Witness Name: Gareth Arthur
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UK COVID-19 INQUIRY

FIRST WITNESS STATEMENT OF GARETH ARTHUR

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6 September 2024

Contents

I, Gareth Arthur, will say as follows:

Introduction

1. The novel Severe Acute Respiratory Syndrome Coronavirus 2 (known as "**SARS-CoV-2**", "**Covid-19**") was declared a pandemic by the World Health Organisation ("**WHO**") on 11 March 2020. There were initially no vaccines and no known effective therapeutics for Covid-19. Therapeutics are treatments to cure, alleviate or prevent a disease.

2. At that stage Covid-19 was understood to affect respiratory functions, leading to high demand for oxygen therapy (including the use of intubation ventilation, normally provided in critical care settings). As Covid-19 became more widespread, the risk of multiple organ failure became better understood.

3. The world faced the challenge of how to suppress the spread of Covid-19, to prevent disease and save lives. In England this included the Government implementing non-pharmaceutical interventions, such as lockdowns and social distancing.

4. Thanks to the NHS, the publicly funded system of thousands of organisations, including NHS bodies (such as Trusts) and independent providers (such as GP practices and pharmacies) and the establishment of clinical trials and the participation of willing patients, existing medicines and other therapeutic treatments were repurposed or became available from 2020 which could be used to prevent severe disease and treat patients.

5. This statement covers therapeutics directly related to the prevention and treatment of Covid-19 only. NHS England understands that management of the supply of supportive medicines, that is those used to manage patients with Covid-19 and/or to alleviate their symptoms – as opposed to therapeutics that directly prevent or treat Covid-19 – will be explored by the Inquiry in Module 3.

6. NHS England played a key role in supporting the prioritisation of key clinical trials in the UK and facilitating their access to clinical data. The UK has established infrastructure in place to carry out clinical trials. The speed at which organisations were able to design and carry these out, along with the willingness of the UK public to be participants in these trials, had an immense impact on identifying therapeutics effective at treating Covid-19.

7. Without any identified effective treatments for Covid-19 at the start of the pandemic, NHS England and its partners came together to rapidly design and implement processes to ensure that well-evidenced therapeutics were available for clinicians to treat patients. The Research to Access Pathway for Investigational Drugs – Covid-19 initiative ("**RAPID C-19**") established by NHS England and partner organisations ensured a rapid, systematic and collective approach to taking promising medicines from clinical trials through assessment and assurance, and out to patients in very short timeframes.

8. The efforts to make therapeutics identified as effective at treating Covid-19 available in very short timeframes – sometimes within a matter of days from a review of evidence – no doubt contributed to reducing mortality rates from Covid-19.

9. For example, the RECOVERY trial showed that the drug dexamethasone (a corticosteroid, which is a type of anti-inflammatory medication) administered to patients in hospital with Covid-19 could reduce intensive care admission and cut the number of deaths by a third for critically ill Covid-19 patients. It has been roughly estimated that the dexamethasone trial has contributed to saving approximately 22,000 lives in the UK and close to one million lives across the world between July 2020 and March 2021 (extrapolated from modelling in Aguas et al, 2021 **[INQ000331013]**.

10. In addition, the NHS was able to rapidly make available oral antiviral and intravenous treatments in the community, shortly after the conditional market approval, The treatments were made available through newly established NHS Covid Medicine Delivery Units (**"CMDUs"**). By 26 June 2023, CMDUs had provided around 115,000 community-based treatments to Covid-positive patients from the highest risk cohort including around 42,000 infusions and around 73,000 oral antivirals.

11. NHS England played a central role in managing shortages of Covid-19 priority medicines, including both supportive medicines and therapeutics (as set out the third witness statement of Professor Sir Stephen Powis provided as part of Module 3, and as set out in Annex Two of this statement).[1] Priority medicines were identified by NHS England and DHSC as medicines for which supply needed to be prioritised. They

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included supportive medicines (i.e. critical care medicines, antibiotics and end of life medicines) and Covid-19 therapeutics.

12. The medicines supply work in particular required clear clinical guidance, analysis of demand and supply, commercial management, and knowledge and coordination of supply chains at a national level, as well as coordination between regions and countries, with Department of Health and Social Care (**"DHSC"**) having overall responsibility for medicines supply). The efforts of wholesalers and NHS organisations to provide accurate information stock levels and medicine usage allowed NHS England to monitor stock and, combined with using information from published clinical guidelines, model anticipated demand. This analysis enabled NHS England to work with system partners to take timely action to ensure adequate stocks of supportive medicines and Covid-19 therapeutics.

13. Accurate information that allowed the effective oversight and management of supply helped ensure that patients with Covid-19 could access the medicines they needed, when required. This meant that no class of Covid-19 priority medicine went out of stock nationally during the response to the pandemic, reflecting the collaboration between government, industry and clinicians, as well the effective management in the NHS.

Corporate witness statement

14. I, Gareth Arthur, am the Director and Senior Responsible Officer (**"SRO"**) of Antivirals Deployment at NHS England. I have been in this role since November 2021. My role reports to the National Medical Director of NHS England.

15. Prior to this, I was the Director of Strategy and Policy, Specialised Commissioning at NHS England from 2016 until February 2021. From March 2020 to February 2021, I was the SRO of the Medicines Cell as part of NHS England's response to the pandemic. From March 2021 to October 2021, I was the Director of Workforce Planning at NHS England.

16. This corporate witness statement (**"Statement"**) was drafted on my behalf, but with my oversight and input, by external solicitors acting for NHS England in respect of the Inquiry. The request received on 28 November 2023 pursuant to Rule 9 of the Inquiry Rules (**"the Module 4 Rule 9 Request"**) to NHS England is broad in scope and goes beyond matters which are within my own personal knowledge. As such, this Statement is the product of drafting after communications between those external solicitors and a number of senior individuals (both current and former NHS England employees) in writing, by telephone and by video conference. I do not, therefore, have personal knowledge of all the matters of fact addressed within this Statement. However, given the process here described, I can confirm that all the facts set out in this Statement are true to the best of my knowledge and belief.

17. Following the period under investigation in Module 4, 30 January 2020 to 28 June 2022 ("**the Relevant Period**"), NHS England merged with:

    a. NHS Improvement on 1 July 2022;

    b. NHS Digital on 1 February 2023; and

    c. Health Education England ("**HEE**") on 1 April 2023.

18. This Statement refers to the legacy organisations above as necessary to respond to the Module 4 Rule 9 Request.

19. As this Statement includes evidence from a breadth of sources, combined to represent the evidence and voice of NHS England, references throughout to 'NHS

England', and 'we' represent the voice of the organisation. I have referred to all individuals (including myself) in the third person, by job title.

20. This Statement has been produced with input from a large number of colleagues across NHS England and following targeted review of emails and other documents collated to date. In the time available it has not been possible to review every potentially relevant document and it is highly likely that relevant documents exist that have not been reviewed. This Statement therefore provides the 'high level summary' requested by the Inquiry and is accurate to the best of our knowledge but we cannot exclude the possibility that it will require updating as further evidence emerges through our ongoing process of internal investigation and document review. NHS England will of course notify the Inquiry as soon as practicable if information comes to light that would have been included in this Statement if it was identified before the deadline for its production.

Approach to the Module 4 Rule 9 Request

21. NHS England welcomes the chance to assist the Inquiry to understand the key issues it has identified as in scope for Module 4 of the Inquiry (and in subsequent engagements with the Inquiry team).

22. We understand that the purpose of this document is to provide a corporate statement on behalf of NHS England to assist the Chair of the Inquiry in understanding a range of matters as set out in the Module 4 Rule 9 Request (both the draft and final requests received).

23. We understand that the scope of Module 4 is focused on a range of issues relating to the development of Covid-19 vaccines and the implementation of the vaccine rollout programme in England, Wales, Scotland and Northern Ireland, specifically during the Relevant Period. We also understand that issues relating to the treatment of Covid-19 through both existing and new medications will be examined in parallel in Module 4.

24. This Statement covers the treatment of Covid-19 through both existing and new medications. NHS England have provided a separate statement focusing on Covid-19 vaccine development and roll-out.

25. Therapeutics refers to treatments to cure, alleviate or prevent a disease. This Statement covers therapeutics related to the prevention and treatment of Covid-19 only. NHS England understands that management of the supply of supportive medicines, that is those used to manage patients with Covid-19 and/or to alleviate their symptoms – as opposed to those used to directly treat or prevent Covid-19 – will be explored in Module 3. Information on the medicines identified as supportive and as Covid-19 therapeutics is set out in Annex Two.

26. As requested by the Inquiry, NHS England has copied and transposed into this Statement a number of paragraphs from the third witness statement of Professor Sir Stephen Powis (M3/NHSE/03). The relevant text has been included in this statement where appropriate, as well as attached as Annex One.

27. The information requested is provided to differing levels of detail. Certain aspects are dealt with at a relatively high level as we understand that many of the issues to be discussed may be addressed in greater detail at a later stage in the Inquiry.

28. To ensure that this Statement is as accessible as possible, material which is primarily required for contextual or reference purposes, including a list of key decision-makers and a list of key milestones, is contained within the annexes at the end of this Statement.

29. In this Statement I have referred to NHS England, the DHSC and the Secretary of State for Health and Social Care ("**SSHSC**") in accordance with how they are structured today, but such references include all predecessor organisations and roles as the context may require.

30. NHS Trusts and NHS Foundation Trusts are referred to collectively as "Trusts" in this Statement unless otherwise stated.

31. NHS England adopts the following definitions of each 'wave' of the pandemic (there is no overarching definition used in England)[2,3]:

Wave and dominant variant	**Dates (approx.)**
Wave 1 – Wuhan variant.	February – May 2020
Wave 2 – emergence of Alpha variant.	September 2020 to January 2021
Wave 2 - reducing and the emergence of Delta variant.	February 2021 to September 2021
Wave 3 – emergence of Omicron variant.	September 2021 to end of the Relevant Period.

Outline of this Statement

32. As suggested by the Inquiry, this Statement adopts its own structure whilst aiming to answer the Inquiry's requests for information in detail.

[2] There were regional variations regarding the impact of each wave.
[3] There is no overarching definition of each wave in England, the above represents the definition being used by NHS England for the purposes of the Inquiry. This definition is taken from the Technical report on the COVID-19 pandemic in the UK **[INQ000205650]**.

33. This Statement comprises seven parts:

a. **Part One**: sets out the role of NHS England and the other organisations involved in identifying, regulating and recommending the use of therapeutics.

b. **Part Two**: covers NHS England's Emergency Preparedness, Resilience and Response and the role of the Specialised Commissioning team.

c. **Part Three**: covers clinical trials, including NHS England's role in these and key Covid-19 clinical trials. It also covers the Early Access Medicines Scheme.

d. **Part Four**: covers how effective Covid-19 therapeutics were identified and how recommendations were shared with clinicians.

e. **Part Five**: covers eligibility criteria for Covid-19 therapeutics and how community access to therapeutics for immunocompromised people was facilitated.

f. **Part Six**: covers how medicine supplies were monitored and future demand modelled. It contains charts indicating stock levels of selected Covid-19 therapeutics during the pandemic. It also covers NHS England's national role in the procurement of remdesivir and reflections on stockpiling therapeutics for future pandemics.

g. **Part Seven**: sets out NHS England's reflections and lessons learnt relating to Covid-19 therapeutics.

34. A chronology of key dates and decisions in respect of NHS England's involvement with therapeutic trials and research is set out in Annex Three of this Statement.

PART ONE: THE LANDSCAPE

35. Part One provides an explanation of the people, organisation and programme context and landscape for Covid-19 therapeutics.

NHS England and the NHS in England

36. In accordance with the framework established by Parliament, the NHS in England is not one organisation. It is a system of commissioners, regulators and service providers, each with their own distinct role. The publicly funded health service (excluding public health) in England comprises primary care, secondary care, tertiary care and community health.

37. In general, it is the responsibility of Government Departments to direct national strategy and set funding levels.

38. The DHSC is responsible for setting policies that deliver the Government's strategic health objectives; and in turn for making sure the legislative, financial, and administrative frameworks are in place to deliver those policies. DHSC oversees the health and social care system through its agencies and public bodies, holding them to account for the implementation of agreed plans and commitments.

39. NHS England is an executive non-departmental public body sponsored by the DHSC. It is referred to as an arm's length body as it is a public body established with a degree of autonomy from the SSHSC. Its primary responsibility is for the co-ordination of the provision of health care services in England and oversight of local commissioners and providers of those health care services.

40. NHS England's core legal function and purpose is to arrange for the provision of services for the purpose of the health service in England, a duty owed concurrently with SSHSC.

41. NHS England also has responsibility for management of national framework agreements for the procurement of medicines and homecare services by hospitals in England.

Organisations involved in identifying, regulating and recommending therapeutics

42. In addition to NHS England, the key organisations involved in identifying and recommending therapeutics are listed below:

    a. DHSC has overall responsibility for ensuring the continuity of the supply of medicines to the NHS in England.

    b. The National Institute for Health and Care Research ("**NIHR**") is the nation's largest funder of health and care research and is directed by the DHSC.

    c. The Medicines and Healthcare products Regulatory Agency ("**MHRA**") is responsible for regulating medicines, medical devices and blood components for transfusion in the UK. It is an executive agency sponsored by DHSC.

    d. The National Institute for Health and Care Excellence ("**NICE**") evaluates new health technologies for NHS use, considering clinical effectiveness and value for money. NICE produces evidence-based guidance for health and care in England and Wales.

PART TWO: EMERGENCY PREPAREDNESS, RESILIENCE AND RESPONSE IN RELATION TO COVID-19 THERAPEUTICS

Emergency Preparedness, Resilience and Response, and the role of the Specialised Commissioning team

NHS England pandemic governance

43. NHS England's general pre-pandemic preparedness is dealt with extensively in Dr Michael Prentice's First Witness Statement, provided during Module 1. Later sections of this Statement refer to pre-pandemic arrangements, and we note in Part Seven that the work on medicine supply carried out in preparing for EU Exit helped introduce new ways of working that informed the response to managing medicine supply during the Covid-19 pandemic.

44. In response to the pandemic, NHS England established a "cell" governance structure. Cells were set up to give a focus to particular issues that arose during the pandemic, with a defined task and team allocated to each cell. NHS England reorganised itself around the cell structure required to respond to the pandemic. Many existing organisational structures, roles and workstreams were placed on hold to enable complete focus on pandemic response.

45. The national structure for cells is set out in detail in NHS England's Second Module 3 Statement. These cells were vital to NHS England's pandemic response and played a key part in gathering information, producing guidelines, and sharing communications with NHS frontline services. This section provides detail of the cells most relevant to Covid-19 therapeutics.

The Clinical Cell

46. NHS England established a clinical cell in February 2020. Its terms of reference were finalised in April 2020 **[INQ000330943]**. The cell's overarching aim was to support recommendations for the treatment and medical management of patients with Covid-19. The specific purpose of the cell was to resolve any clinical questions, issues or tasks from the national incident co-ordination centre and/or other issues that were escalated to a national level.

47. As part of its role, the cell provided guidance on emerging themes arising out of the pandemic, developed policy and provided a strategic response to various issues and

was involved in reviewing and assisting with clinical guidelines. The cell carried out the following specific functions:

a. Identifying tasks which required specialist clinical input;

b. Forwarding tasks to other workstreams;

c. Engaging appropriate clinicians and stakeholders;

d. Collating information provided into a meaningful form;

e. Enabling the senior responsible owner to make informed decisions; and

f. Prioritising tasks based on clinical and operational urgency.

The Specialised Services Cell

48. NHS England has a statutory duty to arrange for the provision of specialised services for the population of England. Specialised services support people with a range of rare and complex conditions. They often involve treatments provided to patients with rare cancers, genetic disorders or complex medical, mental health or surgical conditions. Specialised services are not available in every local NHS hospital because they are delivered by specialist teams of doctors, nurses and other health professionals who have the necessary skills and experience. Unlike most healthcare, which is planned and arranged locally, specialised services are planned nationally and regionally by NHS England although there has been a process ongoing since 2023 to give Integrated Care Boards (**"ICBs"**) a bigger role in commissioning some specialised services.

49. To assist NHS England's specialised commissioning role, there is a standing expert clinical advisory structure in place which includes a number of specialty based Clinical Reference Groups ("**CRG**"). The exact role of a CRG depends on its terms of reference. In general, a CRG is a group of advisers, independent of NHS England, who provide subject matter expertise and clinical advice to support specialised services. Increasingly CRGs are led by a National Clinical Director or National Speciality Advisors.

50. During the pandemic, the specialised commissioning national and regional teams were responsible for commissioning specialised services. National teams, with the

support of CRGs, were also responsible for developing commissioning products (including service specifications and commissioning policies).

51. The Specialised Services Cell (sometimes referred to as the Specialised Commissioning Cell) was established on 9 March 2020 to co-ordinate the maintenance, prioritisation and surge of NHS specialised services in the pandemic.

52. The cell's stated objectives included:

    a. Rapidly forming clinical policy for new treatments or amendments of current treatments;

    b. Supporting the roll out of research for new treatment strategies;

    c. Rapidly forming clinical guidelines in partnership with NICE for Covid-19 specific clinical management scenarios; and

    d. Acting as a single point of contact for key partners including NICE, NIHR and the devolved administrations ("**DAs**").

53. The Specialised Services Cell undertook specific functions as set out in the table below. Issues that could not be managed locally or by national programmes of care and that needed a national resolution or had a national impact were submitted to, and reviewed by, members of the Specialised Services Response team acting within sub-groups carrying out these functions.

Specialised Services Response Team	**Function**
Treatment Medicines	Developed and issued clinical and pharmacy guidance to support the rapid adoption of treatment approaches for Covid-19 and, with the wider Medicines Cell, understood and mitigated any medicines supply issues associated with treatments, either in relation to Covid-19 patients or other patients reliant on that medication.
Research	Supported the identification, prioritisation and roll-out of Covid-19 focused studies in the NHS. National clinical advisory, innovation pathway and other direct commissioning capabilities were used to help identify, prioritise and deliver research findings. The aim was to support the work of NIHR

	and the Chief Medical Officer ("**CMO**") by both supporting prioritised research in the NHS and enabling its rapid dissemination and roll out into front line care.
Clinical Policy	Developed Covid-19 related urgent policies. A three-day rapid evidence review was conducted followed by a two-day expert panel. The aim was to produce the urgent policies within six days.
Clinical Guidelines	Worked in conjunction with NICE to produce Covid-19 related clinical guidelines for specialised services. The aim was for the guidelines to be developed and published on the NICE website within a week.
National Delivery	Reviewed business as usual activities and provided a national response when issues were escalated, and a consistent national position was critical; included linking in with the DAs. In addition, provided commissioner support to the mobilisation of clinical networks to support patient flow and surge management. This response team also provided the link into the national incident management team.
Regional Delivery	Co-ordinated information flows from the central response to regional teams. Identified issues that regions wished to escalate where a national response is required. Identified any national resources which could support regions to manage the incident.

54. The Specialised Services Cell met daily through the first wave of the pandemic. The meetings covered any relevant topics from the sub-groups: treatment medicines, research, clinical policy, clinical guidelines, national delivery and regional delivery.

55. The renal stocktake described in paragraph 3 of Annex One is a good example of how the cells, particularly the Specialised Services Cell, gathered information, used that information to make decisions regarding management (both clinical and operational) and shared that with the system.

56. Given the expected demand from clinicians for clinical guidance on, and access to, treatments for Covid-19, NHS England initiated a novel collaboration with NIHR, MHRA and NICE – the Research to Access Pathway for Investigational Drugs in Covid-19 ("**RAPID C-19**") – led by an Oversight Group with the aim of producing national policy in a much-reduced timescale so that patients across the UK could

access effective treatment for Covid-19 rapidly. The RAPID C-19 Oversight Group is discussed in detail later in this Statement. The Specialised Services Cell carried out most of the NHS England activities as part of the RAPID C-19 Oversight Group and led on the clinical policies issued to the NHS on use of therapeutics for Covid-19.

57. A chronology of key matters is set out in Annex Three of this Statement. This includes decisions related to the subject matter of this Statement, but it should be noted that the Specialised Services Cell also managed non-Covid-19 related treatments. The decision log of the Specialised Services Cell contains a much longer list of decisions.

Covid-19 Therapeutics Cell

58. The Covid-19 Therapeutics Cell co-ordinated the significant clinical access policy work undertaken on behalf of the UK to determine access to evidence-based Covid-19 therapies, working closely with RAPID C-19, DHSC's Therapeutics and Antiviral Taskforces and NHS England's Specialised Commissioning Cell. The Covid-19 Therapeutics Cell also worked closely with the Medicines Cell, which monitored the usage of a number of Covid-19 therapeutics in order to model demand against available known supply where possible.

The Medicines Cell

59. Prior to March 2020, work was undertaken in NHS England to prepare for the expected increased demand for medicines to support Covid-19 patients. Building on the EU Exit programme, work was undertaken to identify the medicines that would be required to manage Covid-19 by NHS England's Medicines Policy team, working with DHSC and with clinical experts. The Commercial Medicines Team identified possible issues in the medicine supply chain resulting from Covid-19, sourcing additional stock to meet an increased demand in patients requiring treatment and stock visibility both in the NHS and wider supply chain. In February 2020, medicine supply chain responsibilities were included in what was then the 'supply chain cell'.

60. The Covid-19 Medicines Cell was formally established in March 2020, to support the continued supply of medicines required for patients in the UK during the pandemic. It aimed to ensure that patients with Covid-19 could access Covid-19 priority medicines, through both proactive management of both the demand and supply side of those medicines across the system. A key element of the Medicines Cell was the allocation

and distribution of supportive medicines for England and the DAs, focussing initially on medicines to support the management of patient. The Medicines Cell was formally stood down in February 2023.

61. The Medicines Cell established seven key workstreams in the first wave of the pandemic alongside a central programme coordination function that was a single point of contact and was responsible for oversight, engagement with key internal and external partners, central reporting and drafting briefs, correspondence and any formal requests. Each workstream was led by a senior clinician or subject matter expert and had distinct purposes and objectives. The workstreams were:

    a. Communications and engagement (throughout the pandemic) - ensuring effective feedback from the NHS, stakeholder groups and clinicians and cascading information to the system as necessary.

    b. Non-Covid-19 medicines (March – June 2020) - identifying any other medicines that were at risk of shortage during the pandemic. For example, ensuring that essential medicines such as insulin were also managed effectively.

    c. Trial and treatment medicines (March – June 2020) - linking to the Covid-19 Therapeutics Cell and Specialised Commissioning Cell to ensure supply of any new treatments following outcomes from clinical trials.

    d. Demand and clinical guidance (March - June 2020) - to provide clinical advice on the most appropriate medicines to manage patients with Covid-19.

    e. Data and analysis (throughout the pandemic) - with oversight of the supply assessment tracker, including demand and supply analysis.

    f. Medicines sourcing and wholesaler/supplier engagement (significant work on sourcing at the start of the pandemic, and wholesaler/supplier engagement throughout) – including the Sourcing Team and engagement for Covid-19 priority medicines.

    g. Allocation and distribution (throughout the pandemic) – to manage the supply of medicines in the NHS and with the other UK nations.

62. Given DHSC's overall responsibility for medicines supply, NHS England worked closely with DHSC to ensure the supply of medicines across primary and secondary care. DHSC identified workstreams and leads within their organisation to align with NHS England counterparts, along with joint governance arrangements. The Medicines Cell reported into the NHS England pandemic arrangements and was not led by DHSC.

63. The Medicines Cell worked closely with colleagues in the Specialised Commissioning Cell and the Covid-19 Therapeutics Cell from the outset to understand the latest information on trial and treatment medicines, including whether there was sufficient stock of these medicines for trial purposes as well as for treatment once the medicines had been deemed effective. An early Medicines Cell workstream (March-June 2020) focused on trial and treatment medicines. After this, the Medicines Cell was kept regularly informed by NHS England colleagues involved in the DHSC Therapeutics Taskforce and RAPID C-19 at the weekly workstream leads meetings, with the Medicines Cell SRO invited to attend the weekly RAPID C-19 Strategic Update meetings from April 2021. Colleagues reported to the cell on, for example, the use of new Covid-19 treatments commissioned under UK wide interim clinical policy arrangements (such as antivirals, neutralising monoclonal antibodies (nMABs) and IL-6 inhibitors via the prior approval system Blueteq), the use of dexamethasone for patients admitted to critical care and stock level discussions with relevant suppliers.

PART THREE: CLINICAL TRIALS

64. This section covers:

    a. Clinical trials; and

    b. The Early Access Medicine Scheme.

65. Key dates and decisions in respect of NHS England's involvement with therapeutic trials and research are included in the chronology set out in Annex Three of this Statement.

Clinical trials

Overview

66. Clinical trials are run to identify effective treatments. Pharmaceutical companies, academics and participants came together to identify effective Covid-19 therapeutics. The UK has a comprehensive and established infrastructure in place for clinical trials which runs independently of NHS England. NHS England (as opposed to the NHS) does not ordinarily have a direct role in coordinating or contributing to research and clinical trials in the UK.

67. Further information on clinical trials is set out in Annex One.

Moving from clinical trials to market authorisation and patient access

68. Following a clinical trial, and where the treatment involves a new medicine, the MHRA (or up to December 2020, the European Medicines Agency) assesses its safety, manufacturing quality and efficacy and determines whether to issue a marketing authorisation.

69. NICE then carries out a technology appraisal for the licensed indication as part of its core role to provide guidance and advice to improve health and social care and treatment. The appraisal process involves a review of clinical evidence to show how well the treatment works and a review of economic evidence to ascertain how much it will cost the NHS and whether this represents value for money. It takes NICE on average 91 weeks to produce a piece of guidance. Each commissioned topic is initially assigned a 'standard (*142 week*)' timeline, 'accelerated *(86 week)*' timeline, or *'short (44 week)*' timeline depending on the expected size of the work required. NICE follows a comprehensive guidance development method and process based on

gathering evidence, analysing that evidence, public consultation at several stages of guideline development, and review and recommendations by independent advisory committees of health care professionals and lay members.

70. The NHS is then legally obliged to fund and make available medicines and treatments recommended by NICE technology appraisals, usually within 90 days.

71. As set out later in this statement, the time taken to approve the use of therapeutics for Covid-19 was significantly reduced during the pandemic.

Key Covid-19 clinical trials

DHSC's support for Covid-19 clinical trials

72. The UK COVID-19 Therapeutics Advisory Panel ("**UK-CTAP**") made recommendations on which therapeutic compounds should be studied through national publicly funded clinical trials, based on submissions from industry and academia. UK-CTAP was established to help prioritise research into the most promising therapeutics during the first year of the pandemic. It ceased operations in September 2021.

73. The role of the DHSC Therapeutics Taskforce, established in April 2020, was to drive forward efforts to ensure that the UK population would have access to clinically safe and effective treatments as soon as possible. From its inception it brought together key clinical, research and industry stakeholders to coordinate and provide oversight to identifying, procuring and deploying treatments for Covid-19. It secured supplies of medicines to support nationally prioritised clinical trials where required and procured central stockpiles for wider population roll-out.

74. The DHSC Antivirals Taskforce, established in April 2021, worked with industry experts to identify, develop and procure novel oral antivirals in pill form that patients can take promptly following infection.

75. The DHSC-led Covid-19 Antivirals and Therapeutics Taskforce co-ordinated the end-to-end provision of treatments for Covid-19 and was responsible for identifying potential Covid-19 therapeutics, trialling these as part of an advanced programme of clinical trials and making effective treatments available to UK patients. It was

established in April 2022, when the DHSC Therapeutics Taskforce and the Antivirals Taskforce were amalgamated.

NHS England's role in Covid-19 clinical trials

76. NHS England was not involved in a formal role with the Covid-19 related clinical trials. NHS England supported trials through its emergency preparedness, resilience and response role by ensuring the NHS was advised to prioritise Covid-19 research. As a result, once key clinical trials had been identified (i.e. the PRINCIPLE, RECOVERY and REMAP-CAP trials), the four CMOs and the National Medical Director for NHS England wrote a letter to the system confirming that these clinical trials were to be national priority clinical trials.

77. Separately, the NIHR established a single UK-wide process to prioritise Covid-19 research as 'Urgent Public Health Research'. This covered Covid-19 studies funded by the public sector, industry or charities. Through this process the NIHR Clinical Research Network ("**CRN**") expedited urgent clinical trials by fast-tracking the local set-up, management and delivery of Covid-19 studies and placing them onto the NIHR CRN Portfolio. The NIHR also announced at the start of the pandemic that new clinical studies not related to Covid-19 would be suspended to prioritise Covid-19 related studies. On 21 May 2020, NIHR set out a framework to guide the restarting of NIHR research activities which had been paused due to Covid-19.

78. Given that NHS England was one step removed from clinical trials research, we set out brief details only of the PROTECT-V, PROTECT-CH, HEAL-COVID and STIMULATE-ICP clinical trials. Information on the RECOVERY, PRINCIPLE and REMAP-CAP clinical trials is included in Annex One. Information on the important role of NHS DigiTrials in providing secure data about people's health and care to researchers during Covid-19 clinical trials is also included in Annex One.

PROTECT-V

79. PROTECT-V (Prophylaxis for patients a risk of Covid-19 infection) is an international, multicentre study. The study opened to recruitment in February 2021 and is enrolling participants who are immunocompromised in order to identify medications which protect vulnerable patients from Covid-19.

80. As of August 2024, the trial is still considering sotrovimab and niclosamide and results are not yet available.

81. NHS England did not have a role in instigating, funding, monitoring or securing the medicines supply for this study.

PROTECT-CH

82. PROTECT-CH (Prophylactic therapy in care homes trial-CH), led by the University of Nottingham, was a platform trial aiming to evaluate prophylactic treatments for Covid-19 in care home residents. Researchers intended to test several treatments intended to reduce the spread of Covid-19 within care homes, and to reduce the risk of hospitalisation and death.

83. The study identified that 200 care homes – around 6,400 residents – would be required for comparison of a treatment. Care homes would be randomised to determine whether they would receive treatment or care. It was expected that most of the treatment would be given for up to two months before it would be known whether they had worked, and whether the treatments were cost effective.

84. Due to the success of the Covid-19 vaccination programme and other measures taken by care homes to reduce the spread, it became clear that the study would require a significantly larger number of care homes and residents to evaluate prophylactic treatments than was assumed when designing the study. The study was deemed no longer feasible after 10 months.

85. NHS England did not have a role in instigating, funding, monitoring or securing the medicines supply for this study.

HEAL-COVID

86. HEAL-COVID (Helping alleviate the longer-term consequences of Covid-19) is a large platform clinical trial designed to compare different treatments to determine whether they can improve the longer-term outcomes for patients who have been hospitalised due to Covid-19. Adults who are expected to be discharged from hospital within five days were eligible to participate in the study. The study involves 1,245 participants across 109 hospitals in the UK.

87. The study examined the effectiveness of apixaban and atorvastatin being taken for a period after hospital discharge. Follow up surveys were sent no more frequently than once a week, and included questions relating to symptoms, quality of life, resource use and experience of participating in research. Results of the study are not yet available.

88. NHS England did not have a role in instigating, funding, monitoring or securing the medicines supply for this study.

STIMULATE-ICP

89. STIMULATE-ICP (Symptoms, Trajectory, Inequalities and Management: Understanding Long-COVID to Address and Transform Existing Integrated Care Pathways) is a two year clinical study of long Covid and involves more than 30 organisations, led by University College London Hospitals NHS Trust and University College London. The study aims to identify what long Covid is, how to diagnose it and how to manage it. Information will be obtained from interviews and NHS records.

90. NHS England did not have a role in instigating, funding, monitoring or securing the medicines supply for this study.

Early Access to Medicines Scheme

91. For medicines that are awaiting marketing authorisation, the Early Access to Medicine Scheme (**"EAMS"**) is a voluntary, manufacturer-led process of engagement with the MHRA that enables drugs to be used in clinical practice during the later stages of the regulatory process. EAMS has been in place since before the pandemic and is only available where there is a clear unmet clinical need for patients with a life threatening or seriously debilitating condition.

92. Under EAMS, the MHRA would give a scientific opinion on the benefit/risk balance of the medicine, based on the data available when the EAMS submission was made.

93. The scheme remained operational throughout the pandemic, ensuring that patients with serious conditions could still be offered new treatment. However, the timescales from submission to receiving a positive opinion could be months, and so was not appropriate for new Covid-19 treatments.

PART FOUR: IDENTIFYING EFFECTIVE TREATMENT FOR COVID-19

94. This Part four provides information on:

    a. How NHS England worked with NICE to produce clinical guidance;

    b. The RAPID C-19 process;

    c. How therapeutics that were not effective at treating Covid-19 were identified; and

    d. How communications about Covid-19 therapeutics were shared with clinicians.

NHS England's collaboration with NICE on guidelines for Covid-19 therapeutics

95. NHS England's collaboration with NICE to produce guidelines during the pandemic is set out in Professor Sir Stephen Powis' Third Witness Statement provided as part of Module 3 and included in Annex One of this statement. A summary of NHS England's collaboration with NICE during the pandemic is set out below.

96. Clinical guidance is ordinarily produced and published by NICE, the Royal Colleges, and regulatory bodies such as the General Medical Council and the Nursing and Midwifery Council, as well as professional societies such as the Intensive Care Society.

97. Outside of pandemics, NHS England has a limited role in issuing guidance on the clinical management of healthcare conditions, although it does produce clinical commissioning polices that support the clinical management of healthcare conditions managed within specialised services.

98. As part of its emergency role during the pandemic, NHS England undertook several extended roles, including the production and dissemination of some specialty clinical guidelines and access policies for clinicians and other healthcare professionals. These guidelines and access policies supported hospitals to treat Covid-19 patients with optimal clinical management and new treatments for Covid-19. They were communicated and introduced rapidly, sometimes within days of approval.

99. Although NHS England does not ordinarily produce clinical guidance, on 11 March 2020, NHS England agreed with NICE that NICE would pause development of its 'business-as-usual' guidance and NHS England would develop and update rapid Covid-19 clinical guidance. NHS England assisted NICE during the pandemic by developing specialty guides drawing from a range of national clinical expertise from within its own organisation (i.e. National Clinical Directors), CRGs and the NHS system more widely.

100. By 27 May 2020 (i.e. within the first two months of the pandemic), NHS England had published 67 specialty guides **[INQ000330861]** not including updates. On 27 May 2020, before transfer to NICE, NHS England's website listed 63 guides (the full list is at Annex Four). As these guides were produced in the early stages of the pandemic, while effective therapeutics were still in the process of being identified, there is limited reference to Covid-19 therapeutics.

101. Further information on NHS England's work with NICE to produce guidelines relevant to Covid-19 as part of RAPID C-19 is set out below.

RAPID C-19

Overview

102. During the pandemic, patients needed access to new and effective treatments (such as those identified in clinical trials) as quickly as possible. RAPID C-19 was established in the early stages of the pandemic. NHS England helped to establish RAPID C-19 and partly funded its work.

103. Outside of the pandemic in BAU, the process to authorise access for new licenced treatments is managed by NICE through their technology appraisal process. The purpose of RAPID C-19 was to join organisations together to create a more rapid appraisal process for Covid-19 treatments. RAPID C-19 ensured safe and timely patient access to medicines and therapeutics which had shown evidence of benefit in treating symptomatic Covid-19 patients. The multi-organisational nature of RAPID C-19 meant that it could align activities and communications and reduce the need for individual agencies to engage bilaterally with sponsors. RAPID C-19 enabled UK-wide adoption of effective Covid-19 therapies in a significantly reduced timeframe compared to prior to the pandemic. RAPID C-19 developed a robust set of procedures

[INQ000315554] **[INQ000330922]** and formally collaborated with the DHSC Therapeutics Taskforce.

104. RAPID C-19 consisted of representatives from the following organisations:

    a. NHS England

    b. MHRA

    c. NIHR

    d. Scottish Medicines Consortium (Healthcare Improvement Scotland)

    e. All Wales Therapeutics and Toxicology Centre

    f. All Wales Medicines Strategy Group

    g. Department of Health in Northern Ireland

    h. Antivirals and Therapeutics Taskforce at the DHSC[4].

105. RAPID C-19 had an Oversight Group that considered potential topics and advised on which should be expedited. Organisations had assigned roles and responsibilities as set out below:

    a. NHS England – clinical services policy development;

    b. NICE – conducted numerous rapid evidence reviews, led the RAPID-C-19 weekly committee and conducted horizon scanning activities;

    c. MHRA – led responsibility for regulatory issues and authorisation functions (including clinical trials, early access and marketing authorisation);

    d. NIHR – coordinated horizon scanning activities alongside NICE; and

    e. DHSC Therapeutics Taskforce – responsible for purchase and supply.

RAPID C-19's process to identify effective Covid-19 therapeutics

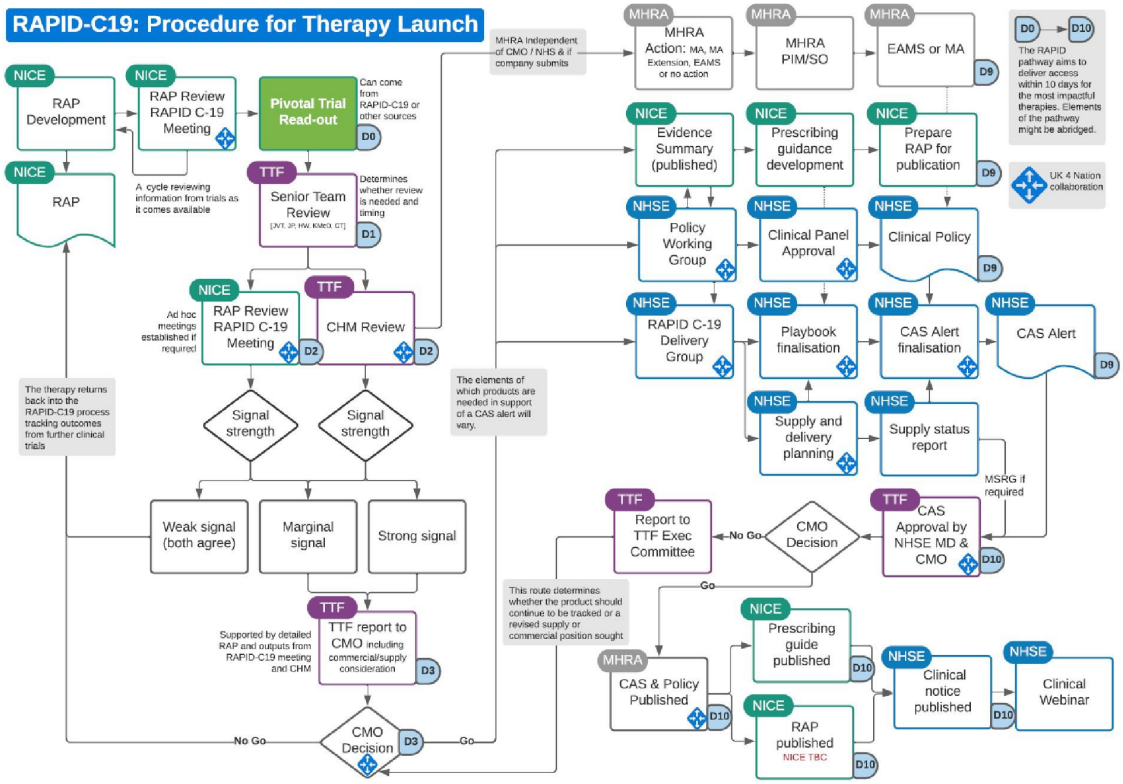
106. In general terms, the DHSC Therapeutics Taskforce identified medicines for research (with NIHR) and secured supply of clinically effective medicines for the UK.

[4] As set out in paragraphs 72 to 74, the Therapeutics Taskforce became part of the Antivirals and Therapeutics Taskforce from April 2022.

RAPID C-19 established whether there was convincing evidence of clinical effectiveness to make the medicine available. The RAPID C-19 Oversight Group met regularly to critically appraise the latest evidence and consider the next steps needed to enable rapid patient access to treatments. If the evidence of benefit was robust, the Oversight Group could then act quickly to make those treatments available promptly through expedited access mechanisms. The NHS England Specialised Commissioning Team built and defined access criteria, published clinical policy (for the UK) and then secured equitable access to supply across the UK. By June 2022, RAPID C-19 had considered briefings on 76 potential treatments.

107. The process broadly followed by the RAPID C-19 Oversight Group is set out in the figure below, and then described in more detail:

Figure 1: RAPID C-19 procedure for therapy launch



108. Covid-19 therapeutics were identified through a horizon scanning approach coordinated by NICE and supported by information from NIHR (in respect of UK clinical trials) and the NHS Innovation Observatory (in respect of international clinical trials) to provide a comprehensive understanding of Covid-19 medicines and

treatments in development. NHS England's role within the RAPID C-19 Oversight Group contributed to NHS England's awareness of Covid-19 related clinical trials and studies.

109. NICE would combine the outputs of the horizon scanning into the RAPID C-19 portfolio. This was supplemented by other information such as intelligence on progress of individual trials and advice from the Committee on Human Medicine's Covid-19 Expert Group. The portfolio was prioritised using scientific criteria based on emerging research/trial evidence of efficacy (for which NIHR had developed a scoring system), medicine safety, whether a licence existed yet and what it covered.

110. NICE presented the RAPID C-19 Oversight Group with regular briefings of the portfolio. A number of Covid-19 medicines and treatments were agreed and prioritised for further development and a rapid action plan was agreed with a shared vision of the approach to development and patient access. In 2021, the rapid action plans were no longer produced; all information that was previously documented in the plans was included in the topic briefings.

111. After consideration of the evidence and other information, the RAPID C-19 Oversight Group would either progress it or:

    a. where evidence of efficacy was insufficient but there were other ongoing trials, the medicine or treatment would continue to be monitored and brought back to the RAPID C-19 Oversight Group when results from identified trials were due; or

    b. where there was no evidence of efficacy and none was likely to be forthcoming, the medicine or treatment would be deprioritised for active monitoring but could be brought back to the RAPID C-19 Oversight Group if new evidence emerged.

112. Where a medicine or treatment was not at a stage where it could be prioritised, it was kept under review with continued monitoring.

113. For those being prioritised, the rapid action plan included plans to progress the medicine or treatment within an expedited or rapid version of the EAMS. This provided the basis for a regulatory opinion, potentially significantly in advance of licensing. Part

of the rapid action plan process was commissioning NHS England to undertake an abridged clinical policy development process to be ready if there was a positive outcome to the rapid EAMS opinion process.

114. The clinical policy workstream undertook the clinical policy development process. The Clinical Director for the National Clinical Policy Team in NHS England's Specialised Commissioning team, in conjunction with NHS England's National Medical Director for Specialised Services, assessed the form of external evidence review required. The clinical policy would be urgently drafted by NHS England's Clinical Policy team, with the input of speciality specific clinicians accessed primarily using NHS England's existing national expert clinical advisory structure and from the other home nations. The policy development process included a Rapid Impact Assessment (RIA) and Equality and Health impact Assessment (EHIA) Review. The EHIA followed the NHS England Specialised Commissioning process for an EHIA. Approval of the policy was through NHS England's Specialised Services Clinical Panel with representation from the DAs (meeting virtually).

115. The national clinical policies defined access to the relevant medicines/treatment for a particular group of patients during the Covid-19 pandemic. All such clinical policies were interim for the Covid-19 period and were reviewed when the pandemic was over, with options including withdrawal, entering the full NHS policy development process, or entering the NICE appraisal process.

116. Subsequently, the Chief Pharmaceutical Officer and NHS England's National Medical Director approved the policy to be submitted to the DHSC's CMO. The CMO approved the policy on behalf of the UK CMOs. On occasion, the four UK CMOs discussed the position of a policy before approval. Publication was approved by the CMO using the established UK-wide alert system. The Central Alerting System ("**CAS**") is a web-based cascading system for issuing patient safety alerts, important public health messages and other safety critical information and guidance to the NHS and others. Further information on CAS alerts is provided later in this Statement.

117. The core difference between the expedited process and the pre-pandemic NICE appraisal process was that under the expedited process the clinical effectiveness of medicines and treatments was considered but cost effectiveness was not. The RAPID C-19 Oversight Group's appraisal relied on pragmatic decision making and

rapidly forming clinical consensus with a focus on medicines that reduced hospital mortality, intensive care requirement or hospital admission.

118. Where clinicians disagreed with the national clinical policies, and there was evidence to support a contrary view, the evidence could be reviewed and considered by the RAPID C-19 Oversight Group. The decision log indicates that a large number of medicines and treatments were considered multiple times as more evidence was received.

119. As an example, the RAPID C-19 Oversight Group was aware that a drug called azithromycin was a regularly used treatment in NHS hospitals. Its use as a treatment for Covid-19 had a growing reputation. It was considered by the RAPID C-19 Oversight Group on 14 May 2020. However, the results of the RECOVERY study showed no significant clinical benefit of either oral or intravenous azithromycin in patients hospitalised with Covid-19. Following consideration by the RAPID C-19 Oversight Group, a CAS alert was issued on 15 December 2020 recommending that azithromycin should not be used to treat patients hospitalised with Covid-19 as the RECOVERY trial showed no significant clinical benefit of either oral or intravenous administration **[GA1/001] [INQ000414411]**

120. The CAS alert also stated that the recommendation would be reviewed as further evidence became available, including from the PRINCIPLE trial.

121. RAPID C-19 was stood down at the end of March 2023 but is able to be re-established at the request of the UK CMOs in a future pandemic response. The oversight of access to medicines in England has returned to NICE through technology appraisals.

Identifying therapeutics that were not effective at treating Covid-19

Overview

122. It was clearly important for RAPID C-19 to identify medicines which were clinically effective. But of equal importance was RAPID C-19's role in identifying those medicines which were not effective, despite in some cases strong public lobbying. Most notably, these medicines included:

a. ivermectin;

b. convalescent plasma;

c. hydroxychloroquine; and

d. tixagevimab and cilgavimab (Evusheld).

123. More detail on these medicines is set out below. Other medicines included canakinumab; doxycycline; aspirin and bamlanivimab. As set out above, the RAPID C-19 Oversight Group applied the same process for all medicines and treatments that were undergoing clinical trials and studies.

Ivermectin

124. Ivermectin is an anti-parasitic agent used in the treatment of onchocerciasis (river blindness), strongyloidiasis and other diseases caused by soil transmitted helminthiasis. It is also used to treat scabies.

125. The RAPID C-19 Oversight Group reviewed the evidence relating to the effectiveness of ivermectin and agreed to monitor it "with low interest" on 14 August 2020. On 21 October 2020, ivermectin was considered again and a decision was made to continue monitoring with elevated interest, awaiting publication of results from further trials. On 6 January 2021, the RAPID C-19 Oversight Group determined that ivermectin should continue to be monitored for meta-analysis results. This was reiterated in decisions made on 11 and 17 March 2021, 28 April 2021, 2 June 2021 and 11 August 2021.

126. The RAPID C-19 Oversight Group made a recommendation on 19 May 2022 that stated that there was a high degree of uncertainty about whether ivermectin was more effective than control for managing Covid-19 in hospital or community settings. There were concerns about the quality of the studies on ivermectin – the certainty of evidence was low to very low for all outcomes. The uncertainty about the overall safety and the possibility of rare serious adverse reactions with ivermectin were noted. Because of the uncertainty in the evidence at that point in time (which included small sample sizes and issues with study quality), it was concluded that ivermectin should only be used to treat Covid-19 in ongoing well-conducted clinical trials. It was noted that there was at least one ongoing trial that might improve certainty in the evidence once the results were available.

Convalescent plasma

127. Convalescent plasma is a transfusion of blood plasma from someone who has recovered from Covid-19 to a person that is unwell with Covid-19.

128. From 13 July 2020 to 20 January 2021, RAPID C-19 agreed to continue to monitor convalescent plasma while waiting for trial results. A decision was made on 11 March 2021 to wait for full results of the RECOVERY trial before taking a decision about the effectiveness of convalescent plasma.

129. Inactivated convalescent plasma was deprioritised by the RAPID C-19 Oversight Group on 14 May 2020.

130. A CAS alert was issued on 17 March 2021 stating that results from the RECOVERY trial showed no significant clinical benefit from treatment with high-titre convalescent plasma in patients hospitalised with Covid-19 **[GA1/002] [INQ000414439]**. The alert indicated that the REMAP-CAP trial had also announced that no significant benefit was seen from treatment with convalescent plasma (up to two ABO-compatible units administered over 48 hours) in patients requiring organ support in an intensive care setting. It was therefore recommended that convalescent plasma was not used in the management of hospitalised patients with confirmed or suspected SARS-CoV-2 infection.

Hydroxychloroquine

131. Hydroxychloroquine is a disease-modifying anti-rheumatic drug used to treat inflammatory conditions and some skin conditions.

132. The RAPID C-19 Oversight Group reviewed a briefing on hydroxychloroquine on 5 May 2020. The briefing set out the existing evidence in relation to its efficacy as a treatment for Covid-19. It was noted that hydroxychloroquine was also being investigated for prevention and post-exposure prophylaxis. The briefing noted that the MHRA expert working group considered that the published trial evidence on the efficacy of hydroxychloroquine was of poor quality and did not contribute much to the evidence base and that the group had noted a well-conducted observational study examining the safety profile of hydroxychloroquine, which showed that serious adverse events did not increase in short-term use, but that cardiovascular mortality

increased with longer term use. Hydroxychloroquine was further considered by the RAPID C-19 Oversight Group on 27 May 2020 and 5 May 2021 with updated evidence, but the assessment did not change.

Tixagevimab and cilgavimab (Evusheld)

133. Tixagevimab and cilgavimab is marketed and sold under the brand name "Evusheld" by AstraZeneca as a pre-exposure prophylaxis for Covid-19. Tixagevimab and cilgavimab is a combination of 2 monoclonal antibodies derived from convalescent patients after SARS-CoV-2 infection. By targeting the virus's receptor binding domain on the SARS-CoV-2 spike protein, tixagevimab and cilgavimab can block viral attachment to human cells, and therefore block infection.

134. We have referred to tixagevimab and cilgavimab, rather than the brand name Evusheld, in this Statement.

135. NHS England's consideration of tixagevimab and cilgavimab as a therapeutic for Covid-19 was via NHS England's role within the RAPID C-19 Oversight Group. An explanation of tixagevimab and cilgavimab and its consideration by the RAPID C-19 Oversight Group is set out below.

136. In December 2021, tixagevimab and cilgavimab was the first treatment to receive approval in America (in the form of emergency authorisation) as a means of protection before exposure to the SARS-CoV-2 virus for adults and children aged 12 and over with compromised immune systems.

137. Tixagevimab and cilgavimab was granted conditional marketing authorisation by the MHRA on 17 March 2022. Clinical trials and UKHSA assessments of tixagevimab and cilgavimab had been limited to its efficacy against previous variants of SARS-CoV-2 and therefore the marketing authorisation was granted on a conditional basis as, at the time of approval, there was not enough data to know how effective tixagevimab and cilgavimab would be against variants of SARS-CoV-2.

138. The RAPID C-19 Oversight Group initially considered tixagevimab and cilgavimab on 3 February 2021. At this first review, the decision was taken to monitor the efficacy of tixagevimab and cilgavimab against the E484K mutation of Covid-19. The decision to monitor (rather than prioritise) was upheld at further RAPID C-19 Oversight Group

meetings on 13 October 2021 and 24 November 2021 whilst key clinical trials were ongoing or whilst full results of those trials were pending.

139. At the 8 December 2021 meeting, the RAPID C-19 Oversight Group suggested that advice should be prepared for the CMO in light of the results from a trial, and on 23 December 2021 formal RAPID C-19 advice to the CMO proposed that NHS England consider preparing a clinical commissioning policy in pre-exposure prophylaxis, to be implemented on receiving marketing authorisation and on confirmation that tixagevimab plus cilgavimab was effective against Omicron, and to consider the options for identifying the potentially eligible patients who might benefit from this medicine.

140. NHS England convened a National Expert Group for tixagevimab and cilgavimab on 26 April 2022 to review the latest evidence. The National Expert Group comprised national experts in relevant medical and scientific fields, as well as representatives from devolved administrations. Its purpose was to advise on the clinical policy, where the Rapid C-19 Oversight Group had recommended the formation of that policy. The meeting invited input from DHSC's Prophylaxis Oversight Group. The Prophylaxis Oversight Group was composed of independent experts and established by DHSC to guide development of pre-exposure and post-exposure prophylaxis for Covid-19 infection. It was invited to contribute to the National Expert Group meeting given that expertise. A statement from the Chair of the Prophylaxis Oversight Group was read out during the meeting **[GA1/014] [INQ000502396]**.

141. The Group noted that marketing authorisation had been received, and went on to consider activity against Omicron. The Group also noted that the consideration of the highest risk patient cohorts was being undertaken by the DHSC-commissioned Independent Advisory Group (discussed below at paragraph 155). The group discussed all the relevant issues at length. A vote was then held and the majority (all members bar one) concluded that there was insufficient evidence at that time to progress a clinical policy, and new academic research in the UK setting was strongly needed. The suggestion for new academic research, including establishing a platform trial to generate evidence relevant to immunocompromised patients, is not a matter within NHS England's scope (as noted in Part Three of this statement, platform trials are run independently of NHS England). Further research could have been undertaken by the manufacturer and/or supported by DHSC's Prophylaxis Oversight Group and NIHR. Following the meeting, a brief was produced on 26 April 2022 for the CMO

confirming the group's view that there was not sufficient evidence **[GA1/003] [INQ000414471]**. Professor James Palmer's statement discusses the 23 December 2021 RAPID C-19 recommendation, and the 26 April 2022 meeting, in further detail at paragraphs 43 to 44, including on the question of cost-effectiveness.

142. At the RAPID C-19 Oversight Group meeting on 18 May 2022, it was suggested that the CMO advice should be updated in light of new information about the efficacy of tixagevimab and cilgavimab against the Omicron BA.2 variant.

143. Following on from the RAPID C-19 Oversight Group Meeting on 18 May 2022, NHS England reconvened the National Expert Group on 19 May 2022. There was an extensive discussion following the presentations which concluded that in the absence of good clinical effectiveness data, the in-vitro data[5] were insufficient to reach a deployment recommendation. There was, at that time, significant scientific uncertainty and clinical equipoise around the efficacy of tixagevimab/cilgavimab against Covid-19, especially in the pandemic context in the UK. The advice noted the need for further data, including pharmacokinetic/pharmacodynamic data ("**PK/PD data**").[6] Again, the question of establishing a platform trial and obtaining further data was not one for NHS England to address. Professor James Palmer's Statement discusses the issue of further research, at paragraph 45. Additional research could have generated further data that may have provided additional evidence as to whether or not tixagevimab/cilgavimab was effective against new Covid-19 variants. The chair asked members of the National Expert Group (but not observers) to vote on whether a UK-wide clinical commissioning policy recommendation should be supported. There was unanimous agreement from the National Expert Group that the recommendation should be that tixagevimab/cilgavimab should not at that time progress to deployment. On 25 May 2022, following the meeting, a further brief was produced which was submitted to the CMO **[GA1/004] [INQ000414472]**.

144. Although outside the Relevant Period, it is worth noting that:

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[5] 'In vitro' data refers to information obtained in studies done 'in the glass' using isolated tissues, organs or cells outside of a living organism.

[6] PK data will typically include measures of the concentration of an administered drug in the body over time, to help understand a compound's absorption, metabolisation, and excretion. PD data relates to the effect on the body of a specific drug concentration, to help understand a compound's ability to interact with its intended target, and its biological effect.

a. on 19 July 2022, the Director of Medicines at DHSC wrote to the Chief Executive of NICE with directions to appraise the clinical and cost effectiveness of tixagevimab and cilgavimab within its marketing authorisation for treating Covid-19 and within the scope of the multiple technology appraisal of therapeutics for treating people with symptomatic Covid-19; and

b. on 12 August 2022, it was announced by the Government that a decision had been made not to deploy Evusheld (tixagevimab and cilgavimab). The announcement stated that there was, at the time, insufficient data on the duration of protection offered by Evusheld (tixagevimab and cilgavimab) in relation to the Omicron variant and, at that time, the Government would not be procuring any doses.

145. In July 2020, DHSC established the COVID-19 Prophylaxis Oversight Group (POG) to guide development of pre-exposure and post-exposure prophylaxis for Covid-19 infection. Tixagevimab and cilgavimab (Evusheld) was the only prophylaxis that reached a decision point in the RAPID C-19 process. Other prophylactics were considered by the NICE-led section of the RAPID C-19 process, but did not reach the point of sufficient evidence to warrant considering introduction. In order to identify an effective prophylaxis a large scale population study is necessary. A study of this type would have been would have been extremely challenging during the pandemic, which may have been one of the factors contributing to the relative lack of evidence of effective prophylactics. The PROTECT-V trial discussed above is continuing research into prophylactics. The rollout of the vaccines had no impact on the prioritisation of work looking into prophylactics. Prophylactics were not introduced because none were shown to be clinically effective when examined through the RAPID C-19 process. NHS England recognised that prophylactic treatment could have been important for a number of clinically vulnerable groups or people for whom vaccination would not be appropriate.

CAS alerts

146. The CAS is managed by the MHRA and is used for issuing patient safety alerts, important public health messages, and other safety critical information and guidance to the NHS and others, including independent providers of health and social care. CAS alerts are generally short urgent messages on specific issues, such as

medicines safety issues. They were a very effective way of getting clear messaging out to the system quickly during the pandemic.

147. Throughout the relevant period, a significant number of alerts were distributed through CAS. Whilst NHS England did not have access to the system to post alerts directly, the CMO was able to post alerts on behalf of NHS England. A number of CAS alerts were tripartite communications between the CMO, Public Health England ("**PHE**") and NHS England. The type of information shared via CAS varied and included alerts on very specific issues such as high flow nasal oxygen during transfers and the use of particular medicines in the treatment of Covid-19, as well as wider alerts on shielding and PPE guidance updates. We have set out examples below of several clinical alerts which assisted in the dissemination of clinical information and advice regarding the optimal clinical management of Covid-19:

    a. 17 March 2020 – anti-inflammatory medicines. This alert from NHS England noted that there had been some concern about the use of non-steroidal anti-inflammatory drugs ("**NSAID**") in relation to Covid-19 following a statement by the French Health Minister advising against the use of ibuprofen. The alert confirmed that there appeared to be no evidence that NSAIDs increased the chance of acquiring Covid-19 **[INQ000330807].**

    b. 16 June 2020 – Dexamethasone in the treatment of Covid-19. This alert confirmed that dexamethasone had been demonstrated to have a clear place in the management of hospitalised patients with Covid-19 and that clinicians should therefore consider using it **[GA1/015] [INQ000283542]**.

    c. 3 July 2020 – Interim Clinical Commissioning Policy for Remdesivir. This alert confirmed that NHS England, working with DAs, had established a rapid policy development process (i.e. RAPID C-19) to aid clinicians in offering best care and clinical advice to patients. This alert set out the interim clinical commissioning position for the use of remdesivir for patients with Covid-19 **[GA1/005]** **INQ000400547**

Prescribing Covid-19 therapeutics

148. Medicines should only be prescribed when they are necessary, and the benefit of administering them should be considered in relation to the risk involved. A prescriber

is responsible for prescribing medications in line with NICE guidance, completing an initial assessment, ensuring there are no contraindications, explaining why the medication is required and any risks or side effects, and ensuring their prescriptions comply with the Human Medicines Regulations 2012 and the Misuse of Drugs Act 1971.

149. In respect of any use of medicines or treatments that were not nationally recommended for treatment of Covid-19, in principle any clinician within the NHS has clinical discretion to prescribe any appropriate medicine as treatment for a particular condition. Identification of an 'appropriate medication' is usually done by referring to NICE guidelines, marketing authorisations issued by the MHRA and through local formularies.

150. As set out in the Government's *Off-label or unlicensed use of medicines: prescribers' responsibilities*[7], there are clinical situations when the use of unlicensed medicines or use of medicines outside the terms of the licence (i.e. 'off-label') may be judged by the prescriber to be in the best interest of the patient on the basis of available evidence. Such practice is particularly common in certain areas of medicine: for instance, in paediatrics where difficulties in the development of age-appropriate formulations means that many medicines used in children are used off-label or are unlicensed.

151. In general, NHS England closely monitored the actual usage of Covid-19 medicine corticosteroid treatments (including dexamethasone and hydrocortisone) along with all other treatment medicines that read out positively from clinical trials and were subsequently licensed for use in Covid-19 patients in the UK. NHS England national teams worked with regional teams to ensure that medicines approved for the treatment of Covid-19 patients were used and prescribed appropriately and adhered to prescribing guidance and recommendations. For example, on 13 November 2020, the Chief Pharmaceutical Officer and NHS England's National Medical Director wrote a letter to Regional Medical Directors, Regional Chief Pharmacists, Provider Trust Medical Directors and Hospital Chief Pharmacists regarding the Covid-19 therapeutic use of corticosteroids, including dexamethasone and hydrocortisone. The letter reiterated the prescribing guidance regarding corticosteroids in Covid-19 patients, and included reference to the WHO recommendations, NICE prescribing briefing and the 3 September 2020 CAS Alert **[GA1/006] [INQ000414401]**.

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7 https://www.gov.uk/drug-safety-update/off-label-or-unlicensed-use-of-medicines-prescribers-responsibilities

152. Notwithstanding clinical discretion, the data held on use of drugs (explained in detail later in this Statement) led to a view by NHS England that it would have been unusual for any drugs or treatments to be used in NHS hospitals to treat Covid-19 that were not specifically recommended in the CAS alerts.

153. NHS England are not aware of any inclusion in local NHS Covid-19 treatment guidelines of therapeutics that were never nationally recommended.

PART FIVE: ELIGIBILITY FOR COVID-19 THERAPEUTICS

154. The following section sets out information on NHS England's role in:

    a. developing eligibility criteria for Covid-19 therapeutics in the community and in hospital; and

    b. ensuring access to therapeutics for people at highest risk of severe Covid-19.

Eligibility criteria

155. During the pandemic, a number of new treatments became available for patients in community settings. Decisions on eligibility for Covid-19 treatments during the pandemic were made by the government. To support those decisions, at the request of the Deputy Chief Medical Officer, DHSC appointed an independent advisory group made up of clinical academics with requisite expertise. The advisory group was overseen by the Covid-19 Therapeutics Clinical Review Panel. The Panel was established to advise on which at-risk patient cohorts should be eligible for Covid-19 therapies. The Panel provided advice on the definition and revision of eligible cohorts for new Covid-19 therapeutics from December 2021 to March 2023. This included a process to provide advice on questions from patient and clinician stakeholders, through a nominated clinician representing a group or individual. (The work of the advisory group and the Panel are discussed further in Professor James Palmer's personal witness statement, at paragraphs 33 to 36).

156. NHS England's National Clinical Policy team had a supporting role in the independent advisory group, with NHS England's Clinical Director of National Clinical Policy in Specialised Commissioning and the National Clinical Policy Lead listed as supporting members in the terms of reference for the advisory group **[GA1/007] [INQ000414511].** Supporting members were available to provide additional support for discussions as required.

157. The work of the group built upon work carried out by the Specialised Services team in NHS England to produce interim clinical commissioning policies as part of their role in RAPID C-19.

158. NHS England's National Medical Director Specialised Services, NHS England's Medical Director of Primary Care and an NHS England Regional Medical Director were on the Panel. The Panel also included senior clinicians from all four nations. It provided advice to the four UK CMOs for agreement of the UK clinical policy.

159. For people admitted to hospital with Covid-19, treatments were administered by clinicians in line with national guidelines based on the individual's presentation and clinical need.

Community access to therapeutics

160. NHS England was responsible for ensuring access to the new treatments that became available in the community. To support timely access, in December 2021, NHS England oversaw the set-up of NHS COVID Medicine Delivery Units ("**CMDUs**") which provided treatments for patients at highest risk of deterioration or death from Covid-19. As set above, out eligibility for treatment was determined by government.

161. The SROs responsible for establishing and overseeing deployment of treatments through CMDUs were myself and Professor James Palmer as Medical Director for Specialised Services. We were both accountable to Professor Sir Stephen Powis (National Medical Director). NHS England worked closely with Charlotte Taylor (Director of the Antivirals and Therapeutics Taskforce) at DHSC to deploy treatments. We also worked with NHS Digital, which developed the digital infrastructure and patient cohorting approach (ie, using health records to identify potential patients), and with UKHSA, which was responsible for providing access to testing for potentially eligible patients and with whom NHS England worked to align communications.

162. Where eligibility criteria changed or treatment changed, a number of different steps were taken, including:
    a. Revising clinical access policies in place for CMDUs, setting out the treatment options. These were cascaded out through CAS alerts.
    b. Updating the digital cohorting algorithms used by NHS Digital to identify any newly eligible patients.
    c. Issuing guidance to GPs, hospital specialists, and NHS111 on revised policy, and signposting to CMDUs.
    d. Updating public-facing communications in place through nhs.uk and gov.uk materials and, where appropriate, writing to patients and sending a test kit.

163. CMDUs provided access to Covid-19 treatments under UK-wide interim clinical access policies ahead of the publication of final NICE technology appraisal recommendations. They began to provide services from 16 December 2021, less than two weeks after the first supply of oral antivirals arrived in the UK. The clinical access policies also covered oral antivirals and intravenous treatments. By 26 June 2023, CMDUs had provided almost 115,000 community-based treatments to Covid-positive patients from the highest risk cohort including ~42,000 infusions and ~73,000 oral antivirals.

164. The new pathway for providing treatments to patients in England was unique in that it enabled a patient to be proactively contacted where they were potentially eligible for treatment and had tested positive for Covid-19. The matching of positive test results and patient data inferring potential clinical eligibility meant that CMDUs were alerted of patients who might be suitable for treatment and could be triaged directly. As an alternative pathway, GPs and hospital specialists were able to directly refer patients to CMDUs.

165. The key challenges in establishing CMDUs included:

    a. Workforce capacity – the number of patients requiring triage (and for some, subsequent treatment) in early stage of deployment were significant and presented challenges to capacity, particularly for specialties already in high demand as the system entered another wave. Although demand fell off, deployment remained a significant demand on specialist workforce. Health systems were reminded to prioritise the deployment of clinical staffing to CMDUs alongside other operational/ COVID programme priorities.

    b. New treatments – new treatments introduced or withdrawn under the revised clinical access policies meant changes in triage and treatment practice. In the case of Paxlovid, its potential contra-indications and drug interactions, could place additional demands on access to clinicians. NHS England provided additional advice to including a summary clinical guide and guidance on drug interactions, as well as making available specialist pharmacy advice to support prescribing decisions.

    c. Awareness – the introduction of new treatments and the new clinical pathway meant that there were some challenges in ensuring that all GPs and other

health professionals remained up to date on referral requirements. Actions were taken to increase awareness amongst primary care and NHS 111 of treatment eligibility, referral time windows and available referral pathways. An e-learning for health module **Error! Hyperlink reference not valid.**was also developed and deployed for clinicians across the NHS including general practice, their teams, community pharmacists and other settings such as NHS111 clinical assessment services.

d. Clarity for patients – NHS England had feedback that the eligibility criteria and the pathway were not always clear. NHS England worked with stakeholder groups to raise awareness of the new pathways and of who was eligible. Identifiable patients in high risk cohorts were contacted proactively by letter to highlight potential eligibility, as well as by SMS if they tested positive. A patient information leaflet (PIL) was developed to support patients taking Paxlovid. Specific work was undertaken with DHSC and social care colleagues to support information cascade in care homes.

166. The medicines were originally made available for around two million people at highest risk from Covid-19, i.e. a smaller population than the product licence. At the time it was anticipated that access would be expanded to a wider population, dependent on the results of a national study: PANORAMIC. However, the results of PANORAMIC were not available until autumn 2022, and they did not demonstrate the relevant medicines met primary end points (to reduce hospitalisations and death) in the wider population.

167. NHS England developed a standard operating procedure for use by CMDUs, which set out expectations of the service **[GA1/008] [INQ000414468]**. This standard operating procedure included arrangements for weekends and evenings, digital infrastructure and clinical requirements.

168. To ensure timely access, the then NHS Digital were commissioned by NHS England to develop new digital infrastructure which was able to link positive test results to patient records and so allow CMDUs to contact patients proactively to provide an assessment of eligibility and to provide treatment if required. NHS Digital was able to identify patients potentially eligible for treatment based on patient records.

169. As well as linking to positive test results and helping CMDUs to identify patients, NHS England was able to use the information to directly contact the majority of people who were highest risk. NHS England wrote to patients regularly to inform them of eligibility and of what to do in the event of symptoms. This information was also used to distribute free Covid-19 tests to potentially eligible patients until early 2023.

170. As not all patients could be digitally identified, NHS England also wrote to ICBs, GPs and to hospital specialists to raise awareness of potential eligibility and of the steps that should be taken in the event of symptoms **[GA1/009] [INQ000414463] [GA1/010]** **INQ000399490** The website was also regularly updated – and NHS England worked closely with stakeholder groups (including, but not limited to, Asthma and Lung UK, Blood Cancer UK, Genetic Alliance, Immunodeficiency UK and Kidney Care UK) to raise awareness and to seek feedback on the roll out of treatments.

171. ICBs noted some issues with referral processes, most significantly the capacity and specialist knowledge required to provide the additional CMDU services. The ordering system for medicines was also new as the medicines came directly from government, rather than through regular wholesalers. GPs and hospital specialists also raised some issues around understanding the new pathway, which provided direct access to CMDUs.

172. To help address these points, the standard operating procedure provided a clear framework for local systems, but also provided flexibility on how to implement locally. NHS England also held regular seminars to help understand and address concerns over how the pathway worked, and provided further guidance to GPs, specialists and CMDUs, including on ordering and prescribing.

173. NHS England had regular stakeholder sessions to get feedback on CMDUs and on access to medicines. NHS England also received direct communications from stakeholder groups and from individual patients. The main issues raised by stakeholders were:

    a. Eligibility – some groups indicated that additional conditions or criteria should be considered for access to treatment. Decisions on eligibility were for DHSC. However, to help address this concern, new arrangements were put in place to manage and consider requests to refine or revise the highest risk cohort.

b. Access to treatment – particularly as the CMDUs were being established, stakeholder groups raised concerns that patients were not able to access treatments, either because they were not referred locally or because they had missed the treatment window. Over the course of the deployment, NHS England provided regular communications to GPs, NHS111 and hospital specialists. NHS England provided additional resources to health care professionals to support decision making, including support for prescribing and flow diagrams for GPs.

c. Access to testing – patients raised concerns that they were not able to access testing, particularly when access was dependent on PCR testing, which involved travel. NHS England worked with UKHSA to review where LFD testing could be used and to support access for patients.

174. NHS England put in place ICB-level monitoring of access to treatments in both hospital and community settings using the Foundry centralised database (**"Foundry"**). NHS England also established weekly (initially daily) operational oversight through regional teams. This information allowed NHS England to monitor local situations and remedy issues as they arose, but also enabled local systems to assess the uptake of treatments and respond appropriately.

175. NHS England established a single point of contact for receiving and addressing issues raised about antivirals from regions, ICBs and CMDUs. This approach meant that the national team could keep track of issues raised and respond appropriately. This single point of contact was in addition to the regular calls with regions to manage the initial implementation and the ongoing delivery.

176. For access to individual treatments, patients were advised to contact their GP for onward referral, rather than for NHS England to arrange treatment.

177. Where system-wide issues were identified, regions were asked to work with the relevant ICB to resolve that issues (e.g, GP awareness, local supply or CMDU capacity). Where individual patient concerns were raised, ICBs were asked to follow up locally.

178. Until mid-2023, NHS England's Covid-19 Antivirals Deployment Steering Group monitored the deployment of Covid-19 therapeutics to non-hospitalised individuals in

highest risk groups through the CMDUs. The information was also shared with the DHSC Antivirals and Therapeutic Taskforce, until it was disbanded in March 2023.

179. The monitoring worked as follows:

    a. Data on access to treatment and on numbers of patients treated was available from the establishment of the CMDUs. This data was made available to regions and ICBs, who had direct responsibility for providing access to treatments.

    b. The key data monitored was the number of patients by ICB and by type of treatment, and the number treated relative to patients identified as potentially eligible. In April the quality of the data was improved by including reasons for patients not being treated.

    c. These figures were not performance figures, but allowed comparisons in terms of types of treatment and numbers of patients treated across local areas and regions. It also enabled local assessment of any potential inequality in access to treatment.

    d. At a national level data, data was monitored on a weekly basis and considered in the routine calls. It was formally monitored as part the Antivirals Deployment Steering Group, which met monthly, and in regular updates provided to DHSC.

180. Within the first two months of the CMDU establishment, an initial review was undertaken with a small sample (fewer than 10) CMDUs, ahead of more granular routine reporting being in place for the triage phase. This review indicated that 19% of patients had treatment planned, with reasons for not being treated including presentation outside the treatment window (19%), symptoms resolving or asymptomatic/mild symptoms (19%) and not eligible following review (19%). A further 17% could not be contacted and 7% left the pathways for unknown reasons.

181. Following this initial review, routine reporting of triage outcomes was put in place. According to those figures, around 25% of identified patients were treated. The two mains reasons for not being treated were the patient's symptoms resolving or not being eligible for treatment. In many cases a patient's symptoms were mild or would

resolve and therefore treatment was not appropriate. The mild symptoms are likely to have been a consequence of the vaccine roll out and the milder strains of COVID.

182. This second reason partly reflects that the algorithm to identify patients was deliberately set broadly to be overinclusive and ensure patients were not excluded. There then necessarily followed a process of confirming eligibility. More detail is provided below from paragraph 221.

PART SIX: MONITORING DEMAND AND SUPPLY

183. Part Six sets out:

    a. how NHS England monitored medicine supply, and modelled future use, using the medicines supply assessment tracker;

    b. how the supply assessment tracker was used to monitor Covid-19 therapeutics in hospitals;

    c. charts showing stock levels of different Covid-19 therapeutics;

    d. how NHS England monitored usage and supply of Covid-19 treatments in the community;

    e. information on NHS England's role in procuring remdesivir; and

    f. reflections on stockpiling therapeutics for future pandemics.

184. Information on NHS England's role in medicine supply during the pandemic is provided in Professor Sir Stephen Powis' third witness statement provided as part of Module 3 and in Annex One of this Statement.

185. All charts included in this section have been produced in response to the Inquiry's request. The charts summarise information that would have been available to NHS England, but not in the format that has been produced for this Statement.

Monitoring medicines supply – medicines supply assessment tracker

186. DHSC has overall responsibility for medicines supply, including as the lead for the supply and procurement of Covid-19 therapeutics. However, early on in the pandemic, NHS England assumed responsibility for developing a Covid-19 supply assessment tracker to help monitor supply, The tracker was initially used for critical care, antibiotic and end of life care medicines (supportive medicines) and later included therapeutics used in hospital once known (for England only).

187. The Medicines Cell developed the medicines supply assessment tracker to assist in forecasting demand and assessing supply of a set of priority medicines that were

used to help manage patients with Covid-19. The tracker was reliably operational by late April 2020, when the first data pack with information on stock in hospitals, stock in wholesalers and future supplies was available. Prior to this, NHS England only had access to hospital pharmacy stock levels (using an IT system that analyses stock control 'Rx-Info Exend') and top-level manufacturing data was provided by those manufacturers who supplied information to NHS England's commercial medicines unit (**"CMU"**). Wholesaler data took more time to come online and was significant as medicines wholesalers held most of the buffer stock in UK.

188. Access to supply data was initially a challenge and took some weeks to fully come onstream. However, NHS England worked with wholesalers and investment was made in the wholesaler and supplier data to accelerate the work needed to secure access to the relevant data. Data sharing arrangements were established so that up-to-date information could be shared with Government regarding medicine stock levels within UK suppliers. By April 2020, the first CMU supplier forward view data collection was shared with NHS England's medicines analysis team, with data collected and then shared daily (and later weekly and fortnightly) and the supply tracker developed to monitor progress.

189. Stock levels for Covid-19 therapeutic medicines were handled differently than for supportive medicines. NHS England engaged with the suppliers to discuss current and forthcoming stock level. For Covid-19 therapeutics there was often a single supplier as the new medicine was still in patent (for example, Gilead for remdesivir). The treatment medicines and presentations in scope were based on reports from NHS England teams involved in work on Covid-19 clinical trials and treatments and were introduced to the tracker in the following order: dexamethasone (June 2020), remdesivir (November 2020), tocilizumab (January 2021), sarilumab (early 2021) and baricitinib (May 2022).

190. The supply assessment tracker contained information on stock in hospitals, stock in wholesalers and future expected supplies (both pre-wholesale and expected supply for the forthcoming 12 weeks). The forecasting relied on engagement with medicines wholesalers as well as an understanding of stock in hospital pharmacies. This engagement allowed NHS England to undertake detailed monitoring of secondary care Covid-19 priority medicines. The modelling had three key components:

a. Covid-19 demand for medicines – estimated by applying clinical usage assumptions to NHS England's Covid-19 bed forecast, taking account of clinically appropriate alternative medicines where relevant;

b. Non-Covid-19 demand for medicines – demand for the Covid-19 medicines for purposes other than Covid-19, estimated based on historic medicines issues data; and

c. Supply levels of available stock of medicines, both in hospital and in the supply chain (based on a bespoke data collection from suppliers/wholesalers covering stock holding and expected deliveries).

191. The analysis, acted as an early warning system that allowed NHS England and other key stakeholders to plan mitigating actions. When stocks were critically low, the modelling was adapted to determine medicine supply allocations to NHS Trusts and other UK nations based on relative criticality of local stockholders.

192. NHS England also developed a Covid-19 medicines forecast model to assess the resilience of medicines supply of the Covid-19 priority medicines under different demand scenarios (including a centrally provided 'reasonable worst-case scenario'). This tracker provided a R/A/AG/G rating (red/amber/amber-green/green) from actual weekly demand and supply data monitoring, alongside additional analysis of medicines that were flagged as at potential risk of shortage.

193. A green rating was given when it was estimated that there was sufficient stock nationally for more than 12 weeks, amber-green where there could be national supply issues between 8-12 weeks, amber where could be national supply issues between 5-8 weeks and a red rating given where there could be national supply issues between 0-4 weeks, i.e. 'critically low'. A summary of that process is set out in **[INQ000409945]**. Further investigation of the supply position and actual usage data was carried out by NHS England CMU, the DHSC MST and the NHS England Medicines Analysis Team if the medicines were rated amber or red.

194. If concerns remained regarding the supply of products, these were escalated to the NHS England's Allocation and Distribution Group (**"ADG"**) and a further RAAGG rating was given to determine whether action should be taken to address a national supply issue (red), the issue should be escalated for discussion (amber), the situation

should be monitored for future review (amber-green) or no action was required (green). ADG was able to support operational decisions through regional teams, but where necessary, ADG made recommendations to the DHSC's Medicines Supply Resilience Group (**"MSRG"**) on action to take, including national allocation of business-as-usual supply, issuance of clinical guidance and supply notifications, and/or release of stockpile products. Two examples of that analysis (one from December 2020 and another from June 2022) show how that process was applied at two different stages of the pandemic **[INQ000409947]** and **[INQ000409946].**

195. Outputs from the supply assessment tracker were included as part of the DHSC Covid-19 medicines analytical pack, the purpose of which was to bring together all medicines data across DHSC and NHS England to provide 'a single version of the truth'. This was shared across all relevant teams and individuals in DHSC, NHS England and the other UK nations. The pack also comprised DHSC-held information on global supply issues; current shortages; progress on procurement of the Covid-19 priority supportive medicines stockpile; stock of the potential medicines used for treatment of Covid-19; and use of primary care supportive medicines.

196. Hospital medicines stock and usage was a particular issue in the first wave of the pandemic. At the start of the pandemic NHS England had access to standardised NHS Hospital medicines stock data from the Rx-Info Exend pharmacy stock control system, that had been used to support EU Exit analysis. This system was rapidly developed further by the system supplier working closely with the NHS during the initial Covid-19 wave to automatically provide stock data on a daily basis and to provide daily data on the issues of medicines associated with management of Covid-19 symptoms, intensive care and end of life.

197. Clinical advice was used to understand and standardise patient level medicines needs to support modelling of stocks to ensure continuity of supply – this then supported the agreement of mitigations and allocation of stock on a UK wide basis by the Allocation and Distribution workstream. Over the course of the Covid-19 response, agreements with suppliers/wholesalers were reached regarding sharing supply/stockholding information for Covid-19 priority medicines, as well as an essential contract extension with Rx-Info (access to which was a key component of managing supply and agreeing mitigations for Covid-19 priority medicines). Further system development then supported monitoring of approved Covid-19 treatments in hospital hubs.

198. ADG and MSRG made recommendations for the release of any Covid-19 supportive medicines from a Covid-19 priority medicines stockpile for which DHSC led a procurement later in the pandemic. However, as Covid-19 therapeutics were not included in this stockpile, decisions regarding central procurement or release of Covid-19 therapeutics were made by the DHSC on recommendation of the DHSC Therapeutics Taskforce. The Taskforce secured supplies of medicines to support nationally prioritised clinical trials where required and procured central stockpiles for wider population roll-out.

199. An example of a mitigation where the Medicines Cell was involved relates to tocilizumab. Following review of tocilizumab stock levels and identification of constrained supply, two Medicines Shortages Notices were jointly issued by DHSC and NHS England on 25 October 2021 and again on 3 February 2022. As the medicine is used for other, non-Covid-19 indications, supply remained constrained despite tocilizumab solution for infusion vials, which are also used in Covid-19 patients, not being covered by the Supply Disruption Alerts.

Monitoring use and supply of Covid-19 therapeutics for hospitalised patients

Overview

200. The Covid-19 supply assessment model was updated weekly, along with data on recent reported medicine usage and daily counts of O, O+ and V patients[8]. Medicines usage included Covid-19 and business as usual use based on historic spend taken from the same month within 12 months prior to the first wave.

201. Using clinical advice, we modelled how Covid-19 therapeutic medicines were used for each group of patients. This assessment focused on medicines that treated patients hospitalised due to Covid-19. Separate arrangements were put in place for community access to Covid-19 therapeutics. Further information on monitoring medicine usage in community settings is included elsewhere in this Statement.

202. In terms of the relevance of particular presentations and cohorts of patients, NHS England modelling analysis was led by and updated in response to the publication of

[8] Patients hospitalised due to COVID-19 were classified into three groups: 'O' requiring low flow oxygen support, 'O+' requiring high flow oxygen support and 'V' mechanically-ventilated patients. A patient could transition between these groups during their time in hospital.

guidance, such as clinical commissioning policies, that were often shared as CAS alerts. As such, the modelling changed over time. For example.

a. A Covid-19 Therapeutic CAS alert was published on 16 June 2020 indicating that dexamethasone had been approved for UK Covid-19 hospital patients requiring oxygen and ventilation and as not being suitable for out of hospital treatment **[INQ000283542]**

b. Remdesivir received Conditional Marketing Authorisation ("CMA") in August 2020 and a CAS alert was issued on 3 July 2020 with a UK-wide interim clinical commissioning policy, which allowed access according to its CMA **[INQ000330872].**

c. NHS England was also led by the updated policy for IL-6 inhibitors issued on 31 January which reflected that tocilizumab (RoActemra®) was licensed for the treatment of adult patients hospitalised due to Covid-19 who were receiving systemic corticosteroids and required supplemental oxygen or mechanical ventilation and that sarilumab (Kevzara), an off-label treatment, should continue to be considered where tocilizumab was not available or could not be used **[GA1/016] [INQ000501970]**.

d. Additionally, a tocilizumab CAS alert issued on 17 February 2021 recommended that NHS Trusts and health boards should consider prescribing a single dose of tocilizumab to eligible hospitalised patients with Covid-19 pneumonia, typically as adjuvant treatment to dexamethasone as standard of care, following the announcement of the findings of the RECOVERY trial. Sarilumab continued to be recommended for critically ill patients being treated with non-invasive ventilation or invasive mechanical ventilation, who had not already received tocilizumab (i.e. as a second-line IL-6 inhibitor). For NHS England's modelling, tocilizumab was only used as a first line therapeutic; then sarilumab was added. In time, tocilizumab was included as a first line and sarilumab as second line, only to be used if tocilizumab was contra-indicated **[GA1/017] INQ000081856]**.

e. The clinical commissioning policy issued on 5 May 2022 included baricitinib alongside remdesivir and IL-6 inhibitors **[GA1/018] INQ000048715]**

203. By June 2022, the Covid-19 treatment medicines set out in the table below were being monitored by the Medicines Cell's weekly tracker. These were largely medicines used to treat patients hospitalised due to Covid-19 or were already routinely used in the NHS and so could be more easily purchased by the NHS. Wholesaler stock and future supply of the relevant presentations included were adjusted to account for usage in the community where relevant, based on a comparison of issue data for both secondary care (using Define) and community care (using ePACT2).

Table: Covid-19 treatment medicines monitored by Medicine Cell's weekly tracker in June 2022

Medicines group	Lead medicine	Alternative medicines
Corticosteroids – IV	Hydrocortisone IV	Dexamethasone IV
Corticosteroids – Solution	Dexamethasone oral solution	
Corticosteroids – Oral	Dexamethasone tablets	
Remdesivir	Remdesivir	
Baricitinib	Baricitinib	
IL-6 inhibitors	Tocilizumab	Sarilumab

204. The Medicines Cell did not track supply of the community-based treatments, including casirivimab/imdevimab (Ronapreve), sotrovimab, molnupiravir and nirmatrelvir/ritonavir (Paxlovid). The Medicines Cell supported the allocations of the first neutralising monoclonal antibody treatment (nMAB) which was casirivimab/imdevimab (Ronapreve). However, stock levels and supply of the new Covid-19 therapeutics were then overseen by the DHSC Antivirals and Therapeutics Taskforce along with the new NHS England antivirals team, which oversaw the CMDUs.

Medicines usage

205. The Covid-19 supply assessment model monitored the use of dexamethasone (split between IV, oral and solution), remdesivir, tocilizumab, sarilumab and baricitinib. It

relied upon clinical input from both DHSC and NHS England. Many of the Covid-19 therapeutic medicines were used for other indications and it is not always possible to distinguish the use of these medicines for different types of patients.

206. The following chart shows modelled use of tocilizumab from April 2022. It should be noted that there were supply issues with tocilizumab, when sarilumab was used as an alternative. Tocilizumab became first-line treatment when it obtained a licence for Covid-19 use, whereas sarilumab became a second line treatment only. Tocilizumab and sarilumab modelling also included non-Covid-19 use. Model 1 and model 2 use slightly different assumptions about daily usage for business as usual and daily dose associated with O+ and V patients. Both models accurately describe demand going into and out of two Covid-19 waves in 2022.

207. While the data was available to decision makers at the time, this chart has been produced for the purpose of this statement.

Figure 2: reported and modelled use of tocilizumab from April 2022 to October 2022

Stock levels

208. In response to the Inquiry's request, NHS England has produced charts for the Inquiry showing the stock levels of dexamethasone, remdesivir, tocilizumab, sarilumab and

baricitinib. While this information was available to decision makers at the time, these charts have been produced for the purpose of this statement.

209. The following charts show stock levels for therapeutic medicines used for Covid-19 patients in hospitals from mid-2020 to the end of June 2022. The charts combine stock held by hospital trusts, wholesalers and pre-wholesalers.

210. Total stock has been recorded in kilogrammes of the active ingredient, which takes account of the variety of presentations (strengths and formulations) used to administer medicines. Hospital trusts were expected to complete Blueteq forms for each patient where remdesivir, tocilizumab, sarilumab and baricitinib were used for Covid-19 treatment.

Dexamethasone

211. Dexamethasone was the first therapeutic medicine used for Covid-19 patients. It was used from June 2020 and could be administered to patients hospitalised due to Covid-19 and who were receiving oxygen therapy, through intravenous (IV) infusion, tablets or oral solution following a Covid-19 therapeutic alert on 16 June 2020.

212. The first chart shows a fall in stock levels of dexamethasone IV from June 2020 to January 2021, in contrast to the second chart where stock levels of tablets fluctuated throughout 2020 but remained good. There was a significant drop in stock levels of oral solution dexamethasone between July and August 2020, but this gradually recovered throughout the rest of the year.

213. IV and oral solution stock levels declined over 2021 through to June 2022. It is worth noting that dexamethasone has non-Covid-19 indications and is therefore widely used in hospitals (available through the business-as-usual supply chain) and so it is not possible to differentiate its use for different indications.

Figure 3: Stock level (kg of active ingredient) for dexamethasone (IV) from June 2020 to June 2022

Figure 4: Stock levels (kg of active ingredient) of dexamethasone (oral) from June 2020 to June 2022

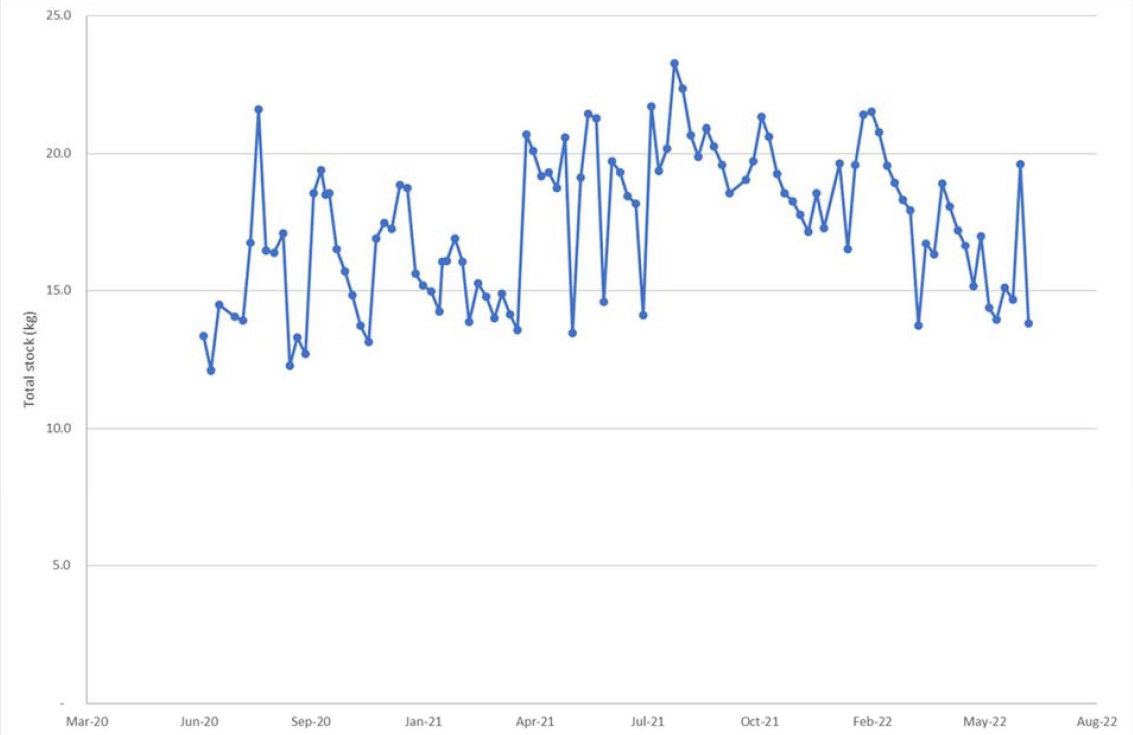


Figure 5: Stock levels (kg of active ingredient) of dexamethasone (solution) from June 2020 to June 2022

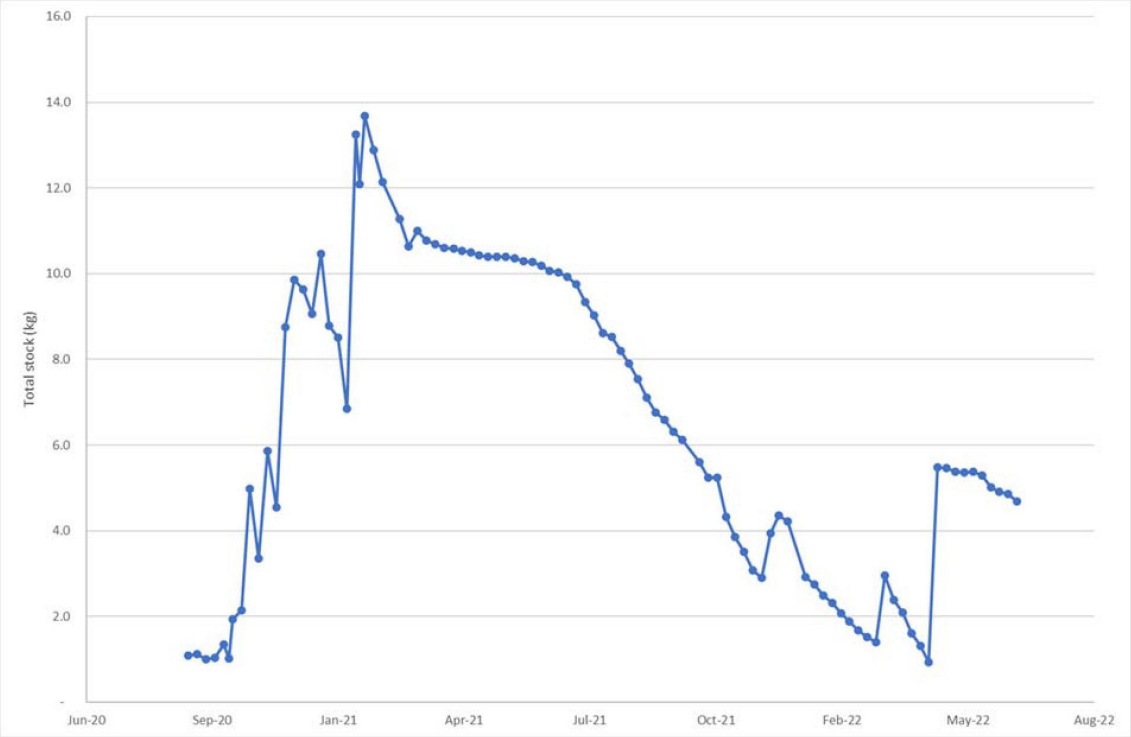
Remdesivir

214. The interim clinical commissioning policy for remdesivir was first issued in July 2020 and it does not have other, non-Covid-19 indications. It was indicated for patients hospitalised due to Covid-19 with pneumonia requiring supplemental oxygen and was administered intravenously over a number of days with a double dose on the first day. It could be co-administered with dexamethasone. Clinical guidance evolved over the period as new therapeutic medicines were introduced and use of remdesivir was later focused on patients hospitalised due to Covid-19 requiring low level supplemental oxygen support. From May 2022 it was also indicated for high-risk patients that had symptomatic hospital-onset Covid-19, having not been admitted to hospital because of Covid-19. A Supply Disruption Alert for remdesivir was issued on 29 September 2020.

215. This medicine was procured centrally from Gilead on a periodic basis by DHSC, which accounts for stock levels falling steadily from January 2021 until May 2022 when new stock was purchased.

216. Further information about remdesivir is provided from paragraph 232 below.

Figure 6: stock levels (kg of active ingredient) of remdesivir from September 2020 to June 2022



Tocilizumab and sarilumab

217. The REMAP-CAP trial demonstrated that tocilizumab and sarilumab (interleukin-6 or IL6 inhibitors) reduced deaths for Covid-19 patients in intensive care. Initial guidance in January 2021 focused on tocilizumab due to the limited supply of sarilumab at the time.

218. Both medicines have other indications (including rheumatoid arthritis) and supply was through the business-as-usual supply chain. The UK supply of tocilizumab by Roche was constrained by global demand and allocations had to be made to hospitals based on existing stock levels and known usage levels covering both Covid-19 and non-Covid-19 indications.

219. The medicines were used for patients hospitalised due to Covid-19 who needed high low supplemental oxygen or mechanical ventilation. Covid-19 use of both medicines was off-label until February 2022 when tociluzumab was licensed for adult patients hospitalised due to Covid-19 that required supplemental oxygen or mechanical ventilation. Supply of sarilumab for Covid-19 was stopped by Sanofi in late 2021. Global supply of tociluzumab improved from early 2022.

Figure 7: stock levels (kg of active ingredient) of tocilizumab from September 2020 to June 2022

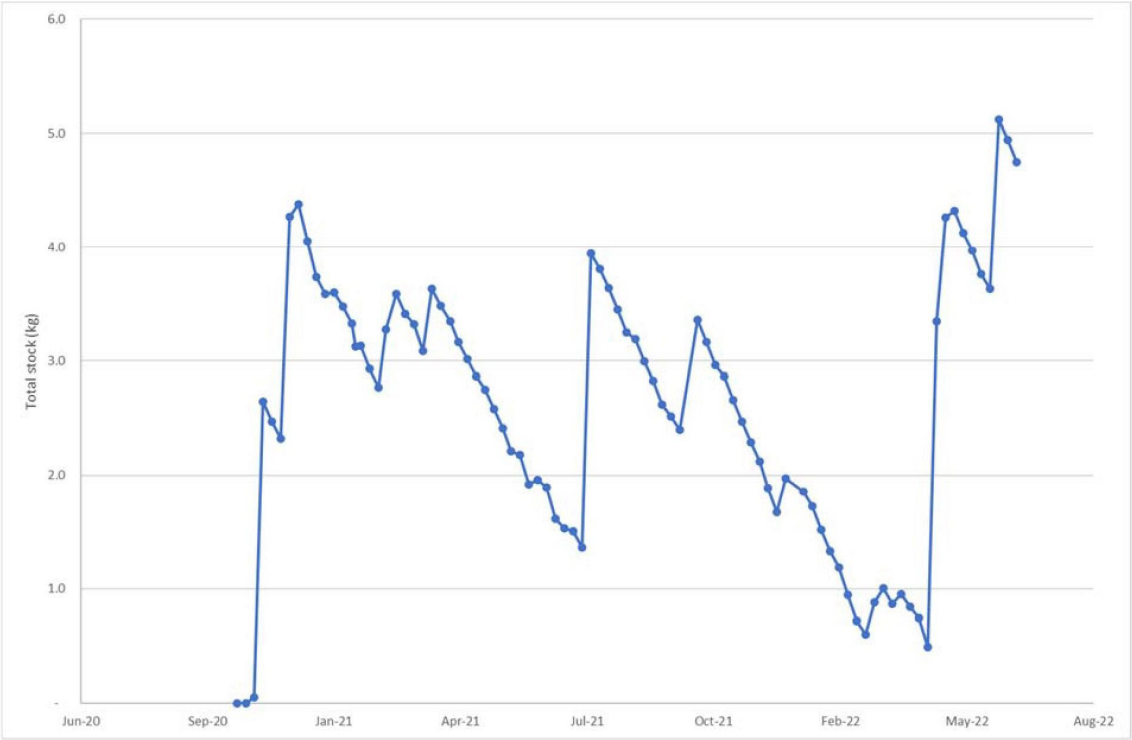
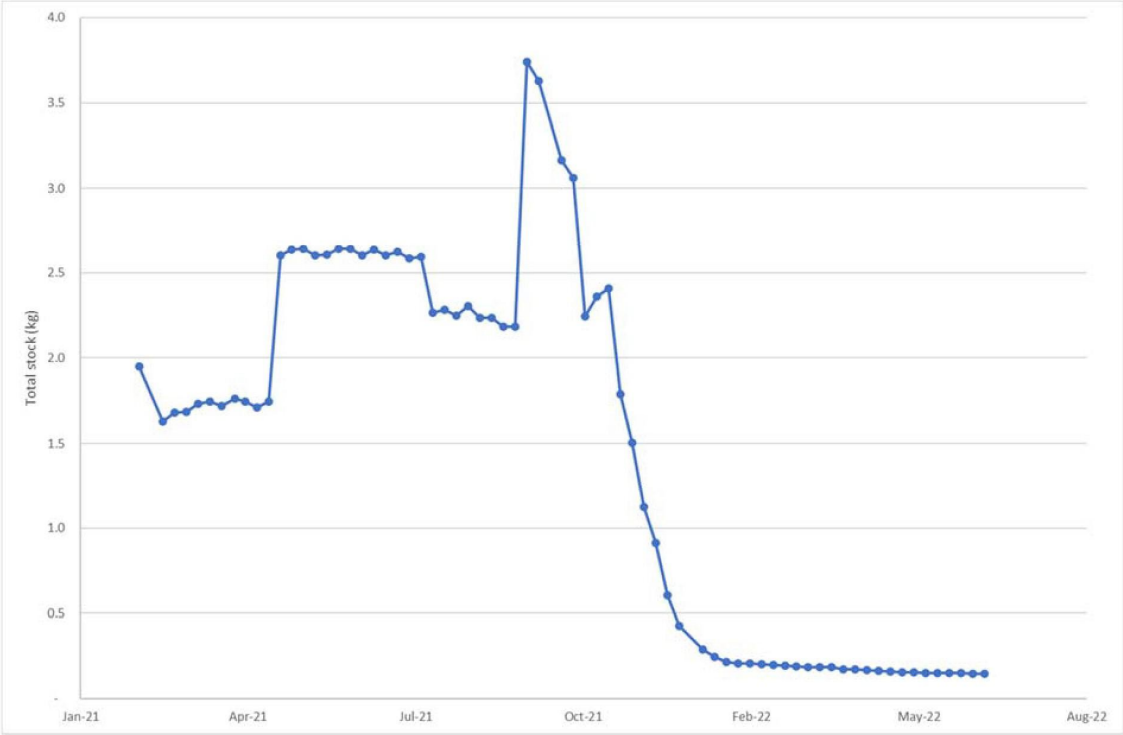


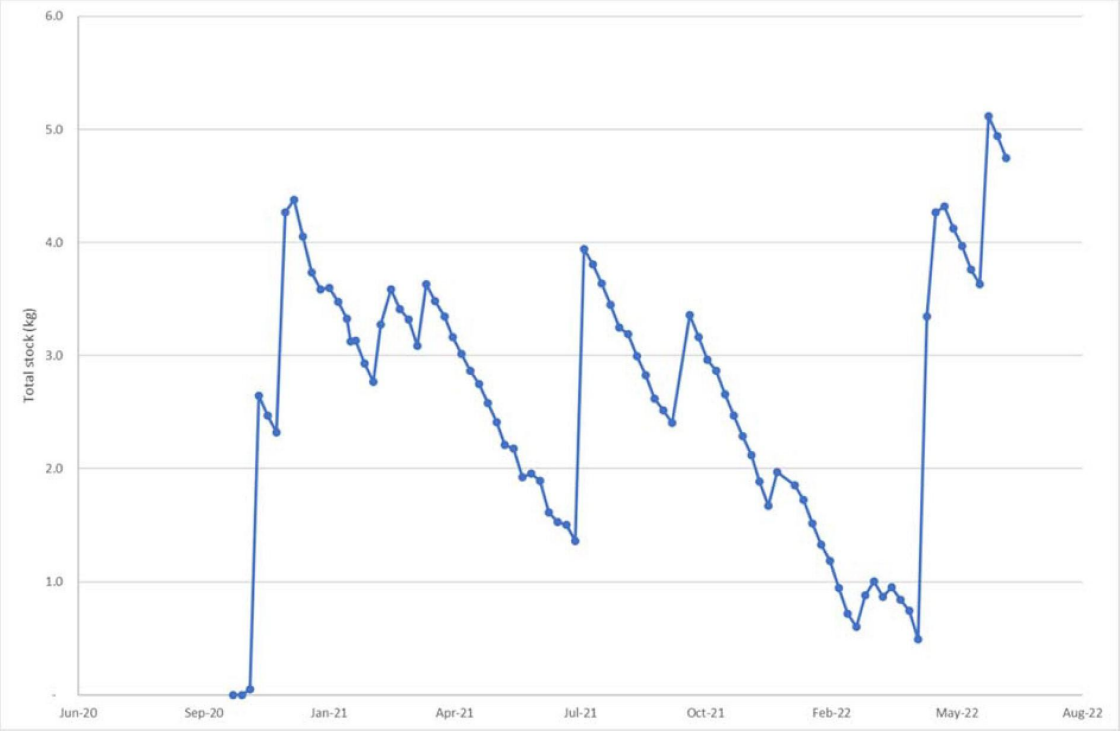
Figure 8: stock levels (kg of active ingredient) of sarilumab from Feb 2021 to June 2022



Baricitinib

220. Clinical guidance on the use of baricitinib for Covid-19 patients was first published in November 2022 (CAS-ViewAlert (mhra.gov.uk)) – noting that this timeline is outside the scope of the public inquiry. Baricitinib was included in the RECOVERY trial between February and December 2021. It has non-Covid-19 indications for rheumatoid arthritis and atopic dermatitis and is supplied through the business-as-usual supply chain.

Figure 9: stock levels (kg of active ingredient) of baricitinib from September 2020 to June 2022



Monitoring use of Covid-19 therapeutics in the community

221. The Therapeutics Cell and Antivirals Programme in NHS England worked together to establish monitoring of the deployment of Covid-19 therapeutics to people in non-hospitalised settings identified as being at higher risk if they have Covid-19. The CMDUs were responsible for delivering treatments and recorded usage using Blueteq, and use was then tracked using a Foundry dashboard. The dashboard enabled the data flows to be automated.

222. The Covid-19 Antivirals Programme, working with DHSC's Covid-19 Antivirals and Therapeutics Taskforce, had oversight of the use of Covid-19 therapeutics in non-hospitalised settings. This information initially included numbers of treatments and numbers of patients triage but was expanded to provide further detail on reasons for triage. The information was shared with ICBs to enable benchmarking and assessment of equitable access.

223. Data on treatments in hospital was later added to the Foundry platform to simplify and consolidate reporting.

224. NHS England published weekly data on the total number of Covid-19 therapeutics provided by the NHS in England, broken down by type of treatment, to:

    a. Eligible individuals hospitalised due to Covid-19, or with hospital-onset Covid-19 in England between 29 June 2020 and 2 July 2023.

    b. Eligible non-hospitalised individuals in England with Covid-19 between 16 December 2021 and 2 July June 2023 **[GA1/011]** **INQ000408766**

225. Treatments administered in clinical trials are not included in the reporting.

226. NHS also published the total number of individuals digitally identified as appropriate for treatment who received treatment, alongside hospital-based and non-hospital-based treatment figures. Figures relate to all individuals who received relevant treatments either as an inpatient, or via CMDUs in England. Relating numbers of treatments to numbers of patients identified indicates that overall around 20% of identified patients went on to receive treatment, although this figure compares numbers from two different sources, and may reflect underreporting of treatments.

227. As noted above at paragraph 180, an early review of CMDUs into the reasons for triage found approximately 19% of those who were either digitally identified or referred to the CMDU through primary or secondary care had treatment planned. The principal reasons for not receiving treatment were that patients were not eligible, symptoms had resolved or were mild, the PCR was outside the 5-day window, or they could not be contacted (together these reasons accounted for 74% of identified patients).

228. Routine reporting on the reasons for triage was subsequently established. The below table shows data between March 2022 and July 2023, as recorded by the CMDUs.

Overall, around 25% of people identified by the CMDU alert system (Webview) were treated in this period. This figures is in line with the estimated 20% set out above, and will reflect differences in reporting by CMDUs.

CMDU Treatments – Triage Outcomes

	Total		Total: no treatment planned	
Eligible: treatment planned	53,074	25.4%		
Ineligible: recovering/no symptoms	45,776	21.9%	45,776	29.3%
Ineligible: clinical	37,782	18.0%	37,782	24.2%
Ineligible: other	28,291	13.5%	28,291	18.1%
Not contactable	15,659	7.5%	15,659	10.0%
Treatment declined	13,078	6.2%	13,078	8.4%
Ineligible: over 5 days	8,833	4.2%	8,833	5.7%
CMDU transfer	6,362	3.0%	6,362	4.1%
Deceased	507	0.2%	507	0.3%
Total	209,362	100%	156,288	100.0%

229. The above data shows that, among those not treated, the most common reasons were:

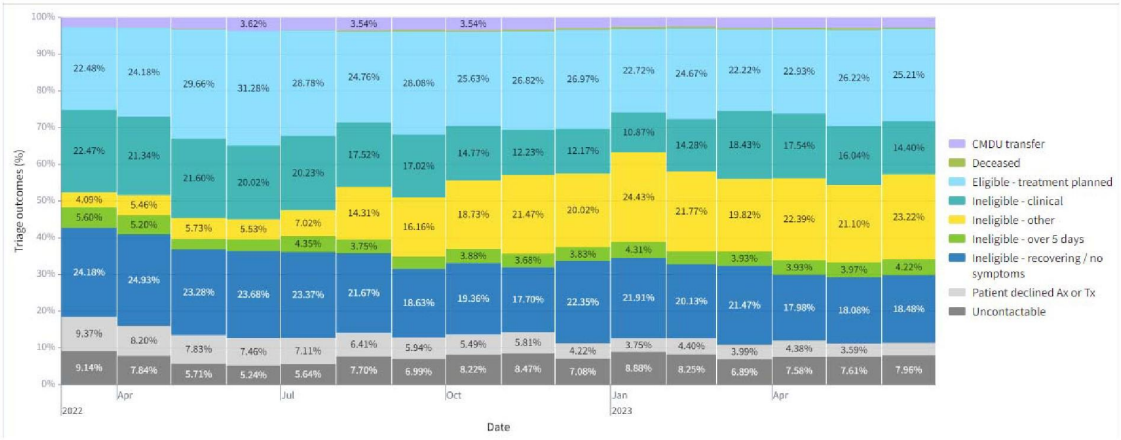
    a. Recovering/no symptoms (29.3% of those not treated) – people who were not eligible because they had mild symptoms and were recovering, or who had no symptoms. The treatments were only appropriate for people who had symptoms.

    b. Clinical reasons (24.2%) – the NHS Digital cohorting rules were set intentionally wide to include all potentially eligible patients. Many of these patients would then be triaged by clinicians for a variety of reasons, for example, no longer receiving a specific treatment.

    c. Other (18.1%)– largely people already in hospital. From August 2022, the CMDUs received alerts through Webview from tests initiated in hospital. The majority of people covered by this testing were still in hospital and therefore not eligible for treatment. However. a small number (around 5%) may have been discharged and therefore eligible, and therefore it was decided that all people should be included in Webview alerts.

230. The chart below shows the changes over time in triage outcomes, including the impact of including hospital testing from July/August 2022.

Figure 10: Chart showing CMDU triage outcomes



231. Further information about use of Covid-19 therapeutics in the community is set out in Part Five of this Statement.

Remdesivir

Overview

232. Further requested information on remdesivir is set out below.

233. Remdesivir, marketed and sold under the brand name Veklury by Gilead Sciences Ltd, is a broad spectrum antiviral medicine. It is used to treat early Covid-19 infection and help to prevent more severe symptoms.

234. Remdesivir was originally developed by Gilead in collaboration with the US Centre for Disease Control and Prevention and the US Army Medical Research Institute of Infectious Diseases, seeking to identify therapeutic agents for treating RNA-based viruses that maintained global pandemic potential. Remdesivir demonstrated activity against a range of coronaviruses including MERS, Ebola, and the causative agents of the common cold. Clinical trials were undertaken but, due to the nature of the viruses which remdesivir treats, these were limited to lab based and animal studies.

235. In January 2020, a Covid-19 positive patient in the USA was given remdesivir under compassionate use access and, following successful treatment, remdesivir was administered to further patients on the same basis. Several clinical trials then commenced to evaluate the safety and efficacy of remdesivir.

236. On 23 March 2020, Gilead Sciences suspended compassionate use access to remdesivir for all cases other than children and pregnant women, with access for other patients limited to those participating in clinical trials. Gilead reported on 28 March 2020 that it had provided over 1000 doses of remdesivir through compassionate use requests.

237. On 26 May 2020, the MHRA, under EAMS, issued a positive scientific opinion to Gilead for remdesivir in the treatment of patients hospitalised with suspected or laboratory-confirmed SARS-CoV-2 infection who meet the clinical criteria.

238. In early June 2020, NICE published an evidence review for remdesivir for treating hospitalised patients with suspected or confirmed Covid-19. NICE reviewed clinical effectiveness, safety and cost effectiveness of remdesivir in adults, young people and children. The studies included in this review suggested some benefit with remdesivir compared with placebo for reducing supportive measures including mechanical ventilation and time to recovery in patients with mild or moderate, or severe Covid-19 disease who were on supplemental oxygen treatment. However, no statistically significant differences were found for mortality and serious adverse events. More treatment discontinuations were reported with remdesivir compared with placebo due to adverse events and a subgroup analysis suggested that some groups may benefit more than others.

239. Conditional marketing authorisation was granted by the European Medicines Agency on 6 July 2020. The marketing authorisation was, at the time, conditional as there was more evidence to come about the medicine. A four nations policy was produced by the RAPID C-19 team and published on 7 July 2020 to coincide with the EMA approval and confirmed the position being taken for use of remdesivir in the UK. The four nations policy set out the interim clinical commissioning position and recommended it was made available as a treatment option through routine commissioning for hospitalised patients (12 years and older) with Covid-19.

240. The 7 July 2020 policy included eligibility criteria from the product licence, namely:

    a. Hospitalised with coronavirus disease 2019 (Covid-19);

    b. With pneumonia requiring supplemental oxygen;

c. Adults, and adolescents ≥ 12 years of age and ≥ 40 kg;

d. eGFR ≥ 30ml/min;

e. Alanine Aminotransferase (ALT) below 5 times the upper limit of normal at baseline.

241. Additional criteria were also included for periods of limited supply, acknowledging that it would then be necessary to allocate the available supply to those with the greatest capacity to benefit. Remdesivir was considered unlikely to improve clinical outcomes in people who appeared clinically to be in the recovery phase of the illness, or those who had required mechanical ventilation or extra corporeal membrane oxygenation for a number of days and did not have ongoing evidence of high viral burden or ongoing viral replication, nor advanced immunosuppression that may put them at risk of reactivation. Supply was therefore prioritised to patients in the earlier stages of respiratory failure, with the following factors also taken into account:

a. At the time of decision to treat with remdesivir patients should not be receiving ongoing mechanical ventilation or extracorporeal membrane oxygenation (ECMO). Patients who present with an initial rapid deterioration can, however, be considered for treatment with remdesivir.

b. A multi-disciplinary team assessment should determine if patients not suitable for escalation would benefit from initiation of treatment with remdesivir.

c. If patients on remdesivir require escalation, continuation of the drug should be considered by a multi-disciplinary team assessment.

242. On 29 September 2020 a CAS alert was issued for remdesivir **[GA1/012] [INQ000414395]**. The alert stated that due to increased demand against available supply, clinicians were asked to apply the full eligibility criteria and to adhere to a standard treatment course of 5 days. This alert was issued to a wider group than would ordinarily have received a supply disruption alert given the nature of the alert.

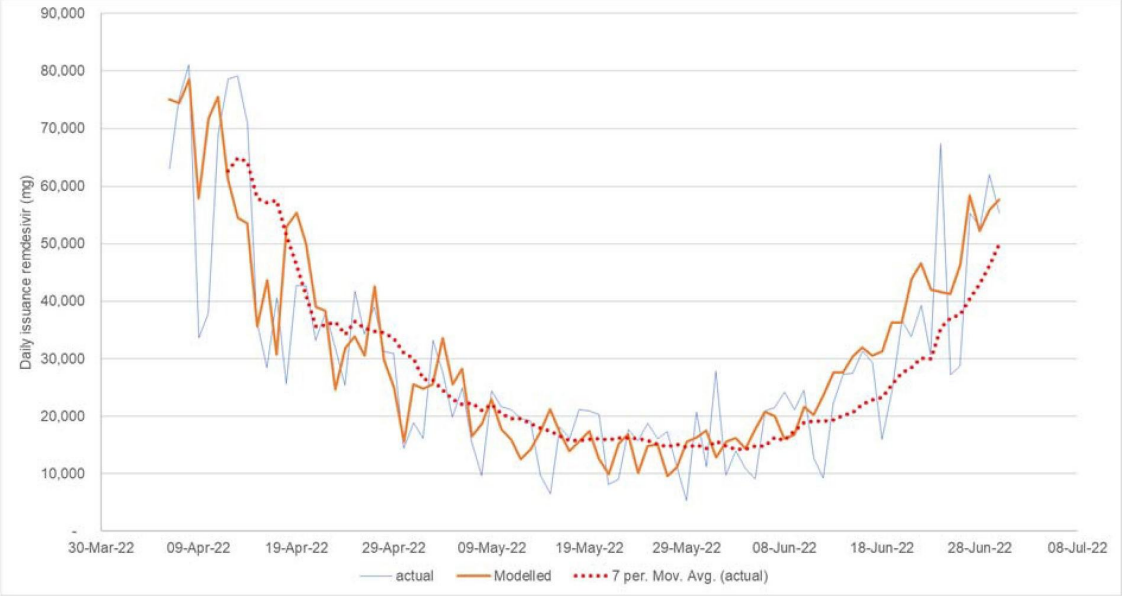
Monitoring remdesivir stock

243. During the pandemic therapeutics effective at treating Covid-19 were in high demand globally, placing additional pressure on supply chains. Although there was a Supply Disruption Alert issued, there was no 'stock out' of remdesivir in the UK. NHS England's work to closely monitor stock and model future requirements of different medicines, and to share this analysis on with system partners, enabled an early intervention, in the form of a supply disruption alert, to help preserve continued availability of remdesivir.

244. NHS England's work to monitor stock levels of therapeutics – including remdesivir – is set out earlier in this Statement.

245. While the information was available to decision makers at the time, the chart below has been produced for the purpose of this statement. The chart is an example of modelled demand for remdesivir between April and June 2022 (orange line) compared with reported actual issuance (blue line) and 7-day moving average of actual daily issuance (red dotted line). Modelled demand takes account of the change in demand through successive Covid-19 waves through 2022. Overall demand takes into account that generated by patients hospitalised due to Covid-19 and needing oxygen support (O patients) as well as hospital onset cases. Treatment for O patients consists of two doses on the first day and a single dose for subsequent four days, whereas for hospital onset cases it is a double dose on first day followed by two days of a single dose. Because remdesivir requires sequential days of IV treatment it was rarely used for non-hospitalised patients. Medicine issuance by NHS Trusts is not differentiated by patient cohort so it is not possible to know how much was issued to patients hospitalised due to Covid-19 and hospital-onset patients. There is no non-Covid-19 related indication for remdesivir.

Figure 11: daily use (actual and modelled) of remdesivir from April 2022 to June 2022



Procurement of remdesivir

246. Remdesivir was centrally procured by DHSC. NHS England's role was to provide information on demand and supply, as described earlier in this statement, to inform purchasing decisions and other actions taken to manage supply.

Stockpiling medicines for future pandemics

247. The work on medicine supply carried out by NHS England and system partners in preparing for EU Exit and during the pandemic has introduced new ways of working that would inform the response to managing medicine supply in any future pandemics.

248. As with Covid-19, medicines supply resilience will depend on processes for quickly understanding pathogens of concern and appropriate clinical treatment, demand and usage modelling, supply chains and procurement arrangements. The relationships built between organisations and collaborative approach taken, as well as the lessons learned, puts RAPID C-19 in a good position to rapidly mobilise if requested to identify future therapeutics for Covid-19 and as a way of working on other pathogens of concern.

249. As this Statement sets out, medicines supply resilience is the responsibility of DHSC. Medicines shortages are part of routine business for NHS England, and we work collaboratively with DHSC on managing shortages. During the pandemic when supply chains were severely affected by increases in global demand and manufacturing disruption, stockpiles of some routinely used medicines played an important role that we have described.

250. When considering the role of stockpiles for pandemic response, a number of factors are relevant, in particular:

    a. the choice of which medicines to stockpile;

    b. the cost and arrangements for storage; and

    c. the cost and arrangements for disposal at expiry (including the financial and Net Zero impacts of wastage) and any replenishment plans.

251. On the choice of medicine, Part Four of this Statement sets out the process for identifying clinically effective medicines (and those which were ineffective) for treating Covid-19, a previously unknown virus. For more routinely used medicines, including for managing patients with respiratory illness, other approaches to managing shortages and supply chain resilience can include manufacturer held buffer stocks to mitigate supply disruptions, as well as ensuring plurality of supply. NHS England has recently changed the terms and conditions of the secondary care medicines frameworks it tenders which now require suppliers to hold eight weeks' buffer stock in the UK.

252. Based on current arrangements, DHSC would be responsible for any plans for medicines supply in future pandemics including any central procurement and/or stockpiles.

253. NHS England is aware that DHSC has established processes for procuring medicines in such circumstances as required. NHS England and DHSC meet regularly to review demand for different medicines by the NHS and to discuss any emerging challenges.

PART SEVEN: REFLECTIONS AND LESSONS LEARNT

254. NHS England recognises the importance of learning lessons and being better prepared for future pandemics and other crises as emerging zoonotic infectious diseases become more common. NHS England recognises the importance of health protection in the design, definition and implementation of any future therapeutics' strategy for a pandemic.

255. Reflections on the medicines supply chain from Professor Sir Stephen Powis' third witness statement provided in Module 3 are set out in Annex One. NHS England would also like to make the following reflections specific to Covid-19 therapeutics.

256. While vaccines remain the first line of defence against Covid-19 for at-risk groups, in part given the wider impact on transmission, proven therapeutics are complementary to vaccines and can be particularly beneficial for the protection of people who are immunocompromised and other groups subject to lower vaccine efficacy.

257. For Covid-19 therapeutics to be at their most effective, treatment needs to be done within around five days of symptoms developing. They also rely on a positive confirmation of COVID, and so require routine access to testing. The ongoing mutation of the virus means some treatments can quickly become less effective.

258. The UK's research friendly environment, alongside the willingness of academia and industry to identify new treatments and to repurpose widely used treatments, allowed evidence about therapeutics that are effective at treating Covid-19 to be identified at pace. The success of the UK's clinical research programme has been partly down to the ability to consider using both novel therapeutics and repurposed medicines against Covid-19, as repurposed medicines can more quickly enter trials and routine use and are often already familiar to NHS clinicians.

259. Whilst we should recognise the pandemic's impact on non-Covid-19 research, the UK research response to Covid-19 has provided evidence of global significance in prevention and treatment, including from internationally renowned UK-based platform studies such as RECOVERY and REMAP-CAP. The more than one million individuals in the UK who participated in Covid-19 trials also played a crucial role in identifying therapeutics effective at treating Covid-19.

260. The NHS operating as a single integrated healthcare system, along with its digital infrastructure, strong local clinical leadership and support from consistent national clinical access policies, allowed treatment pathways for Covid-19 to be established at scale.

261. A key plank of any future strategy should involve a RAPID C-19 type collaboration. As a result of RAPID C-19, there are now stronger working relationships and coordination across NHS England, DHSC, NICE, NIHR and MHRA and an improved understanding of process and comparative advantages between these organisations.

262. RAPID C-19 played an important role in expediting access to Covid-19 therapeutics, including:

    a. fostering greater collaboration, collective intelligence and leadership during the unprecedented pandemic;

    b. helping to inform NHS England's prevention and treatment strategies in an exceptionally rapid timeframe;

    c. evaluating and identifying a wide range of potential treatments in clinical trials. The development and deployment of a diverse portfolio of Covid-19 therapeutics to address varying virus variants and better patient outcomes was an essential tool in fighting the pandemic, enabling the best choice for each patient and increasing public confidence in therapy;

    d. rapidly identifying those medicines which were not effective or even harmful, despite in some cases strong public lobbying;

    e. developing and issuing clinical guidance to support the rapid adoption of treatment approaches; and

    f. ensuring consistency across the four nations.

263. Taking the above together mortality and hospitalisation was reduced. RAPID C-19 was instrumental and effective in combating Covid-19.

264. NHS England also developed a process to produce rapid clinical policies during the pandemic, a process that was a highly compressed version of the standard process used outside of emergencies. The development of these access policies enabled new treatments for Covid-19 to be communicated and introduced rapidly, sometimes within days, based on a review of clinical evidence and the consensus support of national clinical experts and devolved nation colleagues, and built on NHS England's expertise in national clinical policy formulation. Subsequently this guidance was communicated to the four nations via a CAS alert.

265. For clinicians, CAS alerts provided a source of precise information on the use of treatments that were demonstrated to be clinically effective as well as those that did not. CAS alerts allowed instant access to information, improved treatments, led to discontinuation of ineffective medication (based on the latest scientific evidence) and ensured consistency across the four nations.

266. The existence of RAPID C-19 and the collaborative processes it adopted meant:

    a. for patients, rapid access to the most promising new treatments for Covid-19 much faster than usual and in some cases within just days of the evidence being gathered to show how well they work;

    b. for clinicians, the programme provided a source of precise information on the use of treatments that were demonstrated to be clinically effective as well as those that did not, along with educational webinars helping them understand the treatments that were mostly likely to benefit patients, when and how to use them;

    c. for industry, streamlining existing processes and running them in parallel to enable access to UK markets at pace, an advantage of having one single healthcare system;

    d. for Government, greater collaboration and leadership during an unprecedented crisis;

    e. for the world, providing leadership in establishing clinical trials for promising new treatments for Covid-19 and moving treatments from research into clinical practice as fast as possible for the benefit of patients.

267. A system similar in terms of participants, objectives, responsibilities and ways of working can be re-established at short notice at the request of the UK Chief Medical Officers in response to a future pandemic.

268. While the RAPID C-19 process enabled effective therapeutics to be identified at pace during the pandemic, NICE's rigorous appraisal processes offer thorough consideration of clinical and cost effectiveness of different treatments before they are offered by the NHS. These considerations, including consultation with stakeholders, ensure that technologies recommended to be funded by the NHS represent good value for public money and support positive outcomes for patients. Processes introduced to respond to an emergency are not always appropriate for normal service delivery conditions.

269. NHS England welcomes the technology appraisal work NICE has carried out on Covid-19 therapeutics as these appraisals have brought health economic rigour to the review of their clinical and cost effectiveness and will inform future clinical access decisions.

270. The reflections of the first few weeks of CMDUs demonstrated the importance of establishing and prioritising the capacity locally to ensure access to medicines, along with clear communication with clinicians and with patients. It is also worth highlighting some of the challenges of moving from the appropriate pandemic specific arrangements to routine access. Close working with stakeholder groups as well as the ongoing engagement with the NHS and locally were important as the pandemic-specific arrangements were stood down.

271. Finally, it is important to recognise the dedication of the frontline NHS clinicians and other staff who were able to rapidly provide access to new life-saving treatments, particularly the CMDUs.

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.

Personal Data

Signed:

Date: 6 September 2024

ANNEX ONE: Paragraphs from Module 3 witness statement

The below paragraphs have been taken from Professor Sir Stephen Powis' Third Witness Statement provided as part of Module 3. As requested, identified paragraphs from that statement are set out below. Please note that as the paragraphs below are a direct extraction of the relevant paragraphs from that statement they repeat in places, wording contained in the main body of this Statement. The paragraphs below may also contain explanations of defined terms that have already been defined in the main body of this Statement.

Commissioned reports/clinical monitoring (paragraphs 76-80)

1. Various organisations developed and ran clinical trials during the pandemic to assist with the world's clinical understanding of the virus and its clinical management. In addition to these trials, external stakeholders, for example the UK's Intensive Care National Audit and Research Centre ("**ICNARC**"), carried out clinical audit reports and developed risk models which helped to improve the clinical understanding of risk factors for poor outcomes. NHS England paid particularly close attention to ICNARC's reports published in the pandemic. It had undertaken a similar role during the previous 2009/10 (H1N1) flu pandemic. ICNARC is a UK based organisation, established in 1994. Its aim is to improve the quality of critical care through national clinical audit and research. The centre manages national clinical audits which assess the performance of critical care units in the UK. The audits use quality data to provide feedback to units and the insights generated are used to inform national policy and standards for critical care.

2. NHS England met with ICNARC to discuss reports which would assist the clinical understanding and management of Covid-19, including a proposal to track individual patient adherence to drugs [**INQ000330796] [INQ000330902**] including dexamethasone and a review of mortality. The first ICNARC report produced on Covid-19 during the pandemic included data on 13 patients and was sent to NHS England leadership on 10 March 2020 [**INQ000330801**]. The subsequent report, which was ICNARC's first public report, included data on 196 patients and was published on the ICNARC website on 20 March 2020 [**INQ0003308010**]. These reports were disseminated by ICNARC directly to their contact list in every hospital in England, Wales and Northern Ireland as well as to various media contacts. The reports highlighted a number of issues which were not previously apparent from international reports of Covid-19 virus patterns. The clinical guidance group convened by NHS

England for critical care reviewed these reports with a view to amending clinical guidance accordingly.

3. The following is a specific example to demonstrate the value of ICNARC reports and how they informed NHS England's guidance to the system regarding clinical management, including how that information was then shared with the system, used to amend SitRep data, and produce clinical guidance. On 17 April 2020, ICNARC published a report which noted that 28.8% of patients on advanced respiratory support needed renal support for a median of 4 days. Prior to this, the evidence from China (as mentioned above) was that only a small number of Covid-19 patients developed renal problems. On 21 April 2020, following the ICNARC report, the Specialised Services Cell sent out an urgent letter to managers and operational leads in Incident Co-ordination Centres (**"ICCs"**), regional directors of commissioning, critical care networks and renal networks regarding patients who required access to renal replacement therapy ("**RRT**") [**INQ000330989**]. The letter cited ICNARC's findings and explained that discussions had been taking place between manufacturers and clinical leads involved in the national response to maintain the capacity to delivery RRT by way of haemofiltration. The letter recommended that clinicians conserve both fluids and sets used in RRT. The letter also confirmed that the daily national Covid-19 SitRep had been amended to include identification of the number of patients on RRT within critical care and the relevant guidance for patients receiving RRT within critical care had also been updated.

4. In addition to ICNARC reports, NHS England also monitored other expert external stakeholders and systems which produced key clinical information on Covid-19 during the pandemic, such as Blueteq (a system used by NHS England and secondary care providers for the management of high-cost medicines).

5. NHS England specifically monitored the following reports:

    a. the use of Covid-19 treatments commissioned under UK wide interim clinical policy arrangements such as antivirals, monoclonal antibodies and IL-6 inhibitors via the prior approval system Blueteq.

    b. the use of dexamethasone for patients admitted to critical care through a new process audit commissioned by NHS England and delivered by ICNARC.

    c. the treatment and outcome of patients treated within intensive care units in England, Wales and Northern Ireland reported by ICNARC.

Trackers (paragraphs 104-105)

6. In addition to dashboards, NHS England developed more specific trackers. For example, a Covid-19 priority medicines supply assessment tracker [**INQ000330849**], developed by the NHS England medicines cell, was developed to assist in the demand and supply forecasting for identified Covid-19 priority medicines. This was reliably operational by early May 2020. Prior to this, NHS England had access to only hospital pharmacy stock levels and top-level manufacturing data provided by those manufacturers who supplied information to the Commercial Medicines Unit ("**CMU**") for those on CMU frameworks (secondary care only). This priority medicines supply assessment provided an estimate of potential shortages over the forthcoming three months. The assessment supported DHSC and NHS England medicines analysis and allowed actions to conserve supplies, prioritise products for commercial procurement by DHSC and its partners, and allocate to the NHS based on patient need informed by clinical guidance. It comprised Covid-19 demand for medicines (by applying clinical usage assumptions to NHS England Covid-19 bed forecast), non-Covid-19 demand for medicines (based on historic issues data) and the available supply of medicines in hospital and the supply chain (with a bespoke data collection from suppliers). The supply assessment was updated daily in the initial stages of the pandemic, moving to weekly and then fortnightly in the latter stages. It drew on the priority medicines identified by clinical experts used to treat Covid-19 patients in Intensive Therapy Units ("**ITU**") (supportive medicines), antibiotics, palliative medicines and some treatment medicines. The forecasting relied on engagement with medicines wholesalers as well as an understanding of stock in hospital pharmacies to inform the supply position of these drugs to inform operational planning and mapped against a real-time demand scenario.

7. These forecasts acted as an early warning system that allowed NHS England and other key stakeholders to plan mitigating actions, including DHSC and its partners procuring additional stock, sharing clinical guidance with the system on alternative treatments and releasing stock from the Covid-19 stockpile. When stocks were critically low, the modelling was adapted to determine medicine supply allocations to Trusts and DAs based on relative criticality of local stockholders.

CAS alerts (paragraphs 118-119)

8. The CAS is managed by the Medicines and Healthcare products Regulatory Agency ("**MHRA**"). The MHRA regulates medicines, medical devices and blood components for transfusion in the UK. It is an executive agency, sponsored by the Department of

Health and Social Care. CAS is an MHRA web-based cascading alert system for issuing patient safety alerts, important public health messages, and other safety critical information and guidance to the NHS and others, including independent providers of health and social care. CAS alerts are generally short urgent messages on specific issues, such as medicines safety issues. They were a very effective way of getting clear messaging out to the system quickly during the pandemic.

9. Throughout the relevant period, a significant number of alerts were distributed through CAS. Whilst NHS England did not have access to the system to post alerts directly, the CMO (who did have access to the system) was able to post alerts on behalf of NHS England at our request. A number of CAS alerts were tripartite communications between the CMO, PHE, and NHS England. The type of information shared via CAS varied and included alerts on very specific issues such as issues with high flow nasal oxygen during transfers and the use of particular medicines in the treatment of Covid-19, to wider alerts on shielding and PPE guidance updates. We have set out examples below of several clinical alerts which assisted in the dissemination of clinical information and advice regarding the optimal clinical management of Covid-19:

   a. 17 March 2020 – anti-inflammatory medicines. This alert from NHS England noted that there had been some concern about the use of non-steroidal anti-inflammatory drugs ("**NSAID**") in relation to Covid-19 following a statement by the French Health Minister advising against the use of ibuprofen. The alert confirmed that there appeared to be no evidence that NSAIDs increased the chance of acquiring Covid-19. [**INQ000330807**]

   b. 6 June 2020 – Dexamethasone in the treatment of Covid-19. This alert confirmed that dexamethasone had been demonstrated to have a clear place in the management of hospitalised patients with Covid-19 and that clinicians should therefore consider using it.

   c. 3 July 2020 – Interim Clinical Commissioning Policy for Remdesivir. This alert confirmed that NHS England, working with DAs, had established a rapid policy development process (RAPID C-19) to aid clinicians in offering best care and clinical advice to patients. This alert set out the interim clinical commissioning position for the use of remdesivir for patients with Covid-19. **[INQ000414391]**

The Clinical cell (paragraphs 137-141)

10. NHS England established a clinical cell in February 2020. Its terms of reference were finalised in April 2020 [**INQ000330943**]. NHS England used the framework designed for EU Exit as a foundation for the structure of the cell, which meant that it was able to set up the cell quickly. The cell's overarching aim was to support recommendations for the treatment and medical management of patients with Covid. The specific purpose of the cell was to resolve clinical questions/issues/tasks from the national incident co-ordination centre and/or other workstreams.

11. As part of its role, the cell provided guidance on emerging themes arising out of the pandemic, developed policy and provided a strategic response to various issues and was involved in reviewing and assisting with clinical guidelines. The cell carried out the following specific functions:

    g. Identifying email tasks which required specialist clinical input

    h. Forwarding tasks to other workstreams

    i. Engaging appropriate clinicians and stakeholders

    j. Collating information provided into a meaningful form

    k. Enabling the senior responsible owner to make informed decisions

    l. Prioritising tasks based on clinical & operational urgency

The Specialised Commissioning/Specialised Services Cell

12. The Specialised Commissioning/Specialised Services Cell co-ordinated the maintenance, prioritisation and surge of NHS specialised services in the pandemic.

13. The cell's stated objectives included:

    e. Rapidly forming clinical policy for new treatments or amendments of current treatments

    f. Supporting the roll out of research for new treatment strategies

    g. Rapidly forming clinical guidelines in partnership with NICE for Covid-19 specific clinical management scenarios.

    h. Acting as a single point of contact for key partners including NICE, NIHR and DAs.

14. The example of the renal stocktake given above at paragraph 92 is a good example of how the cells, particularly the Specialised Services cell, gathered information, used that information to make decisions regarding management (both clinical and operational) and shared that with the system.

NHS England's collaboration with NICE (paragraphs 146-162)

15. Outside of pandemics, NHS England has a limited role in issuing guidance on the clinical management of healthcare conditions, although it does produce clinical commissioning polices that support the clinical management of healthcare conditions managed within specialised services.

16. Clinical guidance is ordinarily produced and published by NICE, the Royal Colleges, and regulatory bodies such as the GMC and NMC as well as professional societies such as the Intensive Care Society.

17. As part of its emergency role during the pandemic, NHS England undertook several extended roles, including the production and dissemination of some specialty clinical guidelines and access policies for clinicians and other healthcare professionals. These guidelines and access policies supported hospitals to treat Covid-19 patients with optimal clinical management and new treatments for Covid-19. They were communicated and introduced rapidly, sometimes within days.

18. As above, it is NICE's core role to provide guidance and advice to improve health and social care and treatment. It takes NICE on average 91 weeks to produce a piece of guidance. Each commissioned topic is initially assigned a *'standard (142 week)*' timeline, *'accelerated (86 weeks)*' timeline, or *'short (44 week)*' timeline depending on the expected size of the work required. NICE follows a comprehensive guidance development method and process based on gathering evidence, analysing that evidence, public consultation at several stages of guideline development and review and recommendations by independent advisory committees of health care professionals and lay members.

19. The fast-moving nature of the pandemic meant that clinicians and patients did not have time to wait this long for clinical guidance and, more importantly, bearing in mind that NICE's guidance process is heavily dependent on evidence - at the early stages of the pandemic there was often no firm body of evidence that could be relied upon given that Covid-19 was a new virus.

20. Recognising the urgent need for clinical guidance. On 3 March 2020 the Clinical Cell within NHS England drafted and published guidance titled *'Clinical management of persons admitted to hospital with suspected Covid-19 infection'*. On 11 March 2020 [**INQ000330803**] NHS England asked NICE to produce guidelines on Covid-19 topics at pace. It requested that NICE significantly condensed the development process to 5-10 days so that it could publish guidance rapidly as was necessary. NICE recognised that the volume of guidance required at speed was considerable.

21. Although NHS England does not ordinarily produce clinical guidance, on 11 March 2020, NHS England agreed with NICE that NICE would pause development of its 'business-as-usual' guidance and NHS England would develop and update rapid Covid-19 clinical guidance. NHS England therefore assisted NICE during the pandemic by developing specialty guides drawing from a range of national clinical expertise from within its own organisation (i.e., National Clinical Directors), CRGs and the NHS system more widely.

22. NHS England created a Standard Operating Procedure for the development and publication of specialty clinical guidance at pace [**INQ000330802**]. This was developed by NHS England's Deputy Strategic Incident Director.

23. On 13 March 2020, NHS England commissioned the first three Covid-19 rapid guideline topics from NICE, followed thereafter by regular commissions. The first guidelines were published by NICE on 20 March 2020.

24. As Covid-19 was a predominantly new virus and there was no established body of available evidence, NHS England and others recognised that any clinical guidance produced would need to draw from clinical expert opinion (in the absence of established evidence base) to a greater extent than would ordinarily be the case. In order to do this, NHS England drew from a range of national clinical expertise from within its own organisation (i.e., National Clinical Directors), CRGs, the NHS system more widely and other professional bodies and organisations.

25. NHS England spoke with behavioural experts to establish the most effective way of setting out guidelines to ensure that they were clearly received and understood by clinicians working extremely hard in a high-pressured environment. Guidelines needed to be direct and concise so as not to overload clinicians with unnecessary detail or cause potential misinterpretation or confusion. NHS England created a clear template for all guidelines to ensure consistency in approach so that clinicians would become

familiar with the layout of each guideline and know how to navigate their way round the documents.

26. NHS England appointed leading clinical experts to produce particular specialty guidelines where needed. These clinical experts largely came from the NHS and were often NHS England National Clinical Directors. There were several clinical experts and responsible authors appointed for each guideline. The expert groups would seek input on drafting as necessary or appropriate from other sources, such as the Royal Colleges and Specialist societies. Once the expert group had produced a draft of the guidelines, the draft was then reviewed by a clinical review group. The clinical review group comprised of clinical fellows in the NHS and also clinical consultants. The purpose of this review was to correct any errors and ensure consistency with other guidelines. The guidelines would then pass through the publications central content team and a final version check by the responsible authors. The final stages of the process involved a clinical review by either NHS England's National Clinical Director for Trauma, the Medical Director for Professional Leadership and Clinical Effectiveness, or the National Medical Director for Specialised Services. It would then pass to the National Strategic Incident Director or Deputy to sign off, with final sign-off from the Chief Executive office [**INQ000330991**].

27. During the first wave of Covid-19, NHS England worked with the Royal Colleges to develop clinical guidance to ensure the appropriate use of medicines and to manage demand pressures of identified products. It enabled changes in clinical practice, supporting clinicians to substitute suitable products to help conserve and manage supply. It also identified priority products for further procurement. In normal times, this work would be done in response to shortages for an individual medicine or medicine group level. However, Covid-19 necessitated a different scale and pace. Importantly, clinical guidance to manage and conserve supportive medicines for the treatment of patients admitted to ICU was jointly developed between DHSC, NHS England and the Royal College of Anaesthetists.

28. By the 27 May 2020, NHS England published 67 specialty guides [**INQ000330861]** in the first two months of the pandemic (not including updates). In addition to the guidelines published by NHS England, NICE produced 20 rapid guidelines (not including updates). The specialty guides fell into four categories:

    a. Specialty Guides for managing pandemic Surge

    b. Specialty Guides for the specific treatment of Coronavirus and its complications

c. Specialty Guides for continued care of specialty patients during the pandemic to endemic phase

d. Rapid learning guides - What had been learned about the provision of care during a crisis the NHS has never faced before, based upon multiple interviews with front-line clinicians during surge & recovery.

The vast majority of the guides were about service organisation but did cross over into some specific treatment regimens. Specialty guides were published on the NHS England website, and cascaded through the usual channels, including SPOCs, regional teams, and updates.

29. In subsequent discussions with NICE following Wave 1 it was agreed that, by the Autumn, all specialty guides published by NHS England would be (appropriately) transitioned to the NICE website and re-branded as NICE documents. NHS England convened a small group with leads from the NICE Covid-19 rapid guidelines team to agree the transition practicalities including scope and mapping, the process for integration and updating equality impact assessments and governance. The joint transition work progressed until NHS England transitioned the speciality guides at the end of October 2020.

30. It was also agreed with NICE that, following transition, NICE would undertake a review process to identify those specialty guides requiring more immediate development or updating, in light of changing pandemic circumstances. Some areas required a more detailed review by specialists to support full integration into NICE guidelines. All the above work was underpinned by NICE's emerging evidence base processes.

31. NHS England expects that, were another pandemic to occur in the UK, NICE would now be in a better position to respond to that emergency and would be able to adapt their standard guidance procedures such that NHS England would not need to provide such significant assistance.

SECTION 2: NHS ENGLAND'S ROLE IN CLINICAL TRIALS, RESEARCH AND MEDICINES SUPPLY (paragraphs 241-332)

32. This section provides an overview of clinical trials and medicines shortages, including:

a. NHS England's role in supporting clinical trials and research, including the role of NHS DigiTrials; and

b. How NHS England managed medicines supply continuity and mitigated

medicines shortages.

33. NHS England played a role in supporting the prioritisation of key clinical trials in the UK and facilitating their access to clinical data and played a key role in managing concerns regarding shortages of Covid-19 priority medicines. The medicines supply work in particular required sophisticated clinical guidance, analysis of demand and supply, commercial management, and knowledge and coordination of supply chains at a national level, as well as coordination between regions and countries (with DHSC having overall responsibility for medicines supply).

Clinical Trials

Introduction to clinical trials

34. One of the major benefits of the NHS, even though it is a devolved matter for each UK nation and is a diverse ecosystem of organisations and providers of care, is that it has several features (set out below) which promote and facilitate research at scale:

    a. A large and diverse population use the NHS and every patient should have a unique NHS number from birth. This number links up to a patient's medical records. This aids research in several ways, for example by providing clinical details for a vast number of diverse patients.

    b. The NHS system therefore attracts funding from the charitable and academic sectors and the life sciences industry.

    c. Staff are experienced and well-trained to support the opt-in process (to clinical trials) and monitoring of patients. Patients on the whole are happy to contribute to and participate in research and want to 'give something back'.

35. In addition, NHS DigiTrials plays an important role in clinical trials, providing secure data about people's health and care to researchers.

36. At the start of the pandemic there were no known effective therapeutics for Covid-19. The UK capitalised on the strengths of the NHS system described above, which could allow research to take place at scale, to find out how to treat f Covid-19. The National Medical Director of NHS England and the four CMOs sent a letter to NHS colleagues to ensure that every effort was made to enrol Covid-19 patients in national priority clinical trials **[INQ000068589]** .

37. Over one million individuals in the UK agreed to participate in studies regarding Covid-19. The research community, particularly within the UK, rapidly focussed efforts to find treatments for Covid-19. The UK research response to Covid-19 provided evidence of global significance in prevention and treatment, including from internationally renowned UK-based platform studies such as RECOVERY and REMAP-CAP. NHS hospitals and primary care teams were at the forefront of recruitment into and delivery of clinical trials which identified effective Covid-19 treatments benefitting patients across the NHS and around the world.

38. The RECOVERY trial involved tens of thousands of patients and 175 NHS hospitals. The scale and pace of the research into repurposing this drug was possible in part due to the NHS operating as a single integrated healthcare system. It has been roughly estimated that the Dexamethasone trial has contributed to saving approximately 22,000 lives in the UK and close to one million lives across the world between July 2020 and March 2021 (extrapolated from modelling in Aguas et al, 2021 [**INQ000331013**]).

How clinical trials work

39. Before setting out further detail about the Covid-19 clinical trials run during the pandemic, it may first be helpful to explain how clinical trials are usually organised and funded. Each proposed treatment for a health condition in the UK (and generally worldwide) needs to go through a clinical trial process to ensure that it has been satisfactorily tested with sufficient evidence to support the use of the treatment. The clinical trials process is governed by the Medicines and Healthcare products Regulatory Agency ("**MHRA**"). Pragmatic clinical trials of larger populations can focus on the clinical outcomes of treatment in real world settings ensuring the results are relevant to changing circumstances of a pandemic.

40. The UK has a comprehensive and established infrastructure in place for clinical trials which runs independently of NHS England. NHS England (as opposed to the NHS) does not ordinarily have a direct role in coordinating or contributing to research and clinical trials in the UK. The National Institute for Health and Care Research ("**NIHR**") is the national funder of clinical, public health, social care and translational research.

41. Generally, clinical trials are sponsored by pharmaceutical companies or academic institutions as part of the development of new treatments and products. These groups run their own trials looking at drugs they have developed. If a pharmaceutical company is running a trial and they wish to use hospital equipment and/or services,

they must pay the hospital for the costs of any tests carried out and any in-patient stays required as a result of the trial. These agreements are made directly between the pharmaceutical company running the trial and the hospital they are using. Many UK universities have substantial research and clinical trial capabilities and carry out large research and clinical trial projects. They are independent from the NHS.

42. In addition to private investment, the Government can fund health research through organisations such as the NIHR, which is funded by DHSC and is directed by the Chief Scientific Adviser at DHSC. The NIHR was established in 2006 under the Government's health research strategy 'Best Research for Best Health'. Its purpose is to *"create a health research system in which the NHS supports outstanding individuals, working in world-class facilities, conducting leading-edge research focused on the needs of patients and the public"*.

Key Covid-19 clinical trials

43. NHS England was not involved in a formal role with the clinical trials set out below, but it contributed to identifying them as a priority and it had an EPRR role to support the trials by ensuring the NHS was advised to prioritise this research. As a result, once key clinical trials had been identified (i.e. the PRINCIPLE, RECOVERY and REMAP-CAP trials), the CMOs for all four administrations and the National Medical Director for NHS England wrote a letter to the system confirming that these clinical trials were to be national priority clinical trials.

44. Given that NHS England was one step removed from clinical trials research, we set out brief details of key clinical trials here only.

45. Separately, the NIHR established a single UK-wide process to prioritise Covid-19 research as 'Urgent Public Health Research'. This covered Covid-19 studies funded by the public sector, industry or charities. Through this process the NIHR Clinical Research Network ("**CRN**") expedited urgent clinical trials by fast-tracking the local set-up, management and delivery of Covid-19 studies and placing them onto the NIHR CRN Portfolio. The NIHR also announced at the start of the pandemic that new clinical studies not related to Covid-19 would be suspended to prioritise Covid-19 related studies. (On 21 May 2020, NIHR set out a framework to guide the restarting of NIHR research activities which have been paused due to Covid-19.)

RECOVERY trial

46. In March 2020, the RECOVERY (Randomised Evaluation of COVid-19 Therapy) trial was established as a randomised clinical trial to test a range of potential treatments for Covid-19, including tocilizumab (an anti-inflammatory used to treat rheumatoid arthritis). Over 35,000 patients were enrolled from 175 NHS hospitals in the UK. Collaborative buy-in was highlighted in the joint letter written by the UK's four medical officers and the medical director for NHS England on 6 May 2020. This letter encouraged physicians and hospitals to enrol patients into the RECOVERY trial and three other platform trials (i.e., ACCORD, PRINCIPLE, and REMAPCAP).

47. Conducted by researchers at Oxford University, the RECOVERY trial involved all major hospitals in the UK on an unprecedented scale and as many as 3,500 doctors, nurses, and research staff, including consultants, junior doctors, and those newly graduated. Within its first three months it reported its first policy changing result namely that the widely promoted antimalarial drug hydroxychloroquine was ineffective. This was swiftly followed by the extremely positive news that dexamethasone was effective in the treatment of severe Covid-19. The NHS Blood and Transport Clinical Trails Unit was also responsible for the management of the convalescent plasma aspects of the RECOVERY trial.

48. In total, the RECOVERY Trial found four treatments (tocilizumab, Regeneron's monoclonal antibody combination, dexamethasone, baricitinib) that were effective for severe Covid-19.

PRINCIPLE trial

49. Also launched on March 2020, PRINCIPLE (Platform Randomised Trial of Treatments in the Community for Epidemic and Pandemic Illness) grew to become the world's largest Covid-19 treatments trial for recovery at home in the UK.

50. The PRINCIPLE trial platform was the national urgent public health trial for primary care and aimed to find treatments for Covid-19 for people at most risk of serious illness. The trial looked at medicines that could help people with Covid-19 symptoms to recover at home, get better quickly and stop them needing to go to hospital. NHS Digital ensured that data and analyses was shared to support research, enabling evaluation of different response interventions and increasing the understanding of coronavirus (Covid-19) transmission, immunity and clinical outcomes. NHS Digital enabled a significant improvement in the recruitment of patients for the PRINCIPLE

trial through the provision of lists of patients that tested positive for coronavirus in community settings as further described below.

51. Unlike many trials that took place in the community, PRINCIPLE adopted an innovative remote model that recruited participants online from anywhere in the UK, as well as via more than 1000 GP practices across the UK.

52. PRINCIPLE was designed to rapidly identify treatments that showed promise and rule out treatments that did not work. Early in the pandemic, the antibiotics azithromycin and doxycycline were being widely used around the world to treat acute Covid-19; PRINCIPLE was the first major trial in the community to show that, in the absence of other indications, these antibiotics did not benefit COVID patients and so merely put them at unnecessary risk of side effects and added to the problem of antibiotic resistance. PRINCIPLE also found that the anti-inflammatory drug, colchicine, did not help people get better any quicker.

53. A key finding from the trial was that the commonly used asthma steroidal drug, inhaled budesonide, was effective in reducing recovery time by around three days and that there was a high probability that it also reduced hospital admission.

REMAP-CAP

54. REMAP-CAP was an international adaptive platform trial involving 15 different countries. It focussed on community acquired pneumonia and was specifically designed to be employed in a pandemic to evaluate multiple interventions simultaneously in critically ill patients. In addition to recruiting patients with community acquired pneumonia who had been admitted to critical care, the trial also recruiting patients with Covid-19 to understand optimal treatment strategies.

55. The NHS Blood and Transport Clinical Trials Unit was responsible for the management of the convalescent plasma aspects of the REMAP-CAP trial. The convalescent plasma treatment in this trial was for people who had been in intensive care for less than 48 hours and had tested positive for Covid-19.

DigiTrials service

56. Whilst NHS England was not materially involved in clinical trials, the utility of NHS data was seen across a number of clinical trials particularly through the NHS DigiTrials service. Those contributions included:

a. Enabling access to data to support the RECOVERY trial. The trial was first conceived in March 2020 and utilised NHS DigiTrials to draw together clinical trials, NHS and other datasets;

b. Support to the PRINCIPLE trial. Although the study commenced in April 2020, the participant numbers over the first 6 months were low because it was hard to find and engage with patients in the community when they were feeling unwell. The window for recruiting relevant participants following a positive Covid-19 test was only seven to ten days. By providing the PRINCIPLE team with a daily flow of Covid-19 test data records as well as access to the Summary Care Record, NHS Digital helped them to identify suitable trial participants and enable efficient and safe prescribing of trial treatment, resulting in recruitment into the trial doubling to 200 per week. DigiTrials also provided outcomes data to enable the trial to quickly and efficiently analyse their results;

c. Provision of demographics data to Imperial College to enable recruitment of a nationally representative cohort of participants for the REACT study, which was established in May 2020 by Imperial College London on behalf of DHSC. It provided monthly estimates of the prevalence of the virus and bi-monthly estimates of the prevalence of antibodies to the virus in the general population of England (using data collected from home test kits). NHS Digital subsequently shared health records of consenting participants in the study. These records were linked to study data to advance understanding of the risks of infection and reinfection with Covid-19 and people's future health following Covid-19 infection; and

d. Development and administration of the Covid-19 Vaccine Registry, working closely with NIHR. This comprised a database of individuals who had registered via NHS.UK to volunteer to be contacted about opportunities to participate in Covid-19 Vaccine trials. This enabled suitable trial cohorts to be easily and rapidly identified and quickly recruited.

RAPID C-19 Group

57. During the pandemic, patients needed access to new and effective treatments (such as those identified in clinical trials) as quickly as possible. The Research to Access Pathway for Investigational Drugs in Covid-19 ("**RAPID C-19**") Group was established in the early stages of the pandemic. NHS England had overarching responsibility for the establishment of the RAPID C-19 Group and partly funded its work.

58. Outside of the pandemic in BAU, the process to authorise access for new treatments is managed by NICE via their technology appraisal process. The purpose of the RAPID C-19 Group was to join organisations together to create a more rapid appraisal process for Covid-19 treatments. The Group ensured safe and timely patient access to medicines and therapeutics which had shown evidence of benefit in treating symptomatic Covid patients. The multi-organisational nature of the Group meant that it could align activities and communications and reduce the need for individual agencies to engage bilaterally with sponsors. The Group enabled UK-wide adoption of effective Covid-19 therapies in an average of just 6 days from material research findings becoming available to treating patients in the NHS. It developed a robust set of procedures [**INQ000315554**] , **INQ000330922**] and formally collaborated with the DHSC Therapeutics Taskforce.

59. The group consisted of the following organisations which each had assigned roles and responsibilities:

    a. MHRA – had lead responsibility for regulatory issues and authorisation functions (including clinical trials, early access and marketing authorisation).

    b. NHS England specialised commissioning – on clinical services policy development

    c. NICE and NIHR - both coordinated horizon scanning activities. NICE conducted numerous rapid evidence reviews and led the RAPID-C19 weekly committee.

60. The Scottish Medicines Consortium, All Wales Therapeutics and Toxicology Centre, All Wales Medicines Strategy Group, Department of Health in Northern Ireland and Antivirals and Therapeutics Task Force at the Department of Health and Social Care, all formed part of the group.

61. In general terms, the DHSC Therapeutics Taskforce identified medicines for research (with NIHR) and secured supply of clinically effective medicines for the UK. RAPID-C19 established whether there was convincing evidence of clinical effectiveness to make the medicine available. RAPID C-19's oversight group met regularly to critically appraise the latest evidence and consider the next steps needed to enable rapid patient access to treatments. If the evidence of benefit was robust, the group could then act quickly to make those treatments available promptly through expedited access mechanisms. The NHS England Specialised Commissioning Team built and defined access criteria, published clinical policy (for the UK) and then secured

equitable access to supply across the UK. By June 2022, RAPID C-19 had considered briefings on 76 potential treatments.

62. The NHS England Specialised Commissioning team led the following medicines notifications to the UK health system:

a. 26 May 2020 - Early Access Scheme for Remdesivir [**INQ000330860**] – published on the same day as a MHRA positive scientific opinion and followed the publication of the trial results on 22 May 2020 in the New England Journal of Medicine. A four-day turnaround to launch a medicine.

b. 3 June 2020 - Updated criteria for the Early Access Scheme for Remdesivir [**INQ000330863**]

c. 9 June 2020 - Second update for the Early Access Scheme for Remdesivir [**INQ000330867**].

d. 16 June 2020 - Dexamethasone for hospitalised patients **[INQ000283542]**. The RECOVERY trial results were published in the New England Journal of Medicine on 17 July 2020

e. 6 July 2020 - Interim Clinical Commissioning Policy Remdesivir for patients hospitalised with Covid-19 (adults and children aged 12 years and older) [**INQ000330872**]

f. 3 September 2020 - Corticosteroids in the treatment of suspected or confirmed Covid-19 followed the results of the REMAP-CAP trial published on 2 September 2020 in JAMA.

g. 3 September 2020 - Publication of an interim clinical commissioning policy: Remdesivir for patients hospitalised with Covid-19. Remdesivir becomes the first medicines licenced for treatment of COVID. Updates on supply published 29 September 2020, 6 November 2020 **[GA1/013]** **INQ000385828**

h. 25 November 2020 - Publication of an interim position statement: Tocilizumab for patients admitted to ICU with Covid-19 pneumonia (adults). Access to tocilizumab is planned as emergent (non-published) data from the immune modulation arm of the REMAP-CAP trial indicate positive benefits with the use of tocilizumab in patients admitted to an intensive care unit (ICU).

i. 15 December 2020 - Publication of statement to NOT use azithromycin in the Management of Covid-19 (SARS-CoV-2) Positive Patients. The trial was published on 2 February 2021.

j. 8 January 2021 - Interleukin-6 inhibitors (tocilizumab or sarilumab) for patients admitted to ICU with Covid-19 pneumonia (adults). The trial was published in the NEJM on 25 February 2021. With updates on 1 February 2021, 17 February 2021, 12 September 2021.

k. 17 September 2021 - Casirivimab and imdevimab for patients hospitalised due to COVID-19 **[INQ000257052]**. This was the first monoclonal antibody. MHRA gave approval for on 20 August 2021. This development needed the established of antibody testing. Revised 4 November 2021.

l. 14 December 2021 - Withdrawal of the Recommendation for Consideration of Inhaled budesonide as a Treatment Option for Covid-19.

m. 16 December 2021 - Neutralising monoclonal antibodies or antivirals for non-hospitalised patients with Covid-19.

63. It was clearly important for RAPID C-19 to identify medicines which were clinically effective. But of equal importance was RAPID C-19's role in identifying those medicines which were not effective, despite in some cases strong public lobbying. These included: convalescent plasma; canakinumab; doxycycline; hydroxychloroquine; aspirin; bamlanivimab; ivermectin.

64. RAPID-C19 was stood down at the end of March 2023 but is able to be re-established at the request of the UK CMOs in future pandemic response. The oversight of access to medicines in England has returned to NICE through technology appraisal.

Medicines Supply

Introduction to medicines supply

65. The following NHS England cells and groups are referred to below: the Medicines Cell, Covid Therapeutics Cell, Medicines Supply Strategic Advisory Group (MSSAG), National Clinical Group, Medicine Shortage Response Group (MSRG), Covid Medicines Shortage Response Group (CMSRG), Allocation and Distribution Group and Commercial Medicines Unit (CMU). We have set out a brief overview of the governance of these cells and groups in Annex 4 of this statement.

66. The production and supply of medicines is complex and highly regulated. Materials and processes must meet rigorous safety and quality standards. Supply chains are complex, global and very commercial. The production of a medicine starts with the manufacture of the active ingredients and related materials, which will then be incorporated into a finished product dosage. Each component of a medicine may come from a different country, with manufacture of the final product often being outside the UK.

Medicines supply overarching governance pre- pandemic

67. DHSC holds overall responsibility for continuity of supply of medicines in England, including shortages management and, whilst it is a devolved matter, in some circumstances also for the other nations of the UK and Crown Dependencies. Manufacturers have a legal requirement to inform DHSC of any supply problems. DHSC works closely with NHS England, the MHRA, the wider NHS, pharmaceutical companies, wholesalers and others in the supply chain to ensure the consistency and stability of supply of medicines. DHSC is also responsible for engagement with the Devolved Administrations (DAs).

68. The Commercial Medicines Unit ("**CMU**"), which is part of NHS England's Commercial Medicines Directorate (now called Medicines Value and Access), has specific responsibilities relating to any secondary care medicines and certain homecare services included on CMU frameworks in England. These frameworks support the medicines purchasing activities of NHS Trusts. The CMU Pharmacy Supply Team works closely with a wide range of stakeholders and suppliers in monitoring and managing medicine supply issues, working in close collaboration with the DHSC Medicines Supply Team, the Specialist Pharmacy Service and the Regional Pharmacy Procurement Specialists. This occurred both during the pandemic and as part of business as usual.

69. Any operational shortages are normally managed locally or regionally. However, if there are any widespread shortages, they may be escalated to the Medicines Shortages Response Group ("**MSRG**"), which is a multi-disciplinary group with members from across DHSC, NHS England and the wider NHS and was formed in 2019 in preparation for EU Exit. We provide more detail on the MSRG below and in Annex 5.

70. Until shortly before the Covid-19 pandemic, there had been no formal governance to coordinate with DHSC and across NHS England teams working on medicines and

medicines supply – including the CMU, Specialised Commissioning, Community Pharmacy, Hospital Pharmacy and the regional teams. However, the work undertaken to prepare for EU Exit identified the relevant roles and helped to establish close working practices and engage meaningfully with clinicians regarding medicines of interest. A document titled *"A guide to Managing Medicines Supply and Shortages"* was jointly published by NHS England and DHSC in November 2019 [**INQ000330790**]. The document details the national, regional and local management and escalation processes and communication routes for medicines supply issues.

71. NHS England does not have structures in place to manage the medicines supply chain or act as central procurer of stock. It has no Wholesale Distributor Authorisation (WDA) to purchase or hold medicines and does not hold the mandate to coordinate the medicines needs of the DAs or make volume commitments or purchase stock from manufacturers on their behalf.

Overview of NHS England's role in medicines supply during the pandemic

72. During the Covid-19 pandemic, NHS England took a more involved role – beyond its BAU role - in medicines supply to assist its partners, including DHSC. It took on additional activities, including measures to source additional stock in Wave 1 of the pandemic, and actions to allocate and distribute stock within the NHS, using a newly established Allocation and Distribution Group ("**ADG**") (described in more detail below) as required. NHS England worked in close partnership with DHSC and the DAs to identify priority products, manage demand across the NHS using mitigations such as the clinical advice contained within supply disruption notices, work with Royal Colleges to identify alternative treatment, source additional supplies of critical secondary care products, and support appropriate allocation and distribution across NHS organisations, including the DAs.

73. At the outset of the pandemic, NHS England recognised that supply chain pressures, global shortages and competition for scarce resources would risk supply issues for a number of vital medicines. The very nature of a global pandemic meant that there was world-wide demand for the same medicines to treat the virus (or symptoms of the virus). NHS England put in place various measures quickly and effectively to mitigate these concerns, working closely with partners. NHS England's strategic knowledge of the pharmaceutical industry and supply chains – for example, the Commercial Medicines Negotiations team, building on their experience in negotiating with industry, and CMU, with its specialist knowledge of procurement and supply – along with existing professional relationships and processes meant that it was able to source

sufficient supply of these medicines in an emergency. It also established a clinical group, working closely with frontline clinicians to help identify and update the critical medicines required for Covid-19 treatment, and put in clear governance through regional pharmacy teams to help manage allocation and distribution within the NHS.

The Medicines Cell

74. Prior to March 2020, work was undertaken in NHS England to prepare for the expected increased demand for medicines to support Covid-19 patients. Building on the EU Exit programme, work was undertaken to identify the medicines that would be required to manage Covid-19. In addition, the Commercial Medicines Team, identified possible issues in the medicine supply chain resulting from COVID-19, sourcing additional stock to meet an increased demand in patients requiring treatment and stock visibility both in the NHS and wider supply chain. In February 2020, medicine supply chain responsibilities were included in what was then the 'supply chain cell'.

75. The Covid-19 Medicines Cell was formally established in March 2020, to support the continued supply of medicines required for patients in the UK during the pandemic. It aimed to ensure that patients with Covid-19 could access Covid-19 priority medicines, through both proactive management of both the demand and supply side of those medicines across the system. The Cell formally stood down in February 2023

76. The Cell established seven key medicines workstreams in Wave 1 alongside a central programme coordination function that was a single point of contact and responsible for oversight, engagement with key internal and external partners, central reporting and drafting briefs, correspondence and any formal requests. Each workstream was led by a senior clinician or subject matter expert and had distinct purposes and objectives. The workstreams were:

    h. Communications and engagement (throughout the pandemic) - ensuring effective feedback from the NHS, stakeholder groups and clinicians and cascading information to the system as necessary.

    i. Non-Covid-19 medicines (March – June 2020) - identifying any other medicines that were at risk of shortage during the pandemic. For example, ensuring that essential medicines such as insulin were also managed effectively.

j. Trial and treatment medicines (March – June 2020) - linking to the Covid-19 Therapeutics Cell and Specialised Commissioning Cell to ensure supply of any new treatments following outcomes from clinical trials.

k. Demand and clinical guidance (March - June 2020) - - to provide clinical advice on the most appropriate medicines to manage patients with Covid-19.

l. Data and analysis (throughout the pandemic) - with oversight of the supply assessment tracker, including demand and supply analysis.

m. Medicines sourcing/wholesaler and supplier engagement - (significant programme of work at the start of the pandemic and supplier engagement throughout) – including the Sourcing Team and supplier engagement for Covid-19 priority medicines.

n. Allocation and distribution (throughout the pandemic)– to manage the supply of medicines in the NHS and with the devolved countries.

77. Given DHSC's overall responsibility for medicines supply, close working and governance arrangements were essential, not least to ensure the supply of medicines across primary and secondary care. Concurrently, DHSC identified workstreams/leads within their organisation to align with NHS England counterparts. The Medicines Cell reported into the NHS England pandemic arrangements and was not led by DHSC.

The MSRG and CMRSG

78. The MSRG was originally set up as part of EU Exit preparations, but with the intention it would become part of BAU operations to support DHSC Medicines Supply Team ("**MST**") and NHS England CMU in managing significant medicines shortages. It is a pharmacy-led cross-organisational group of senior clinicians and professionals that is part of established systems and processes for the management and mitigation of medicines supply shortages and discontinuations. It oversees high and critical impact issues and develops appropriate mitigation plans, for example changes to clinical guidance or use of products. It often draws on the expertise of relevant specialist clinical specialist advisors to make considered changes to clinical guidance or the use of products in the event of a medicine shortage. It was chaired by the Deputy Chief Pharmaceutical Officer during the pandemic and continues to operate. From June 2020, it took over Covid-19 responsibilities (as set out below) from the Covid-19

Medicines Shortage Response Group ("**CMSRG**") as it was no longer deemed necessary to have both groups running concurrently.

The CMSRG

79. During the Covid-19 pandemic, a separate, but related, group was established in May 2020 as the Covid-19 Medicines Shortage Response Group ("**CMSRG**"). It formed part of the Medicines Cell activities and it met more frequently than MSRG and its membership was widened to include specialist input on Covid-19. It replaced MSRG for all Covid-related issues and was chaired by the Chief Pharmaceutical Officer for England. It also acted as a clinically chaired decision-making body to ratify and oversee decisions of the new Allocation and Distribution Group ("**ADG**") with regard to the management of supply issues. The CMSRG ran until the end of May 2020, when all responsibilities passed to MSRG.

80. The CMSRG's main functions were to:

a. receive intelligence on supply issues that the ADG felt needed discussion and potential escalation/de-escalation;

b. commission the ADG to manage the day-to-day allocation of a specified medicine or category of medicines;

c. agree the content and dissemination routes for communications to the system, including overseeing the issuing of Medicine Supply Notifications (MSNs) / Supply Disruption Alerts (SDAs);

d. sign off management and communications plans that were brought before the group for consideration; and

e. alongside ADG, recommend any requests for Covid stockpile release or diversion, prior to sign off by the DHSC and NHS England MSSAG co-chairs.

The ADG

81. In addition to the MSRG and CMSRG, the ADG was set up in April 2020 during Wave 1 of Covid-19. This group formed part of the Medicines Cell's activities and met regularly throughout the pandemic, mainly weekly (and twice weekly at the height of the pandemic.

82. NHS England took on additional activities via the ADG, including measures to source additional stock in Wave 1 and actions to allocate and distribute stock, facilitating

central allocations to ensure equitable access (making allocations of medicines across the UK based on the Barnett Formula, and in response to the needs of local population at a regional and hospital trust level). Regular updates were provided to the CMSRG/MSRG on the current supply position, any anticipated issues and the planned mitigations to be deployed. The latest position and recommendations were also presented to MSSAG. A more detailed description of this process and how it was used when Medicines stocks were assessed as being critically low is set out below.

83. Options for mitigation of supply issues included:

a. Temporarily re-directing stockpile supply into the BAU supply chain.

b. Advising switching to alternative suppliers of the same medicine.

c. Advising switching to alternative presentations / strengths.

d. Advising on the availability of non-UK licensed imports or other unlicensed medicines available in the UK.

e. Advising switching to alternative medicines, as identified in clinical management plans.

f. Consideration of mutual aid – sharing stock between trusts within/between regions.

g. Release of permitted or preferred medicines and presentations from the Covid stockpile.

h. Regional and national allocation of medicines.

84. During Wave 1, medicines not originally destined for the UK market or unlicensed versions of products were sourced. In all cases, Quality Assurance (QA) colleagues from the NHS Specialist Pharmacy Service undertook thorough assessments to ensure the products were appropriate and safe for use. Where necessary, clinical input was sought and supporting documentation was issued prior to these medicines being made available.

85. The regional pharmacy teams provided feedback on local supply disruptions, as well as cascading national messages at a local level. They also played a crucial role in managing mutual aid between trusts, regions and the DAs.

Covid-19 Medicines Oversight Group and Medicines Supply Strategic Oversight Group

86. The purpose of the Covid-19 Medicines Oversight Group (**"CMOG"**) (established by NHS England in February 2020 and joined by DHSC in March 2020) was to provide strategic advice on the management of interdependencies and risks relating to medicines supply. The group consisted of clinical and expert staff from DHSC, NHS England, DAs, MHRA, NICE, Regional Chief Pharmacists and the NHS Specialist Pharmacy Service.

87. In August 2020 it became the Medicines Supply Strategic Advisory Group ('MSSAG') and provided a forum to bring together the different national organisations to discuss and advise on issues regarding medicines supply – work on trials and treatments supply, stockpile procurement, contingency planning and any medicines shortages response. CMOG was chaired by NHS England initially, but then jointly by both NHS England and DHSC. MSSAG still operates as a jointly chaired group.

The Sourcing Team

88. The Sourcing Team was established early on in the pandemic, prior to the establishment of the Medicines Cell, to focus on sourcing priority ITU medicines. The team included members of NHS England Commercial Medicines Negotiations team, building on their experience in negotiating with industry, and CMU colleagues, with their knowledge of procurement and supply. The Sourcing Team's initial priority was to maximise use of the normal NHS supply chain by working with existing market authorisation holders to access stock. It worked alongside the British Generic Manufacturers Association (the trade body for generics companies) to discuss:

    i. Rationalising medicines and presentations in line with the priority list of medicines

    j. Rationalising manufacturing – reduce duplication of effort between manufacturers so that they each focus on key molecules (subject to competition rules)

89. The team also met with all the major Pharmacy Wholesalers and requested they triple their stockholding of these priority ITU medicines immediately which would both support the increasing demand and also ensure suppliers would respond by increasing manufacture. Using Pharmacy Wholesalers allows NHS provider trusts to use the business as normal UK supply chain using the established national supply and logistics arrangements as much as possible and ensures hospitals have access to the stock of these priority medicines at the earliest opportunity.

90. It was immediately clear that for the majority of products on the priority list additional sources outside of the supply chain would need to be found and so the Sourcing Team needed to:

a. Identify opportunities and import these priority products from other countries

b. Work with the MHRA and NHS Quality Assurance team to create a rapid task force to ensure that these supplies meet with the required safety standards for use in the NHS

c. Work with Pharmacy Wholesalers to purchase these products for use in the NHS.

Summary of key work undertaken on medicines supply

Monitoring medicines stock – medicines supply assessment tracker

91. DHSC has overall responsibility for medicines supply, including as the lead for the supply and procurement of Covid-19 therapeutics. However, early on in the pandemic, NHS England assumed responsibility for developing the Covid-19 medicines forecast model or supply assessment tracker – initially for critical care, antibiotic and end of life care medicines (supportive medicines) and later including some therapeutic medicines once known (for England only). The Medicines Cell developed a Covid-19 priority medicines supply assessment tracker to assist in the demand and supply forecasting for the priority medicines referred to above. The tracker was reliably operational by late April 2020, when the first data pack with information on stock in hospitals, stock in wholesalers and future supplies was shared with the allocation and distribution workstream. Prior to this, NHS England only had access to hospital pharmacy stock levels (via an IT solution 'Rx-Info Exend') and top-level manufacturing data was provided by those manufacturers who supplied information to CMU. Wholesaler data took more time to come online and was critical as medicines wholesalers held most of the buffer stock in UK. Access to supply data was therefore a challenge and took several weeks to fully come onstream, but NHS England worked with wholesalers and investment was made in the wholesaler and supplier data to accelerate the work needed to secure access to the relevant data. Data sharing was established with the Healthcare Distribution Association (HDA) so that up-to-date information could be shared with Government regarding medicine stock levels within UK suppliers. By April 2020, the first CMU supplier forward view data collection was shared with NHS England's medicines analysis team, with data collected and then shared daily (and later weekly and fortnightly) and a stock tracker developed to monitor progress.

92. The above tracker contained information on stock in hospitals, stock in wholesalers and future supplies over the forthcoming 12 weeks. The forecasting relied on engagement with medicines wholesalers as well as an understanding stock in hospital pharmacies. This allowed NHS England to undertake detailed monitoring of secondary care Covid-19 medicines, i.e., medicines used to treat Covid-19 patients in ITU (supportive medicines), antibiotics, palliative medicines and some treatment medicines. The modelling had three key components:

a. Covid-19 demand for medicines – estimated by applying clinical usage assumptions to NHS England's Covid-19 bed forecast, taking account of clinically appropriate alternative medicines where relevant.

b. Non-Covid-19 demand for medicines – demand for the Covid-19 medicines for purposes other than Covid-19, estimated based on historic medicines issues data.

c. Supply – levels of available stock of medicines, both in hospital and in the supply chain (based on a bespoke data collection from suppliers/wholesalers covering stock holding and expected deliveries).

93. The analysis – initially updated weekly (and then fortnightly during the latter stages of the pandemic) acted as an early warning system that allowed NHS England and other key stakeholders to plan mitigating actions. When stocks were critically low, the modelling was adapted to determine medicine supply allocations to Trusts and DAs based on relative criticality of local stockholders.

94. NHS England's Covid-19 medicines forecast model assessed the resilience of medicines supply of the Covid-19 priority medicines under different demand scenarios (including a centrally provided 'reasonable worst-case scenario') and highlighted those at risk of supply issues. This model provided a RAG rating (Red /Amber/Amber-Green/Green) from actual weekly demand and supply data monitoring, alongside additional analysis of R/A/AG medicines that were flagged as at potential risk of shortage. A green rating was given when it was estimated that there was sufficient stock nationally for more than 12 weeks, green-amber where there could be national supply issues between 8-12 weeks, amber where could be national supply issues between 5-8 weeks and a red rating given where there could be national supply issues between 0-4 weeks, i.e. 'critically low'. A summary of that process is set out in **[INQ000409945].** Further investigation of the supply position and actual usage data was carried out by NHS England CMU, the DHSC MST and the NHS England

Medicines Analysis Team if the medicines were rated amber or red. If concerns remained regarding the supply of products, these were escalated to the ADG and a further RAG rating was given to determine whether action should be taken to address a national supply issue (Red), the issue should be escalated for discussion (Amber), the situation should be monitored for future review (Amber-Green) or no action was required (Green). Where necessary, ADG made recommendations to the MSRG on action to take, including national allocation of business-as-usual supply, issuance of clinical guidance and supply notifications, and/or release of stockpile products. Two examples of that analysis (one from December 2020 and another from June 2022) show how that process was applied at two different stages of the pandemic - [**INQ000409947** and **INQ000409946]**.

95. Outputs from the model were also included as part of the DHSC Covid-19 medicines analytical pack, the purpose of which was to bring together all medicines data across DHSC and NHS England to tell 'one single version of the truth'. This was shared across all relevant teams and individuals in DHSC, NHS England and the DAs. The pack also comprised DHSC-held information on global supply issues; current shortages; progress on procurement of the Covid-19 priority supportive medicines stockpile; stock of the potential medicines used for treatment of Covid-19; and use of primary care supportive medicines.

96. Hospital medicines stock and usage was a particular issue in the first wave of the pandemic. At the start of the pandemic NHS England had access to standardised NHS Hospital medicines stock data from an IT solution ('Rx-Info Exend') that was developed to support EU Exit. This system was rapidly further developed by the system supplier working closely with the NHS during the initial Covid-19 wave to provide stock data, automatically, on a daily basis and also to provide daily data on the issues of medicines associated with management of COVID symptoms, intensive care and end of life.

97. Clinical advice was used to understand and standardise patient level medicines needs to support modelling of stocks to ensure continuity of supply – this then supported the agreement of mitigations and allocation of stock on a UK wide basis including all the Devolved Administrations by the Allocation and Distribution workstream. Over the course of the Covid-19 response, agreements with suppliers/wholesalers were reached regarding sharing supply/stockholding information for Covid-19 priority medicines, as well as an essential contract extension with Rx-Info; access to which was a key component of managing supply and agreeing mitigations for Covid-19

priority medicines. Further system development then supported monitoring of approved Covid treatments in Hospital Hubs.

Medicines and supplier engagement

98. The medicines supply chain in the UK is highly integrated, with fewer than ten wholesalers supplying over 90% of medicines to the NHS across the four nations of the UK. The majority of ICU medicines, which were critical during the Covid-19 pandemic, came from five wholesalers. Some pharmaceutical manufacturers do not use a wholesale and distribution model, instead choosing to supply directly to Trusts, but these are in the minority. The continuity of NHS medicines supply depends heavily on the successful operation of the wholesale model. The NHS England CMU Pharmacy Supply Team worked closely with suppliers in monitoring and managing medicine supply issues throughout the pandemic. It also worked in close collaboration with the DHSC MST and the NHS SPS.

99. As set out above, NHS England does not have the structures in place to manage the medicines supply chain or act as central procurer of stock. It has no Wholesale Distributor Authorisation (WDA) to purchase or hold medicines and does not hold the mandate to coordinate the medicines needs of the DAs. There is also no single UK body to make volume commitments or purchase stock from manufacturers. However, in the pandemic NHS England saw the need to fill a critical gap in medicines supply chain management. Sourcing medicines is usually the responsibility of each DA but, given the pressures, DHSC and the DAs requested that NHS England supported UK-wide priorities and an informal agreement was put in place for NHS England to source medicines on behalf of all DAs.

100. NHS England established memoranda of understanding (MoU) with key wholesalers, setting out expectations of the supply data that would be provided to NHS England as well as the maximum mark-ups expected for priority ICU medicines. In return, and to provide the wholesalers with financial assurance to secure identified supplies, the MoU set out the conditions by which NHS England would underwrite unsold medicines stock. These financial assurances were essential to enable the wholesalers to purchase priority medicines on behalf of the NHS from manufacturers often on global markets. As NHS England could not purchase or store medicines, it instead offered 'letters of intent' to manufacturers. These were non-binding agreements that gave manufacturers assurance that their products would be used in the NHS. NHS England worked closely with the MHRA to ensure that appropriate regulatory standards were met when sourcing medicines.

101. Throughout March-May 2020, NHS England also worked with the Foreign and Commonwealth Office/Department for International Trade and several industry associations to identify and directly source priority medicines from around the world. Examples included sourcing propofol from India and noradrenaline from the USA.

102. Over the course of the Covid-19 response, NHS England reached agreements with different suppliers and wholesalers regarding sharing supply and stockholding information for Covid-19 priority medicines, as well as an essential contract extension with Rx-Info (software developer for Trust pharmacies and finance departments). Access to Rx-Info was a key component of managing supply and agreeing mitigations for Covid-19 priority medicines.

103. During Wave 1, to ensure that the UK had sufficient stock of critical priority medicines, the UK sourced medicines which were not originally destined for the UK market or were exceptionally unlicensed versions of products. In all cases, Quality Assurance ("**QA**") colleagues from the NHS SPS undertook thorough assessments to ensure the products were appropriate and safe for use. Where necessary, clinical input was sought and supporting documentation was issued prior to these medicines being made available.

104. Following the emergency response to Wave 1, DHSC wanted to prepare for further waves and sought to pre-emptively source additional supplies in anticipation. NHS England's Commercial Medicines Directorate was tasked to support DHSC to design and implement the sourcing exercise. The team had three main objectives outlined for the tender:

    a. Acquisition of the required volume of each medicine;

    b. Staying within the budgetary mandate; and

    c. Completing the tender(s) within the indicated timeframe, in preparation for an expected second wave during Winter 2020/1.

105. The final outcome of this process fulfilled these objectives. As a result of the two tenders, the required volume of each of the 49 identified medicines were acquired, with 36% of volume to be delivered within the first month of the contract and 64% within the first three months.

106. The CMU pharmacy supply team continued to work closely with suppliers in monitoring and managing medicine supply issues throughout the pandemic, working in close collaboration with the DHSC MST and the NHS SPS.

Development of clinical guidance

107. As set out above, during Wave 1 of Covid-19, NHS England worked with Royal Colleges to develop and publish clinical guidance to ensure the appropriate use of medicines and to manage demand pressures of identified products. Additionally, clinical groups fed into the NHS England medicines demand assessments for secondary care, based on actual use of medicines for Covid-19 patients and emerging evidence. These assumptions were fundamental to effective planning and were continually reviewed and updated. This included the regular meetings led by the Chief Pharmaceutical Officer for England, along with the NCD for Critical and Peri-operative Care, with colleagues from the Royal College of Anaesthetists, Faculty of Intensive Care Medicine and UK Clinical Pharmacy Association from May 2020 onwards to discuss medicines usage and potential shortages on the frontline.

Summary of NHS England's role in managing the medicines supply chain during Covid-19

108. In summary, NHS England's Medicines Cell's response to the pandemic primarily consisted of the following actions:

a. It worked with national Clinical Directors, Royal Colleges, and clinical specialists to identify over 100 Covid priority medicines required to support and treat Covid-19 patients. It developed clinical management plans for Covid priority medicines (ITU, end of life care and antibiotics), it ascertained first line medicines ('preferred medicines') and second/third line alternatives ('permitted medicines').

b. Based on these priority medicines, it developed and implemented a comprehensive Covid medicine supply forecast model and supply tracker. The modelling used the cross-government SAGE narrative scenarios, to forecast secondary care demand and supply for Covid supportive medicines in England.

c. It oversaw the allocation and distribution of limited medicines supply, including mutual aid between providers, regions and countries, and putting in place effective mitigation measurers

d. It sourced additional supportive medicines stock from medicine suppliers to support the Covid response, and informed DHSC work to procure central

stockpiles of critical Covid priority medicines as an insurance policy to mitigate the risk of insufficient supplies during future waves of the disease.

e. It worked closely with colleagues in the Specialised Commissioning and Covid-19 Therapeutics Cells from the outset to understand the latest information on trial and treatment medicines, including whether there was sufficient stock of these medicines for trial purposes as well as once the medicines had been deemed effective.

f. It maintained close engagement with industry via close supplier engagement and monitoring and regular discussions with trade associations, such as British Generic Manufacturers Association (BGMA), Healthcare Distribution Association (HDA) and the Ethical Medicines Industry Group (EMIG). This engagement included establishing data sharing with the Healthcare Distribution Association (HDA) so that, for the first time, there was up-to-date information shared regarding medicine stock levels within UK suppliers.

109. No COVID-19 priority medicine, or class of medicine, went out of stock nationally during the response, reflecting the collaboratively with government, industry and clinicians, as well the effective management in the NHS. This oversight and management of supply helped ensure that patients with COVID-19 could access the medicines they needed, when required.

110. The summary below provides an overview of some of the key actions that NHS England took in relation to particular Covid-19 priority medicines at risk of shortage (and working to support DHSC medicines supply colleagues on many others). This is a small sample of the work that was undertaken; the Decision Register details over 1,000 specific actions:

a. In April and May 2020, NHS England wrote Letters of Intent for 11 suppliers to source Covid-19 priority medicines in line with the principles agreed with the Chief Financial Officer. Fourteen additional commitments were made via email to seven suppliers to provide assurance regarding the UK purchase of Covid-19 priority medicines.

b. NHS England issued various Medicines Shortage Notices, for example levomepromazine (February 2020), noradrenaline (April 2020), propofol and midazolam (April 2020), fentanyl (May 2020), propofol (June 2020).

c. NHS England issued various Supply Disruption Notices, for example

diamorphine hydrochloride (February 2020), neuromuscular blocking agents (atracurium, cisatracurium and rocuronium) (April and updated May 2020), lorazepam (April 2020), methylprednisolone (January 2021).

d. NHS England approved Covid priority medicines stockpile releases, for example rocuronium (January 2021), midazolam (February 2021) and remifentanil (February 2022)

e. ADG advised allocations for various medicines, including for atracurium and rocuronium, propofol and tocilizumab.

Medicines supply - the role of regional pharmacists

111. The regional pharmacy teams are key to the distribution and supply of medicines throughout the UK and were critical to the distribution of medicines during the Covid-19 response. They support trusts in the procurement of medicines, working closely with suppliers to issues such as shortages, as well as providing advice on the use of medicines.

112. During the pandemic, the regional pharmacy teams provided feedback on local supply disruptions, as well as cascading national messages at a local level. They also played a crucial role in managing mutual aid between Trusts, regions and the DAs.

Community Pharmacy

113. When the Covid-19 pandemic first began to peak in England, community pharmacies across the country saw increased demand for medicines and healthcare advice. NHS England provided necessary support to pharmacies to enable them to remain open where possible so that they could continue to provide medicines to their local communities.

114. Community pharmacies in England provide services under the NHS Community Pharmacy Contractual framework (CPCF). Services sit within the following categories:

a. Essential services – these are provided by all pharmacy contractors under a clinical governance framework that includes clinical audit and information governance requirements.

b. Advanced services – which can be provided by all contractors once accreditation requirements have been met and are commissioned by NHS

England.

c. Locally commissioned services – these are local public health services commissioned mostly by local authorities. CCGs/ICSs may also commission local services from community pharmacy to meet the needs of their patients.

115. While pharmacy contractors must provide Essential services, they can choose whether they wish to provide Advanced and Enhanced services.

116. Community pharmacy is often the first point of contact for patients. NHS England encouraged pharmacies to extend their opening hours to cope with the initial significant increase in workload. Pharmacies also provided a delivery service to all patients who were shielding or considered to be at high risk for Covid-19.

117. To ensure that pharmacies complied with social distancing, the Chief Pharmaceutical Officer for England, and NHS England Director of primary care strategy, wrote to pharmacists indicating that they would give all pharmacies a £300 payment to support the installation of physical barriers, such as screens and retractable tape barriers or other adjustments to help enforce social distancing.

118. NHS England provided a range of PPE to pharmacies and on 9 March 2020 advised community pharmacies that gloves, aprons and fluid repellent face masks should be ordered via wholesalers in small quantities, with the intention of being used by staff (i.e., not to be sold to the public).

119. NHS England recognised that stores needed to close when staff were unavailable to work. To mitigate the consequences of this, they asked pharmacies to notify them immediately if they were going to close the pharmacy and asked that the pharmacy's NHS 111 directory services profile was updated accordingly. NHS England also encouraged the use of "buddy arrangements" to help encourage local pharmacies to maintain continuity of service.

120. On 29 September 2021 NHS England announced that to help provide support to people who have been notified of the need to self-isolate by NHS Test and Trace, the Community Pharmacy Home Delivery Service – an NHS funded service - was to be commissioned from 1 October 2021 to 31 March 2022 (inclusive) for anyone living in England who has been notified by NHS Test and Trace to self-isolate. Pharmacies across England were required to ensure that those people who had been requested

by NHS Test and Trace to self-isolate could receive their prescription medicines and appliances by home delivery during the ten-day self-isolation period, if they were unable to arrange for medicines to be picked up.

121. Alongside those arrangements, from 16 March 2021 to 30 September 2021 people who had been notified to self-isolate by NHS Test and Trace and provided with a unique Test and Trace ID number were able to access support for the delivery of their prescription items.

122. These services also built on pre pandemic Essential and Advanced Services that predated the commissioning of the NHS Home Delivery Service, under which community pharmacies and dispensing doctors already provided "backstop deliveries" to patients who had no family or carers who could collect prescriptions

Reflections on NHS England's role in medicines supply

123. There were a number of lessons learned in both preparing for and responding to the pandemic in respect of medicines supply. NHS England has been able to build on this learning as we continue our BAU work on medicines supply and future resilience of the medicines supply chain. These are summarised below:

a. Governance and collaboration. Clearly agreed and defined aims of the Medicines Cell were essential, and the importance of adjusting these as different waves evolved. Collaboration and coordination across several NHS England teams was important, along with the Specialist Pharmacy Service - and also DHSC colleagues - to take on different roles to support the pandemic response outside day-to-day and traditional responsibilities. There were occasions where NHS England had to step outside its usual areas of responsibility. Providing early clarity on roles between DHSC and the NHS – including where they may be shared – would have been helpful.

b. Clinical engagement. Developing and publishing clinical guidance that had been agreed with clinicians, professional bodies and Royal Colleges, to ensure the appropriate identification of and management of demand pressures on identified critical products, was important. Regular engagement with the Royal Colleges and frontline clinicians regarding the pandemic response and how NHS England could best support shortages worked well. Input from the NHS England national clinical group that advised on the most appropriate Covid priority medicines (including alternatives) meant that the relevant cells and groups could always look ahead to

what the next best medicines might be within a class should the first one look to be in short supply.

c. Demand and supply modelling, and supply chain information. Developing medicines demand assessments based on Covid-19 planning to support the effective management and mitigation to potential disruptions in priority medicines was central to the successful management of medicines by forecasting expected usage. The team based the models on BAU usage data and usage profiles across different patient demographics, although central planning assumptions were often difficult to access. Additionally, the use of standardised structured data was essential and beneficial (e.g., using the dictionary of medicines and devices). There are many BAU opportunities that would be directly helped by systematic adoption of this approach going forwards.

d. Industry engagement. Sourcing and securing medicines is a very different model than for other NHS product procurements. It was essential to have a team who knew the market and how to engage effectively with providers. Investing substantial additional capacity in improving data and information on the supply chain (focused on critical care, antibiotics and end of life care medicines) to inform decision-making was critical and enabled NHS England to model supply against likely demand so that it could better flag where shortages might occur. It has been useful to have developed the understanding and robustness regarding hospital pharmacy stocks with access to live data to inform decision-making.

e. Allocation and distribution. The newly established function to develop and run a national allocation process for limited supplies of particular medicines to Trusts and the DAs was a key part of the process to ensure that Covid-19 patients did not go without the medicines they needed. This function is now dormant but could be stood up again should this be required. Decisions were informed to a great extent by the daily (and then weekly and fortnightly) data packs which gave a weekly update on the medicines and medicine groups at risk of shortage and were an excellent resource. Joint working with DHSC regarding the development of processes for drawing down of the Covid-19 supportive medicines stockpile worked well and can easily be built upon for any future release of medicines from Government-held stockpiles.

f. Communication. The cell worked collaboratively and successfully with a wide range of clinicians and numerous professional bodies to produce guidance regarding medicine formularies and medicine management, as well as regularly updating the

Medical Directorate SMT and supporting webinars for clinicians, Royal Colleges and the system.

ANNEX 4: Medicines Groups

Further information and context is set out below on cells and groups of particular relevance to SECTION 2, specifically:

1. Commercial Medicines Unit
2. Covid Therapeutics Cell
3. Medicines cell
4. Medicines Supply Strategic Advisory Group ('MSSAG')
5. Medicine Shortage Response Group ('MSRG')
6. Covid Medicines Shortage Response Groups ('CMSRG')
7. Allocation and Distribution Group

Commercial Medicines Unit

The CMU unit existed before Covid; it was instrumental in the management of medicines during the pandemic. It is predominantly responsible for the management of national framework agreements for the procurement of medicines and homecare services by hospitals in England. Any supply issues for products on a framework were reported directly to the team by manufacturers and suppliers, or by pharmacy procurement teams. The team managed supply issues in close collaboration with the DHSC Medicines Supply Team and the Specialist Pharmacy Service medicines information function and the Regional Pharmacy Procurement Specialists and other stakeholders, seeking their advice and support on potential management options.

The CMU was also responsible for coordinating operational management of supply problems for medicines procured for hospitals on CMU frameworks. For Covid priority medicines, an enhanced process was followed to manage shortages and mitigate potential shortages. Supply issues or shortages were identified by:

- Ongoing monitoring – the data and analysis team developed long-term demand and supply modelling data and also provided twice weekly updates identifying medicines where supply issues were expected.

- Regional intelligence – National Delivery Group input from regional chief pharmacists and regional pharmacy procurement specialists
- Suppliers and wholesalers – through the supply workstreams engagement with suppliers and wholesalers

Covid Therapeutics Cell

This cell co-ordinated the significant clinical access policy work undertaken on behalf of the UK to determine access to evidence-based Covid-19 therapies. Working closely with RAPID C-19, DHSC's therapeutic and antiviral taskforces, and the CMO's office to ensure a single point of UK sign-off, the cell worked closely with expert clinical and academic advisors, DHSC on Covid-19 medicines procurement and supply, and with the MHRA to enable the rapid publication of interim policy through the CAS alert system.

By Summer 2021, with the anticipated arrival of new oral antiviral treatments, the cell had also taken on a national leadership role for the roll out of community based Covid-19 treatments, working alongside local systems on the specification and rapid establishment of CMDUs, a key part of the ongoing pandemic response at the point at which the Omicron variant was emerging.

Coming out of the pandemic, the determination of routine access to Covid-19 treatments in the NHS has reverted to the NICE technology appraisal system.

Medicines cell

The Covid-19 Medicines Cell was formally established in March 2020 to support the continued supply of medicines required for patients in the UK during the pandemic. It aimed to ensure that patients were able to access COVID-19 priority medicines, through modelling and management of use and supply of those medicines, including sourcing of medicines from the global supply chain and allocation and distribution for England and the DAs. Workstreams were led by pharmacist, analyst and policy and strategy professionals from across the organisation. The cell operated in the context of DHSC's overall responsibility for medicines supply (including sourcing and stock management), and close working arrangements were in place to ensure access to medicines across primary and secondary care. The cell formally stood down in February 2023 as the medicines management activities returned to 'Business as Usual' (BAU) activities.

The medicines cell was predominantly formed using the resource of BAU teams in medicines policy, pharmacy and analysis (including Specialised Commissioning, Medicines Policy Unit

and Medicines Analysis Team and Hospital Pharmacy Team colleagues and Medicine Supply (including CMU) and communications, and the NHS Specialist Pharmacy Service (SPS)). Clinical oversight was provided by the NCD for Critical Care and the Office of the Chief Pharmaceutical Officer. From June 2020 (following Wave 1), most medicine supply colleagues working within the cell moved back to their BAU roles, which then included the monitoring and management of COVID-19 medicines. Cell activity was coordinated by a team within the Medicines Policy Unit.

Medicines Supply Strategic Advisory Group ('MSSAG')

The MSSAG was formerly known as the Covid Medicines Oversight Group (CMOG). It was established in August 2020. The purpose of this group was to provide strategic advice on the management of interdependencies and risks relating to medicines supply. The group consisted of clinical and expert staff from DHSC, NHS England, DAs, MHRA, NICE, Regional Chief Pharmacists and the NHS Specialist Pharmacy Service. CMOG (from February to August 2020 and joined by DHSC in March 2020), and then MSSAG, provided a forum to bring together the different national organisations to discuss and advise on issues regarding medicines supply - work on trials and treatments supply, stockpile procurement, contingency planning and any medicines shortages response. CMOG was chaired by NHS England initially, but then jointly by both NHS England and DHSC. MSSAG still operates.

Medicine Shortage Response Group ('MSRG')

The 'MSRG' acted as a clinically chaired decision-making body to ratify and oversee decisions of the **Allocation and Distribution Group and** support the DHSC Medicines Supply Team and NHS England Commercial Medicines Unit ('CMU') with the management of supply issues of high (tier 3) or critical (tier 4) impact. The Medicines Supply Strategic Advisory Group ('MSSAG') agreed the role of the MSRG in overseeing the development of appropriate mitigation plans for managing shortages and discontinuations.

The MSRG escalated matters to EPRR where necessary for tier 3 and 4 shortages. It also provided advice on communications content and dissemination. It commissioned the NHS England Medical Directorate to obtain clinical advice on medicines supply issues (in addition to the information provided by the UK Medicines Information). It also advised whether the development of Serious Shortage Protocol would be beneficial to help mitigate a shortage and provided a recommendation to the National Medical Director and Chief Pharmaceutical Officer on this basis. The NMD and CPO then provided a final recommendation to Ministers.

This group evaluated the medicines position and then ratified recommendations from ADG where appropriate. The MSRG commissioned ADG to progress the agreed mitigating actions.

Covid Medicines Shortage Response Groups ('CMSRG')

During Covid, an extra allocation and distribution group was set up to manage the distribution of medicines where there were shortages of Covid-priority medicines. The MSRG was focused on BAU shortages, whereas the COVID Medicines Shortage Response Group ('CMSRG') focused on the close management of priority medicines.

The functions of the group were delegated to the MSRG by NIRB. The CMSRG operated under the remit of the MSRG and provided regular updates to the MSRG on the current supply position along with any anticipated issues and the planned mitigations to be deployed.

The CMSRG acted as a clinically chaired decision-making body appointed to oversee the management of Covid priority medicines shortages. In addition, it carried out the following roles:

1) to receive intelligence on supply issues that the COVID Medicines Allocation & Distribution Group feel needs discussion and potential escalation/de-escalation.

2) to determine and oversee escalation and de-escalation for Tier 3 shortages, and any Tier 2 issue that COVID Medicines Allocation & Distribution Group feel require referral to MSRG;

3) to commission the COVID Medicines Allocation & Distribution Group to manage the day-to-day allocation of a specified medicine or category of medicines;

4) to ensure sufficient clinical advice has been obtained, commissioning additional advice from the COVID Medicines Clinical Group where needed;

5) to agree the content and dissemination routes for communications to 'the system', including overseeing the issuing of MSNs/SDAs;

6) to sign off management and communications plans that are brought before the group for consideration; and

7) to share decisions with the National Medical Director (and nominated DA representatives where appropriate) for final sign-off.

Allocation and Distribution Group

The 'ADG' managed stockpile release and allocations of medicines in short supply to secondary and primary care as appropriate. It also identified and considered options to address BAU supply shortages and made recommendations to MSRG. This included recommending release of medicines from Covid, PIPP and EMBS stockpiles. Where stockpile release was agreed by DHSC and NHS England, ADG managed the release and the allocation of the medicines into the supply chain.

This group evaluated what action needed to be taken to mitigate against and manage medicine shortages. Recommendations were then presented to MSRG for ratification.

ANNEX 5: Table of medicines groups meetings

Frequency	Group/Team/ Cell
Daily	1. IMT 2. Rapid-C19 Delivery Group
More than once a week	1. Allocation and Distribution group. A&DG was set up in April 2020 and has been re-operationalised to meet current needs. The group will operate under the remit of the clinically chaired, cross-organisational Medicines Shortage Response Group (MSRG) and provided regular updates to it on the medicines supply position, any anticipated issues and the planned mitigations to be deployed. 2. Rapid C-19
Weekly	1. Covid-19 workstream leads 2. Covid-19 supply pillar leads 3. Medicine supply coordination meeting 4. Tactical fusion 5. Weekly review of amber/red medicines 6. Rapid-C19 7. Covid-19: Supply and Information
Fortnightly	1. EU Exit steering group 2. UK medicine supply working 3. Medicines Supply Strategic Advisory Group (MSSAG) 4. Covid-19 medicines supply 5. Medicines Shortage Response Group
As required	1. Medicines Resilience Planning Meeting 2. Medicines Supply Privy Council

ANNEX TWO: List of priority medicines (supportive and Covid-19 therapeutics)

Covid-19 Priority Medicines (Supportive) (as at June 2022)

The Medicines Cell brought together a National Clinical Group comprised of a group of senior specialist clinicians and specialist pharmacists to establish priority medicines lists[9] for Covid-19 patients for critical care, end of life care and antibiotics, including preferred presentations – please see below. This information was used to assess the demand for these medicines under reasonable worse case scenarios on accordance with DHSC assumptions. Set alongside information on stocks in the UK and planned deliveries, NHS England was able to provide estimates of how long supplies would last, allowing mitigations to be put in place.

Critical Care Medicines

Medicines group	Lead medicines	Alternative medicines
Antipyretics	Paracetamol	-
Electrolytes - Magnesium Sulphate	Magnesium Sulphate	-
Electrolytes - Potassium Chloride	Potassium Chloride	-
Insulin	Insulin	-
Neuromuscular Blocking Agents – Maintenance	Rocuronium	Atracurium, Cisatracurium, Pancuronium
Neuromuscular Blocking Agents – Intubation	Rocuronium	Suxamethonium
Opioids - Anaesthesia – Continuous	Remifentanil	-
Opioids - Anaesthesia – Induction	Fentanyl	-
Opioids – Continuous	Alfentanil	Fentanyl, Morphine
Sedatives – Continuous	Propofol	Midazolam
Sedatives – Continuous Supportive	Clonidine	Dexmedetomidine
Sedatives – Intubation	Propofol	Thiopental
Stress Ulcer Treatment – Proton Pump Inhibitor	Pantoprazole	*Clinical alternatives exist but not included in modelling*
Thromboprophylaxis/ Anticoagulation for Continuous Renal Replacement Therapy (CRRT) / Extra Corporeal Membrane Oxygenation (ECMO)	Dalteparin	Enoxaparin, Tinzaparin, Heparin
Vasopressors and inotropes – Adrenaline	Adrenaline	-
Vasopressors and inotropes – General	Noradrenaline	Metaraminol
Vasopressors and inotropes – Other	Argipressin	-

Palliative Care medicines

[9] Additionally, a primary care priority medicines list and self-care medicines list (over the counter medicines) were also developed with relevant clinicians, although these were then passed to DHSC to manage. The primary care priority medicines and self-care medicines lists are not included in this Annex.

Medicines group	Lead medicines	Alternative medicines
Antipsychotic - Injection	Haloperidol	Levomepromazine
Antipsychotic - Oral	Haloperidol	Levomepromazine
Antipyretic	Paracetamol	-
Anxiety - Type 1	Lorazepam (oral)	-
Anxiety - Type 2	Midazolam	-
Opioids - Modified Release	Morphine	Oxycodone
Opioids - Subcutaneous	Morphine	Oxycodone
Opioids	Morphine	Oxycodone
Secretions/Colic	Hyoscine butylbromide	Glycopyrronium

Antibiotics

Medicines group	Lead medicines	Alternative medicines
Hospital Acquired Pneumonia (HAP) Methicillin-resistant Staphylococcus aureus (MRSA) Dual Therapy – Intravenous	Teicoplanin	Vancomycin, Linezolid
HAP MRSA Dual Therapy – Oral	Linezolid	*Clinical alternatives exist but not included in modelling*
HAP Severe/Ventilator Associated Pneumonia (VAP)/Sepsis	Piperacillin/Tazobactam	Ceftazidime, Levofloxacin, Meropenem
HAP Non-severe – Oral	Co-amoxiclav	Doxycycline, Co-trimoxazole, Levofloxacin
CAP Moderate/Severe – Intravenous	Cefuroxime	Levofloxacin
CAP Moderate/Severe - Oral	Doxycycline	Levofloxacin
CAP Moderate/Severe Dual Therapy - Med 1 – Intravenous	Clarithromycin	*Clinical alternatives exist but not included in modelling*
CAP Moderate/Severe Dual Therapy - Med 2 – Intravenous	Co-amoxiclav	*Clinical alternatives exist but not included in modelling*
CAP Moderate/Severe Dual Therapy - Med 1 – Oral	Co-amoxiclav	*Clinical alternatives exist but not included in modelling*
CAP Moderate/Severe Dual Therapy - Med 2 – Oral	Clarithromycin	*Clinical alternatives exist but not included in modelling*

Covid-19 Treatment/Therapeutic Medicines (as at June 2022)

One of the biggest clinical challenges at the start of the pandemic was how to treat worsening symptoms of Covid-19. There were no known effective therapeutics for Covid-19. The research community rapidly focussed efforts to find treatments for Covid-19 and the results of these clinical trials informed the analysis undertaken to determine supply and usage of relevant medicines once confirmed as effective.

The Covid-19 therapeutics listed in the table below were used in a hospital setting:

Medicines group	Lead medicine	Alternative medicines
Corticosteroids – Intravenous	Hydrocortisone Intravenous	Dexamethasone Intravenous
Corticosteroids – Solution	Dexamethasone oral solution	
Corticosteroids – Oral	Dexamethasone tablets	
Antiviral	Remdesivir	
Baricitinib	Baricitinib	
Interleukin-6 inhibitors	Tocilizumab	Sarilumab

The Covid-19 therapeutics listed in the table below were used in community settings. These treatments were delivered by CMDUs, and use tracked using the Foundry platform and through the COVID-19 Therapeutics Programme, working with DHSC's Covid-19 Antivirals and Therapeutics Taskforce:

Medicines group	Lead medicine	Alternative medicines
Monoclonal antibodies	Casirivimab/imdevimab (Ronapreve)	
	Sotrovimab	
Antiviral	Nirmatrelvir/ritonavir (Paxlovid)	
	Remdesivir	
	Molnupiravir	

ANNEX THREE: Therapeutics chronology

Date	Event
31 January 2020	DHSC Medicines Supply Team and NHS England EPRR Team ask NHS England's CMU to identify "a list of 'supportive' medicines which UK hospitals should have in stock to support the treatment of patients with Covid-19 (it was assumed that these will largely be medicines that treat respiratory conditions). Key things that were required to be identified were: •What medicines should be on this supportive medicines list •What volume of these medicines will be needed? Once they have this information, the DHSC Medicines Supply Team and NHS England's CMU can engage with suppliers providing these supportive medicines to identify their stock and try to secure adequate supply
February 2020	CMOG established.
3 February 2020	CAS Alert Advice for primary care and community settings including pharmacy This alert highlights the advice for primary care and pharmacies relating to the evolving situation regarding the novel coronavirus (2019-nCoV).
11 February 2020	Covid-19 supportive medicines list finalised by NHS England's Head of Medicines and Diagnostics Policy Unit and shared with the dCPO. This was a list of products required by NHS acute organisations managing cases of UK patients presenting with Covid-19.
17 February 2020	CAS Alert This alert addresses recent concern about the use of non-steroidal anti-inflammatory medications (NSAIDs) in relation to Covid-19.
28 February 2020	Covid-19 Self Care Medicines list shared with DHSC and NHS England Clinical Cell by NHS England Medicines and Diagnostics Policy Unit
March 2020	RECOVERY trial established.
3 March 2020	NHS England published 'Clinical management of persons admitted to hospital with suspected Covid-19 infection'.
9 March 2020	Specialised Services Cell established.
11 March 2020	NHS England asked NICE to produce guidelines on Covid-19 topics at pace.
13 March 2020	NHS England commissioned the first three Covid-19 rapid guideline topics from NICE
20 March 2020	NICE published first guidelines.
23 March 2020	Collaboration between NHS England, NICE, MHRA, NIHR initiated by NHS England's Medical Director Specialised Services NHS England
30 March 2020	The Chief Pharmaceutical Officer wrote to all NHS Trusts to confirm that products should only be used for their licensed indications and potential treatments should only be used in a clinical trial setting.

April 2020	PRINCIPLE trial commenced. ADG established. First CMU supplier forward view data collection was shared with NHS England's medicines analysis team
1 April 2020	CAS alert sent by England's CMO encouraging NHS bodies to enrol Covid-19 patients in the national priority clinical trials.
1 April 2020	Confirmation of antibiotics to be added to the Covid-19 supportive medicines list sent by the Medicines Cell.
3 April 2020	First meeting of RAPID-C19.
17 April 2020	DHSC finance approval to spend up to £45m for Covid-19 therapeutic medicines.
30 April 2020	Guidance published on priority medicines, advising on available alternatives and substitute availability. Developed in conjunction with NHS England.
May 2020	REACT study established. CMSRG established.
5 May 2020	RAPID C-19 Oversight Group considered hydroxychloroquine.
6 May 2020	Letter issued encouraging hospitals to enrol patients in clinical trials.
14 May 2020	RAPID C-19 Oversight Group considered azithromycin.
14 May 2020	RAPID C-19 Oversight Group deprioritised convalescent plasma.
18 May 2020	RAPID-C19 to develop a process to ensure that treatment medicines are distributed appropriately, working with regions and the other UK nations.
26 May 2020	CAS Alert indicating: • a positive scientific opinion for remdesivir; and • hospitals who have registered an interest in participating in EAMS can apply for access to remdesivir for eligible patients.
27 May 2020	RAPID C-19 Oversight Group again considered hydroxychloroquine.
16 June 2020	CAS Alert indicating: • dexamethasone demonstrated to have a clear place in the management of hospitalised patients with Covid-19; and • clinicians should consider dexamethasone for the management of hospitalised patients with Covid-19 who require oxygen or ventilation.
3 July 2020	Interim clinical commissioning policy put in place to define routine access to remdesivir in the treatment of Covid-19 across the UK.
13 July 2020	RAPID C-19 decided to monitor convalescent plasma
August 2020	CMOG becomes MSSAG.
14 August 2020	RAPID C-19 Oversight Group considers ivermectin.

18 August 2020	CAS Alert indicating: • Over 110,000 UK participants enrolled in Covid-19 urgent public health research supported by the NIHR and its devolved nations equivalents; • RECOVERY will continue to be supported as the national clinical trial platform for Covid-19 phase III therapeutics trials.
3 September 2020	CAS Alert indicating corticosteroids, and in particular dexamethasone and hydrocortisone, have been demonstrated to have a place in the management of patients with Covid-19. CAS Alert indicating an interim clinical commissioning policy for remdesivir for patients hospitalised with Covid-19 (adults and children aged 12 years and older).
October 2020	NHSE National clinical group re-convene to review ITU medicines clinical management plans on Covid-19 supportive medicines list
21 October 2020	RAPID C-19 Oversight Group considers ivermectin.
25 November 2020	CAS Alert indicating publication of an interim position statement for tocilizumab for patients admitted to ICU with Covid-19 pneumonia (adults).
2 November 2020	Approval for revised remdesivir clinical commissioning policy
15 December 2020	CAS alert recommending that azithromycin should not be used to treat patients hospitalised with Covid-19.
2 January 2021	CAS Alert indicating that antimicrobials (azithromycin and doxycycline) are not beneficial in the management of Covid-19 positive patients.
6 January 2021	RAPID C-19 Oversight Group determined ivermectin should continue to be monitored for meta-analysis results.
13 January 2021	RAPID C-19 decided to continue to monitor convalescent plasma.
20 January 2021	RAPID C-19 decided to continue to monitor convalescent plasma.
3 February 2021	RAPID C-19 considered tixagevimab and cilgavimab (Evusheld).
4 February 2021	CAS Alert indicating an interim clinical commissioning policy for tocilizumab for critically ill patients with Covid-19 pneumonia (adults) - tocilizumab is recommended to be available as a treatment option through routine commissioning for adult patients (aged 18 years and older) hospitalised with Covid-19 in accordance with the criteria set out. Also an interim clinical commissioning policy for sarilumab for critically ill patients with Covid-19 pneumonia (adults) - sarilumab is recommended to be available as a treatment option through routine commissioning for adult patients (aged 18 years and older) hospitalised with Covid-19.
17 February 2021	CAS Alert indicating interim clinical commissioning policies for: • tocilizumab for hospitalised patients with Covid-19 pneumonia (adults) • sarilumab for critically ill patients with Covid-19 pneumonia (adults)
11 March 2021	RAPID C-19 Oversight Group determined ivermectin should continue to be monitored for meta-analysis results.
11 March 2021	RAPID C-19 decided to wait for full results before taking a decision to stand down convalescent plasma.

17 March 2021	RAPID C-19 Oversight Group determined ivermectin should continue to be monitored for meta-analysis results.
17 March 2021	CAS Alert indicating no significant clinical benefit from treatment with high-titre convalescent plasma in patients hospitalised with Covid-19.
28 April 2021	RAPID C-19 Oversight Group determined ivermectin should continue to be monitored for meta-analysis results.
5 May 2021	RAPID C-19 Oversight Group considered hydroxychloroquine.
2 June 2021	RAPID C-19 Oversight Group determined ivermectin should continue to be monitored for meta-analysis results.
14 June 2021	CAS Alert indicating interim clinical commissioning policy for remdesivir for patients hospitalised with Covid-19 (adults and children 12 years and older) Version 3.
11 August 2021	RAPID C-19 Oversight Group determined ivermectin should continue to be monitored for meta-analysis results.
25 August 2021	Preparation for COVID-19 antivirals deployment.
12 September 2021	CAS Alert indicating interim clinical commissioning policy for IL-6 inhibitors (tocilizumab or sarilumab) for hospitalised patients with Covid-19 (adults).
17 September 2021	CAS Alert indicating interim clinical commissioning policy for casirivimab and imdevimab for patients hospitalised due to Covid-19.
13 October 2021	RAPID C-19 Oversight Group determined to monitor tixagevimab and cilgavimab (Evusheld).
4 November 2021	CAS Alert indicating interim clinical commissioning policy for casirivimab and imdevimab in the treatment of Covid-19 in hospitalised patients.
24 November 2021	RAPID C-19 Oversight Group determined to continue to monitor tixagevimab and cilgavimab (Evusheld).
December 2021	COVID Medicines Delivery Units established.
8 December 2021	CAS Alert indicating interim clinical commissioning policy for neutralising monoclonal antibodies or antivirals for non-hospitalised patients with Covid-19.
8 December 2021	RAPID C-19 Oversight Group suggested advice should be prepared for the CMO on tixagevimab and cilgavimab (Evusheld).
14 December 2021	CAS Alert indicating interim clinical commissioning policy for withdrawal of the Recommendation for Consideration of Inhaled Budesonide as a Treatment Option for Covid-19.
16 December 2021	CAS Alert indicating interim clinical commissioning policies for: • Neutralising monoclonal antibodies or antivirals for non-hospitalised patients with Covid-19; and • Neutralising monoclonal antibodies in the treatment of Covid-19 in hospitalised patients
24 December 2021	CAS Alert indicating interim clinical commissioning policy for neutralising monoclonal

	antibodies and intravenous antivirals in the treatment of Covid-19 in hospitalised patients.
27 January 2022	CAS Alert indicating interim clinical commissioning policy for antivirals or neutralising monoclonal antibodies in the treatment of Covid-19 in hospitalised patients (Version 5).
31 January 2022	CAS Alert indicating interim clinical commissioning policy for IL-6 inhibitors (tocilizumab or sarilumab) for hospitalised patients with Covid-19 (adults).
24 February 2022	CAS Alert indicating interim clinical commissioning policy for: • antivirals or neutralising monoclonal antibodies for non-hospitalised patients with Covid-19 (Version 5); and • antivirals or neutralising monoclonal antibodies in the treatment of hospital-onset Covid-19 (Version 6).
26 April 2022	RAPID C-19 submitted brief to the CMO on tixagevimab and cilgavimab (Evusheld).
5 May 2022	CAS Alert indicating interim clinical commissioning policy for baricitinib for patients hospitalised due to Covid-19 (adults and children aged 2 years and over).
18 May 2022	RAPID C-19 decided to update CMO advice on tixagevimab and cilgavimab (Evusheld).
19 May 2022	RAPID C-19 concludes that ivermectin only be used to treat Covid-19 in ongoing well-conducted clinical trials.
25 May 2022	RAPID C-19 submitted further brief to the CMO on tixagevimab and cilgavimab (Evusheld).
30 May 2022	CAS Alert indicating interim clinical commissioning policies for: • Antivirals or neutralising monoclonal antibodies in the treatment of hospital-onset Covid-19 (Version 7); and • Antivirals or neutralising monoclonal antibodies for non-hospitalised patients with Covid-19 (Version 6).

ANNEX FOUR: List of clinical guides on NHS England's website on 27 May 2020

Coronavirus treatment

Title	Date published/updated
Management of persons admitted to hospital with suspected COVID-19 infection	19-Mar-20
Guidance for the role and use of non-invasive respiratory support in adult patients with coronavirus (confirmed or suspected)	06-Apr-20

Adult critical care

Title	Date published/updated
Clinical guide for use of anaesthetic machines to provide continuous invasive ventilatory support for adult patients during the coronavirus pandemic	29-Apr-20
Clinical guide for the management of stroke patients during the coronavirus pandemic	16-Apr-20
Clinical guide for renal replacement therapy options in critical care during the coronavirus pandemic (amended version)	15-Apr-20
Clinical guide for extra corporeal membrane oxygenation (ECMO) for respiratory failure in adults during the coronavirus pandemic	10-Apr-20
Clinical guide for the optimal use of oxygen therapy during the coronavirus pandemic	09-Apr-20
Management of critical care patients	09-Apr-20
Critical care and anaesthesia service reorganisation	17-Mar-20
Principles for increasing the nursing workforce in response to exceptional increased demand in adult critical care	25-Mar-20
Clinical guide to adult critical care during the coronavirus pandemic: staffing framework	01-Apr-20
Clinical guide for the management of surge during the coronavirus pandemic: critical care rapid learning	16-May-20

A&E

Title	Date published/updated
Management of emergency department patients	17-Mar-20
Reference guide for emergency medicine	22-Apr-20

Medicine

Title	Date published/updated
Clinical guide for acute kidney injury in hospitalised patients with COVID-19 outside the intensive care unit during the coronavirus pandemic	22-Apr-20

Management of acute diabetes patients	19-Mar-20
Management of non-coronavirus patients requiring acute treatment: general and internal medicine	20-Mar-20
Management of rheumatology patients	14-Apr-20
Management of cardiology patients	20-Mar-20
Management of ophthalmology patients	23-Mar-20
Provision of tuberculosis services	26-Mar-20
Management of respiratory patients	26-Mar-20

Cancer

Title	Date published/updated
Management of non-coronavirus cancer patients	23-Mar-20
Management of proton beam referrals	03-Apr-20

Surgery

Title	Date published/updated
Clinical guide for the management of urgent and emergency spinal surgical patients during the coronavirus pandemic	15-Apr-20
Management of trauma and orthopaedic patients	14-Apr-20
Management of neuro trauma patients	14-Apr-20
Clinical guide to surgical prioritisation during the coronavirus pandemic	11-Apr-20
Management of general surgical patients	16-Mar-20
Management of cardiothoracic surgery patients	20-Mar-20
Management of patients requiring plastics surgery treatment	20-Mar-20
Management of vascular surgery patients	20-Mar-20
Management of patients requiring spinal surgery	20-Mar-20
Management of patients requiring oral and maxillofacial surgery	23-Mar-20
Perioperative care of people with fragility fractures	26-Mar-20
Management of major trauma patients	27-Mar-20
Management of acute burns patients	17-Mar-20
Clinical guide for open foetal surgery to treat foetuses with open spina bifida during the coronavirus pandemic	01-Apr-20

Children

Title	Date published/updated
Clinical guidelines for children and young people with palliative care needs in all care settings during the COVID19 pandemic	24-Apr-20
Management of paediatric patients	17-Mar-20
Management of paediatric critical care patients	26-Mar-20

Coronavirus: Parent information for newborn babies	08-Apr-20
Illness in newborn babies	08-Apr-20

Obs and Gynae

Title	Date published/updated
Clinical guide for the temporary reorganisation of intrapartum maternity care during the coronavirus pandemic	09-Apr-20
ICON for midwives during the coronavirus pandemic	02-Apr-20
ICON letter for midwives	02-Apr-20
ICON Poster	27-Mar-20

Radiology

Title	Date published/updated
Management of Radiology patients	20-Mar-20

Palliative care

Title	Date published/updated
Clinical guide for supporting compassionate visiting arrangements for those receiving care at the end of life	11-May-20
Management of palliative care in hospital during the coronavirus pandemic	22-Apr-20

Musculoskeletal

Title	Date published/updated
Urgent and emergency musculoskeletal conditions in children (under 16) requiring onward referral	14-Apr-20
Management of patients with musculoskeletal and rheumatic conditions on corticosteroids	25-Mar-20
Urgent and emergency musculoskeletal conditions requiring onward referral	23-Mar-20

Other

Title	Date published/updated
Principles for increasing the nursing workforce in response to exceptional increased demand in adult critical care	25-Mar-20
Management of patients with a learning disability, autism or both	24-Mar-20
Management of patients with a learning disability, autism or both: Easy read	01-Apr-20

Clinical guide for the management of remote consultations and remote working in secondary care during the coronavirus pandemic	27-Mar-20
Management of patients requiring immunoglobulin treatment	31-Mar-20
Clinical guide for the management of anticoagulant services during the coronavirus pandemic	01-Apr-20
Clinical guide for the management of patients requiring transfer for specialist rehabilitation during the coronavirus pandemic	06-Apr-20
Clinical guide for the management of patients requiring endoscopy during the coronavirus pandemic	06-Apr-20
Clinical guide for the management of people with alcohol dependence during the coronavirus pandemic	08-Apr-20
NHS e-Referral Service – guidance to help providers manage referrals during the coronavirus pandemic	04-May-20

ANNEX FIVE: Larger versions of charts

Figure 2: Chart showing reported and modelled use of tocilizumab from April 2022 to October 2022

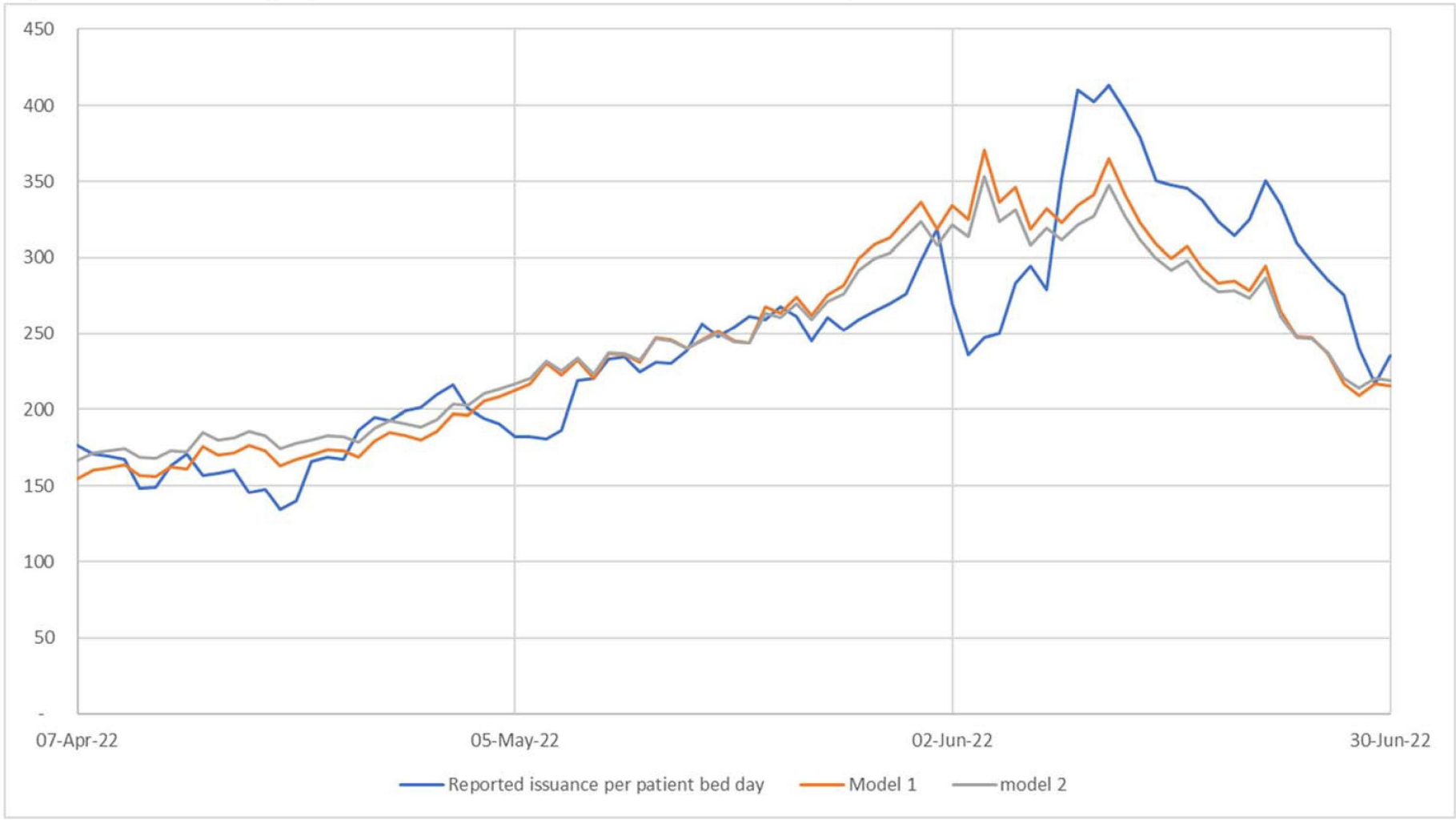


Figure 3: Chart showing stock level (kg of active ingredient) for dexamethasone (IV) from June 2020 to June 2022

Figure 4: Chart showing stock level (kg of active ingredient) for dexamethasone (oral) from June 2020 to June 2022

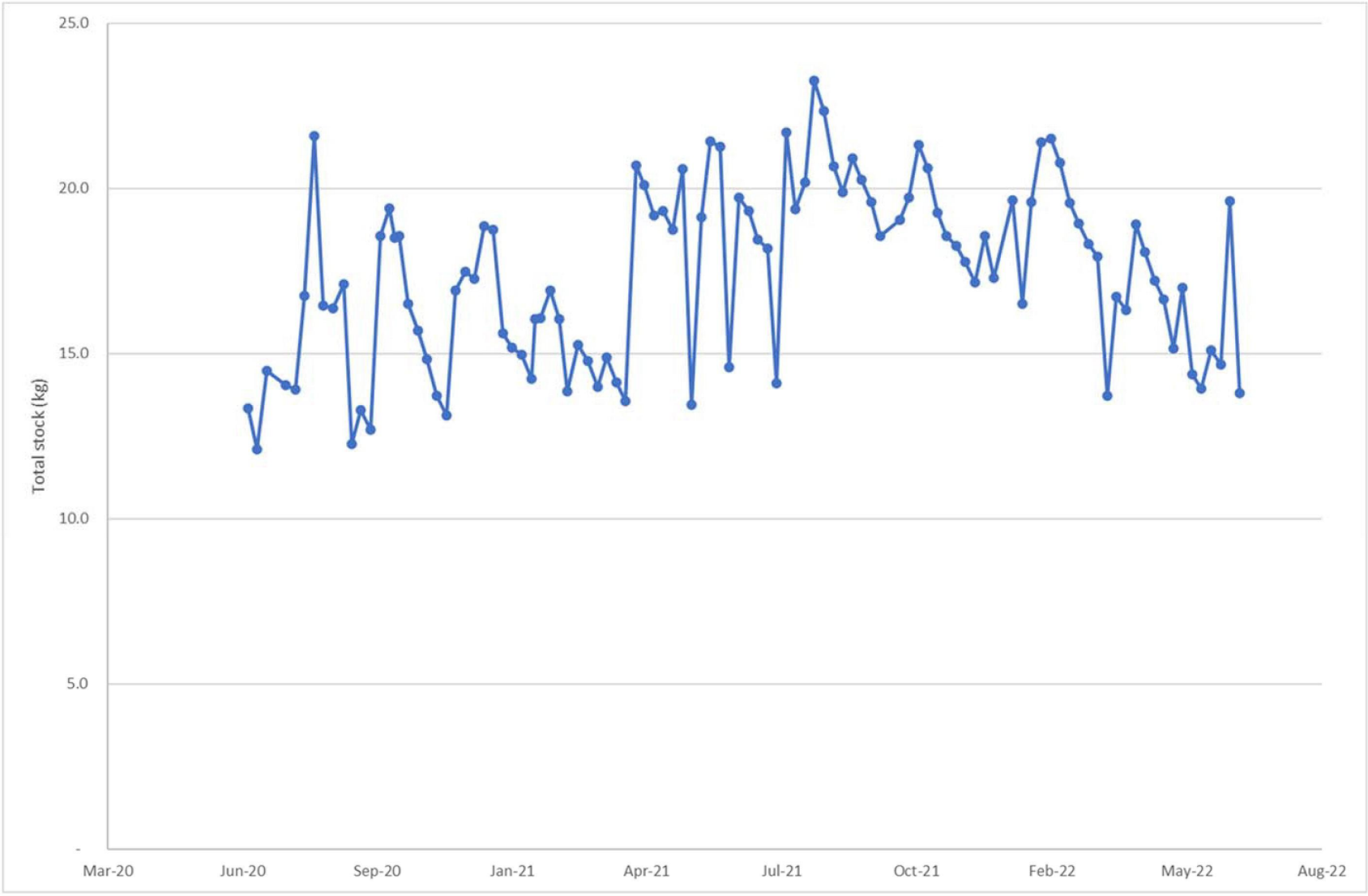


Figure 5: Chart showing stock level (kg of active ingredient) for dexamethasone (solution) from June 2020 to June 2022

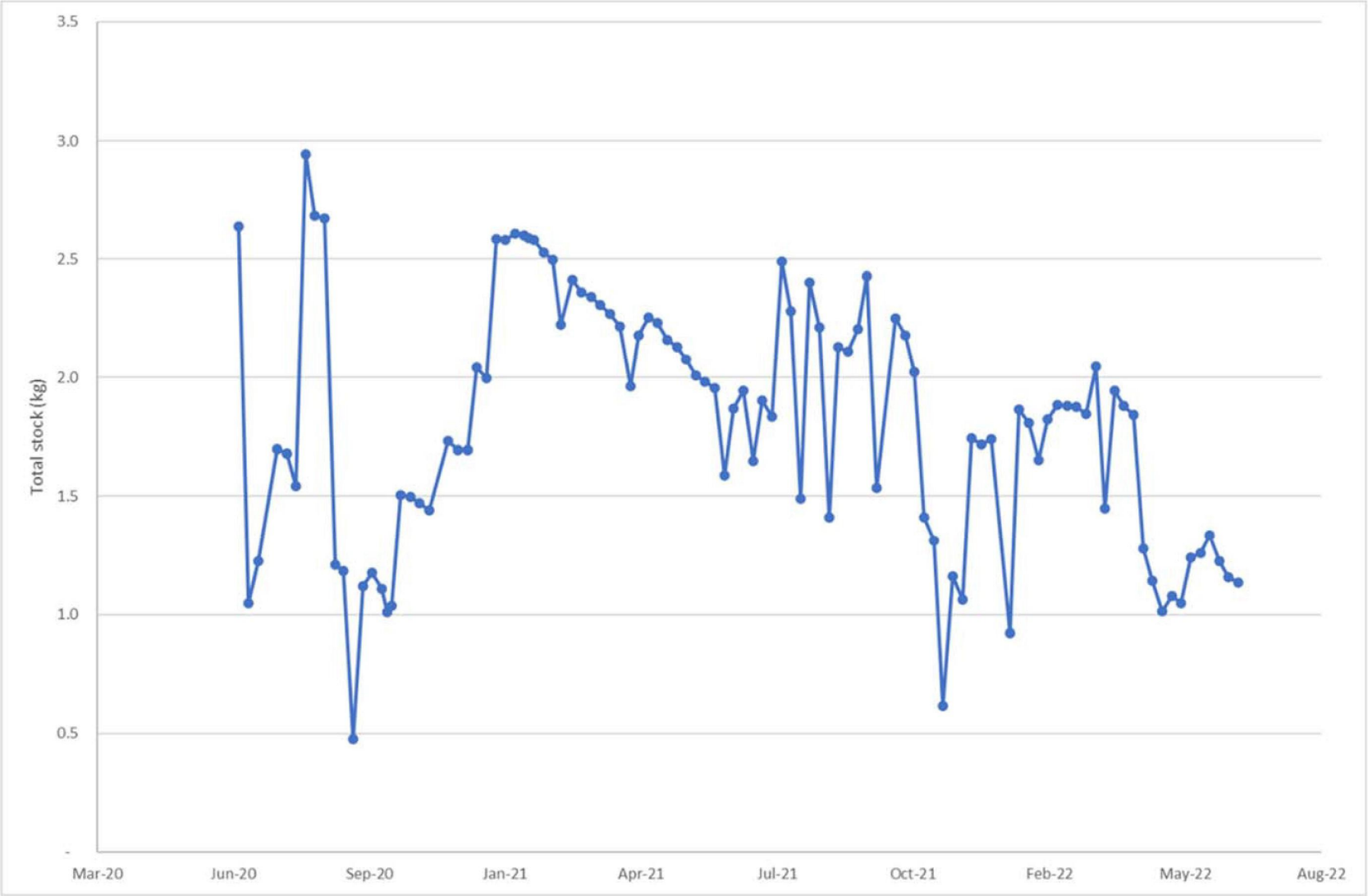


Figure 6: Chart showing stock level (kg of active ingredient) for remdesivir from September 2020 to June 2022

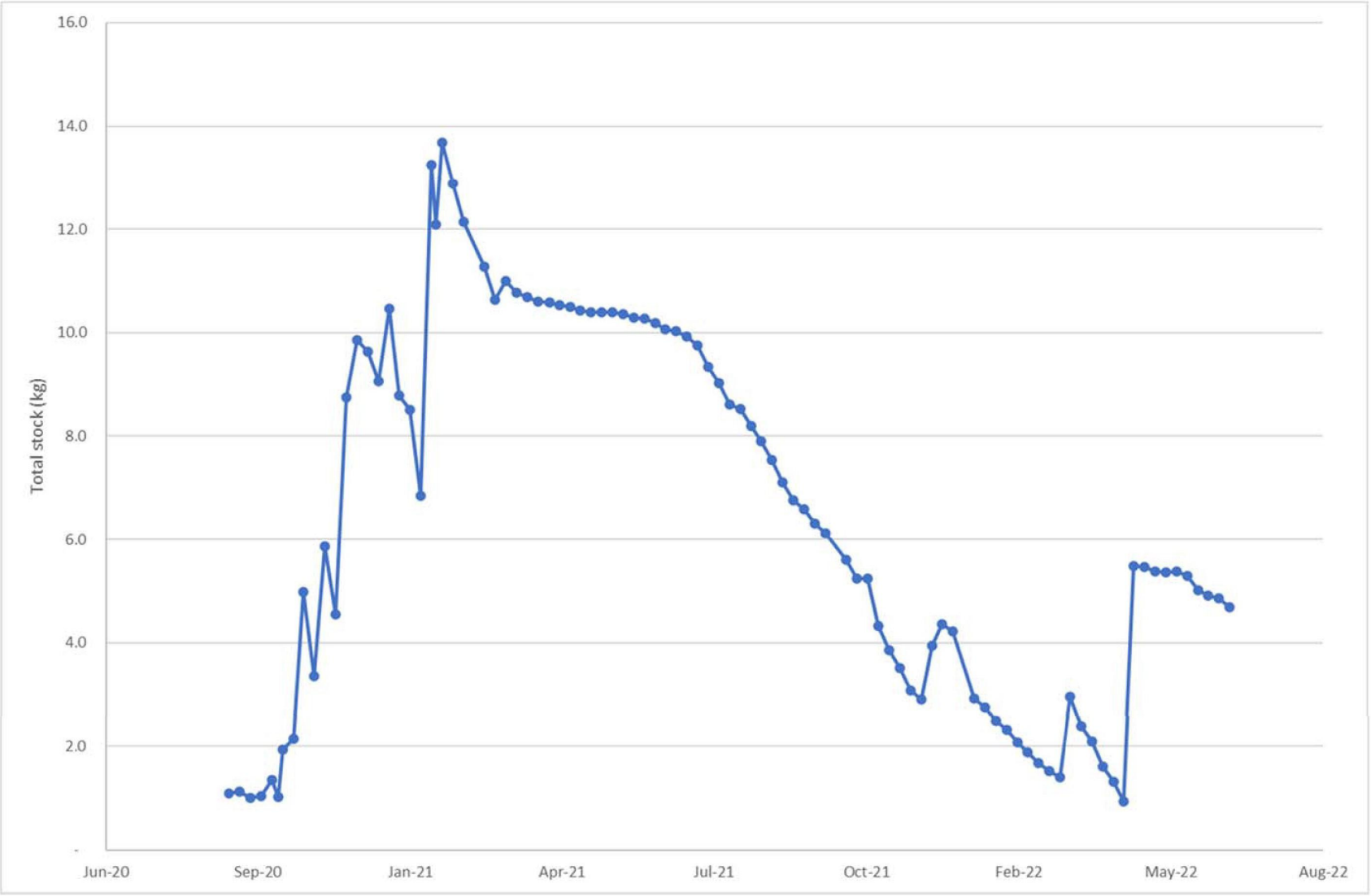


Figure 7: Chart showing stock level (kg of active ingredient) for tocilizumab from September 2020 to June 2022

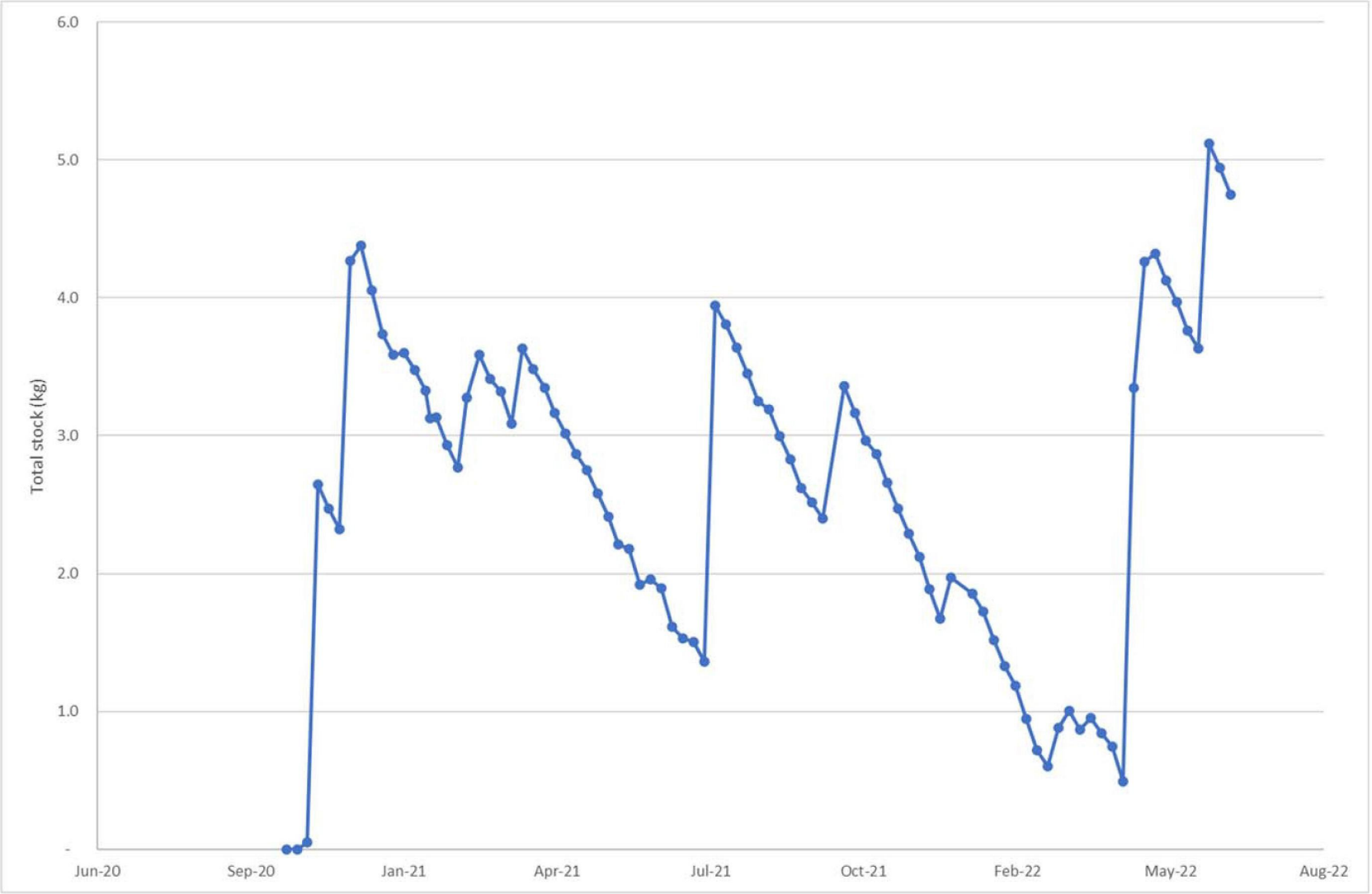


Figure 8: Chart showing stock level (kg of active ingredient) for sarilumab from February 2021 to June 2022

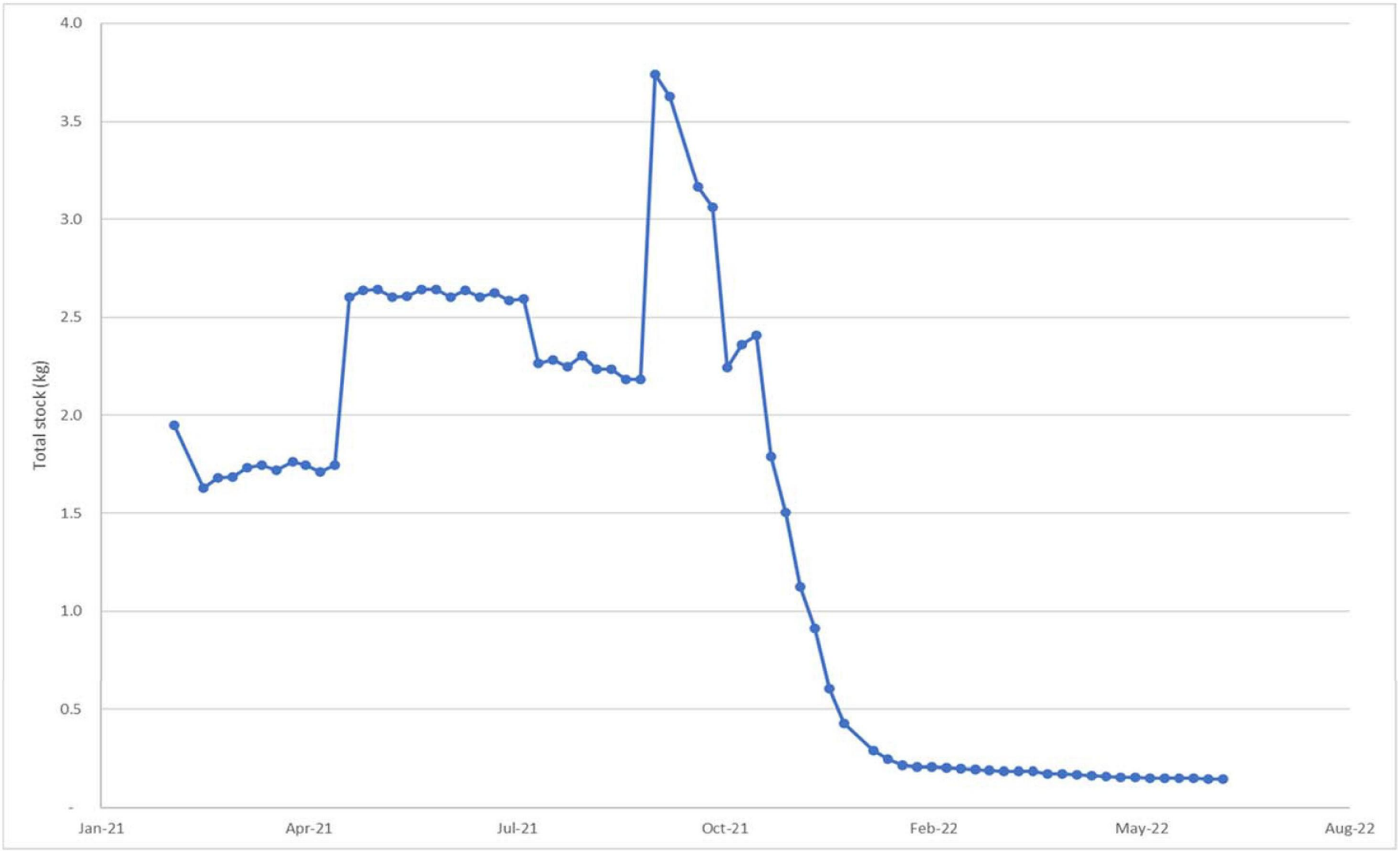


Figure 9: Chart showing stock level (kg of active ingredient) for baricitinib from September 2020 to June 2022

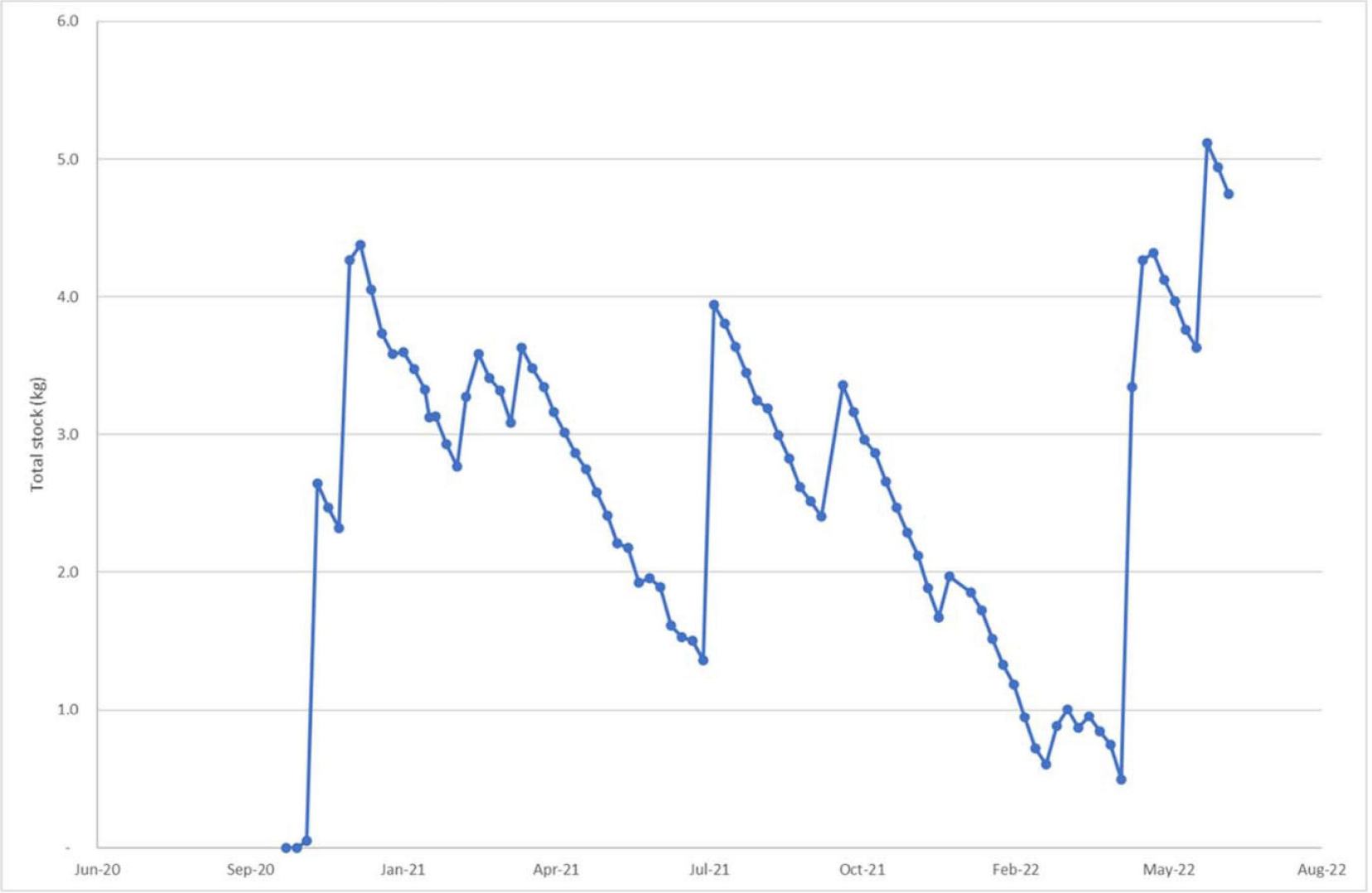


Figure 10: Chart showing CMDU triage outcomes

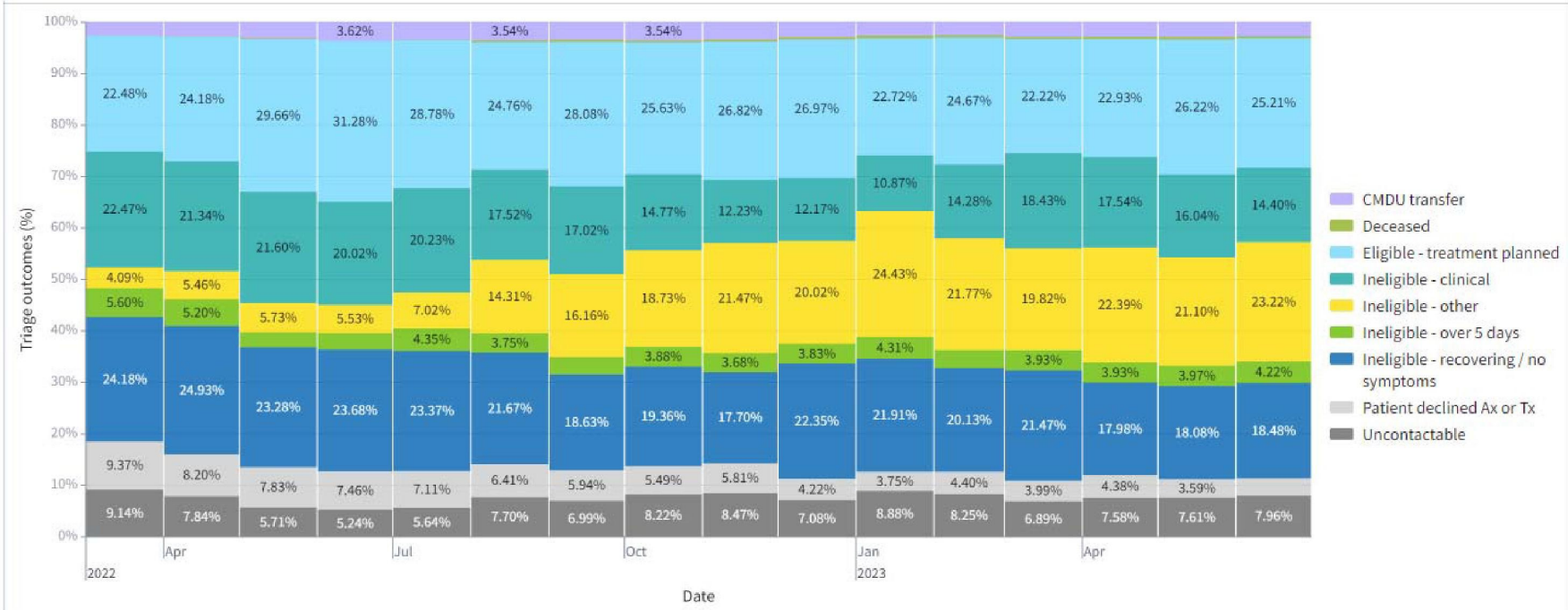


Figure 11: Chart showing daily use (actual and modelled) of remdesivir from April 2022 to June 2022