Witness Name: Ruben Rizzi
Statement No.: 1
Exhibits: RR/1–RR/23
Dated: 27.00ctober 2024

UK COVID-19 INQUIRY

CORPORATE WITNESS STATEMENT OF RUBEN RIZZI ON BEHALF OF BIONTECH UK LIMITED

I, Ruben Rizzi, will say as follows:

Introduction

1. This is a corporate witness statement made on behalf of BioNTech UK Limited in response to the Rule 9 Request for Module 4 of the UK COVID-19 Public Inquiry (the "**Inquiry**") dated 29 November 2023 (the "**BioNTech Rule 9 Request**"), and related questions from the Inquiry.

2. BioNTech UK Limited was incorporated on 24 November 2020 and is part of the BioNTech group ("**BioNTech**"). BioNTech's response to the COVID-19 pandemic in the UK was handled by personnel from different parts of the BioNTech group. This witness statement focuses on the information most relevant to BioNTech's involvement with the response to the COVID-19 pandemic in the UK.

3. I am Senior Vice President of Global Regulatory Affairs at BioNTech SE (BioNTech UK's parent company). I have extensive experience in the pharmaceutical and biotechnology industry, specialising in regulatory aspects. I hold a medical doctorate from Università degli Studi di Milano-Bicocca. After obtaining my doctorate in 2012, I worked in several medical roles before joining the Menarini Group, an international pharmaceutical and diagnostics company. From 2013 to 2017, I was a Medical Advisor for Corporate Direction Regulatory Activities and Market Access at the Menarini Group. In this role I was responsible for the medical and regulatory evaluation of potential in-licensing opportunities, and provided regulatory and medical support for development programs and approved products.

In January 2018, I became a Regulatory Development Manager & Medical Advisor with the Menarini Group. In that role, I led the newly created Global Regulatory Development team responsible for regulatory development planning and defining global regulatory strategies for the corporate research and development pipeline, including oncology and infectious disease (antimicrobial and prophylactic vaccine) candidates, while continuing to be internally responsible for regulatory due diligence activities and working as global lead for the evidence generation strategy of liquid biopsy platforms.

4. In December 2019, I joined BioNTech as a Regulatory Affairs Strategist, initially providing regulatory support to advance the clinical development of key oncology candidates from BioNTech's pipeline. Beginning in February 2020, I was involved in planning activities for the development of a COVID-19 vaccine. Since then, I have been directly involved with work on the Vaccine (as defined below) and responsible for global regulatory strategy and execution, including joint program governance with Pfizer. I became Director of Global Regulatory Affairs in November 2020, Vice President of Global Regulatory Affairs in July 2021, and Senior Vice President of Global Regulatory Affairs in 2024. In my current position, I co-lead the Global Regulatory Affairs department and am focused mainly on regulatory activities in support of BioNTech's clinical pipeline, including development activities for the Vaccine, labelling, and post-approval and regulatory intelligence matters.

5. The BioNTech Rule 9 Request seeks information on a wide range of topics, some of which are outside my own knowledge and experience. Thus, the information provided in this statement is informed by my own personal knowledge and experience, as well as the knowledge and experience of other individuals at BioNTech and BioNTech's documentary records.

6. In addition, as discussed further below, BioNTech partnered with the Pfizer group ("**Pfizer**") to develop, manufacture, procure, obtain regulatory approval of, and commercialise the Pfizer-BioNTech COVID-19 vaccine (the "**Vaccine**"). In broad terms, in the UK, BioNTech led interactions with the Medicines and Healthcare products Regulatory Agency (the "**MHRA**"); whereas Pfizer was responsible for managing the arrangements for procurement, contracting and distribution of the

Vaccine in the UK with Government and NHS bodies, and for delivering supplies of the Vaccine to meet UK requirements. A more detailed overview of this split of responsibilities can be found at Annex 7 to the Pfizer Statement.

7. I understand that Pfizer Limited (an English company that is part of the Pfizer group) has also received a Rule 9 Request from the Inquiry that is very similar to the BioNTech Rule 9 Request. Accordingly, with the Inquiry's agreement, and to avoid duplication, this witness statement refers to the witness statement of Ben Osborn for Pfizer Limited (the "**Pfizer Statement**") on certain topics. Insofar as my witness statement does not address a particular question or topic in the BioNTech Rule 9 Request, it is because Pfizer took the lead on certain activities in the UK and is in a better position to address those topics in the Pfizer Statement.

8. There is now produced and shown to me a bundle of true copy documents marked "RR/1–RR/23" (indexed in Annex A hereto), to which I refer in this statement (together with the document reference in the format "INQ000000000").

Structure, Role, People and Processes

9. BioNTech is a next-generation immunotherapy group of companies researching and developing novel therapies for cancer and other serious diseases. Among other things, BioNTech has expertise in messenger ribonucleic acid ("**mRNA**") vaccine development and is developing multiple investigational mRNA vaccines (also known as "**vaccine candidates**") for a range of infectious diseases.

10. mRNA is a nucleic acid present in all living cells that carries instructions for the manufacture of specific proteins. Vaccines that rely on mRNA technology to prevent viral diseases provide human cells with the building plan for a specific non-infectious protein that can be found on the surface of a virus. Following administration of an mRNA-based vaccine, these viral proteins are recognised by the immune system as a foreign protein and trigger an immune response that includes antibodies and T-cells. Antibodies are known as the first line of defence as they can assist in protecting the vaccine recipient against infection by binding to the virus and blocking it from entering the cells. Antibodies produced by the vaccine recipient's immune system after vaccination remain in the body for some time and can prevent infection. The second line of defence are T-cells, which

recognise and attack infected cells. They are important to protect the vaccine recipient from severe cases of disease and remain in the body longer than antibodies.

11. Vaccines that rely on mRNA vaccine technology may offer benefits over other types of vaccines,[1] including, for instance, that mRNA vaccines can be manufactured and adapted rapidly.[2]

BioNTech's Role in Responding to SARS-CoV-2

12. On 9 January 2020, the World Health Organisation (WHO) reported that Chinese authorities had determined a novel coronavirus to be the cause of an outbreak of respiratory infections in China. BioNTech recognised this novel coronavirus as a potential global threat and in late January 2020 applied its significant mRNA vaccine development experience to begin developing a potential mRNA-based COVID-19 vaccine. In particular, BioNTech began development by designing and manufacturing multiple vaccine candidates, conducting non-clinical studies,[3] and designing a "first-in-human" clinical trial in Germany to start exploring such candidates.

13. On 17 March 2020, BioNTech and Pfizer announced a letter of intent to co-develop and co-commercialise a potential COVID-19 vaccine.[4] The two companies had been collaborating to develop mRNA-based vaccines for the prevention of influenza since 2018, and aimed to build on that collaboration to accelerate the

---

[1] There are several types of vaccines, each of which are designed to teach an individual's immune system to fight particular germs. These include: (1) inactivated vaccines, which contain the "killed" version of a germ that causes disease, (2) live-attenuated vaccines, which use a weakened form of the germ, (3) subunit, recombinant, polysaccharide, and conjugate vaccines, which use specific pieces of a germ (e.g., its protein, sugar, or the casing around a germ), (4) toxoid vaccines that use a harmful product made by the germ that causes a disease, and (5) viral vector vaccines, which use a modified version of a different virus. *See* RR/1 INQ000485946.

[2] *See id.*

[3] Non-clinical development means the research and development that is conducted in the laboratory and/or in animals, before research in humans begins.

[4] RR/2 INQ000485947.

development of a COVID-19 vaccine. From this point, the two companies began working together to bring a COVID-19 vaccine to market expediently.[5]

14. Human clinical trials commenced in April 2020 and these trials resulted in the selection of a lead vaccine candidate, BNT162b2, to be administered in a two-dose regimen, based on available non-clinical and clinical Phase 1/2[6] data.[7] The efficacy and safety of BNT162b2 was subsequently further investigated in a large Phase 1/2/3[8] clinical trial[9] and on 1 December 2020 — following assessment of data by the MHRA[10] — the United Kingdom granted a temporary authorisation under Regulation 174 of the Human Medicines Regulations 2012 for use of the Vaccine in individuals above the age of 16.[11]

15. Other regulatory approvals followed, including in the United States (Emergency Use Authorisation on 11 December 2020), Switzerland (Conditional Marketing Authorisation on 18 December 2020), and the European Union (Conditional Marketing Authorisation on 21 December 2020).

16. The Vaccine received a standard Marketing Authorisation, applicable in Great Britain, in November 2022.

---

[5] *Id.*

[6] "Phase 1/2" trials refer to clinical trials that combine (1) small Phase 1 clinical trials that primarily are designed to establish a vaccine's safety and tolerability, with (2) Phase 2 clinical trials designed to demonstrate the immune response and appropriate dose of a vaccine, into a single clinical trial protocol.

[7] *See* RR/3 INQ000485948.

[8] A Phase 2 clinical trial is designed to demonstrate the immune response and appropriate dose of a vaccine. A Phase 3 clinical trial involves several thousand volunteers, and is designed to generate additional data regarding a vaccine's safety and efficacy.

[9] *See* RR/4 INQ000485949.

[10] The MHRA regulates medicines, medical devices and blood components for transfusion in the UK. Its responsibilities include: ensuring medicines meet applicable standards of safety, quality and efficacy; securing safe supply chains for medicines; educating the public and healthcare professionals about the risks and benefits of medicines; enabling innovation and research and development; and collaborating with partners to enable the earliest access to safe medicines to protect public health. RR/5 INQ000485950.

[11] RR/6 INQ000485951and RR/16a INQ000485961.

17. BioNTech and Pfizer have continued to study the safety, efficacy, and tolerability of the Vaccine in accordance with regulatory requirements, and to develop variant-specific vaccine candidates.

Key Decision-Makers

18. The speed with which BioNTech and Pfizer advanced the Vaccine to market was a result of the parties' effective collaboration, which allowed BioNTech and Pfizer to work together—with BioNTech and Pfizer each taking the lead on different development, regulatory, manufacturing, commercialisation, and distribution responsibilities—to enable the most efficient availability of the Vaccine.[12]

19. On BioNTech's side, the key decision-makers in respect of matters discussed in this statement were:

a. Professor Ugur Sahin, M.D., Co-Founder and the Chief Executive Officer of BioNTech SE.
b. Professor Özlem Türeci, M.D., Co-Founder and the Chief Medical Officer of BioNTech SE.
c. Sean Marett, CMG, the Chief Business and Chief Commercial Officer of BioNTech SE (Mr Marett retired from BioNTech's Management Board in June 2024 and is currently a specialist advisor to the company).
d. Sierk Poetting, the Chief Operating Officer of BioNTech SE.
e. Dr. James Ryan, Chief Legal Officer (September 2023–present) and Chief Business Officer (July 2024-present) of BioNTech SE, and former Vice President Legal & IP, General Counsel (January 2022–September 2023) and Vice President of Legal (until 1 January 2022).
f. Oliver Hennig, Senior Vice President Product Supply (January 2023–present) and former Senior Vice President Operations (November 2020–January 2023).
g. Andreas Kuhn, Senior Vice President RNA Biochemistry & CMC Development (June 2023–present) and former Senior Vice President RNA Biochemistry & Manufacturing (May 2019–June 2023).

[12] *See* Annex 7 of the Pfizer Statement.

h. Dr. Constanze Blume, Senior Vice President Global Regulatory Affairs (since July 2021) and former Vice President Global Regulatory Affairs (since September 2018).

i. Dr. Ruben Rizzi, M.D., Senior Vice President Global Regulatory Affairs (January 2024–present) and former roles summarised earlier in this statement.

j. Shanti Pather, Senior Director Global Medical Affairs.

k. Dr. Annette Vogel, Senior Director Infectious Disease Vaccines (February 2022–present) and former Director Infectious Disease Vaccines (November 2020–February 2022) and Head of Infectious Disease Vaccines (until November 2020).

l. Dr. Claudia Lindemann, Director Non-Clinical Safety (September 2022–present) and former Associate Director Non-Clinical Safety (until September 2022).

m. Dr. Anette Jork, Vice President Quality for BioNTech's Mainz site (Oct 2022–present) and former Director of Quality/Qualified Person (January 2018–September 2022) and Head of Quality Control in Mainz (October 2020–October 2022).

20. BioNTech's key decision-makers had a number of interactions with UK Government officials in their effort to respond to the COVID-19 pandemic. For instance, as explained in further detail below, BioNTech's then Chief Business and Chief Commercial Officer, Sean Marett, led BioNTech's interactions with the UK Vaccine Taskforce (the "**VTF**"). While he primarily communicated with Kate Bingham, the Chair of the VTF,[13] BioNTech also interacted at times with other individuals including Sir Patrick Vallance, Chief Scientific Advisor; Professor Jonathan Van-Tam, Clinical and Public Health Adviser to the VTF; Clive Dix, Deputy Chair of the VTF; Nick Elliot, Director-General of BEIS; Ben Pledger, Deputy Director of the VTF; Madelaine McTernan, Director UK Government Investments; Deborah Marmot, Legal Advisor to the VTF; Ian McCubbin,

[13] The titles/roles of various non-BioNTech personnel stated in this witness statement are given to the best of BioNTech's knowledge, but it is possible that such individuals may have held other titles/roles during the relevant time period.

Manufacturing Policy Advisor to the VTF; Devina Banerjee, Manufacturing Policy Advisor to the VTF; Andy Jones, ISCF Challenge Director for Medicines Manufacturing; Divya Chada Manek, VTF Clinical Trials Workstream Lead; Matt James, Commercial Director of the VTF; Steve Bagshaw, Industry Adviser to the VTF; and Tim Cullen, VTF Programme Director.

21. BioNTech also interacted frequently with the MHRA. Pfizer was also typically involved in these interactions. As explained in further detail later in this Statement, BioNTech's interactions with the MHRA related to all aspects of the authorisation and regulatory maintenance of the Vaccine (initially under the Regulation 174 procedure alone, beginning 1 December 2020; then also as a centrally approved product with conditions authorised by the European Commission from 21 December 2020, which, once Brexit took effect from 1 January 2021, was converted to a Great Britain Product Licence ("**PLGB**") with conditions (referred to as the "**Marketing Authorisation**" or the "**MA**")).

22. The MHRA assembled a team dedicated to the review of the Vaccine, which served as the primary point of contact for BioNTech and Pfizer. This team included, amongst others, Julian Bonnerjea, Group Manager of the MHRA Biologicals & Biotechnology Unit, Clinical Trials Unit, Innovation Office, Parallel Imports Unit, and Statistics and PK Unit; Tracy Moore, Expert GMDP Inspector; Samantha Atkinson, Interim Chief Quality & Access Officer; Gill Simeon, Pharmaceutical Assessor; and Zoran Simic, Unit Manager. In addition, BioNTech interacted with Nicola Rose, Head of Virology, National Institute for Biological Standards and Control in relation to the lot release testing of the Vaccine.

23. Additional details regarding BioNTech's interactions with the VTF and the MHRA, and how these worked in practice, are set out below.

Key Decisions, Actions and Documents

24. An index of documents referenced in this statement is provided as Annex A hereto. In addition, BioNTech refers the Inquiry to Annex 2 to the Pfizer Statement, which lists additional documents (which in some cases are referred to in this statement, so as to avoid duplication between exhibits), as well as to Annex 4 of the Pfizer

Statement which provides a chronology of the main stages in the development, manufacture, procurement, approval and supply of the Vaccine in the UK.

Vaccine Preparedness

25. BioNTech was not involved in preparedness planning in the UK before the COVID-19 pandemic. Nevertheless, based on its subsequent work in the UK, BioNTech understands that in early 2020, the UK had certain measures and infrastructure in place that enabled its pandemic response.

26. In fact, several countries—including the UK—had pandemic preparedness frameworks in place, which were informed by government responses to previous epidemics and pandemics. In particular, the UK's Influenza Preparedness Strategy[14] was issued in 2011 and built upon the UK's previous national framework for responding to an influenza pandemic by taking into account lessons learned from the Swine flu A/H1N1 pandemic of 2009. The Influenza Preparedness Strategy, while not directly applicable to the COVID-19 pandemic, included guidance regarding support for the development of pandemic-specific vaccines, as well as plans to use advance purchase agreements to secure sufficient UK supply of such vaccines.[15]

27. The UK's existing regulatory framework was also important. The Human Medicines Regulations 2012 included "Regulation 174",[16] which allowed for the temporary authorisation of medicines in response to a public health emergency. The option for and the use of the temporary authorisation was a key factor that led to the UK becoming the first Western nation to authorise use of a COVID-19 vaccine.

---

[14] RR/7 INQ000102974.

[15] *Id.* at 42–44.

[16] "The prohibitions in regulation 46 (requirement for authorisation) do not apply where the sale or supply of a medicinal product is authorised by the licensing authority on a temporary basis in response to the suspected or confirmed spread of—(a) pathogenic agents; (b) toxins; (c) chemical agents; or (d) nuclear radiation, which may cause harm to human beings." (The Human Medicines Regulations 2012, reg. 174)

28. Further, a number of well-established pharmaceutical manufacturing sites are located in the UK. While BioNTech understands that the presence of such manufacturing sites may assist the UK's pandemic preparedness as a general matter, BioNTech and Pfizer's COVID-19 Vaccine was the first in a novel class of mRNA-based vaccines. This meant that, shortly after the start of the pandemic, BioNTech and Pfizer were unable to locate appropriately equipped and experienced manufacturing sites in the UK on short notice to assist with the manufacture of the Vaccine. I return to this point below.

Development of COVID-19 Vaccine

Key Stages of Development of BioNTech and Pfizer's COVID-19 Vaccine

29. In response to the COVID-19 pandemic, BioNTech initiated its COVID-19 vaccine development program, internally referred to as BNT162, in late January 2020. Using its proprietary mRNA platform,[17] BioNTech began non-clinical development of its vaccine immediately by designing and testing potential mRNA vaccine candidates.

30. Based on preliminary data collected by its researchers, BioNTech selected four clinical vaccine candidates: BNT162b1, BNT162b2, BNT162a1, and BNT162c2. Beginning in March 2020, the vaccine candidates were evaluated in a repeat dose toxicity study[18] in rats, which was designed to evaluate the safety of the vaccine candidates, and also to confirm the immunogenicity of the dose administered.[19]

31. Based on an interim report from that study, and following approval from the relevant competent authority (the Paul Ehrlich Institute in Germany), BioNTech initiated a Phase 1/2 clinical trial of its four vaccine candidates in healthy volunteers. This clinical trial took place in Germany and was designed to

[17] A "platform" is a type of technology or technologies that can be used as the basis for developing multiple different medicinal products or candidates. Vaccine technology platforms can accelerate the production and development of new candidates because companies do not have to start from scratch each time they seek to develop a new product.

[18] A "repeat dose toxicity" study is designed to determine the toxicological profile of a pharmaceutical product following the administration of multiple doses of the product being studied.

[19] BNT162c2 was checked by comparison with BNT162b1 and BNT162b2 data.

determine the safety, immunogenicity, and optimal dose level of BioNTech's four vaccine candidates, as well as to assess the effects of repeated vaccination. Shortly after the beginning of the first clinical trial in Germany, a second Phase 1/2 trial was initiated in the United States in collaboration with Pfizer. In parallel to these Phase 1/2 clinical trials, BioNTech/Pfizer initiated a "proof-of-concept" study of relevant vaccine candidates in non-human primates to assess the immunogenicity of the vaccine. In July 2020, BioNTech and Pfizer then initiated a second repeat-dose toxicity study of selected candidates in Wistar Han rats to confirm previously collected safety data.

32. BioNTech's non-clinical studies demonstrated antiviral activity against SARS-CoV-2 in mouse and non-human primates with no signs of systemic toxicity (i.e., no signs that the Vaccine affected multiple organs or the entire body) and all participants in the Phase 1/2 study showed manageable reactogenicity and a broad immune response. After extensive review of the non-clinical and clinical data from its Phase 1/2 clinical trials, and in consultation with a number of regulators from different regions, Pfizer and BioNTech chose to advance their BNT162b2 vaccine candidate into a Phase 1/2/3 study using a schedule of two 30 µg doses 21 days apart.

33. In general, the clinical development of the vaccine was accelerated compared to standard timelines. This was mainly achieved with (1) prioritisation of resources "above any other business" from BioNTech and Pfizer, i.e. significant allocation of internal resources; (2) availability and prioritisation from external stakeholders: for example, competent authorities (including MHRA) being available to review documents faster and/or outside standard procedural timetables, sites and vendors prioritising COVID-19-related activities, volunteers being willing to contribute to the development of the vaccine by participating in clinical trials; and (3) willingness from BNT and PFE to commit resources / invest "at risk", for example preparing for large clinical trials before having data available from prior studies, or setting up manufacturing before knowing whether the vaccine would work. These factors significantly contributed to acceleration. However, none of these factors had an impact on safety, efficacy and quality assessments, the safeguarding of study subjects or vaccine recipients, or on oversight by the regulatory authorities and ethic committees on the vaccine.

34. Pfizer took the lead conducting this Phase 1/2/3 study in adults and adolescents, which was designed as a study to describe the safety, tolerability, immunogenicity, and efficacy of the Vaccine against COVID-19. The trial began on 27 July 2020 and completed enrolment of over 43,000 participants at over 150 clinical trial sites in Argentina, Brazil, Germany, Turkey, South Africa, and the United States.

35. On 18 November 2020, Pfizer and BioNTech announced that a final efficacy analysis in their ongoing Phase 3 study demonstrated that the Vaccine was 95% effective against COVID-19.[20]

36. After this, Pfizer and BioNTech continued to collect efficacy and safety data from participants in this Phase 1/2/3 study, and the companies continued their joint efforts to conduct further studies designed to assess the safety and efficacy of the Vaccine in particular populations, and to evaluate the Vaccine's efficacy. Further details regarding Vaccine clinical studies are set out in the Pfizer Statement.

37. As these clinical studies were conducted, non-clinical work on the Vaccine also continued. For instance, as part of BioNTech and Pfizer's effort to prepare for global supply of the Vaccine, non-clinical studies were conducted to support the production process and the adaptation of the production process—particularly with regard to product stability, upscaling, and transfer to manufacturing sites. Furthermore, there were studies assessing reproductive safety of the vaccine (i.e. looking for any effects on fertility and pregnancy), and studies determining the distribution in the body of the intact lipid nanoparticle and the lipids it contains (the "lipid nanoparticle" is the vehicle for delivering the Vaccine's mRNA into the body's cells). These studies were later complemented with experiments looking at mRNA distribution, as well as where in the body this mRNA is then translated into proteins. Among other things, the outcome of these studies showed that the formulation of the Vaccine did not lead to the distribution of mRNA and/or protein in or near the heart, which at the time was one hypothesis for linking the Vaccine and cases of myocarditis. Further studies were also performed, which, among other things, helped to show which type of cellular response the vaccine induces. These further experiments/studies were completed in 2023. In addition, further non-clinical

[20] RR/8 INQ000485953.

studies were (and are still) being conducted to understand the immunogenicity of the Vaccine against COVID-19 variants (e.g., Omicron BA.1, Omicron BA.4-5, XBB.1.5, JN.1 and KP.2) and to adapt the Vaccine to such variants.[21]

38. Any studies revealing new information affecting the assessment of the benefits and risks of the vaccine would, in line with applicable legislation, be reported to the MHRA forthwith. To date, no such situations have arisen, and accordingly the outcomes of such studies have been and will continue to be reported to the MHRA at appropriate time points in line with applicable legislation and guidance.

Key Stages of Manufacturing the Vaccine[22]

39. When BioNTech began its vaccine development efforts in January 2020, no mRNA-based drug or vaccine products were available on the market. This meant manufacturing sites with the necessary equipment, experience, and scale to support the global supply of a successful mRNA-based vaccine were unavailable. BioNTech and its partners were able to provide early supply from BioNTech's GMP-certified[23] mRNA manufacturing facilities to support clinical development activities, but understood that additional work was needed to prepare for the potential worldwide supply of a successful COVID-19 vaccine.

40. After BioNTech and Pfizer announced their collaboration in March 2020, the companies began working at risk to develop and scale up a manufacturing process capable of supporting worldwide vaccine supply, all while non-clinical and clinical development was ongoing.[24]

---

[21] *See, e.g.*, RR/9 INQ000485954.

[22] BioNTech understands that the Vaccines Manufacturing and Innovation Centre ("VMIC") participated in the development and manufacture of certain COVID-19 vaccines. The VMIC did not, however, play a role in BioNTech and Pfizer's development or manufacture of the Vaccine. BioNTech has no view on the sale of the VMIC.

[23] GMP (Good Manufacturing Practice) describes the minimum standard that a medicines manufacturer must meet in their production processes. *See* RR/10 INQ000485955.

[24] *See, e.g.*, RR/11 INQ000485956 (describing BioNTech's 2020 acquisition of a manufacturing facility in Marburg, Germany to expand COVID-19 vaccine production capacity by up to 750 million doses per year).

41. Teams at two Pfizer manufacturing facilities in Puurs, Belgium and Kalamazoo, Michigan, United States, began work to build formulation labs, design an industrial process, develop methods to purify RNA, embark on a sterilisation process that would make the Vaccine safe for injection, establish a filling process, source necessary equipment (e.g., deep freezers), and manufacture initial batches of the Vaccine in anticipation of regulatory approval.

42. At the same time, BioNTech and Pfizer worked to identify reliable suppliers and contract manufacturers, including facilities with the capability and capacity to fill vaccine vials and package the Vaccine for distribution. For instance, beginning in March 2020, BioNTech made enquiries about possible "fill-finish" facilities in the UK and liaised with the UK's VTF about identifying facilities with such capacity.

43. In addition, while the vaccine manufacturing processes were being advanced, BioNTech and Pfizer worked together to develop vaccine labelling, packaging, and analytical testing strategies that would comply with applicable regulatory requirements. Under the conditions of Regulation 174, for instance, the MHRA permitted the supply of the Vaccine in the UK only on a batch-by-batch basis. Thus, before BioNTech and Pfizer could ship Vaccine doses to the UK, BioNTech was required to conduct "QP" certification of the batches allocated for UK supply in close contact with the Good Manufacturing Practices inspectors at MHRA. As part of the final batch certification process, BioNTech's QP[25] conducted additional reviews of batch documentation, checked to confirm the approved specifications were met in accordance with regulatory requirements, and would prepare a batch genealogy tracing the manufacturing process. Oversight of the manufacturing facilities was conducted in accordance with Good Manufacturing Practices (GMP), which are internationally recognised standards for the manufacture of biopharmaceutical products. BioNTech's manufacturing facilities have been inspected by the competent authorities in Germany and those of certain non-EU countries.[26] At the time of the Vaccine's Conditional Marketing Authorisation, the

[25] "Qualified Persons" are highly skilled scientists with defined qualifications who certify every batch of a pharmaceutical product before the batch can be released and distributed to consumers.

[26] Annex B sets out further details of inspections carried out by the German authorities in the Inquiry's date range.

UK remained part of the EU's centralised marketing authorisation procedure, and so no separate GMP inspection was required by the MHRA.

44. mRNA was manufactured both in small-scale ("Process 1") and large-scale ("Process 2") manufacturing processes, which both provided mRNA of comparable quality. This was tested and confirmed through side-by-side comparability studies and heightened characterization testing. Drug substance for the COVID-19 vaccine produced by both "Process 1" and "Process 2" were included in the pivotal clinical trial (C4591001) with no findings with regards to the efficacy, safety or quality. The process was validated at all relevant manufacturing sites from Pfizer and BioNTech and submitted for review and approval to many health authorities throughout the world. The MHRA's Public Assessment Report – Authorisation for Temporary Supply concluded that "The manufacturer has performed a comparability assessment of drug substance batches used in the clinical trial programme and batches representative of the subsequent manufacturing changes occurring during product development, such as introduction of new manufacturing sites, manufacturing process changes and increase in batch scale, including full scale validation batches. The drug substance batch release data for essential parameters that control the quality of the active RNA and several extended characterisation test parameters were considered. These data demonstrate consistency between the drug substance described for this application and those used in the pivotal clinical study."[27]

45. In summary, Pfizer and BioNTech manufactured the Vaccine at their full capacities, in accordance with applicable regulatory standards, to meet global demand (including UK demand), utilising a joint international network comprising both internal manufacturing sites and contract manufacturing organisations. The manufactured batches allocated to the UK were stored at BioNTech and Pfizer warehouses until they were released and subsequently supplied to the UK. Pfizer then distributed designated Vaccine batches to the UK.

[27] RR/17 at 8 INQ000485963.

Obstacles Faced in the Development and Manufacture of the Vaccine

46. While BioNTech and Pfizer were able to advance the development of the Vaccine from discovery to temporary authorisation in under a year, the rapid non-clinical and clinical development of the Vaccine was a challenge for a number of reasons.

47. For instance, BioNTech faced difficulty locating clinical research organisations with availability to conduct vaccine studies on short notice. In February 2020, several UK-based clinical research organisations were unable to accommodate BioNTech's requests to conduct repeat-dose toxicity studies of its vaccine candidates, indicating that such studies could not begin before the summer of 2020 and would not be completed before December 2020. This timeline would have delayed BioNTech's vaccine development by at least nine months.

48. In addition, when conducting the first Phase 1/2 clinical trial of the Vaccine, BioNTech selected external vendors (e.g., clinical research organisations and central laboratories) that BioNTech had already contracted with. While BioNTech was able to conduct necessary development work in a timely fashion by working with known external vendors, this limitation could have caused delay if additional vendors had been necessary or if BioNTech had not had such relationships already. Selecting new vendors with appropriate capabilities, vetting their qualifications, and negotiating contracts can be a time-consuming process with the potential to delay vaccine development. The UK could support future rapid development efforts by maintaining and making available information regarding the capabilities and qualifications of clinical research organisations, laboratories, and other relevant vendors with the availability to take on pandemic-related work.

49. The limited availability of the supplies and materials necessary for BioNTech's non-clinical and clinical studies also posed significant challenges in the development of the Vaccine. BioNTech had difficulty obtaining reagents (e.g., specific antibodies for the novel COVID-19 pathogen), swabs, PCR machines, and other key materials that were in short supply. Making resources available for the production of materials to support pandemic-related research efforts could reduce the risk of shortages delaying future vaccine development.

50. Another challenge arose in relation to Regulation 174's batch-specific release requirements. BioNTech and Pfizer, with the assistance of MHRA and the MHRA's National Institute for Biological Standards and Control ("**NIBSC**"), had to develop a specific batch-release process to demonstrate that the relevant requirements and conditions of Regulation 174 were fulfilled for each individual batch of the Vaccine that was designated for supply in the UK, while at the same time ensuring compliance with the European Union's Good Manufacturing Practice requirements (as BioNTech and Pfizer's relevant manufacturing sites and qualified persons were located in the European Union). Defining a process that would demonstrate compliance with both sets of regulations simultaneously, on a batch-by-batch basis, was complex given the significant time constraints BioNTech and Pfizer faced to supply the Vaccine to the UK. NIBSC also needed to establish, within very tight timelines, the product-specific analytical testing protocols and standards for batch testing of the Vaccine. A particular challenge in this regard was that mRNA vaccines were a novel drug class which required new analytical methods. Now that NIBSC is familiar with typical analytical methods for mRNA-based products, setting up testing for future mRNA vaccines is likely to be more streamlined. There is however a risk of similar challenges arising in the future for other novel technologies. An additional challenge for NIBSC at this time was that they were coping with Brexit simultaneously, and had to set up as an independent laboratory as a result.

51. The Pfizer Statement summarises additional stages of Vaccine development, procurement, and manufacture as well as key obstacles faced.

Overview of BioNTech's Relationship with the UK VTF / UK Government

52. Pfizer took the lead in negotiating commercial arrangements for the supply of the Vaccine to the UK. The Pfizer Statement therefore summarises key aspects of discussions with the UK VTF and other UK representatives. The following information supplements the Pfizer Statement.

53. In the weeks after the COVID-19 pandemic was declared by the World Health Organisation in March 2020, BioNTech approached and/or was introduced to various UK government/civil service representatives, including Sir Patrick Vallance

of the VTF and others from the Department of Business, Innovation and Skills (BEIS) Office for Life Sciences, and UK Research and Innovation (*see supra* 20). At that point, BioNTech had recently announced its partnership with Pfizer, and, as discussed above, was seeking support from governments to ensure sufficient manufacturing capacity would be in place to support rapid worldwide supply of the Vaccine (which was at that time still in development).

54. In May 2020, Kate Bingham contacted Sean Marett, BioNTech's then Chief Business and Chief Commercial Officer. Mr Marett and Ms Bingham had known each other professionally for over twenty years, through their broader work in the biopharmaceutical industry. Ms Bingham explained that she had been appointed as Chair of the VTF and set up a call to discuss how the VTF could work with BioNTech in relation to the Vaccine. Initial exploratory discussions with Ms Bingham and other members of the VTF continued for the next few weeks.

55. In June 2020, Mr Marett introduced Ms Bingham to Janine Small, Pfizer's President of International Developed Markets. Ms Small involved (among other Pfizer colleagues) Pfizer's Managing Director and Country Manager UK, Mr Ben Osborn.

56. Thereafter, Ms Bingham introduced other members of the VTF team to move the negotiation of a supply agreement forward. The VTF's Deputy Chair, Clive Dix, led the diligence process; Director of UK Government Investments, Madelaine ("Maddy") McTernan, led contracting; Legal Advisor to the VTF, Deborah Marmot, managed the negotiation of a Confidential Disclosure Agreement; and the VTF's Director-General, Nick Elliott, provided additional support and oversight.

57. Over the following weeks, BioNTech and Pfizer presented the Vaccine's concept to the VTF and negotiations began regarding the terms for the supply of the Vaccine to the UK. BioNTech was involved alongside Pfizer in much of those discussions, particularly in the early stages of negotiations. On occasion, members of the VTF and Mr Marett also discussed points relating to the negotiations directly, with Mr Marett keeping Pfizer closely informed. A more detailed summary of the contractual arrangements ultimately agreed with the UK is set out in the Pfizer Statement.

58. As time went on, BioNTech was less frequently involved in communications with the VTF, which were handled mainly by Pfizer.

59. Nevertheless, on some occasions Mr Marett and others at BioNTech were involved with further discussions with the VTF on certain issues. For example:[28]

a. In the second half of 2020, BioNTech was involved in discussions about the UK's plans to conduct "Heterologous Prime-Boost Studies" to evaluate the viability of patients receiving an initial dose of one vaccine, and a booster dose of a different vaccine. This included discussion and consideration with the VTF's Divya Chadek Manek (National Institute for Health and Care Research's Head of Business Development) and Matthew Snape (Associate Professor in Paediatrics and Vaccinology at the University of Oxford). BioNTech and Pfizer did not support the Vaccine being used in this study given the stage of development of COVID-19 vaccines at the time (i.e., prior to marketing authorisation), and because the study would have diverted vaccine doses in an already highly constrained supply environment (at the time, commercial manufacturing of mRNA did not exist as it was a new technology and both BioNTech, Pfizer, and third parties had to develop processes and scale-up manufacturing capacity to meet global demand for the Vaccine). After the UK granted the Vaccine Marketing Authorisation, a study along these lines was progressed.

b. Pfizer and BioNTech participated in discussions with members of the VTF about certain aspects of the Vaccine's label. Further details of discussion about the Vaccine's dosing interval, for instance, are set out at paragraph 86 below.

c. In December 2020 and early 2021, there were discussions about the VTF's proposal to create a "Rapid Response Vaccine Unit". The VTF sought permission to use the Vaccine's mRNA template as part of a library of COVID-19 variants against which vaccines could be tested. After BioNTech shared

[28] These are examples only. During this period, BioNTech personnel were involved in a variety of interactions with the VTF and MHRA on regulatory-focused topics about the vaccine.

the UK's proposal with Pfizer, Pfizer expressed an interest in developing a global surveillance project that would include the UK. Later in 2021, BioNTech was involved in further discussion with the VTF regarding vaccine response to COVID-19 variants. This was particularly so after the "Omicron" variant emerged in November 2021. Most discussion with the VTF regarding the response to COVID-19 variants was however led by Pfizer. The Pfizer Statement gives further details about cooperation with the UK in relation to responding to new virus variants.

d. In early 2022, Mr Marett contacted Ms McTernan of the VTF to discuss the UK's potential interest in "BioNTainers". BioNTainers are portable mRNA manufacturing units that, at that time, BioNTech had recently launched. In February 2022, Sierk Poetting, BioNTech's Chief Operating Officer, and Mr Marett met with the VTF's Commercial Director, Matt James; Industry Advisor, Steve Bagshaw; and Programme Director, Tim Cullen regarding BioNTainers' potential to advance the UK's pandemic preparedness and independence by establishing local and scalable mRNA vaccine production platforms with reserved manufacturing capacities. While discussions regarding BioNTech's BioNTainer offering continued through May 2022, the UK opted not to proceed with BioNTech's proposal.

Innovative Aspects of the Vaccine's Development and Manufacturing Processes

60. The development of the Vaccine required reliance on a variety of innovations to ensure that a vaccine candidate could be successfully brought to market.

61. In the early stages of the pandemic, BioNTech and Pfizer began a number of vaccine development processes in parallel and at-risk. Assisting BioNTech and Pfizer with this effort, regulators including the MHRA dedicated resources to frequent communications with BioNTech, thereby enabling an efficient approach that allowed BioNTech to adjust its development activities in real-time in response to regulatory feedback. The fast development of the manufacturing process and the required analytical tests was only possible due to BioNTech's prior years of experience with manufacturing and testing mRNA-based products.

62. In addition, the rapid start of the "first-in-human" trial in Germany was made possible by an expedient approach to non-clinical toxicology, which provided supportive data for all clinical vaccine candidates, due to a platform-based design consistent with the considerations published by the International Coalition for Medicinal Regulatory Agencies on 18 March 2020.[29]

63. BioNTech's pre-existing clinical experience with mRNA-based candidates was also instrumental in accelerating early development of the Vaccine. Before starting its COVID-19 vaccine development program, BioNTech had already developed multiple candidates using the same RNA formats and similar lipid formulations as ultimately used in the Vaccine as part of its product pipeline. This experience was useful when rapidly defining dose levels and predicting the reactogenicity of the vaccine candidates. A summary of BioNTech's experience with prior mRNA-based investigational products was made available to regulators and to investigators outside of the UK as part of the early versions of the Investigator's Brochure for the BNT162 COVID-19 vaccine development program.[30]

64. In the subsequent development and approval of variant-adapted COVID-19 vaccines (bivalent Original / Omicron BA.1, bivalent Original / Omicron BA.4-5, monovalent XBB.1.5, JN.1 and KP.2), platform-based approaches were used by the MHRA, as well as other regulators, who considered the totality of the evidence available for the original BNT162b2 vaccine, clinical data from multiple variant-adapted vaccines, and nonclinical immunogenicity data to support the approval of variant-adapted vaccines.

65. In BioNTech's view, the innovative principles discussed above should become a permanent part of the UK's vaccine preparedness strategy. In addition, the definition of vaccine technology platforms would ideally become a key part of pandemic preparedness frameworks, allowing a more rapid response in future pandemics and supporting the objectives of the "100 Days Mission".[31] For

---

[29] *See* RR/12 INQ000485957.

[30] *See* RR/13 at § 3.2 INQ000485945.

[31] In March 2022, the UK Government cohosted the Global Pandemic Preparedness Summit in London to explore the potential response to the next "Disease X". During the

example, regulators in the UK could make it possible to obtain approval of vaccine technology platforms, which would allow pre-approval of a platform dossier based on quality, nonclinical and potentially also early clinical data which could be used as the basis for approval of multiple vaccine candidates. In case of an epidemic or pandemic outbreak, the platform dossier could be rapidly integrated with the information relevant only to a new vaccine candidate targeting the specific pathogen / strain that needs to be added. Such a process would follow principles similar to those adopted for the approval of the Original / Omicron BA.4-5 vaccine, and would follow the concepts already outlined in flu pandemic models.

Approval Process

66. On 25 August 2020, BioNTech and Pfizer had a meeting with the MHRA to begin focusing on the regulatory approval process. During the meeting, BioNTech and Pfizer shared information regarding the development of the Vaccine, expected clinical trial timelines, and the possible timing for regulatory filings. At the time, BioNTech and Pfizer communicated to MHRA that they intended to begin rolling regulatory submissions to the European Union in October 2020.

67. On 10 September 2020, the MHRA sent a letter to BioNTech and Pfizer requesting that the companies simultaneously submit all European Union regulatory filings to the MHRA.[32] BioNTech agreed, confirming a target submission timeline with the MHRA, and scheduling a follow-up meeting in early October to discuss the procedure for submission and review.

68. Beginning in October 2020, and on a rolling basis, BioNTech and Pfizer submitted substantial data to the MHRA related to the safety and efficacy of the Vaccine, including data from two clinical trials:

Summit participants discussed the possibility of making safe, effective vaccines, therapeutics, and diagnostics within 100 days of Disease X's identification. The UK Government named this the "100 Days Mission". *See* RR/14 INQ000485958.

[32] RR/15 INQ000485959.

a. Study BNT162-01: a Phase 1/2 clinical trial conducted in 60 adults aged 18-55 years (with immunogenicity data available up to one month after the second dose of the Vaccine); and

b. Study C4591001: a Phase 1/2/3 clinical trial conducted in adults and adolescents, aged 12-15 years, 18-55 years, and 65-85 years (at the time of initial authorisation, data was submitted relating to 43,651 first doses—21,823 doses of the Vaccine and 21,828 doses of placebo—and 41,102 second doses—20,565 doses of the Vaccine and 20,536 doses of placebo).

69. The MHRA established a team dedicated to the review of data related to the Vaccine. Following initial data submissions, BioNTech and Pfizer spoke frequently with this team regarding a variety of topics, including, for instance, the content of BioNTech and Pfizer's regulatory submissions and clinical trial data, the requirements of Regulation 174, and the expected batch testing and release process. As BioNTech, Pfizer, and the MHRA were dedicated to advancing toward regulatory approval as quickly as possible, these discussions were often scheduled on short notice and outside of ordinary working hours.

70. During the regulatory authorisation application process, the applicant is required to share with the health agency (in this case, the MHRA) all the information and data that are required for the agency to conduct an assessment of the safety, efficacy and quality of the product. An applicant may not withhold such information, as it constitutes the basis for a regulatory approval. The format and content of the documentation submitted is strictly regulated and defined in detail by international standards and national/country-specific requirements and guidance. Different country requirements mean that the applications submitted for the Vaccine are not identical in all jurisdictions, but the core data submitted are the same. In addition, marketing authorisation applicants must by law submit any new information relevant to the evaluation of the safety, quality or efficacy of the product, and marketing authorisation holders must (among other things) inform the MHRA of any new information which might affect the evaluation of the benefits and risks of the medicinal product, as soon as reasonably practicable after becoming

aware of it.[33] Marketing authorisation holders must also ensure that the product information is kept up to date with current scientific knowledge.[34]

71. In summary, applicants compile a submission dossier that is compliant (from a content as well as a format perspective) with the above standards, and then during the review process the MHRA can require additional data or further information to be provided in case their initial assessment concludes that further information about some parts of the application would be helpful. In addition, the MHRA can at any time require the MA holder to submit additional information relating to the benefit-risk assessment of the product.

72. Based on the substantial data submitted by BioNTech and Pfizer, the MHRA granted the Vaccine authorisation for temporary supply under Regulation 174 of the Human Medicines Regulations 2012 on 1 December 2020.[35] Under this authorisation, the Vaccine was indicated for "active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 16 years of age and older".[36]

73. The overall conclusion of the MHRA, following its assessment of the Vaccine, was that "[t]he non-clinical and clinical data submitted have shown the positive benefit/risk of this product for active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus…".[37] Similar conclusions were also reached in the subsequent weeks by the European Medicines Agency, the US Food and Drug Administration, and other regulatory authorities around the world.

74. The European Commission granted the Vaccine a Conditional Marketing Authorisation ("**CMA**") on 21 December 2020.[38] This CMA was effective

---

[33] See e.g. Human Medicines Regulations 2012, Regulations 57 and 75.
[34] Human Medicines Regulations 2012, Regulation 76.
[35] RR/16 INQ000485960.
[36] RR/17 at 5 INQ000485963.
[37] *Id.* at 50.
[38] RR/18 INQ000485964.

throughout the EU and in Northern Ireland, and on 1 January 2021 was converted to a Great Britain CMA.[39]

75. Regular interactions with the MHRA continued after the Vaccine was granted authorisation under Regulation 174. For instance, BioNTech and Pfizer attended biweekly meetings with the MHRA beginning in December 2020 to discuss the safety of the Vaccine as well as BioNTech and Pfizer's work on submission of adverse event reports. Beginning in April 2022, similar meetings were held on a monthly instead of biweekly basis.

76. BioNTech and Pfizer also frequently interacted with the MHRA to discuss the detailed conditions of Regulation 174 authorisation applied by the MHRA, and other post-authorisation commitments. The conditions of Regulation 174 were broad—covering for instance obligations relating to the manufacture, pharmacovigilance, further clinical trials, supply, and distribution of the Vaccine—and provided that product information for the Vaccine[40] must be agreed with MHRA. Thus, BioNTech and Pfizer communicated with MHRA often through 2022.

77. A standard Marketing Authorisation applicable in Great Britain was granted in relation to the Vaccine in November 2022.[41] This meant that all the requirements necessary for standard marketing authorisation were met at that time. The Vaccine, as updated to respond to COVID-19 variants, continues to be supplied in Great Britain in accordance with this standard Marketing Authorisation.

Innovative Aspects of the UK's Regulatory Approval Process

78. The UK's use of Regulation 174's temporary authorisation procedure was an innovative regulatory process that BioNTech believes contributed significantly to the expedient launch of the Vaccine in the UK. For instance, while Regulation 174

[39] RR/19 INQ000485965.

[40] Product information for the Vaccine includes information equivalent to that provided in a summary of product characteristics ("SmPC") with information for healthcare professionals and a patient information leaflet ("PIL") with information for patients/users, which is provided in relation to a medicinal product that is the subject of a marketing authorisation.

[41] RR/19 INQ000485965.

was not an innovation specifically developed to respond to the COVID-19 pandemic, BioNTech understands that the UK utilised the temporary authorisation procedures on a widespread basis for the first time in 2020.

79. The MHRA's flexibility in designing and managing the temporary authorisation application process led to significant efficiencies. For instance, instead of waiting until BioNTech submitted all relevant data related to the Vaccine's safety and efficacy to start its review, the MHRA conducted a rolling review of the quality, non-clinical and clinical data that BioNTech submitted on an ongoing basis. This allowed the MHRA to remain informed about the outcomes of BioNTech's studies as data became available, and significantly accelerated the MHRA's ultimate decision to grant Regulation 174 approval for the Vaccine.

Regulatory Classification of the Vaccine

80. The Inquiry has asked BioNTech to comment on whether mRNA vaccines should have been classified as "gene therapies" or "pro drugs" as distinct from "traditional vaccines", and how any related regulatory/safety considerations were addressed.

81. According to the applicable legislation and guidance, the Vaccine is not a gene therapy or a "pro drug". EU Directive 2001/83/EC (Annex I, Part IV, Art. 2.1) governing human medicinal products, as adopted into UK law, is clear that gene therapy medicinal products do not include vaccines against infectious diseases.[42]A "pro drug" has been defined as a compound that, on administration, must undergo chemical conversion by metabolic processes before becoming the pharmacologically active drug for which it is a pro drug.[43] Pro drugs thus have a different mode of operation to mRNA vaccines.

82. It is for the regulator to determine product classification in accordance with applicable laws. However, in BioNTech's view it would have been inconsistent with the existing infectious diseases framework to treat vaccines against infectious diseases in this way.

---

[42] Human Medicines Regulations 2012/1916, regulation 2A(3): "A vaccine against infectious diseases is not to be treated as a gene therapy medicinal product."
[43] RR/23 INQ000508041.

83. BioNTech also does not consider that adjusting the regulatory framework would improve product safety. The regulatory framework for vaccines against infectious diseases requires extremely high safety standards. Vaccines against infectious diseases (unlike many other types of pharmaceutical products) are administered to healthy populations, so it is vital to ensure a clearly positive benefit-risk ratio in favour of the vaccine. Further, the current regulatory framework emphasises the importance of multidisciplinary collaboration and the inclusion of relevant experts to assess the safety of new therapies.

84. It is also worth considering that mRNA vaccines, unlike some gene therapies, do not edit/alter the genomic sequences of a vaccinated person. Moreover, mRNA in the cells of a vaccinated person is only temporarily present in those cells before it is degraded. Classifying mRNA vaccines for infectious diseases as "gene therapies" may fuel public misconceptions and incorrect narratives about mRNA vaccines that could deter vaccine take-up, and ultimately worsen public health outcomes.

Vaccine Delivery and Prioritisation

85. Beyond the submissions that BioNTech made to the MHRA in connection with the regulatory authorisation of the Vaccine, BioNTech did not play a significant role in advising or liaising with the UK Government regarding Vaccine delivery and prioritisation within the UK population.

86. In December 2020, however, Pfizer and BioNTech participated in discussions with members of the VTF, including Professor Jonathan Van Tam, then the UK's Deputy Chief Medical Officer, regarding the UK's consideration of extending the interval between first and second Vaccine doses up to 12 weeks (i.e. beyond the 21-day interval specified in the MHRA approval in force at the time). BioNTech understood the potential benefit of the proposed extended dosing interval, i.e. allowing more people to receive the first dose of a vaccine in circumstances where vaccine supply was limited. However, given that the Vaccine clinical studies evaluated a 21-day dosing interval, with only limited data regarding longer dosing intervals (the actual interval in the clinical trial being 19-23 days per protocol, with outliers at 42 days), BioNTech was not able to confirm or endorse the UK's

proposed longer dosing interval. The UK Government ultimately proceeded with this extension, setting out its reasoning in a letter from the chief medical officers dated 31 December 2020.[44]

Vaccine Safety

BioNTech's Role in Addressing Vaccine Safety

87. As part of BioNTech's collaboration with Pfizer, Pfizer's "Global Safety" team is responsible for the effective intake, evaluation, and databasing of reported suspected adverse events ("**AE**") concerning the Vaccine. In addition, Pfizer took the lead in conducting case processing, medical evaluation, signal management, and signal evaluation work related to the Vaccine, and completed aggregate reports regarding the Vaccine's safety on a monthly basis. More details about these processes are set out in the Pfizer Statement.

88. BioNTech's Head of Safety (Olaf Schickling up to 31 January 2022 and Frank van den Ouweland beginning 1 February 2022) liaised with Pfizer's Qualified Person for Pharmacovigilance in relation to the sharing of information within the collaboration. Beginning in 2022, BioNTech built out its Medical Safety and Pharmacovigilance Department. The relevant colleagues from this department frequently engage with Pfizer's Global Safety team to discuss safety topics, such as management of AE reports and signal evaluation, answers to Health Authority questions and the review of periodic safety reports. Joint safety oversight is also in place regarding ongoing clinical development activities, for example the bivalent Comirnaty Original/Omicron BA.4-5 and the Comirnaty Omicron XBB1, JN.1 and KP.2 targeted line extensions.

89. In relation to signal evaluation in particular, BioNTech representatives would attend signal evaluation meetings together with the Pfizer safety representatives to assess whether additional safety information regarding the Vaccine could be discerned from AE reports and other sources as applicable, and to review the identified signals on an ongoing basis. A safety signal is emerging information on a new or known adverse event that may potentially be caused by a specific

[44] RR/20 INQ000485966.

medicinal product. Safety signals warrant further investigation to understand better whether there is an actual link with the medicinal product or the adverse event arises from alternative causes. Signals can be detected from several sources, like spontaneous reports, clinical studies and the scientific literature. If a safety signal was detected, either by MHRA assessment or following relevant signal procedures adopted by the EMA Pharmacovigilance Risk Assessment Committee (PRAC), the MHRA would typically engage with BioNTech and Pfizer to request follow-up activities and in-depth evaluations in order to perform a complete assessment and decide on the most appropriate measures required, if any. Further details about safety-related additions to the Product Information after the initial authorisation are set out in Annex 6 of the Pfizer Statement.

Observations on the Management of Vaccine Safety

90. While the process of adverse event monitoring for the Vaccine was and is similar to processes applied to other vaccines, there were certain differences.

91. First, the volume of reported suspected adverse reactions that Pfizer and BioNTech needed to monitor was much greater than is typical, due to the number of doses administered worldwide (over 3 billion doses of the Vaccine have been delivered since December 2020) in global mass vaccination campaigns. There was a high interest from the public and primary caregivers in reporting suspected adverse events following the administration of the first mRNA-based vaccine. Furthermore, public health scrutiny regarding suspected adverse events meant that BioNTech and Pfizer, and regulatory authorities around the world, worked on the evaluation of potential safety signals.

92. Second, BioNTech and Pfizer submitted monthly summaries to the MHRA of suspected adverse reactions to the Vaccine. While such reports are not ordinarily required for all vaccine products, this extra step was required to support the MHRA's "Yellow Card" scheme as adapted specifically for COVID-19 vaccines. The Yellow Card system is a public, web-based system that allows users to report suspected adverse events and look up safety data related to pharmaceutical products. During the pandemic, a Yellow Card reporting website dedicated to COVID-19 vaccines was established that allowed MHRA to publish regular

summary reports with a complete listing of all suspected adverse reactions reported to MHRA (by healthcare professionals, members of the public and pharmaceutical companies) sorted by vaccine brand. The submission of BioNTech and Pfizer's monthly summaries supported the MHRA's publication of these monthly COVID-19 vaccine reports. In addition to information from the UK under the Yellow Card scheme, the MHRA also requires Marketing Authorisation Holders to submit adverse event information from other countries, meaning that the MHRA has a view of adverse events reported internationally.

93. Third, a Risk Management Plan was developed for the Vaccine (as for all newly authorised medicines) detailing the risks of the Vaccine, how such risks could be minimised, the uncertainties/missing information regarding the Vaccine, and how more information would be obtained about important risks and uncertainties. The risk minimisation measures as defined in the Risk Management Plan were regularly amended based on global new information, meaning that the degree of scrutiny applied to ensure the safe administration of the Vaccine was greater than normal.[45]

BioNTech's Relationship with the MHRA

94. BioNTech's relationship with the MHRA is that of a regulated biopharmaceutical company with its medicines regulatory authority. MHRA undertakes its regulatory decision making, including on vaccine safety, independently, and although it seeks information from marketing authorisation applicants / holders, it has its own systems and processes for managing risk assessment, to which BioNTech has no access. Interactions are managed by MHRA according to established and standard ways of working, including submission procedures, meeting procedures, template documents, submissions portals and the like, together with adherence to their conflicts of interest policies and procedures. In this way, MHRA maintains its independence from industry. Although during the pandemic there were more meetings and communications between MHRA and BioNTech than would normally

[45] RR/21 INQ000485967.

be needed, these were undertaken in accordance with the usual principles of the independence of the MHRA in its decision making and actions.

95. BioNTech's financial relationship with the MHRA relates only to the payment of the routine fees for the MHRA's regulatory activities, such as meetings and submissions. These fees are publicly disclosed by the MHRA[46] and are invoiced by the MHRA to Clinical Trial Sponsors / Marketing Authorization Holders depending on the activities conducted.

Therapeutics

96. BioNTech was not involved in the research or development of new COVID-19 therapies and did not investigate the potential effectiveness of existing medications for the treatment of COVID-19.

UK Vaccine Damage Payment Scheme

97. BioNTech does not have any experience with the UK Vaccine Damage Payment Scheme and has no observations to offer regarding this program.

Lessons Learned and Preparing for a Future Pandemic

98. The response to the COVID-19 pandemic has shown that vaccines can be made available on a global scale under exceptional timelines without compromising on quality or the robustness of clinical evidence and end-product. The development of multiple vaccine candidates under unprecedented timelines was made possible by the joint efforts of vaccine developers, governments, regulators, laboratories and manufacturing sites, and clinical investigators and researchers, among others.

Building on Strengths

99. New technologies such as those using mRNA allowed expedited development of initial COVID-19 vaccines, as well as a rapid introduction of subsequent variant-adapted vaccines. This is due in large part to the intrinsic characteristics of the

[46] RR/22 INQ000485968.

platform, such as flexibility to adjust the Vaccine to target specific antigens,[47] and its readily reproducible design and manufacturing process.

100. SARS-CoV-2 is however a relatively "simple" virus, belonging to a known family (Coronaviruses), and its spike protein (i.e. a protein on the surface of the SARS-CoV-2 virus) offered a clear and obvious target to induce protective immune responses. The genomic sequence of the SARS-CoV-2 virus was published soon after the virus was discovered. This, in turn, allowed BioNTech quickly to identify and develop the required mRNA template targeting the virus's spike protein. BioNTech was also able to make use of its pre-existing experience with mRNA and with the lipid "envelope" nanotechnology needed to deliver the mRNA into the body's cells. In case of a more complex pathogen, or if BioNTech's previous experience in mRNA was not applicable to vaccine development, the development of a vaccine could have taken considerably longer and presented greater challenges.

101. Now that mRNA technology is more established, new regulatory definitions and guidelines may help in the future to realise the potential utility of mRNA technology, allowing a more rapid development of vaccines for potential future pandemics.

102. In addition to novel underlying technology, the availability of publications that reported data was also a key factor in expedient vaccine development and deployment. The rapid deployment of COVID-19 vaccines on a global scale resulted in an unprecedented amount of real-world data being generated and published in parallel to ongoing clinical trials of the Vaccine post-authorisation. Publications with data on special populations, such as immunocompromised subjects or pregnant and breastfeeding women, were used by regulators and vaccine developers globally to inform label updates during the pandemic.

103. In this regard, one of the UK's particular strengths is the existence of an established, country-wide healthcare provider. During the pandemic, the NHS was able to use existing distribution networks to facilitate a coordinated and speedy vaccine roll-out. In turn, those same networks facilitated the rapid gathering and

[47] An antigen is any substance that causes the body to make an immune response against that substance. The antigen targeted by the Vaccine is the SARS-CoV-2 spike protein.

feedback of country-wide data being reported in publications. These kinds of publications proved an extremely useful basis for decision-making as the pandemic progressed.

104. Beyond technology and data, cooperation between governments, regulators, and industry was also critical to rapid vaccine development and deployment. The UK was the first country to approve the Vaccine, thanks in large part to its effective cooperation with Pfizer and BioNTech during the early phase of the pandemic. The VTF, led by Kate Bingham, displayed a deep understanding of both the scientific and commercial aspects of bringing the Vaccine to market, and adopted a cooperative approach that was highly effective. Likewise, the MHRA adopted a flexible and innovative approach in implementing the Regulation 174 approval process (*see supra* ¶¶ 73–74) and a pragmatic approach to handling the complexity of the post-Brexit transition phase. The MHRA has provided continued guidance on regulatory requirements and has offered clear communication channels to ensure that rapid advice could be obtained on important matters. These efforts effectively secured a key role of the UK in the global deployment of COVID-19 vaccines.

Addressing Challenges

105. Despite the many successes of the vaccine response to the pandemic, there were also challenges.

106. The effort and investment required not merely to develop a new vaccine product, but also to manufacture it in sufficient quantities to provide billions of doses, should not be underestimated. The costs and resources involved are substantial, and potentially require vaccine developers to make at-risk investments in the billions. While BioNTech's partnership with Pfizer demonstrates that it is possible to bring products like the Vaccine to market quickly and effectively, there is a risk that in future pandemics smaller biotechnology and pharmaceutical companies with viable products may not have the resources or established relationships (e.g. with contract manufacturers, suppliers, or clinical research organisations) needed for vaccine deployment at the pace required to respond to a global emergency.

107. In addition, the roll-out of a new vaccine with novel technology in the context of a fast-moving global pandemic meant that the Vaccine faced virtually unprecedented levels of scrutiny. While effective scrutiny of all vaccines is vital and welcome, in a pandemic context in particular, it is important that such scrutiny is based on factually correct information and scientific understanding. Internationally, vaccine developers and others in the scientific community sometimes encountered misunderstandings about how vaccines work. In the context of a pandemic, it is especially important that complex scientific information is conveyed both accessibly and accurately, in order to avoid misunderstandings or information gaps among the public, which in turn have the potential to adversely affect the acceptance of innovative medicines. While public messaging in the UK during the pandemic was strong, and such challenges were by no means limited to the UK, the importance of correct information and messaging should not be underestimated when preparing for future pandemics. It can often be challenging for the public to distinguish valid scientific information (which can change over time) from incorrect or incomplete information from untrustworthy sources. Governments and health authorities have an important role to play in supporting the public, and others involved in informing them (such as news media), in making these distinctions.

108. Further, despite the efforts for global harmonisation, internationally a number of different country- and region-specific requirements were still in place during the COVID-19 pandemic. These included, for example, differences in labelling, language, and artwork requirements, periodic safety reporting, and regulatory dossier format and structure. A global regulatory framework for pandemic vaccines, agreed between relevant regulators in different countries, would significantly improve biotechnology and pharmaceutical companies' ability to respond rapidly to future pandemics, and would allow more manufacturers to contribute to the development of vaccine candidates on an international scale.

109. The need for international harmonisation is potentially a particularly acute consideration for the UK. The end of the Brexit transition period on 31 December 2020 brought specific complexities and challenges. While the MHRA adopted a pragmatic and sensible approach, the transition from the Vaccine's Regulation 174 approval to the pre-Brexit Centrally Approved Marketing Authorisation, and then to

the post-Brexit GB Marketing Authorisation, occupied considerable time and resource from a regulatory and procedural perspective.

110. Accordingly, the streamlining of processes and minimising variance between international regulatory regimes has the potential to create considerable efficiencies. In particular, now that the UK is no longer an EU member state and so is not part of the centralised European procedures, the MHRA will need to perform either a full regulatory assessment of a Marketing Authorisation application alone, or be willing to rely on the international recognition procedure to recognise a Marketing Authorisation granted by countries recognised under that procedure. A solo assessment by the MHRA would require significant MHRA resources.

BioNTech's Role in Preparing for a Future Pandemic

111. BioNTech, among others, is closely collaborating with the Coalition for Epidemic Preparedness Innovations (CEPI) and other international stakeholders, including UKHSA, to leverage the experience gathered during the development of pandemic COVID-19 vaccines for the improvement of pandemic preparedness frameworks globally. These initiatives include, among other things, work towards the "100-day mission" for development of vaccines for potential future pandemics and epidemics, for known pathogen and pathogen families, as well as for the so-called "Disease X", i.e. a yet unknown potential future pandemic pathogen. Several proposals in the context of these initiatives go in the direction of "proactive vaccinology": for instance, for pathogen families with known epidemic potential (as Coronaviruses were before the emergence of SARS-CoV-2), early research work can be done in advance. For example, this could involve developing "response playbooks" that provide early guidance to potential vaccine developers or developing prototype vaccines that can be rapidly deployed or adapted, if needed, in case of a pandemic outbreak. BioNTech is actively collaborating with relevant stakeholders on these activities to ensure that its experience with COVID-19 can help improve responses to future global health threats.

112. Other areas of work towards "proactive vaccinology" include developing proposals for a regulatory framework that includes the concept of "platform technologies" for vaccine development. BioNTech believes that such a framework would help

leverage some of the advantages offered by the messenger RNA technology and expedite the ability to respond to future pandemics by re-using existing experience. More generally, BioNTech is also involved in the areas of regulatory harmonization and collaboration, to support a global harmonization of regulatory requirements for pandemic products based on some of the challenges that were faced for COVID-19.

Conclusion

113. Overall, the UK's vaccine response to the pandemic demonstrated its ability to adopt a flexible, innovative approach, drawing on its deep bench of scientific, regulatory, and commercial industry expertise to deliver the Vaccine at pace. As described above, the existence of the NHS as an established, country-wide healthcare provider was also a significant factor in swift vaccine delivery and the availability of publications offering timely national data. In BioNTech's view, as outlined above, greater recognition and readiness for the use of mRNA technology in future vaccines, and smoother, more internationally harmonised regulatory rules and processes would be particularly welcome in laying the groundwork for a rapid response to future pandemics.

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: 27-Oct-2024

Annex A

Index of Exhibited Documents

RR/1	U.S. Dep't of Health & Human Servs., 'Vaccine Types' (last reviewed 22 December 2022) <https://www.hhs.gov/immunization/basics/types/index.html> accessed 14 March 2024.	INQ000485946
RR/2	BioNTech, 'Pfizer and BioNTech to Co-develop Potential COVID-19 Vaccine' (17 March 2020) <https://investors.biontech.de/news-releases/news-release-details/pfizer-and-biontech-co-develop-potential-covid-19-vaccine> accessed 14 March 2024.	INQ000485947
RR/3	U.S. National Library of Medicine, 'A Trial Investigating the Safety and Effects of Four BNT162 Vaccines Against COVID-2019 in Healthy and Immunocompromised Adults' (last updated 13 January 2022) <https://classic.clinicaltrials.gov/ct2/show/NCT04380701> accessed 14 March 2024.	INQ000485948
RR/4	U.S. National Library of Medicine, 'Study to Describe the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals' (last updated 28 February 2023) <https://clinicaltrials.gov/study/NCT04368728> accessed 14 March 2024.	INQ000485949
RR/5	GOV.UK, 'About Us' <https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/about> accessed 14 March 2024.	INQ000485950
RR/6	GOV.UK, 'UK medicines regulator gives approval for first UK COVID-19 vaccine' (2 December 2020) <https://www.gov.uk/government/news/uk-medicines-regulator-gives-approval-for-first-uk-covid-19-vaccine#:~:text=Press%20release-,UK%20medicines%20regulator%20gives%20approval%20for%20first%20UK%20COVID%2D19,products%20Regulatory%20Agency%20(MHRA).> accessed 14 March 2024.	INQ000485951
RR/7	Department of Health, Social Services and Public Safety, 'UK Influenza Pandemic Preparedness Strategy 2011' (10 November 2011) <https://assets.publishing.service.gov.uk/media/5a7c4767e5274a2041cf2ee3/dh_131040.pdf> accessed 14 March 2024.	INQ000102974
RR/8	BioNTech, 'Pfizer and BioNTech Conclude Phase 3 Study of COVID-19 Vaccine Candidate, Meeting All Primary Efficacy Endpoints' (18 November 2020) <https://investors.biontech.de/news-releases/news-release-details/pfizer-and-biontech-conclude-phase-3-study-covid-19-vaccine> accessed 14 March 2024.	INQ000485953
RR/9	BioNTech, 'Pfizer and BioNTech Announce Updated Clinical Data for Omicron BA.4/BA.5-Adapted Bivalent Booster Demonstrating Substantially Higher Immune Response in Adults Compared to the Original COVID-19 Vaccine' (4 November 2022) <https://investors.biontech.de/news-releases/news-release-details/pfizer-and-biontech-announce-updated-clinical-data-omicron> accessed 14 March 2024.	INQ000485954
RR/10	GOV.UK, 'Good manufacturing practice and good distribution practice' (27 December 2020) <https://www.gov.uk/guidance/good-manufacturing-practice-and-good-distribution-practice> accessed 14 March 2024.	INQ000485955
RR/11	BioNTech, 'BioNTech to Acquire GMP Manufacturing Site to Expand COVID-19 Vaccine Production Capacity in First Half 2021' (17 September	INQ000485956

	2020) <https://investors.biontech.de/news-releases/news-release-details/biontech-acquire-gmp-manufacturing-site-expand-covid-19-vaccine> accessed 14 March 2024.	
RR/12	International Coalition of Medicines Regulatory Authorities, 'Summary Report: Global regulatory workshop on COVID-19 vaccine development' (18 March 2020) <https://www.icmra.info/drupal/sites/default/files/2020-03/First%20regulatory%20COVID-19%20workshop%20-%20meeting%20report_March%202020.pdf> accessed 14 March 2024.	INQ000485957
RR/13	BioNTech, 'Investigator's Brochure BNT162/PF-07302048' (12 August 2020) <https://www.tga.gov.au/sites/default/files/foi-2183-09.pdf> accessed 14 March 2024.	INQ000485945
RR/14	Gouglas, D. et al, 'The 100 Days Mission—2022 Global Pandemic Preparedness Summit' (14 February 2023) <https://wwwnc.cdc.gov/eid/article/29/3/22-1142_article> accessed 14 March 2024.	INQ000485958
RR/15	MHRA Letter to Blume, C. (BioNTech) and Boyce, D. (Pfizer) (10 September 2020).	INQ000485959
RR/16 RR/16a RR/16b	MHRA Email to Blume, C. (BioNTech) et al. (1 December 2020) and Attachments.	INQ000485960 INQ000485961 INQ000112703
RR/17	MHRA, 'Public Assessment Report Authorisation for Temporary Supply COVID-19 mRNA Vaccine BNT162b2 (BNT162b2 RNA) concentrate for solution for injection' (dated 1 December 2020, last updated 2021 June 4) <https://assets.publishing.service.gov.uk/media/63529601e90e07768265c115/COVID-19_mRNA_Vaccine_BNT162b2__UKPAR___PFIZER_BIONTECH_ext_of_indication_11.6.2021.pdf> accessed 14 March 2024.	INQ000485963
RR/18	European Medicines Agency, 'EMA recommends first COVID-19 vaccine for authorisation in the EU' (21 December 2020) <https://www.ema.europa.eu/en/news/ema-recommends-first-covid-19-vaccine-authorisation-eu> accessed 14 March 2024.	INQ000485964
RR/19	GOV.UK, 'Decision: Regulatory approval of Pfizer/BioNTech vaccine for COVID-19' (22 December 2023) <https://www.gov.uk/government/publications/regulatory-approval-of-pfizer-biontech-vaccine-for-covid-19> accessed 14 March 2024.	INQ000485965
RR/20	GOV.UK, 'Correspondence: Letter to the profession from the UK Chief Medical Officers regarding the UK COVID-19 vaccination programmes' (31 December 2020) <https://www.gov.uk/government/publications/letter-to-the-profession-from-the-uk-chief-medical-officers-on-the-uk-covid-19-vaccination-programmes/letter-to-the-profession-from-the-uk-chief-medical-officers-regarding-the-uk-covid-19-vaccination-programmes#:~:text=We%20are%20confident%20that%20based,in%20particular%20severe%20COVID%20disease.> accessed 14 March 2024.	INQ000485966
RR/21	BioNTech, 'Comirnaty, Comirnaty Original/Omicron BA.1, Comirnaty Original/Omicron BA.4-5, Comirnaty Omicron XBB.1.5 (COVID-19 mRNA Vaccine) Risk Management Plan' <https://www.ema.europa.eu/en/documents/rmp-summary/comirnaty-epar-risk-management-plan_en.pdf> accessed 26 September 2024.	INQ000485967

RR/22	GOV.UK, 'Statutory Guidance: Current MHRA fees' (20 November 2023) <https://www.gov.uk/government/publications/mhra-fees/current-mhra-fees> accessed 14 March 2024.	INQ000485968
RR/23	United States National Library of Medicine, definition of “Prodrugs”, https://www.ncbi.nlm.nih.gov/mesh/?term=PRODRUGS (last accessed 4 October 2024)	INQ000508041

Annex B

Summary of Vaccine-related GMP Inspections by German Authorities at BioNTech Group Manufacturing Sites during Inquiry Date Range (30 January 2020 to 28 June 2022)

BioNTech Manufacturing GmbH site "Goldgrube"

7-9 Jul 2020	Landesamt für Soziales, Jugend und Versorgung (Regional Office for Social Affairs, Youth and Supply), Rhineland-Palatinate Paul Ehrlich Institute, Langen, Germany
3-4 Dec 2020	Landesamt für Soziales, Jugend und Versorgung (Regional Office for Social Affairs, Youth and Supply), Rhineland-Palatinate

BioNTech Manufacturing Marburg GmbH

14 Jan 2021	Hessisches Landesamt für Gesundheit und Pflege (HLfGP former Regional council Darmstadt) Paul Ehrlich Institute, Langen, Germany
25 & 27 Jan 2021	Hessisches Landesamt für Gesundheit und Pflege (HLfGP former Regional council Darmstadt) Paul Ehrlich Institute, Langen, Germany
04 Mar 2021	Hessisches Landesamt für Gesundheit und Pflege (HLfGP former Regional council Darmstadt) Paul Ehrlich Institute, Langen, Germany
29 Apr 2021	Hessisches Landesamt für Gesundheit und Pflege (HLfGP former Regional council Darmstadt) Paul Ehrlich Institute, Langen, Germany
02 Sep 2021	Hessisches Landesamt für Gesundheit und Pflege (HLfGP former Regional council Darmstadt) Paul Ehrlich Institute, Langen, Germany
08 Feb 2022	Hessisches Landesamt für Gesundheit und Pflege (HLfGP former Regional council Darmstadt)

	Paul Ehrlich Institute, Langen, Germany

BioNTech Innovative Manufacturing Services GmbH:

08 Dec 2020	Landesamt für Soziales, Jugend und Versorgung (Regional Office for Social Affairs, Youth and Supply), Rhineland-Palatinate
17/18 Jun 2021	Landesamt für Soziales, Jugend und Versorgung (Regional Office for Social Affairs, Youth and Supply), Rhineland-Palatinate
09/10 Jun 2022	Landesamt für Soziales, Jugend und Versorgung (Regional Office for Social Affairs, Youth and Supply), Rhineland-Palatinate