Witness Name: Helen Knight
Statement No: 1 [Module 4]
Exhibits: HK4-1 to HK4-290
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UK COVID-19 PUBLIC INQUIRY

MODULE 4 WITNESS STATEMENT OF HELEN KNIGHT

I, Helen Knight, will say as follows:

1. I make this witness statement further to receipt of the Rule 9 letter from the Public Inquiry addressed to the Chief Executive of the National Institute for Health and Care Excellence ["NICE"] dated 8 August 2023. I have prepared this witness statement to assist the UK COVID-19 Public Inquiry in its understanding of NICE and NICE's response to the pandemic, particularly in relation to those areas covered by the Provisional Outline of Scope for Module 4. As requested, this statement will mainly focus on the period between 30 January 2020 and 28 June 2022 ["the relevant period"]. It should be read in conjunction with the witness statement provided by former NICE colleague Dr Paul Chrisp (former Head of Publishing and Products and Director of the Centre for Guidelines, at NICE).

2. On behalf of everybody at NICE, I would like to start by expressing my deepest sympathy to all those who lost loved ones during the COVID-19 pandemic and those affected in many other ways, including those that continue to be affected.

3. I am Director of Medicines Evaluation, Centre for Health Technology Evaluation ["CHTE"] at NICE - a position I have held since December 2022. I joined NICE in November 2007 as a Technical Analyst before progressing to Technical Advisor, where I was responsible for ensuring the technical quality of outputs of the Appraisals Team and for the line management of a group of Health Technology Analysts.

4. In May 2011, I became Associate Director, providing support to the Programme and Centre Director in all aspects of the management and delivery of the Technology Appraisals ["TA"] and Highly Specialised Technologies ["HST"] Programme within CHTE, before being promoted to Programme Director in July 2018.

5. My role as Director of Medicines Evaluation involves being responsible for the delivery of the methods, process and guidance for the Medicines Evaluation programmes (namely the TA & HST Programmes) within CHTE. I direct the work of the team which produces guidance on medicines for the NHS in England. I oversee topic selection activities and monitor the delivery of appraisals and evaluations across 2 sites (London and Manchester), directing a portfolio of complex projects, including the recent review of the methods used for health technology evaluation which resulted in an updated methods and process manual being published in January 2022.

6. My substantive role at the start of the pandemic was Programme Director, TA & HST. This covered all types of health technologies. This included medicines, Advanced Therapy Medicinal Products, diagnostics and health technologies. During the pandemic, my role narrowed to focus primarily on medicines.

7. At the start of the pandemic, Meindert Boysen was the Director of CHTE. Meindert went on a period of absence in July 2020 and then again between November 2021 and March 2022, at which point he returned to a special project role, reporting to the Chief Executive Officer ["CEO"]. In July 2020, I was appointed as one of two deputy directors for CHTE, along with Jeanette Kusel, Director of Scientific Advice, within CHTE. Between November 2021 and March 2022, both myself and Jeanette Kusel jointly covered the CHTE director role. Jeanette focused largely on the internal running of CHTE, and I focused on our external relationships, covering our stakeholder meetings and external outputs.

8. In March 2022, the director role was more permanently split in 2, with myself taking on the role of Acting Director for Medicines Evaluation, and Jeanette Kusel taking on the role of Acting Director of Medical Technology and Digital Evaluation. In May 2022, Mark Chapman took up the post of Interim Director of Medical Technology and Digital

Evaluation and in December 2022 I was appointed substantively as NICE's Director of Medicines Evaluation.

9. During the relevant period, as Programme Director and subsequently Deputy Director, I reported directly to Meindert Boysen. During Meindert Boysen's absence and then following my appointment as Acting Director in March 2022, I reported directly to the CEO. The CEO reports to the Board and is the Chair of the Executive Team ["ET"], which until January 2021 was known as the Senior Management Team ["SMT"]. I am also a member of the ET and a member of NICE's Guidance Executive ["GE"], which, on behalf of the Board, approves NICE guidance, advice and other products for publication.

10. **Exhibit HK4-01/INQ000252455** is a copy of the Senior Leadership Organogram, which shows the NICE management structure between March 2020 and June 2022 and also details the changes of leadership within CHTE during the relevant period.

11. NICE has a number of directorates, including CHTE and the Centre for Guidelines ["CfG"]. An overview of NICE's centres and directorates as of June 2022 can be found at **Exhibit HK4-02/INQ000252457**. An organogram for CHTE dated 2020 is produced as Exhibit **HK4-03/INQ000316242.** CHTE and CfG are the two directorates that are primarily relevant to the Provisional Outline of Scope for Module 4, particularly relating to 'the development, trials and use of new therapeutics during the pandemic, in addition to the use of existing medications'.

12. CHTE's role is to undertake heath technology evaluations within the following programmes:

    - Diagnostics Assessment Programme
    - Medical Technologies Evaluation Programme
    - Highly Specialised Technologies Evaluation Programme
    - Technology Appraisal Programme
    - Interventional Procedures Programme.

13. Health technology evaluations, also known as appraisals, are designed to provide recommendations, in the form of NICE guidance, on the clinical and cost effectiveness of new and existing therapeutics, health technologies and treatments in the NHS. In the case of Interventional Procedures, recommendations are provided on the safety and efficacy of procedures.

14. The role of CHTE relevant to Module 4, was to oversee the Research to Access Pathway for Investigational Drugs in COVID-19 ["RAPID C-19"]. RAPID C-19 was a multi-agency initiative aimed at ensuring safe and timely access to therapeutics that show evidence of benefit in preventing and treating COVID-19, as part of temporary emergency pandemic arrangements. Its role was to, where necessary, provide advice to England's Chief Medical Officer ["CMO"] on the strength of the clinical effectiveness evidence for the therapeutics proposed for treating COVID-19.

15. Dr Paul Chrisp provides further details about the role of CfG relevant to Module 4 within his witness statement, but by way of overview, the CfG is responsible for overseeing the production of guidelines. Its primary objective is to develop and maintain high quality, timely, evidence based, cost effective guidance and advice on the prevention, treatment and care of people for practitioners and commissioners of services. The CfG role relevant to Module 4 was to deliver the COVID-19 rapid guideline programme and produce rapid evidence reviews, which made recommendations on COVID-19 therapeutics. The statement of Dr Paul Chrisp also includes a corporate overview of NICE and its response to the pandemic.

16. NICE also has a role in monitoring therapeutics after they have been rolled out by the NHS. CfG undertook ongoing surveillance activity in relation to monitoring the effectiveness of COVID-19 therapeutics once they have been rolled out to patients. Surveillance is a process by which NICE conducts frequent updated searches of literature, research and guidance. In the pandemic, this surveillance process was enhanced to identify any emerging evidence that was potentially relevant to COVID-19 therapeutics and could lead to a rapid update in guideline recommendations. (See Dr Paul Chrisp's witness statement for further information).

17. In addition, the Medicines and Healthcare products Regulatory Agency ["MHRA"] is responsible for the safety of therapeutics. The MHRA produces a monthly drug safety

update newsletter. This advises healthcare professionals about new safety advice for licensed medicines. The newsletter can include new safety warnings, including about the balance of risks and benefits, product withdrawals and other important changes to the marketing authorisation. NICE's Patient Safety Oversight group leads on monitoring and assessing any specific patient safety signals that may impact upon existing NICE guidance. They highlight and co-ordinate any additional work that might be required to provide any additional flags within NICE guidance.

Personal background and experience

18. Prior to joining NICE in 2007, I was a Senior Research Associate at Mapi Values Limited, where I was involved in both leading projects and working as part of the project team in health economics and market access.

19. In terms of formal qualifications, I have a Degree in Biochemistry from the University of Leeds, and a Postgraduate Certificate in Health Economics from the University of Aberdeen.

CHTE – Role and function during the pandemic

20. NICE operates in an environment that by its very nature has a high interest in its outputs. It already had established robust and transparent methods and processes to provide the necessary reassurance of the quality and resilience of its guidance and advice. It is recognised as a world-leading organisation in health technology assessment and clinical guidelines development. When COVID-19 became a national health and care emergency, there was a need to quickly adapt ways of working, consider innovative solutions and revise the approach to meet the health care system's need for speedy and trusted guidance and advice. An innovative solution and key priority for CHTE during the relevant period was the development and implementation of RAPID C-19.

21. In addition, on 17 March 2020, in view of the impact of COVID-19 on the NHS - and in conjunction with the letter from Sir Simon Stevens, NHS Chief Executive (**Exhibit HK4-04/INQ000087317**) - NICE's SMT decided to only publish work on topics that were therapeutically critical and/or addressed COVID-19 diagnostic or therapeutic

interventions, until further notice. This approach was supported by NICE's sponsor team at the Department of Health and Social Care ["DHSC"]. The SMT agreed prioritisation criteria and the CHTE work programme, including TA, HST, Interventional Procedures, Medtech and Diagnostic Assessments, was reviewed in line with the following criteria:

a. Guidance that was therapeutically critical.
b. Guidance that addressed COVID-19 diagnostic or therapeutic interventions.
c. Guidance that was post consultation and could be completed by developers without engagement of stakeholders and/or committee members.
d. Topics which did not fall into any of the above categories, but where staff, if available, could work without engaging stakeholders and/or committee members, for example in carrying out evidence reviews.

22. The purpose at the time was to avoid distracting the NHS when it was facing unprecedented pressure; releasing frontline health care staff who might otherwise have been engaged in NICE guidance/guideline committees and as stakeholders on draft guidance/guidelines; and to focus NICE resources on guidance and advice that was needed to support the NHS response to the pandemic.

23. All CHTE guidance topics that were in development at the start of the pandemic or were due to be started in the 3 months from March 2020, were assessed and reviewed against the criteria above. On 20 March 2020, NICE's GE approved this approach. Although, not technically relevant to Module 4, the following summarises the guidance that was selected as therapeutically critical to continue for the health technology evaluation programmes:

- All TA's involving a cancer medicine were considered therapeutically critical, with the exception of reviews of drugs provided through the Cancer Drugs Fund. This was because patients were currently accessing these drugs via the Cancer Drugs Fund, and it was therefore not considered of critical importance to engage the appraisal committee and frontline staff to developing new/final guidance for those. NHS England ["NHSE"] supported this approach.

- Phenylketonuria - sapropterin dihydrochloride. Improved phenylketonuria control would result in fewer NHS appointments and fewer avoidable or emergency hospital admissions.
- Anticoagulation - andexanet alfa. This treats life-threatening bleeding.
- Cardiomyopathy (transthyretin amyloid) - tafamidis. Individuals with cardiomyopathy may be at increased risk of developing a severe illness should they contract COVID-19.
- Thrombocytopenic purpura (acquired, acute) - caplacizumab. This has the potential to reduce demand on wider NHS resources, such as time spent in intensive care.
- Haemophagocytic lymphohistiocytosis (primary) - emapalumab. This treats a group of highly vulnerable patients for whom social shielding was recommended.
- Cystic fibrosis (F508del homozygous, aged 12 and over) - elexacaftor–tezacaftor–ivacaftor. Social shielding was recommended for people with cystic fibrosis.
- Ulcerative colitis (moderate, severe, active) - ustekinumab. Originally not prioritised for continued development. After representation from stakeholders that this should be classed as therapeutically critical, the topic continued.

24. CHTE also produced a commissioning support briefing on remdesivir for treating COVID-19. In August 2020 NICE received a referral from the DHSC for a TA of remdesivir. However, the company who produces remdesivir requested to delay the TA to enable them to collect further trial data, in order to provide a submission to NICE[1]. NICE agreed to this as it cannot progress a TA without a company submission. In January 2021, DHSC requested that NICE review the evidence for remdesivir to inform its procurement negotiations. NICE adapted its standard TA methods and process (see **Exhibit HK4-05/INQ000316244**) to undertake a rapid value assessment of the medicine. This assessment was called a Commissioning Support Briefing. The driver for this work was that remdesivir was one of the first new active substances to be approved for use by the MHRA on 26 May 2020, specifically for treating some people with COVID-19. It also had an anticipated end to its existing procurement agreement.

[1] Companies are invited to submit evidence on the technology or technologies being evaluated. They should identify all evidence relevant to the evaluation, including all studies known to them, including clinical trials, follow-up studies and evidence from registries. In a single technology evaluation, the company must provide a systematic review of the clinical and cost evidence and an economic evaluation.

25. The briefing's aim was to assist in future procurement decisions on the medicine. This commissioning support briefing provided a summary of the best available clinical evidence for remdesivir within its licensed indication. It also summarised a cost-effectiveness model that was developed for this and provided maximum prices for remdesivir using NICE's normal methods for assessing cost-effectiveness. It also identified the gaps and limitations of the evidence base and cost effectiveness model. The briefing was shared with DHSC on 6 May 2021. (A copy of the commissioning support briefing is exhibited as **Exhibit HK4-21/INQ000494528).**

NICE Fast track advice service

26. NICE does not play a role in the initiation and delivery of clinical research. It does have interests in clinical trial design and broader evidence generation activities, such that evidence to support NICE's evaluation of clinical and cost effectiveness is of the best quality and becomes available in a timely manner to support patient access to beneficial innovative therapeutics. NICE supports the life sciences industry to generate high quality evidence through NICE Advice, which is a fee-for-service, offered to the life sciences industry that was called NICE Scientific Advice during the relevant period.

27. During the pandemic, in relation to Module 4, NICE provided a free fast track advice service for researchers developing novel diagnostics or therapeutics for COVID-19 to help to expedite breakthroughs in care and support the life sciences industry. This helped researchers from around the world optimise their approach to generating the essential evidence required to inform decision-making. Outside of a pandemic situation, NICE normally charges for these services, but because of the unprecedented need to accelerate these technologies into the NHS during the COVID-19 outbreak, NICE waived its fee and provided a free service. 17 free fast-track advice projects were provided in total: 4 for pharmaceuticals, 8 for medical technologies (including diagnostics) and 5 for digital health technologies.

28. The nature and size of the advice projects varied depending on the type and stage of development of the technology. The high-priority pharmaceuticals were offered a full scientific advice project, which involved the submission of a briefing book from the company, the convening of a virtual meeting with the company, NICE staff and clinical and health economic experts and the provision of a written advice report.

29. The nature of the advice delivered as part of these projects ranged from advice on the value proposition of the product, the clinical evidence requirements to demonstrate that the technology had clinical benefit, and the economic modelling that may be required to show the technology was a good use of NHS resources.

Standard CHTE Methods and Processes

30. By way of background information, (although not directly relevant to Module 4) the standard process for health technology evaluations is set out in the 'NICE Health Technology Evaluation – The Manual - Process and Methods'. The manual sets out the process and methods used, including expected timescales, for health technology evaluations. The most recent iteration of the manual was published on 31 January 2022. During the Module 4 relevant period, the majority of CHTE evaluations of therapeutics followed the single technology appraisal ["STA"] process previously published in 2018. This process is set out in the "Guide to the Processes of Technology Appraisal (2018)" produced as **Exhibit HK4-05/INQ000316244.** The TA programme evaluates the clinical and cost-effectiveness of all new active substances and significant licence extensions, aiming to produce guidance as close to marketing authorisation as possible. Therapeutics are formally referred to NICE by the DHSC. NICE can only produce TA guidance on therapeutics that have a marketing authorisation for use in Great Britain.[2]

31. When a NICE TA recommends a technology as a clinical and cost-effective use of resources, the regulations require commissioners to provide funding within the period specified in the guidance. This is usually 3 months, except when particular barriers to implementation are identified, within that period. Since 2019, NICE has been asked to appraise most new therapeutics and significant licence extensions. The NHS in England does not normally provide funding for medicines until they receive a positive TA recommendation.

[2] NICE TA recommendations are described in Regulation 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013.

32. Any guidance or advice produced by CHTE, including updates to guidance, is approved by NICE's GE. None of the TAs published during the relevant period are relevant to the scope of Module 4. RAPID C-19 was a standalone multi-agency initiative that developed a new approach outside of the standard route to medicines access, as explained below.

Research to Access Pathway for Investigational Drugs for COVID-19 ("RAPID C-19")

Introduction

33. RAPID C-19 was established on 29 April 2020 at the request of NHSE and was stood down at the end of March 2023. On 6 April 2020, following discussions between Meindert Boysen and James Palmer (National Medical Director, Specialised Services and Senior Responsible Officer COVID-19 Specialised Services Cell, NHSE), work commenced on the multi-agency initiative.

34. RAPID C-19 was established as part of temporary emergency pandemic arrangements to facilitate rapid patient access to therapeutics for COVID-19 when they were proven to be clinically beneficial and before more formal mechanisms of clinical and cost-effectiveness assessments were undertaken. Its role was to identify and monitor the development of potential medicines/therapeutics and their associated clinical evidence and licensing status/timelines; and to rapidly assess the emerging evidence to help support a route to patient access if the evidence of benefit was strong. RAPID C-19 would communicate its consensus opinion to the CMO and others in the DHSC, who would decide whether to expedite the availability of therapeutics, as appropriate. This included both new therapeutics in development and the repurposing of existing ones. RAPID C-19 did not have a role in monitoring the effectiveness of therapeutics in clinical practice once rapid access had been granted. However, RAPID C-19 continued to monitor emerging evidence for all therapeutics. If new trial data became available for a therapeutic that had already been granted access that could potentially impact the existing access policy or the NICE clinical guideline, it was considered. This complemented the surveillance work being undertaken by CfG and the involvement of representatives from CfG in RAPID C-19 ensured joined up consideration by system partners.

35. The pandemic triggered the mobilisation of system partners to work collaboratively in an unprecedented way to bring clinically effective treatments for COVID-19 to patients as quickly as possible. It was innovative in that it was a deviation from standard routes of access to therapeutics available on the NHS, which in normal circumstances requires a company to submit evidence to NICE so it can undertake a health technology assessment of the clinical and cost effectiveness of a new therapeutic being licensed. This would normally take time. For example, a standard STA usually takes about 44 weeks. Scheduling of an appraisal is aligned closely to the regulatory timeline, with details and timings of the marketing authorisation known well in advance, normally 18 months to 2 years, to allow for timely NICE guidance. The standard TA process supports decision-making related to routine NHS commissioning of medicines and so requires cost-effectiveness analysis to ensure value for the taxpayer and the financial sustainability of the NHS. The work of RAPID C-19 was to support decision-making about temporary access arrangements in an emergency pandemic situation, before more formal mechanisms were applied for any consideration of more permanent commissioning arrangements. The RAPID C-19 process did not include consideration of cost-effectiveness. NICE believes that the expedition of processes for RAPID C-19 and the quality of decision-making were appropriate given the unprecedented and emergency circumstances. The challenge was the availability of evidence and the quality of the data produced within a fast moving and ever-changing environment.

36. The RAPID C-19 pathway was co-designed by the key agencies involved in the development and access pathway for therapeutics in England, including the regulatory authority (MHRA), evidence funders (National Institute for Health and Care Research ["NIHR"]), evidence assessors (NICE), and clinical commissioning (NHSE). They came together in early conversations in March 2020 to explore what could be done to enable effective treatments to come out of research studies and into clinical practice as quickly as possible.

37. It is important to note that RAPID C-19 did not formulate or provide clinical guidelines, guidance, advice or recommendations for clinicians in the NHS. Its role was to provide advice to the CMO, in the form of a short report that contributed to DHSC decision-making and subsequent NHSE policy development regarding the provision of patient

access to therapeutics during the pandemic. As such, the CMO report was not intended for publication. Furthermore, RAPID C-19 outputs do not constitute NICE outputs. The short reports to the CMO represented the agreed consensus of the Oversight Group decision makers on the strength of the evidence of clinical benefit for a therapeutic and its opinion on whether the evidence warranted consideration for rapid interim access to that therapeutic.

38. RAPID C-19 generally provided advice to the CMO where it was considered that the evidence of clinical benefit was sufficient to warrant consideration for rapid interim patient access. RAPID C-19 also provided advice to the CMO on 6 topics where the evidence was not considered sufficient to warrant consideration for rapid interim access, but where there was high interest. The requests for RAPID C-19's advice as a result of high interest from government ministers, the public or the media, came from the DHSC Antivirals and Therapeutics Task Force ["ATTF"]. These were baricitinib (in 2020 – later trial results resulted in interim access), hydroxychloroquine, colchicine, budesonide, fluvoxamine and tixagevimab plus cilgavimab (Evusheld). The high interest usually stemmed from trial results that had been widely reported in the media, for example the results of the TOGETHER trial of fluvoxamine, and the COLCORONA trial of colchicine.

39. RAPID C-19 also advised the CMO of a positive signal from a trial that warranted consideration for rapid interim patient access but preparations for access were not subsequently progressed for various reasons (e.g., the emergence of more information, regulatory developments). This applied to anakinra, casirivimab plus imdevimab (for post-exposure prophylaxis), bamlanivimab plus etesevimab, and regdanvimab.

40. There was no positive signal from a sufficiently robust trial of ivermectin that warranted a CMO report. NICE also supported the DHSC with their response to a letter before action pursuant to the Pre Action-Protocol for Judicial Review, regarding the use of ivermectin to treat and prevent COVID-19. The claimant challenged the DHSC's failure to grant authorisation and approve NHS use of ivermectin, suggesting that it was unlawful. As NICE held the secretariat for the RAPID-C19 initiative, including all the documentation and technical work, NICE had been asked to provide supporting information to DHSC to assist in their response to the claims regarding the evidence of effectiveness for ivermectin.

41. It is also important to note that decision-making on interim therapeutic access arrangements within England rested with the CMO and DHSC. RAPID C-19's view was one of several sources of information and advice that informed this decision. Where interim access was supported, this was taken forward by NHSE through development of interim access policies. (please see paragraph 57 for information on devolved nations)

42. RAPID C-19 contributed to decisions to make treatments available during the pandemic, which saved lives. Its cross-agency consideration of the clinical evidence played a key role in enabling this rapid availability of treatments. A copy of the RAPID C-19 Oversight Group ["Oversight Group"] achievements summary slides can be found at **Exhibit HK4-06/INQ000316245**.

43. Some statistics illustrating the scale of the work undertaken (as at December 2022) are provided below:

- 92 Oversight Group meetings held.
- 89 topics reviewed.
- >24,000 papers screened.
- >100 trial investigators contacted.
- 551 completed actions
- 10 treatments had access
- <10 days from key trial readout[3] to patient access (for repurposed medicines)

44. In addition, RAPID C-19 submitted 20 reports to the CMO, as detailed in **Table 1** below:

Table 1: Reports submitted to the CMO

Date	Therapeutic	Exhibit reference
21/12/2020	Baricitinib	**HK4-102/INQ000315940**

[3] Key trial readout refers to the result of a key trial, which would serve to indicate whether or not a therapeutic is likely to be beneficial.

06/01/2021	Tocilizumab & Sarilumab	**HK4-109/INQ000494427**
15/01/2021	Hydroxychloroquine	**HK4-112/INQ000316184**
29/01/2021	Colchicine	**HK4-122/INQ000316198**
12/02/2021	Tocilizumab	**HK4-130/INQ000494448**
08/04/2021	Budesonide	**HK4-155/INQ000316019**
18/06/2021	Budesonide	**HK4-192/INQ000494510**
18/06/2021	Sotrovimab	**HK4-206/INQ000494524**
18/06/2021	Casirivimab plus Imdevimab	**HK4-207/INQ000316094**
29/06/2021	Anakinra	**HK4-211/INQ000316100**
23/07/2021	Casirivimab plus Imdevimab (prophylaxis)	**HK4-220/INQ000316118**
28/07/2021	Bamlanivimab plus Etesevimab	**HK4-221/INQ000316121**
11/10/2021	Molnupiravir & Remdesivir	**HK4-238/INQ000316150**
04/11/2021	Fluvoxamine	**HK4-244/INQ000316159**
23/12/2021	AZD7442 (Evusheld)	**HK4-256/INQ000316179**
06/01/2022	PF-07321332 plus Ritoinavir (Paxlovid)	**HK4-259/INQ000316200**
18/01/2022	Regdanvimab	**HK4-261/INQ000316218**
09/03/2022	Baricitinib	**HK4-269/INQ000316232**
30/05/2022	AZD7442 (Prophylaxis)	**HK4-276/INQ000316210**
23/06/2022	Tixagevimab plus Cilgavimab (Evusheld, AZD7442)	**HK4-278/INQ000316214**

45. The RAPID C-19 initiative and its advice to the CMO, resulted in over 200,000 patients receiving treatments for COVID-19 in the UK (as at the end of October 2022).

RAPID C-19 Oversight Group

46. The Oversight Group was responsible for considering potential COVID-19 therapeutics in development and to identify, prioritise and monitor those likely to be expedited for patient access in the NHS. The group had a Terms of Reference, approved by the 4 key organisations, which was updated over time; a copy of the first iteration dated May 2020 is exhibited as **Exhibit HK4-07a/INQ000471160**. A copy of the final version dated July 2022 is exhibited as **Exhibit HK4-07b/INQ000316247.**

47. A spreadsheet, which provides a timeline of all Oversight Group meetings and outputs for COVID-19 therapeutics during the relevant period is exhibited as **Exhibit HK4-08/INQ000494417.** This spreadsheet details all Oversight Group meetings and process changes, as well as reports to the CMO and summary briefings presented to the Oversight Group. A full list of the RAPID C-19 briefings and reports to the CMO identified within **Exhibit HK4-08/INQ000494417** can be found in appendix 1 at the end of this statement.

48. The Oversight Group was considered an advisory group. While members were described as 'decision-makers', these decisions related to operational matters, next steps and sign-off of the group's advice to CMO. The Oversight Group did not have decision-making responsibility for the provision of interim access to therapeutics for COVID-19; this rested with the DHSC and the CMO (see paragraph 89 for further information).

49. The group's considerations were informed by briefings prepared predominately by NICE staff. The group worked at pace, meeting regularly on a weekly basis, in the evening (with additional ad hoc meetings as necessary), as new evidence emerged. The Oversight Group meetings were not minuted, but a decision and action log was maintained – a copy of which, as at 17 June 2022, is produced as **Exhibit HK4-09/ INQ000316249.** As RAPID C-19 was required to operate at pace and with agility due to the emergency nature of the pandemic situation, the priority was to consider potential therapeutics for COVID-19. To optimise the available resources for this purpose, it was considered that the action and decision log was sufficient for record-keeping, rather than formal minutes. The group functioned well as a collaborative with all involved demonstrating a clear commitment to supporting, via advice to the CMO, rapid access to therapeutics with proven clinical benefit. Prior to each meeting, all members of the Oversight Group were required to declare any conflicts of interest that were relevant or potentially relevant, in line with NICE and NHSE policies for managing interests. Further detail regarding conflicts of interest can be found at paragraph 60 below.

50. RAPID C-19 'recommendations' (advice to CMO) were submitted to the CMO via the DHSC ATTF. RAPID C-19 did not otherwise report or disseminate any recommendations. RAPID C-19 received confirmation from the ATTF of receipt of the report and brief high-level feedback on the CMO's response. Any system actions in

response to a CMO decision on rapid interim patient access to a therapeutic for COVID-19 were taken forward by the relevant organisations.

Key health care bodies and individuals involved

51. The Oversight Group consisted of decision makers and advisory members. The decision makers were senior representatives of NICE, MHRA, NHSE, and NIHR. Decision-makers were required to nominate formal deputies to cover absence. These senior representatives identified additional staff from their organisations who would need to be involved in an advisory capacity. All members of the group had a role in advising on the suitability of a product for consideration for rapid interim access, based on the evidence available.

52. The designated decision-maker for NICE was initially Meindert Boysen. I was the deputy decision maker and became the decision maker in November 2021, when Meindert stood down. Advisory members from NICE included staff from CHTE, CfG and the Science, Evidence and Analytics Directorate.

53. In addition, the Oversight Group facilitator was the Programme Director for Commercial and Managed Access, within CHTE, who also had overall responsibility for the operation of the RAPID C-19 secretariat function. During the relevant period, that person was Carla Deakin. The Life Sciences Team ["LST"] within CHTE provided the RAPID C-19 secretariat. A copy of the RAPID C-19 NICE Secretariat Organogram April 2020 – June 2022, is produced as **Exhibit HK4-10/INQ000316250.**

54. Other advisory members were identified as and when their expertise was needed or their involvement in related activities meant it was important for them to be aware of and participate in discussions at the Oversight Group. Overall, the group included clinicians, pharmacists, evidence assessors and researchers, those involved in clinical policy development and implementation and service delivery. Expertise in pharmacology was consulted periodically and brought into the initiative more formally during the second half of 2021. No drug company representatives were involved in RAPID C-19.

55. It is important to note that access to therapeutics is a devolved activity in the UK. Consequently, the RAPID C-19 Oversight Group, as per the terms of reference, focused

on access to therapeutics in England. As stated above, the RAPID C-19 pathway was co-designed by the key agencies involved in the development and access pathway for medicines and therapeutics in England. In addition to NICE, this included NHSE, MHRA and NIHR. They worked collaboratively to rapidly develop the initiative, in response to the urgent pandemic situation. This included agreeing each partner agency's role and responsibilities (as outlined in the terms of reference), decision-making responsibilities and lines of communication with the CMO for England via the ATTF. **Exhibit HK4-07a/ INQ000471160** identifies the decision-making members as:

- Director of CHTE, NICE
- Programme Director CHTE, NICE
- National Medical Director – Specialised Services, NHSE
- NIHR representative
- MHRA representative.

The latest version of the Terms of Reference (**Exhibit HK4-07b/INQ000316247**) identifies the decision makers as:

- Medical Director – Specialised Services, NHS England and NHS Improvement
- Programme Director CHTE, NICE
- Director, National Institute for Health Research
- Deputy Director, Medicines and Healthcare products Regulatory Agency

56. The Terms of Reference states that "*Decisions will be made on consensus wherever possible. Only in exceptional circumstances, if consensus cannot be reached, decision making-members of the group will be asked to vote*". A vote was not required during the operation of RAPID C-19; all decisions were reached by consensus.

57. In addition, given access arrangements for therapeutics are devolved, it was also desirable to support the devolved nations' participation in the initiative. The Scottish Medicines Consortium ["SMC"] contributed technical resource to the development of briefings. Representatives from the devolved nations attended the meetings in an advisory capacity to identify any specific medicines access arrangements that might be required for their jurisdictions, including lines of communication with their CMO's.

58. Further details of the key bodies and individuals involved in RAPID C-19 are outlined in **Table 2** below.

Table 2: Key bodies and individuals associated with RAPID C-19

CMO's in England, Wales, Scotland and Northern Ireland	NICE, through its role in RAPID C-19 and provision of the secretariat for this initiative, engaged with the CMO for England indirectly via the DHSC ATTF. RAPID C-19 did not engage with the CMO's for Scotland, Wales and Northern Ireland, but it is understood that its outputs were shared with them.
NHSE	James Palmer, National Medical Director, Specialised Services (RAPID C-19 decision maker) Anthony Kessel, Clinical Director, National Clinical Policy, Specialised Commissioning (RAPID C-19 deputy decision maker) <u>Advisory members:</u> Ann Jarvis, Programme Director (Clinical Strategy), Specialised Commissioning Malcolm Qualie, Medicines Lead, Specialised Commissioning (until January 2022) Miranda Matthews, Medicines Lead, Specialised Commissioning (from January 2022) National Clinical Policy Fellows (NHS clinicians on temporary work placements with NHSE) – Matthew Newton, Christin Henein, Dhivya Subramaniam
MHRA	Keith McDonald, Deputy Director, Licensing Division (RAPID C-19 decision maker until February 2021) Krishna Prasad, Deputy Director (interim), Licensing Division and Principal Assessor to Commission on Human Medicines (RAPID C-19 decision maker from February 2021)

	Daniel O'Connor, Expert Medical Assessor, Licensing Division (RAPID C-19 deputy decision maker)
NIHR	Hywel Williams, Scientific and Coordinating Centre Programmes Contracts Advisor (RAPID C-19 decision maker until September 2021) Daniel McAuley, Director, Efficacy and Mechanism Evaluation Programme (RAPID C-19 decision maker from September 2021) Nick Lemoine, Medical Director, Clinical Research Network (RAPID C-19 deputy decision maker) <u>Advisory member:</u> Dawn Craig, Director, NIHR Innovation Observatory
SMC	<u>Advisory members:</u> Anne Lee, Chief Pharmaceutical Adviser Helen Wright, Principal Pharmaceutical Analyst Note: analytical staff within SMC supported the NICE technical secretariat for RAPID C-19.
All Wales Therapeutics and Toxicology Centre ["AWTTC"]	<u>Advisory members:</u> Karen Samuels, Head of Health TA, Medicines Management and Programme Director Kath Haines, Head of Welsh Analytical Prescribing Support Unit Anthony Williams, Head of Patient Access to Medicines
All Wales Medicines Strategy Group ["AWMSC"]	RAPID C-19 did not engage with the AWMSC. By way of explanation, this body constitutes the equivalent of the independent TA committees that advise NICE. The Welsh perspective was therefore covered by the AWTTC (essentially the equivalent body to NICE).
Department of Health in Northern Ireland ["DHNI"]	Lynn Keenan, Pharmacy Co-ordinator (Specialist Medicines) (Advisory member)
DHSC	Lucy Chappell, Chief Scientific Adviser (Advisory member)

ATTF	Advisory members: Lucy Darling, Head of Supply and International Sophia Berry, Head of Regulation and Clinical Access Charlotte Taylor, Acting Director Alexander Churchill, Deputy Director David Hayward, Deputy Director Nikki Pitt, Deputy Director Other Taskforce representatives including Rachel Mumford, Trudy Netherwood, Rebecca Wilkinson, Marjia Monsur, Bindiyah Shah, Daniel Glaholm, Aidan McIvor, Dafni Moschidou, Aniyah Steadman.
Clinical trials and their principal investigators and senior management	Investigators of around a hundred clinical trials were contacted by the RAPID C-19 secretariat. See **Exhibit HK4-14/INQ000252477**.
Any international organisations	Information about the operation of RAPID C-19 was shared with partner organisations in Australia and Canada through existing interfaces but there was no collaboration with these bodies as part of RAPID C-19. The RAPID C-19 secretariat utilised publicly available information from several international sources when developing topic briefings, such as the US National Institutes for Health and the COVID-NMA initiative (an international research initiative supported by the World Health Organisation ["WHO"] and Cochrane Collaboration which produced a 'living' evidence synthesis from emerging trial results), and various online 'dashboards' that collated non-clinical evidence on the activity of neutralising antibodies against identified variants.
Any other relevant bodies or individuals	UK COVID-19 Therapeutics Advisory Panel ["UK-CTAP"][4]. Patrick Chinnery, Chair. Alastair Lamb, Head of Operations and Governance

[4] 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 helped

	National Institute for Health Research Innovation Observatory ["NIHRIO"] Prophylaxis Oversight Group (David Lalloo, Andrew Owen) National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre ["NETSCC"] Vaccine Taskforce at the UK Government Department for Business, Energy and Industrial Strategy ["BEIS"] UK Health Security Agency ["UKHSA"] UK Clinical Trials Forum ["UKCTF"]

The roles and responsibilities of key health care bodies

59. An overview of the nature of the key system partners and their roles and responsibilities relationships within RAPID C-19 can be found in **Table 3** below.

Table 3: Roles and responsibilities of key health care partners associated with RAPID C-19

ATTF	RAPID C-19 operated within the governance framework of the DHSC Antivirals and Therapeutics Taskforce, representatives of which regularly attended RAPID C-19 Oversight Group meetings. Representatives of the Vaccine Taskforce at the BEIS attended an Oversight Group meeting in August 2020 to present an overview of their antibodies work programme.
NHSE	Had overall responsibility for RAPID C-19.
NICE, NHSE, MHRA, NIHR	Key decision-making members, contributing expertise in evidence critique and their specific perspectives, for example: • NHSE – implementation and deployment considerations, clinical policy development • NICE – medicines access, technology appraisal, clinical guideline development • MHRA – regulatory and safety considerations • NIHR – research operation and co-ordination

prioritise research into the most promising therapeutics during the first year of the pandemic, before ceasing operations in September 2021.

NICE	As explained above, NICE was a key (decision-making) member of the RAPID C-19 initiative. It also led the development of the initiative and provided the project and technical secretariat that facilitated its operation. The role was to: • Provide the RAPID C-19 Oversight Group with the most accurate and up to date information on potential COVID-19 therapeutics in ongoing trials, in the form of topic briefings (also supported by analysts from the SMC, the national source of advice on the clinical and cost-effectiveness of all new medicines in Scotland). • Undertake various surveillance and monitoring activities to ensure the Oversight Group was aware of any developments regarding these therapeutics such as new evidence and regulatory plans. This included enrichment of horizon scanning information and briefing preparation, topic monitoring and rapid evidence synthesis and critique to support the Oversight Group (and included analytical staff from the SMC). • Co-ordinate partner agency involvement. • Co-ordination (project) activities including Oversight Group meeting administration, declarations of interests, agenda planning, circulation of papers, maintaining action and decision logs, maintaining webpage information and engagement with trial investigators (including pharmaceutical companies).
SMC, AWTTC, DHNI	Advisory members (with analytical staff from SMC supporting the RAPID C-19 technical secretariat at NICE through collaborative working).
NIHRIO	NIHRIO was responsible for the horizon scanning that underpinned the operation of RAPID C-19, and the NIHRIO Director regularly attended Oversight Group meetings. The RAPID C-19 secretariat worked closely with the NHRIO.
Prophylaxis Oversight Group	The secretariat reached out to members of the Prophylaxis Oversight Group ["POG"] in May 2021 because of the difficulties encountered in assessing the evidence for neutralising antibodies in the face of changing variants, and they subsequently became advisory members who attended the Oversight Group regularly.
Other relevant bodies	UK-CTAP and NETSCC

	The secretariat also sought specialist input from other organisations such as UK-CTAP and NETSCC as needed, to supplement its information on therapeutics being investigated for the treatment of COVID-19. The chair of UK-CTAP attended the Oversight Group in November 2020 to provide an overview of its work. UKHSA There was some interaction with UKHSA in the spring of 2022 due to their role in testing neutralising antibodies against variants, with Meera Chand, Director of Clinical and Emerging Infection and Mary Ramsay, Head of Immunisation, attending the Oversight Group in April 2022.

Managing Conflicts of Interest

60. Effectively managing interests – and identifying potential conflicts – is essential if health and care professionals and the public are to maintain confidence in NICE's independence and work. It is central to how NICE develops guidance and appoints members to its independent committees that develop this guidance.

61. NICE's approach to identifying and managing conflicts of interest is set out in our policies for declaring and managing interests. One policy is focused on board members and staff, with the other focused on the advisory committees. This latter policy applies both to the members of the committees and those who attend in a non-decision-making capacity to give evidence to the committees.

62. The policy on declaring and managing interests for NICE advisory committees was developed in January 2018 and the policy focussing on board members and staff was updated in May 2018, to align with this policy. The policies, which draw upon the model NHS policy published by NHSE, replaced a combined policy that previously encompassed committees, board members and staff. The policy for advisory committees was subject to public consultation before approval by the Board. It supports a culture of transparency about the interests of the advisory committee members, and the people who work with the committee. This means the effect of any potential interests is known, understood and managed. It aims to ensure that the advisory committees have access to the appropriate expertise in the areas under consideration, while minimising the risks to their perceived ability to objectively consider the evidence.

63. The policies set out the requirements for staff and those working with the committees to declare their interests before involvement with NICE (and then keep these declarations updated) and the approach for managing any actual or perceived conflicts that may arise from these interests.

64. Both policies are kept under regular review and underwent minor revisions during the relevant period. The amendments are summarised in the version control table in each policy.

65. For the Oversight Group, a procedure for declaring and managing interests was utilised, which was derived from existing NICE and NHSE policies. The approach for identifying and managing conflicts of interest is set out in the document titled 'RAPID C-19 Oversight Group Procedure – Declaring and Managing Interests'. A copy of this is attached at **Exhibit HK4-11/INQ000316251.**

Funding

66. The RAPID C-19 initiative did not receive any specific funding. The constituent organisations dedicated their existing resource to it. The RAPID C-19 secretariat at NICE was provided by the LST, which repurposed its resource from supporting Accelerated Access Collaborative projects, funded by NHSE, when these were put on hold and staff deployed elsewhere because of the pandemic. From April 2022 until the end of the initiative, secretariat activities were funded by the DHSC.

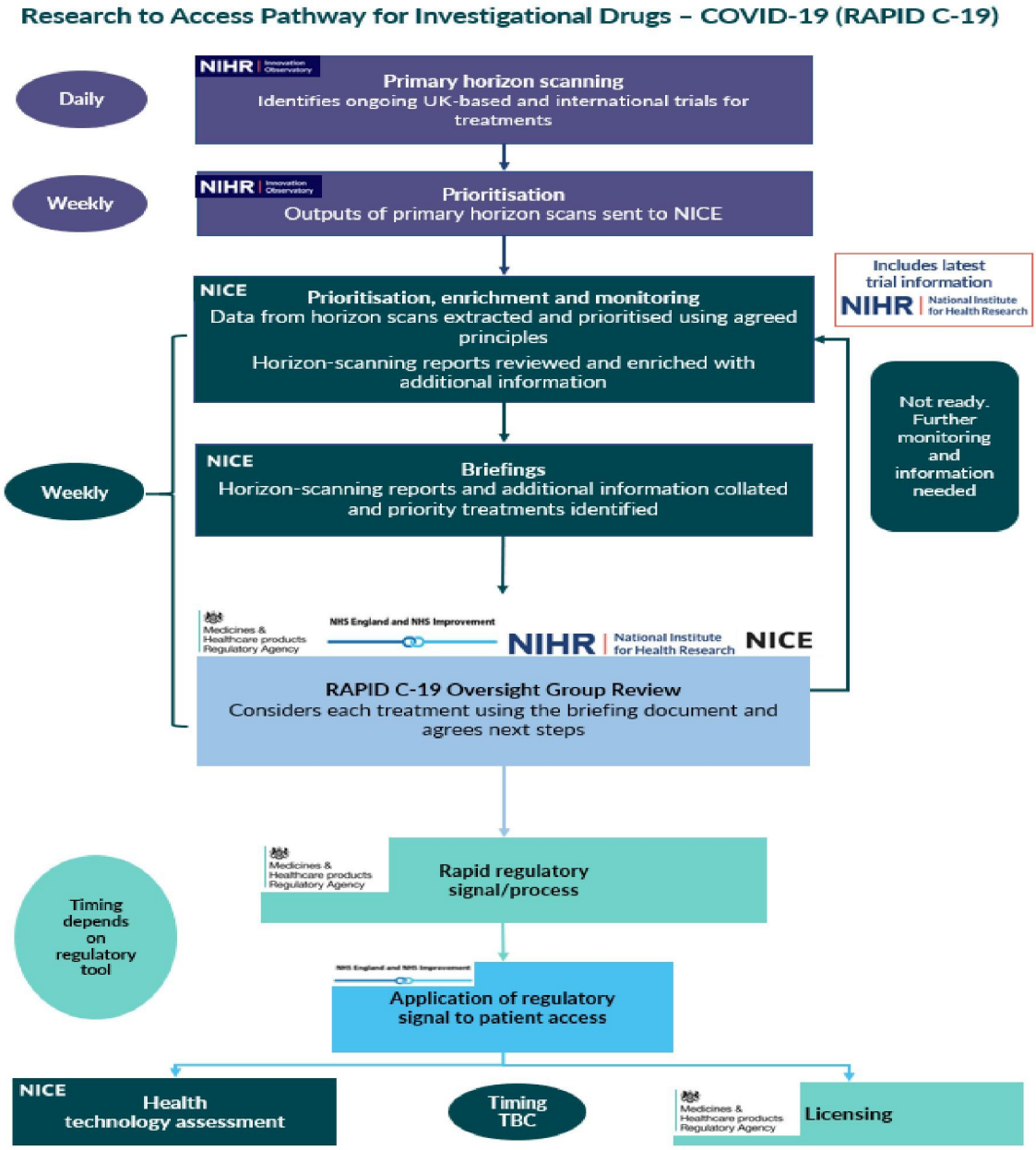
67. The RAPID C-19 initiative ended in March 2023 as the UK moved from emergency pandemic arrangements towards routine commissioning of COVID-19 therapeutics. During the pandemic, COVID-19 therapeutics were centrally funded by the DHSC, and rapid interim access was granted before more formal mechanisms of clinical and cost-effectiveness assessments were undertaken. The return to routine commissioning arrangements from April 2023 required patient access to be determined by NICE assessment in the standard way.

RAPID C-19 Pathway Stages

68. To guide the work of the pathway a RAPID C-19 process was developed, titled 'Research to Access Pathway for Investigational Drugs in COVID-19 (RAPID C19): interim process for NICE activities'. This was made publicly available via the NICE website from August 2020. This document, which sets out the main stages of the RAPID C-19 process, was developed and updated over time. A copy of the guide, last updated in 2021, is exhibited as **Exhibit HK4-12/INQ000316252.**

69. A summary of the standard process of RAPID C-19 is summarised in **figure 1** below.

Figure 1: RAPID C-19 Process Diagram



70. Please note the following sections provide more detail on each stage of the process. The role of the Oversight Group is explained above.

Primary horizon scanning

71. The NIHR Innovation Observatory ["NIHRIO"] provided information on all registered clinical trials around the world investigating treatments for COVID-19. This served as a single data feed for cross-planning between partner organisations within the healthcare system. The scan was provided by the NIHRIO. The information was made available publicly through an online dashboard as well as an excel spreadsheet sent directly to those involved in the oversight and development of the horizon scanning, which included advisory members from NIHRIO, NICE, MHRA and NHSE. This spreadsheet was initially sent twice weekly, then weekly from September 2020, fortnightly from August 2021 and finally monthly from September 2022 until the end of the initiative at the end of March 2023.

Prioritisation

72. The NIHRIO scan identified all registered trials for COVID-19 therapeutics worldwide. The identified therapeutics were then ranked against a set of criteria comprised of investigative features that could be considered a proxy for the most promising therapeutics, that is, those considered most likely to be beneficial. These criteria were applied in a scoring matrix. The therapeutics with the highest scores were prioritised for consideration by RAPID C-19. This matrix was developed collaboratively by the 4 key RAPID C-19 partners: NHSE, MHRA, NICE and NIHR (see **figure 2** below). The initial criteria and rudimentary scoring were firstly put together at NICE as a way to manually filter the horizon scanning information coming through the NIHRIO. It was then further iterated, tested and defined with NHSE, MHRA and NIHRIO colleagues as RAPID C-19 was being established. Once agreed, NIHRIO automated the operationalisation of the scoring to its horizon scanning spreadsheets which enabled stratification of the horizon scanning information. The initial approach and any further iterations were agreed at the Oversight Group.

73. At the time, the key priority was to identify treatments that were considered the most likely candidates for accelerated rapid access based on likelihood of sufficient evidence of effectiveness (which would usually come from phase 2 or 3 trials). In the prioritisation

criteria, a higher score was applied to treatments in later stage trials because more robust and clinically interpretable data (providing more confidence in any positive results) is expected from trials in later phases. Treatments in early phase trials would require further testing in larger trials to establish benefit even if the results from those early phase trials were positive, which would of course take time. This is why treatments only in early phase trials (phase 0 or 1) scored lower in the prioritisation matrix. This did not preclude them from being considered by RAPID C-19 and the phase of trial was only one element of the prioritisation criteria used.

74. Special populations were considered for the prioritisation criteria in June 2020, as it was considered important to capture any evidence for populations that are not routinely included in trials such as pregnant women, children and ethnic minority groups. However, the criteria applied in the scoring matrix was limited in terms of what could be easily extractable from the clinical trial registries from which NIHRIO generated the horizon scanning information in order to automate the scoring and stratify the treatments in the horizon scanning spreadsheets. Further detail on the populations included in the relevant trials was provided in the treatment-specific briefings that were considered by the Oversight Group. The gap in trial activities in paediatric patients was because in general, i.e. not specific to COVID-19, clinical trials in children are rarely undertaken except when the disease or condition being addressed primarily affects children. Paediatric clinical trials can be more challenging to conduct for various reasons, including ethical considerations. In general, it is not unusual for there to be gaps in trial activities for certain populations, including pregnant women, children, older people, immunosuppressed or immunocompromised people or other high-risk populations with multiple comorbidities. Clinical trial participants in general rarely include vulnerable groups.

75. As explained above, it is likely that any further detail to be specifically included in the scoring matrix was limited to what could be easily extractable from the trial registries. The inclusion of an additional point for therapeutics that were in trials that included children in the scoring matrix had little impact on the treatments included in the prioritised list and/or selected for consideration by RAPID C-19, mainly because not many trials included children. The briefing documents considered by the Oversight

Group contained more detail on any special populations that were included in the relevant trials of that treatment.

Figure 2: RAPID C-19 horizon scanning scoring matrix.

Criterion	Scoring Matrix	Score	Rationale
High level of investigative activity (volume of trials)	1 trial only	1	A potential indicator of early positive evidence of efficacy and strong scientific rationale for activity.
	2-5 trials	2	
	More than 5 trials	4	
Locations of trials	Rest of world	1	Potentially easier to obtain access to results of trials conducted in the UK based on strong links with UK trial investigators, and results likely to be most relevant / generalizable to NHS clinical practice.
	EU/US/Canada/Australia	2	
	UK	4	
Trial phase / design	Unknown or phase 0-1	1	More robust clinically interpretable data expected from trials in later phases, potentially including comparative efficacy evidence.
	Phase 2+	2	
	Phase 2+ and randomised	4	
Trial size	<100 participants	0	Larger trials will likely provide more robust evidence with less bias.
	100-999 participants	2	
	>1,000 participants	3	
Regulatory status	No UK/EU licence	0	The access pathway for treatments with a UK licence likely to be quicker from an assessment and supply perspective.
	EU licence (not UK)	1	
	UK licence	2	
Special populations	Active paediatric trials	1	To address the gap in trial activities in paediatric patients.

Figure 3: RAPID C-19 horizon scanning scoring matrix updated October 2020

Criterion	Scoring matrix	Score	Rationale
High level of investigative activity (volume of trials)	1 trial only	1	A potential indicator of early positive evidence of efficacy and strong scientific rationale for activity.
	2-5 trials	2	
	More than 5 trials	4	
Locations of trials	Rest of world	1	Potentially easier to obtain access to results of trials conducted in the UK based on strong links with UK trial investigators, and results likely to be most relevant/generalisable to NHS clinical practice.
	~~EU/~~US/Canada/Australia	2	
	UK/~~EU~~	~~43~~	
Trial phase/design	Unknown or phase 0-1	1	More robust and clinically interpretable data expected from trials in later phases, potentially including comparative efficacy evidence.
	Phase 2+	2	
	Phase 2+ and randomised	4	
Trial size	<100 participants	0	Larger trials will likely provide more robust evidence with less bias.
	100-999 participants	2	
	≥1,000 participants	3	
~~**Regulatory status**~~	~~No UK/EU licence~~	~~0~~	~~The access pathway for treatments with a UK licence likely to be quicker from an assessment and supply perspective.~~
	~~EU licence (not UK)~~	~~1~~	
	~~UK licence~~	~~2~~	
Special populations	Active paediatric trials	1	To address the gap in trial activities in paediatric patients.

76. The scoring matrix was amended in October 2020 (**see figure 3** above-changes marked in red) to ensure that any novel therapeutics in development were not missed. The initial prioritisation criteria prioritised therapeutics in UK trials because it was considered potentially easier to obtain access to results of trials conducted in the UK based on strong links with UK trial investigators and results likely to be most relevant/generalisable to NHS clinical practice. There was no guarantee that any new therapeutics in development would have trial sites in the UK and so the amendments to the scoring in relation to trial location could increase the likelihood of novel therapeutics appearing in the prioritised list if they scored highly on the other criteria relating to the investigative features of the trials.

77. The initial prioritisation criteria prioritised therapeutics that were already licensed because it was considered that the access pathway was likely to be quicker from an assessment

and supply perspective. So, the scoring matrix included reference to regulatory status, with a score of 0 if the medicine was not yet licensed in the UK or EU, 1 if it was licensed in the EU but not UK and 2 if it was licensed in the UK. Novel therapeutics in development for COVID-19, that is, new molecules, would not yet be licensed and so this meant that potentially interesting new therapeutics without a licence could be potentially omitted from the prioritisation list. So, removing these extra 'points' for already licensed medicines, would increase the chances of novel therapeutics being included in the prioritised list if they scored highly on the other criteria relating to the investigative features of the trials. Consideration of the regulatory status of a product could be given later in the process, that is, in the briefing documents considered by the Oversight Group.

78. RAPID C-19 did not necessarily consider all therapeutics in the prioritised list and did consider therapeutics outside of the prioritised list. The stratification of the horizon scanning information was simply a way to prioritise what therapeutics to look at and did not constitute eligibility for consideration. Other intelligence also informed what topics RAPID C-19 considered. This was obtained either through further information gathering by the NICE team or insight from members of the Oversight Group or the DHSC ATTF and included considerations such as biological plausibility, UK platform trial activity, and the regulatory intentions of sponsors.

79. Furthermore, the prioritised list did not remain static as the trial landscape evolved. As noted in paragraph 77, the initial prioritisation criteria prioritised therapeutics that were already licensed because it was considered that the access pathway was likely to be quicker from an assessment and supply perspective. However this was changed in October 2020 to ensure that any novel therapeutics in development were not missed. The RAPID C-19 process itself did not differ at all between new therapeutics in development and repurposed existing drugs. It should be noted however that new therapeutics in development required UK marketing authorisation before rapid access could be granted.

Enrichment and monitoring

80. The NICE technical team within the RAPID C-19 secretariat augmented the horizon scanning information produced by NIHRIO (as explained above) to develop topic briefings for the Oversight Group. The briefings were 'living documents', kept up to date by the NICE team with emerging evidence and other information that related to the potential for rapid access. A weekly literature search was undertaken by NICE Information Services which fed into RAPID C-19's monitoring processes. This included newly published papers, conference abstracts, preprints and international guideline developments. The results from the broad search were triaged to specific topic categories for detailed consideration.

81. The RAPID C-19 secretariat contacted the lead investigators of many trials, which included both academic sponsors and companies to understand when trial results might be available and if investigators would be willing to share them with RAPID C-19. A spreadsheet outlining the extent of trial engagement is produced as **Exhibit HK4-13/ INQ000316253.** The information the secretariat did get from investigators was helpful in prioritising and planning activity, and where draft manuscripts or submitted papers were shared it enabled RAPID C-19 to consider the evidence as soon as possible. Some investigators did not respond to the emails from the secretariat, and some responded agreeing to share information in future which did not transpire; it is likely that this is because the trial findings did not suggest the treatment was beneficial or the trial did not complete for some reason.

82. Information on the progress and likely readout timings of the key UK platform trials (for example, RECOVERY, REMAP-CAP, PRINCIPLE) was obtained largely through contacts at the DHSC ATTF and insight from RAPID C-19 members. The secretariat, and RAPID C-19 members, were also linked in with the meetings of the UKCTF.

83. Trial investigators were not invited to the Oversight Group, with the exception of the chief investigators of key UK platform trials. Co-chief investigators of the RECOVERY trial, Peter Horby and Martin Landray, attended an Oversight Group meeting in June 2020 to provide an update on the medicines included in the trial and anticipated readout times where known. RECOVERY was an international adaptive platform trial led by the

University of Oxford comparing several treatments with standard care in hospitalised patients with clinically suspected or laboratory confirmed SARS-CoV-2 infection. Chief investigator of the Post-hospitalisation COVID-19 ["PHOSP-COVID"] trial, Chris Brightling, attended an Oversight Group meeting in November 2020 to talk about the establishment of this study. The PHOSP-COVID study was being set up to understand the long-term impact of COVID-19 on patients who had been hospitalised, led by the University of Leicester. On a few occasions, separate meetings were arranged with investigators, including Christopher Butler (PRINCIPLE trial co-chief investigator) and Anthony Gordon (REMAP-CAP UK chief investigator). PRINCIPLE was a UK-based adaptive platform trial comparing several treatments with standard care in patients in the community at higher risk of complications from COVID-19 (aged 65 and over or aged 50 and over with comorbidity), who had been unwell for up to 14 days with suspected or confirmed COVID-19. It was led by the University of Oxford. REMAP-CAP was an international adaptive platform trial comparing several treatments with standard care in patients in critical care requiring respiratory or organ support with suspected or confirmed COVID-19. In the UK, the trial was led by Imperial College London and the Intensive Care National Audit and Research Centre.

84. RAPID C-19 members also attended meetings with non-UK trial investigators (for example, of the SAVE-MORE trial, a study undertaken in Greece to investigate anakinra, and of the DORM trial, a study undertaken in Singapore to investigate povidone-iodine amongst other treatments). These meetings were usually arranged by NHSE, and they were intended for RAPID C-19 members to understand more detail about the trial results of interest and to ask questions of the investigators, to inform its considerations about whether the results warranted consideration for rapid access where the trial results were unclear or ambiguous. Meetings with companies sponsoring trials of new therapeutics in development were generally initiated by the DHSC ATTF, with RAPID C-19 members invited.

Briefings

85. The briefings were intended to provide the information needed to judge whether a treatment warranted consideration for rapid access. They included information about the existing evidence for efficacy in treating COVID-19, the ongoing trials, and the

regulatory status and commercial availability (where known) for the product. The sources for this information included the NIHRIO scan, clinical trial registries, company websites, literature searches and press alerts, as well as soft intelligence from Oversight Group members, the DHSC ATTF and trial investigators where available. Where evidence was available, the briefing documents were designed to provide a rapid overview of it to support the considerations of the Oversight Group in relation to rapid access and did not represent a comprehensive evidence review with associated formal methodology. The briefings were kept up to date, by the on-going monitoring explained above, as evidence emerged. Please see **Table 4** below:

Table 4: RAPID C-19 briefings: Oversight Group considerations and information needed.

Oversight Group consideration	Information needed
Is existing evidence sufficient to warrant consideration for interim patient access?	Is there existing evidence? If so, of what type and quality? Are the results positive, negative or mixed?
Which are the trials that are likely to provide robust, generalisable and timely results that constitute a strong signal (or not) as to whether the treatment warrants consideration for rapid access? When are they likely to read out?	Are there ongoing trials? If so, of what design and size and in which populations and locations? Which are the key trials?
Could the drug be used immediately (e.g., off-label)?	Is the product already licensed in the UK/elsewhere? If not, when is it likely to be licensed?
Is the drug currently available in the UK?	Is the product currently available and are stocks sufficient? Will stocks be purchased?

RAPID C-19 Oversight Group review

86. As stated above, the Oversight Group's considerations were informed by the briefings prepared by the secretariat. When topics were first presented to the Oversight Group it was unlikely that there was yet sufficient evidence to warrant consideration for rapid access, and so these topics were then monitored by the secretariat. The topics were brought back to the Oversight Group when there was a substantive new development to discuss. This could relate to emerging evidence or regulatory or other developments that could impact on the group's considerations around potential rapid access.

87. The Oversight Group agreed the next steps for each therapeutic (also called 'topics'), considering the emerging evidence. The options included a combination of the below:

a. **Progress:** Where good evidence of efficacy is sufficient for further action to be taken. The Oversight Group's assessment of the evidence and suggested next steps were summarised in a report to the CMO submitted via the ATTF. This was often produced a day after the Oversight Group's consideration of the evidence. The CMO report included a brief summary of the evidence considered, and any other considerations relating to regulatory status or potential use in clinical practice and constituted a summary of the Oversight Group's consensus opinion on the evidence and its conclusions relating to rapid access.

b. **Monitor:** Where good evidence of efficacy was currently insufficient but there were other ongoing trials. The topic would remain in the enrichment and monitoring stage and would be brought back to the Oversight Group when results from the identified key trial(s) became available.

c. **Stand down:** Where there was no evidence of efficacy and none likely to be forthcoming. The topic was deprioritised for active monitoring but could be brought back to the Oversight Group if new evidence emerged.

88. Where new key evidence was available, the NICE team would present a high-level overview of the evidence, highlighting important aspects relevant to a critique of the trial's quality, generalisability and robustness of results that would then be discussed by the Oversight Group. Members of the Oversight Group would indicate whether a CMO report would be needed to communicate its conclusions. In circumstances where a key trial had reported clear and unambiguous evidence of benefit (for example, the tocilizumab results from RECOVERY trial), a subset of the Oversight Group comprising the senior decision-making members would be quickly set up outside of the usual weekly Oversight Group schedule. This resulted in the CMO being informed of beneficial medicines at the earliest opportunity.

89. Details of the key trials whose results prompted a RAPID C-19 response in the form of a CMO report, are attached at **Exhibit HK4-14/INQ000252477.** Also included within this exhibit are key trials whose results prompted rapid interim patient access prior to the CMO report being included in RAPID C-19 processes. Due to the nature of the pandemic emergency, RAPID C-19 processes iterated over time and CMO reports - as a formal summary of RAPID C-19's opinion - were added to the process in December 2020. Decision-making on interim access arrangements rested with the CMO and DHSC and was not dependent on a RAPID C-19 CMO report. Furthermore, RAPID C-19 may have advised the CMO of a positive signal from a trial that warranted consideration for rapid interim patient access but preparations for access were not subsequently progressed for various reasons (e.g. the emergence of more information, regulatory developments). Information on the provision of patient access via the RAPID C-19 process is included within **Exhibit HK4-14/INQ000252477** for additional context. This applied to anakinra, casirivimab plus imdevimab (for post-exposure prophylaxis), bamlanivimab plus etesevimab, and regdanvimab.

90. Where RAPID C-19 submitted CMO reports suggesting a therapeutic should be considered for rapid access, the fact that rapid access did not subsequently progress was not due to the DHSC/CMO disagreeing with that position, but more that on further consideration undertaken by the relevant organisations, it was not appropriate or feasible to proceed to rapid access. Some illustrative examples are provided below:

- A CMO report on anakinra proposed that it could be considered for rapid patient access, but on further interrogation of the data and anticipated implementation issues, NHSE did not continue to policy development.
- A CMO report on regdanvimab proposed that it could be considered for rapid patient access subject to it receiving marketing authorisation from the MHRA and confirmation of activity against the currently circulating Omicron variant. Neither of these eventualities subsequently materialised.

No therapeutics were granted rapid access against RAPID C-19's advice.

91. RAPID C-19 were aware of the trials that were prioritised by NIHR, including those designated as Urgent Public Health trials, which included trials such as RECOVERY

and REMAP-CAP. The RAPID C-19 secretariat provided by NICE, as part of its role in monitoring the emerging evidence, was kept up to date on the progress of these trials through contacts at the DHSC ATTF, as well as insight from RAPID C-19 members.

92. With regard to PROTECT-V, PROTECT-CH and PANORAMIC, there were no results during the Module 4 relevant period for RAPID C-19 to consider. For information, (although outside of the relevant period) RAPID C-19 did consider the results from PANORAMIC when they became available in September 2022 and submitted a report to the CMO dated 21 September 2022. PANORAMIC was a randomised, controlled, open-label UK-based adaptive platform trial led by the University of Oxford, comparing treatments with standard care in patients in the community at higher risk of complications with COVID-19 (at least 50 years old, or 18 and over who were considered clinically vulnerable), who had been unwell for 5 days or less with confirmed COVID-19. Patients were randomised to the molnupiravir arm from 8 December 2021 until 27 April 2022. The results showed that molnupiravir did not reduce hospitalisation or death compared with standard care in people in the community at higher risk of complications from COVID-19. RAPID C-19's response was a report to the CMO not recommending consideration of expanding interim access (interim access to molnupiravir had been granted in December 2021 for the highest risk patients, as defined in the DHSC commissioned Independent Advisory Group Report).

93. The results from SOLIDARITY did not prompt a CMO report from RAPID C-19, primarily because its results did not suggest anything different to the extant understanding of the clinical effectiveness of the therapeutics being investigated (remdesivir, hydroxychloroquine, lopinavir and interferon beta-1a) that would change the current position with regard to consideration of rapid access. Interim access to remdesivir had been granted in July 2020 for hospitalised patients as evidence at that time showed that, although there was no evidence of a mortality benefit, treatment with remdesivir resulted in a significantly shorter time to recovery compared with placebo. There had been no evidence suggesting that hydroxychloroquine, lopinavir or interferon beta-1a should be considered for rapid access. SOLIDARITY was a randomised, controlled, open-label international adaptive trial led by the WHO, comparing treatments with standard care in hospitalised patients with moderate to severe disease. Patients were randomised from 22 March 2020 to 4 October 2020. The interim results published in February 2021

showed that these treatments did not reduce death in people with moderate to severe disease in hospital, compared with standard care. The final results were published in May 2022, which included additional patients randomised up to 29 January 2021, but again, these results did not suggest a change to the current position with regard to rapid access.

94. RAPID C-19 assessed the evidence available for the clinical effectiveness of therapeutics using the standard considerations when reviewing clinical evidence. These include assessing the statistical results alongside the internal and external validity of the trial (that is, an assessment of potential sources of bias), in order to interpret the robustness and reliability of the results, and their relevance to patients in the NHS; details as follows:

    a. **Internal validity:** This includes the design, analysis and conduct of the trial, including for example:
        i. whether the trial was blinded,
        ii. the method of randomisation[5],
        iii. completeness of follow-up,
        iv. size and power of the trial, including number of events[6],
        v. selection and measurement of outcomes[7], including whether pre-specified and whether objective or subjective,
        vi. the inclusion and exclusion criteria[8],
        vii. whether the analysis was methodologically sound,
        viii. whether the trial stopped early, or if any changes were made to the protocol once the trial had started.

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[5] The random allocation of participants in a clinical trial to the intervention and control groups using mechanisms such as random number table or a computer-generated random number list. This type of allocation reduces potential bias in assigning participants to the intervention and control groups and is a key condition for the use of many statistical tests used to analyse trial results.
[6] The number of people in a group in whom an event (for example an outcome of interest such as hospital admission or death) is observed over a specified period of time.
[7] The impact that an intervention or treatment has on people included in the trial (for example, the number of hospital admissions or deaths). It is an event that can be measured and is of importance for the patient, determined on the basis of the health problem being studied.
[8] Defines the sample of patients to be included in a study to determine whether a treatment is effective (for example, in a trial for a therapeutic for COVID-19, the inclusion criteria may stipulate that COVID-19 has been confirmed by a PCR test).

b. **External validity:** This is about whether the trial's results were generalisable to the population of interest, that is, whether the results could be expected to be applicable in people outside of the trial participants and in routine clinical practice. It involves considering whether aspects of the trial were representative of what would be expected to be seen in the UK, such as the following (list not exhaustive):
    i. the location and setting of the trial, and if outside of the UK, whether there were any relevant differences in health systems or health-seeking behaviour that might potentially impact on the interpretation of the outcome data,
    ii. the standard of care and/or other treatments received by patients,
    iii. the inclusion and exclusion criteria,
    iv. the baseline demographic and clinical characteristics of trial participants, including vaccination status (and where relevant, serostatus (whether participants have detectable antibodies against SARS-CoV-2)),
    v. the dominant variant at the time patients were enrolled to the trial, and
    vi. the background (baseline) event rates[9].

c. **Statistical results:** The group considered:
    i. whether the results were statistically significant,
    ii. whether results were consistent across subgroups and secondary outcomes,
    iii. whether the results differed across subgroups, for example if a greater or lesser benefit was seen in certain groups,
    iv. whether the demographic and clinical characteristics were balanced across the intervention and control groups[10],
    v. the magnitude of benefit shown, and whether it was clinically meaningful,
    vi. the proportion of participants completing the full course of treatment,

[9] The set of measurements at the beginning of a study with which subsequent results are compared.
[10] In medical terms the intervention could be a drug treatment, surgical procedure, diagnostic test or psychological therapy. The control group is a group of people in a study who do not have the intervention or test being studied. Instead, they may have the standard intervention (sometimes called 'usual care') or a dummy intervention (placebo). The results for the control group are compared with those for a group having the intervention being tested. The aim is to check for any differences. Ideally, the people in the control group should be as similar as possible to those in the intervention group, to make it as easy as possible to detect any effects due to the interventions.

vii. the 'number needed to treat', that is, based on the results of the trial, the number of patients on average you would need to treat to avoid 1 additional adverse outcome (or achieve 1 additional good outcome).

95. The Oversight Group also took note of adverse events data and whether there were any potential safety concerns, commented on any information available on activity against the currently dominant variant (particularly for neutralising antibodies), and was cognisant of the transparency of the reporting of data, and whether results were peer reviewed.

96. It is the MHRA that is responsible for the safety of therapeutics. Any therapeutics licensed by the MHRA are deemed to be safe for use. Interim access policies included reference to safety reporting via the MHRA yellow card scheme.

Changes in effectiveness of therapeutics

97. Changes in effectiveness of therapeutics due to the evolution of new variants was a key challenge for RAPID C-19; further detail with regard to this is detailed within Lessons Learned below (Page 61). Although potentially relevant to all types of therapeutics it was most immediately relevant to the neutralising antibody technologies because of their mode of action. In general terms, these antibodies bind to the spike protein of the virus in order to neutralise its effect, and so when the virus itself changes, there is no guarantee that this neutralising activity is maintained. The main implications of this were 2-fold.

98. Firstly, it meant that the clinical evidence of effectiveness became outdated – the evidence from trials conducted earlier in the pandemic when a different variant was dominant, or in a country or countries where the dominant variant differed to that in the UK, was not generalisable to the current situation. That is, the results could not necessarily be expected to be representative of its likely effectiveness if used in the current UK population.

99. Secondly, the quickest method for assessing the antiviral activity of these technologies against other variants was to conduct in-vitro (lab-based) experiments. There was little appetite from commercial sponsors to undertake further clinical trials, and indeed, the

speed at which new variants started emerging during the later stages of the pandemic suggested this course of action was unlikely to provide the clarity needed. In-vitro assessments could provide the information needed when the loss of activity was clear cut; for example, in December 2021 Roche had concluded from its own tests that casirivimab plus imdevimab did not exhibit antiviral activity against the Omicron variant and announced this publicly. In cases which were not so clear cut (that is, lab tests suggested reduced activity), there emerged numerous in-vitro studies undertaken by various researchers and with a range of conclusions. It should be noted that in drug development, in-vitro assessments take place in the early stages and provide developers with an indication of whether the molecule has sufficient potential for activity against a disease that it should progress to in vivo (animal) testing and then potential clinical trials in humans. Many drugs can show antiviral activity in the laboratory but are then proven not to be clinically beneficial when investigated in trials.

100. RAPID C-19 had been established to consider the clinical evidence for the effectiveness of therapeutics. It did not have the expertise to review and make conclusions from non-clinical evidence and experts were brought into the Oversight Group from the Prophylaxis Oversight Group[11] on a regular basis as and when RAPID C-19 had questions for them. The POG effectively supported RAPID C-19 to interpret the in-vitro data and provide explanation and context to the issues at hand. This whole issue was not specific to the operation of RAPID C-19, in that there were no agreed standard methods for assessing the quality of in-vitro studies and their results, and there existed no scientific consensus that in-vitro results could be extrapolated into conclusions about clinical effectiveness.

Use of clinical trial and research information

101. Neither NICE nor RAPID C-19 were responsible for registering, selecting, authorising or regulating clinical studies. It is important to note that RAPID C-19 also did not have a role in the operation or approval of clinical trials. Whilst it is noted that the operation of clinical trials are subject to specific ethical standards, as RAPID C-19 had no

[11] This group was established by the DHSC in July 2020 to guide development of pre and post exposure prophylaxis for COVID-19. The group was formed of independent experts and chaired by Professor David Lalloo, Director, Liverpool School of Tropical Medicine.

role in the running of clinical trials, NICE are unable to comment on how these standards were maintained. However, as explained above, RAPID C-19 monitored for the results of clinical trials.

102. For information and to provide an indication of the volume of research being undertaken, a NIHRIO scan from early April 2020 identified 444 registered trials investigating 103 therapeutics. In April 2021 there were 3,886 trials investigating 866 therapeutics. In April 2022 there were 5,743 trials investigating 1,152 therapeutics. At the end of June 2022 there were 5,980 trials investigating 1,194 therapeutics. As indicated, the clinical trials investigating therapeutics for possible treatment of COVID-19 was not a static indicator. Many trials were suspended, withdrawn, or never got started. The reasons for this are likely to vary according to circumstance and are not necessarily known, however it is likely that outcomes from other research was a factor (for example, early in the pandemic there was interest in certain drugs that were subsequently proven not be beneficial and so any planned research into those drugs would then no longer be worthwhile pursuing). Later in the pandemic after vaccination programmes had been rolled out, some trials were stopped early because it was no longer possible to recruit enough participants. Some trials are likely to have completed but their results never published; this could be, amongst other reasons, because of a general tendency seen in clinical research for the results of trials with positive findings being more likely to be published than those with equivocal or negative findings.

103. While the volume of clinical trials being undertaken around the world was substantial, in many cases the individual trials were too small and not sufficiently powered to provide robust and reliable results. The ability of the UK platform trials (RECOVERY, REMAP-CAP, PRINCIPLE) to provide a clear, fast answer on the efficacy of therapeutics particularly repurposed therapeutics, showed the value of a national coordinated approach to investigating treatments in a pandemic emergency.

Relationship with COVID-19 Guidelines

104. The relationship between RAPID C-19 and the COVID-19 guidelines is illustrated in the "RAPID C-19 and COVID-19 guidelines: therapeutics for COVID-19 process map" which is attached at **Exhibit HK4-15/INQ000316255**. A positive signal from the

Oversight Group would form a trigger within the COVID-19 guidelines programme and if it met the required criteria, the therapeutic would be progressed for recommendation development. The required criteria were:

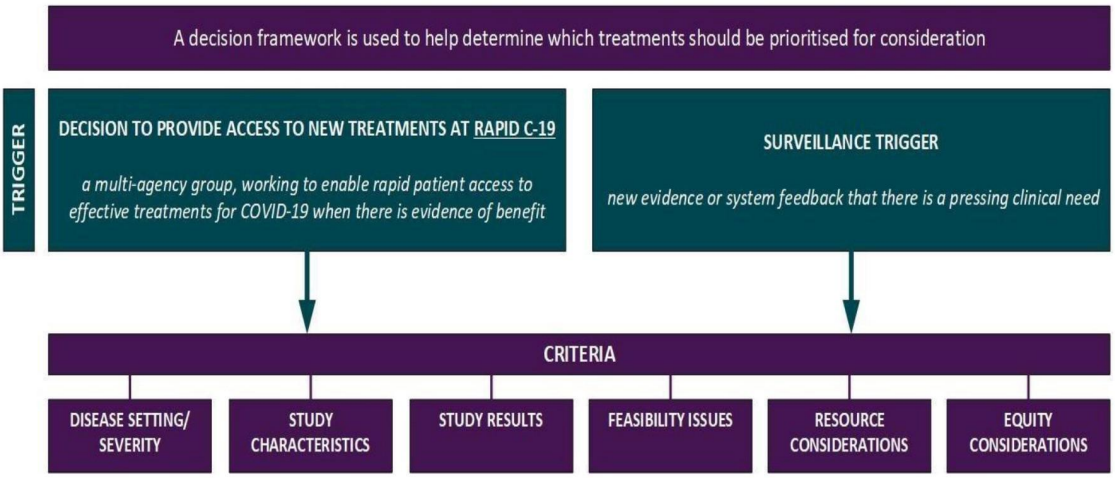
- **Disease setting/severity** – this was where the therapeutic sits within the treatment pathway (prevention/mild/moderate/severe/critical & rehabilitation / community / hospital (ward)/ hospital (ICU)).
- **Study characteristics** – This included any large / pivotal trials and expected date of completion, study size, population studies and publication status.
- **Study results** – This included signal on benefit and harm
- **Feasibility issues** – This included whether the therapeutic was licensed by MHRA, the parameters of licence, existing/developing NHSE guidance and policy, MHRA Central Alerting System ["CAS"][12] alerts and relevance to UK population and practice.
- **Resource considerations** – This was limited to unit costs, any supply issues and/or comments on any resource implications.
- **Equity considerations** – These included pressures on supply chains for existing patients on repurposed medicines and any restrictions to the eligible population from central government or NHSE.

105. The consideration of whether a therapeutic met the required criteria was undertaken by senior managers in NICE's COVID-19 guideline team. Although I am aware of the criteria, I was not involved in the guideline team's work and as such I am unaware how the criteria was weighted and applied.

106. This process is set out in **Figure 4**: COVID-19 guidelines prioritisation criteria for COVID-19 therapeutics, below:

[12] The 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, including independent providers of health and social care.

Figure 4: COVID-19 guidelines prioritisation criteria for COVID-19 therapeutics



107. If a therapeutic with a positive signal was progressed for rapid access and guideline recommendation development, a summary of the RAPID C-19 topic briefing would be published on the NICE website. This provided information about the therapeutic and the key evidence underpinning the rapid access decision, while it underwent a full evidence review by the COVID-19 guideline team.

108. The summary briefings produced and published on the NICE website related to the following therapeutics.

- Budesonide - **Exhibit HK4-228/ INQ000316134**
- Casirivimab plus imdevimab - **Exhibit HK4-231/INQ000316139**
- Sotrovimab - **Exhibit HK4-257/INQ000316180**
- Molnupiravir - **Exhibit HK4-258/INQ000316181**
- Nirmatrelvir plus ritonavir - **Exhibit HK4-262/INQ000316219**

109. Once recommendations on that therapeutic were published in a COVID-19 guideline, the RAPID C-19 summary briefing would be replaced by signposts to the guideline. The guideline content superseded all documentation rapidly developed to support the Oversight Group's considerations, and the guideline evidence review took precedence over any versions of RAPID C-19 briefing documents. For further information, please see Dr Paul Chrisp's statement.

COVID-19 therapeutics

Therapeutics recommended

110. A table summarising the list of therapeutics recommended for consideration for rapid patient access by RAPID C-19 and recommended for use in the treatment of COVID-19 in NICE COVID-19 rapid guidelines, is exhibited at **Exhibit HK4-16/ INQ000316256**.

111. RAPID C-19 had no role in drug discovery (which is the process by which a new chemical or biological substance is identified). It also did not approve trials or treatments. However, the Oversight Group's consideration of the clinical evidence for the effectiveness of treatments contributed to the rapid availability of the following treatments:

- Remdesivir
- Dexamethasone
- Hydrocortisone
- Tocilizumab
- Sarilumab
- Casirivimab plus imdevimab[13]
- Sotrovimab
- Molnupiravir
- Nirmatrelvir plus ritonavir
- Baricitinib

112. NICE had a good system in place to track and monitor the emerging data and make timely judgements. Any decisions regarding the recommendation of therapeutics are always based on clinical effectiveness and are made upon the evidence available at the time. It is often easy to be critical of a decision with hindsight, but all RAPID C-19 decisions were made on the evidence available at a particular moment in time – and at

[13] Please note casirivimab plus imdevimab were granted access and then withdrawn through the process due to lack of effectiveness in circulating variants. See Table 5

a time when the virus was rapidly evolving. RAPID C-19 was not concerned with the cost of a therapeutic as that was a matter for the DHSC once a recommendation for consideration of rapid access had been made to the CMO.

113. **Tables 5 and 6** provide further detail on timescales for treatment access. To further explain, the tables below list the treatments granted rapid access and the date from which access was available (the point an NHSE clinical policy was issued). For repurposed medicines this was the number of days between RAPID C-19 considering the key evidence and access being granted. For new medicines, the timescale from the date of marketing authorisation is considered of most relevance, because this was required before access could be granted (the key evidence may have emerged prior to regulatory approval). The format of the key evidence seen by the Oversight Group varied – for example, it may have been a published paper, press release or draft manuscript shared in confidence. This is also detailed in the tables below. The NHS was informed of the UK position on use of therapeutics for COVID-19 through the MHRA Central Alerting System. The issue of therapeutic alerts and position statements enabled rapid implementation and were quickly followed by the issue of clinical policies that iterated over time to reflect the latest evidence and information.

Table 5: Timescales for treatment access for repurposed treatments

Treatment	**No. days to patient access (calculated from receiving pivotal RCT results or results publication)**	**Date of access**
Dexamethasone	0	16 June 2020 (therapeutic alert)
Hydrocortisone	1 day (from publication) 10 days (from early sighting of results)	3 September 2020 (therapeutic alert)
Tocilizumab	6 days (from press release)	25 November 2020 (interim position statement)
	3 days (from draft pre-print sent to RAPID C-19)	8 January 2021 (updated interim position statement) 1 February 2021 (interim clinical policy)

	7 days (from pre-print publication)	17 February 2021 (interim clinical policy)
Sarilumab	3 days (from draft pre-print sent to RAPID C-19)	8 January 2021 (updated interim position statement) 1 February 2021 (interim clinical policy)
	7 days (from pre-print publication)	17 February 2021 (interim clinical policy)
Baricitinib	64 days (from pre-print publication)	5 May 2022 (interim clinical policy)

Table 6: Timescales for treatment access for new treatments

Treatment	**No. of days to patient access (calculated from marketing authorisation date)**	**Date of access**
Remdesivir	0 days	26 May 2020 (through the Early Access to Medicines Scheme, which aims to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation when there is a clear unmet medical need) 3 July 2020 (interim clinical policy at point of marketing authorisation)
Casirivimab plus imdevimab	29 days	17 September 2021 (interim clinical policy) *24 February 2022 (CAS alert noting withdrawal of product as ineffective against Omicron variant)*
Sotrovimab	14 days	16 December 2021 (interim clinical policy)
Molnupiravir	42 days	16 December 2021 (interim clinical policy)
Nirmatrelvir plus ritonavir	41 days	10 February 2022 (interim clinical policy)

Evusheld

114. The 2 antibodies making up Evusheld are tixagevimab and cilgavimab. In earlier documentation, Evusheld was referred to as AZD7442. In drug nomenclature, the first name is the chemical name used by the company in initial development – which in this case was AZD7442. The International Nonproprietory Name ["INN"] is the generic name of the active ingredient(s) of the drug. There is a standardised approach to assigning the INN, which is usually selected by WHO. In this case, the INN is tixagevimab and cilgavimab. Evusheld is the trade, or brand name. Once a drug goes off-patent and other companies have the ability to produce and market the drug, there may be many brand names for the same drug/active ingredient. A combination of these names was used by RAPID C-19 within the documents referred to in **Exhibit HK4-08 /INQ000494417.** For the purpose of this statement, the therapeutic will be referred to as Evusheld.

115. Evusheld was a new medicine being investigated for pre-exposure prophylaxis[14], post-exposure prophylaxis[15] and treatment (pre-hospitalised and hospitalised patients) of COVID-19. The Oversight Group had considered Evusheld on several occasions, starting in February 2021, when the Oversight Group noted the features of the medicine, the settings in which it was being investigated, the ongoing trials and expected timings of results and any known regulatory plans. The topic was then monitored for key trial readouts.

116. The use of Evusheld in post-exposure prophylaxis was considered by the Oversight Group on 13 October 2021 (see RAPID C-19 briefing AZD7442 exhibited as **Exhibit HK4-235/INQ000316147**). The key trial (STORM CHASER) had not met its primary endpoint of preventing the development of symptomatic COVID-19, therefore suggesting there was no benefit with Evusheld for post-exposure prophylaxis. Evusheld in post-exposure prophylaxis was not considered again by the Oversight Group for rapid access.

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[14] Pre-exposure prophylaxis refers to a preventative intervention given prior to exposure to a virus that is intended to reduce the chance of acquiring it.

[15] Post-exposure prophylaxis refers to a preventative intervention given after exposure to a virus that is intended to reduce the chance of acquiring it. In the context of COVID-19, this could be household contacts of people with confirmed COVID-19, but who are currently testing negative for the virus.

117. The use of Evusheld for treating COVID-19 in hospitalised patients was considered by the Oversight Group on 17 August 2022 (see RAPID C-19 briefing AZD7442 exhibited as **Exhibit HK4-281/INQ000494607**). It was noted that the key trial (ACTIV-3) had not met its primary endpoint of sustained clinical recovery (therefore suggesting there was no benefit with Evusheld for treating COVID-19 in hospitalised patients). Evusheld for treating COVID-19 in hospitalised patients was not considered again by the Oversight Group for rapid access.

118. The use of Evusheld for treating COVID-19 in non-hospitalised patients was considered by the Oversight Group on 15 June 2022 (see RAPID C-19 briefing AZD7442 exhibited as **Exhibit HK4-277/INQ000316211**). The results of the key trial (TACKLE) were discussed and subsequent CMO report submitted (dated 23 June 2022 – **Exhibit HK4-278/INQ000316214**). RAPID C-19 advised the CMO that it considered that the results from the TACKLE clinical trial were not directly relevant to the current situation. This was because the study population were unvaccinated and enrolled when pre-Omicron variants were dominant. Therefore, these results did not warrant action to progress towards patient access.

119. Consequently, RAPID C-19 primarily focused on consideration of Evusheld for pre-exposure prophylaxis use. A chronology and account of RAPID C-19's consideration of Evusheld between February 2021 and June 2022 in pre-exposure prophylaxis is outlined in table 7 below.

Table 7: Chronology of RAPID C-19's consideration of Evusheld for pre-exposure prophylaxis between **February 2021 and June 2022**

Date	Activity	Outcome	Exhibit name	Exhibit reference
03.02.2021	Oversight group meeting	New topic-monitor	RAPID-C19 Briefing: AZD7442	**HK4-126/ INQ000315972**
13.10.2021	Oversight group meeting	Continue to monitor for full results from key trials	RAPID-C19 Briefing AZD7442	**HK4-235/ INQ000316147**
24.11.2021	Oversight group meeting	Continue to monitor for full results from key trials	RAPID C-19 Briefing AZD7442	**HK4-248/ INQ000316167**
08.12.2021	Oversight group meeting	Prepare a report to CMO	RAPID-C19 Briefing AZD7442	**HK4-249/ INQ000316170**

		Continue to monitor for full results from key trials		
22.12.2021	Oversight group meeting	Submit report to CMO	RAPID-C19 briefing AZD7442	**HK4-255/ INQ000316170**
23.12.2021	Report to CMO	Report submitted to CMO. Consideration for progressing towards patient access subject to marketing authorisation and confirmation of activity against Omicron	RAPID C-19 Report to CMO AZD7442	**HK4-256/ INQ000316179**
09.02.2022	Oversight group meeting	Continue to monitor and defer full discussion on next steps with regard to prophylactic use to 16.02.2022 Oversight Group	RAPID C-19 Briefing AZD7442	**HK4-263/ INQ000316222**
16.02.2022	Oversight group meeting	Continue to monitor. Await UKHSA report	RAPID C-19 Briefing AZD7442 (re-presented for information only)	**Exhibit HK4-265/ INQ000316222**
18.05.2022	Oversight group meeting	Continue to monitor. Prepare CMO report	RAPID C-19 Briefing AZD7442	**HK4-275/ INQ000316209**
30.05.2022	Report to CMO	Report submitted to CMO Consideration that this information does not warrant action to progress toward patient access.	RAPID C-19 Report to CMO - Tixagevimab plus cilgavimab (Evusheld, AZD7442; AstraZeneca) in pre-exposure prophylaxis	**HK4-276/ INQ000316210**
15.06.2022	Oversight group meeting	Continue to monitor	RAPID C-19 Briefing AZD7442 (this relates primarily to treatment)	**HK4-08-277/ INQ000316211**

120. To reiterate, the RAPID C-19 briefing documents were intended to provide the information needed for the Oversight Group to judge whether a therapeutic warranted consideration for rapid access. They included information about the existing evidence for effectiveness, the ongoing trials, and the regulatory status and commercial availability (where known) about the product. Where evidence was available, the briefing documents were designed to provide a rapid overview of it to support the considerations

of the Oversight Group in relation to rapid access and did not represent a comprehensive evidence review with associated formal methodology. When topics were first presented to the Oversight Group it was unlikely that there was yet sufficient evidence to warrant consideration for rapid access, so these topics were then monitored by the secretariat. The topics were brought back to the Oversight Group when there was a substantive new development to discuss. This could relate to emerging evidence or regulatory or other developments that could impact on the group's considerations around potential rapid access.

RAPID C-19 Oversight Group – December 2021

121. On the 8 December 2021, the Oversight Group meeting discussed Evusheld. It considered a pre-publication manuscript shared in confidence by the company, with results from the key trial in pre-exposure prophylaxis (PROVENT).

122. The RAPID C-19 briefing paper (**Exhibit HK4-249/INQ000316170)** recommended the next steps as: a) consider preparing advice to the CMO in the light of the results from the pre-exposure prophylaxis PROVENT trial and b) monitor for full published results from ongoing key trials. The next steps were considered to both progress and monitor because the briefing covered Evusheld in different indications, not just pre-exposure prophylaxis. The Oversight Group were still awaiting the full results from the TACKLE trial of Evusheld as a treatment for COVID-19 and so would be continuing to monitor for those.

123. The Oversight Group agreed that the results of the PROVENT trial, detailed in a pre-publication manuscript provided in confidence by the company, represented a positive signal and to prepare advice to the CMO for rapid access consideration and seek input from the POG for inclusion in the CMO report given their specific expertise in this area (see **Exhibits HK4-09/INQ000316249 and HK4-256/INQ000316179**). Oversight Group members were not certain whether the evidence of benefit from the PROVENT trial was robust enough to consider for rapid access, given the lack of

evidence for efficacy against the currently dominant Omicron variant and therefore the lack of generalisability[16] to the then current situation.

124. On 22 December 2021, the Oversight Group meeting continued to discuss Evusheld. It agreed that Evusheld could be considered for rapid access subject to it receiving a MHRA marketing authorisation and confirmation of activity against the Omicron variant. It agreed to submit a CMO report dated 23 December 2021 (see **Exhibit HK4-256/INQ000316179**). The UKHSA (the organisation previously known as Public Health England) had been asked by the ATTF to assess the efficacy of Evusheld against Omicron. The timelines were not known to RAPID C-19 at this time, but the eventual output was the UKHSA report, which was considered by RAPID C-19 at the Oversight Group meeting of 18 May 2022.

RAPID C-19 Oversight Group – February to May 2022

125. On 9 and 16 February 2022 the Oversight Group again discussed Evusheld. On 9 February 2022 there was a brief update on conversations and activities happening elsewhere in the system regarding Evusheld, for example, the DHSC ATTF notifying of meetings it had had with UKHSA and AstraZeneca, and reporting when the POG would next be considering Evusheld. It was agreed to defer further discussion to the next meeting on 16 February 2022, which members of the POG attended (see **Exhibit HK4-09/INQ000316249**).

126. At the Oversight Group meeting of 16 February 2022, Professor David Lalloo provided feedback on the POG's considerations of Evusheld. At this point, the POG's opinion was that the evidence for Evusheld's activity against the Omicron variant was not strong and its own position was that the evidence as a whole was not robust enough to consider Evusheld for rapid access. The Oversight Group agreed that a formal report from UKHSA with its findings in regard to Evusheld's activity against the Omicron variant was needed to inform RAPID C-19's view (see **Exhibit HK4-09/INQ000316249**).

[16] Whether the results of a trial could be expected to be applicable to people outside of the trial population, and in routine, current, clinical practice.

127. Evusheld was therefore not discussed by the Oversight Group until the UKHSA report was received, which was on 17 May 2022. On 18 May 2022, the Oversight group again considered Evusheld in the light of the report shared by UKHSA – a copy of which is produced as **Exhibit HK4-279/INQ000494604.** It also considered a written commentary on behalf of the POG, produced as **Exhibit HK4-280/INQ000494606.** This provided a general introduction to the issue, comment on the UKHSA findings and a description of findings from 2 other papers. Note that the UKHSA report and the POG's commentary refers to both Evusheld and sotrovimab. The POG considered that the UKHSA data had not presented any reason to alter their previous conclusions. The Oversight Group was again attended by Professor David Lalloo who contributed to the discussion. As previously noted, the Oversight Group was not constituted to review non-clinical evidence i.e. in vitro data. All group members agreed that they required the expertise of members of the POG (Professor David Lalloo and his colleague Professor Andrew Owen) to interpret the data and offer some conclusions.

128. The Oversight Group was aware of the importance of greater protection for vulnerable groups who were shielding and of the need to be confident that any medicine provided for this purpose was effective and did not put these vulnerable groups at increased risk. The discussion was comprehensive and lengthy, and different opinions and perspectives were explored. Through this debate the group reached a consensus opinion that the non-clinical data did not provide sufficient confidence that Evusheld would be clinically effective against currently circulating variants.

129. The Oversight Group agreed that the non-clinical evidence, i.e. in vitro data, was not sufficient to support the clinical effectiveness of the treatment against Omicron. The Oversight Group concluded that, because of the difficulties in extrapolating non-clinical data to conclusions about clinical effectiveness, there was no certainty that Evusheld would prevent symptomatic COVID-19 caused by the Omicron variants in the vulnerable population who would potentially be eligible for this treatment. So, the risks of proceeding to patient access were considered to outweigh the risks of not providing this treatment in the pandemic context at the time. RAPID-C19 considered that the new information did not warrant action to progress towards patient access. It agreed to update the advice to the CMO from 23 December 2021 and a report was sent to the CMO on the 30 May 2022- **Exhibit HK4-276/INQ000316210.**

130. The issue regarding neutralising monoclonal antibodies and evolving viral variants was recognised as a much broader issue and the DHSC ATTF noted they would be taking forward some work on this.

RAPID C-19 Oversight Group – post June 2022

131. Following the advice to the CMO in May 2022 (and in the absence of further trial data or a means of extrapolating laboratory data into conclusions about clinical effectiveness), the ATTF requested that RAPID C-19 consider real world (observational) evidence from countries which had deployed Evusheld. This was to assess whether this was sufficiently robust to confirm its activity against Omicron. On 17 and 24 August 2022 the Oversight Group considered this evidence. The RAPID C-19 briefing documents that relate to these meetings are exhibited as **Exhibits HK4-281/INQ000494607** and **HK4-282/INQ000494608** respectively. The real-world evidence that was considered is exhibited as **Exhibit HK4-283/INQ000494609** and **HK4-284/INQ000494610** respectively.

132. The Oversight Group concluded that the quality of this data was insufficient to address the uncertainty or warrant action to progress to consideration for rapid access. The CMO advice was updated in a report dated 1 September 2022, exhibited as **Exhibit HK4-285/INQ000479901**. The updated CMO report included comments on the studies considered and reiterated the extant position, noting that further research should be considered to determine the clinical effectiveness and safety of Evusheld in the current UK population.

133. In summary, the Oversight Group considered that the uncertainties in the evidence base for Evusheld for pre-exposure prophylaxis use were too substantial to warrant consideration for rapid access. Subsequently the CMO and DHSC decided not to support interim access to Evusheld.

134. For information, although covering events outside of the relevant period, on 23 March 2022, NICE received a referral from DHSC to conduct a multiple technology

appraisal ["MTA"][17] of all of the treatments for COVID-19 that were being commissioned by NHSE on an interim basis (in response to the pandemic), as well as those expected to receive a an MHRA marketing authorisation during the time it would take to complete the MTA (**Exhibit HK4-286/INQ000494612).** This was in anticipation of the return to routine commissioning arrangements under the government's return to living with COVID-19 arrangements. On 19 July 2022, NICE received a further referral from DHSC to add Evusheld to the MTA, as it was expected to receive an extension to its marketing authorisation to include treatment of COVID-19 (**Exhibit HK4-287/INQ000494613)**. This licence extension was granted by MHRA in November 2022. On 8 May 2024, the guidance TA971: Remdesivir and Tixagevimab plus Cilgavimab for treating COVID-19 was published on the NICE website. A copy of the guidance is exhibited as **Exhibit HK4-288/INQ000494614;** Evusheld was not recommended for the treatment of COVID-19.

135. On 10 August 2022, NICE received a referral from DHSC to conduct a TA of Evusheld for preventing COVID-19, i.e. prophylaxis use. A copy of the referral letter is exhibited as **Exhibit HK4-289/INQ000494615**. On 14 June 2023, the guidance TA900: Tixagevimab plus Cilgavimab for preventing COVID-19 was published on the NICE website. A copy of the guidance is exhibited as **Exhibit HK4-290/INQ000494617;** Evusheld was not recommended for the pre-exposure prophylaxis of COVID-19.

136. On 9 December 2022, the European Medicines Agency's Emergency Taskforce issued a statement cautioning that monoclonal antibodies currently authorised for COVID-19 (such as Evusheld) were unlikely to be effective against emerging strains of SARS-CoV-2. Similarly, on 26 January 2023, the US Food and Drug Administration ["FDA"] revised the Emergency Use Authorization for Evusheld to limit its use to when the combined frequency of non-susceptible SARS-CoV-2 variants nationally is less than or equal to 90%. Based on this revision, the FDA suspended the authorisation for Evusheld in the US. NICE considers that, with the benefit of hindsight, the UK public health and regulatory system could have looked more intensively at whether or not Evusheld was effective against SARS-CoV-2 variants. This in itself would have been

[17] A NICE technology appraisal reviews the clinical and cost-effectiveness of technologies, typically, new pharmaceutical products or new licensed indications. This is undertaken in accordance with processes and methods set out in the NICE health technologies evaluation manual.

challenging however as the virus was constantly mutating and would require intensive tracking. Inevitably, there would always be a delay before any therapeutic was licensed and administered as a treatment and by that point, variants would likely have progressed and the therapeutic may no longer be as effective. This would cause a substantial concern and uncertainty for those patients who had received the therapeutic, which was given every 6 months, and believed they were protected from the virus, when in fact that may not be the case if the therapeutic was now less effective. Whilst NICE was aware of the progress of variants, UKHSA was responsible for providing that information.

Additional prophylactic treatments considered

137. Casirivimab plus imdevimab (brand name Ronapreve; another monoclonal antibody) was also considered by RAPID C-19 for post-exposure prophylaxis and positive results were reported in June 2021. The Oversight Group reviewed the results and provided a CMO report in July 2021 (**Exhibit HK4-220/INQ000316118)** indicating that it considered the results sufficiently robust to consider for rapid access subject to marketing authorisation but noting remaining unanswered questions regarding the generalisability of the results. Note that in December 2021 the company (Roche) subsequently advised that this therapeutic was not active against the Omicron variant.

138. RAPID C-19 considered other therapeutics that were being investigated in multiple settings that included the prophylactic setting; however, there was no forthcoming evidence that the Oversight Group considered strong enough to warrant consideration for interim patient access, and no other CMO reports were issued in relation to therapeutics for potential prophylactic use.

Equality and health Inequalities

139. RAPID C-19 were aware of the disproportionate impact of COVID-19 amongst different population groups, (such as those with primary or secondary immunodeficiencies and other conditions and as described in the report of the

independent advisory group commissioned by the DHSC[18]) and the continuing need for treatment options to prevent disease progression despite the widespread roll out of the vaccination programme. RAPID C-19's assessment of the effectiveness of therapeutics for COVID-19 and their potential for rapid access was dependent on the clinical evidence available from the trials being undertaken, but it was aware that people such as those on the Shielded Patient List ["SPL"] did not receive the same protection from vaccination as the general population. It is important to note that RAPID C-19's role was to consider the emerging evidence related to therapeutics in treating or preventing COVID-19, not the evidence for the effectiveness of the vaccines, including vaccines in specific population groups.

140. A key element of the Oversight Group's deliberations on specific treatments was the demographic characteristics of the people included in the trials. The CMO reports generally included comments on when there was a lack of evidence for efficacy in certain groups. For example, pregnant women, children, older people or immunosuppressed or immunocompromised people, or other high-risk populations. Information on any potential side effects or drug-drug interactions also formed part of the Oversight Group's deliberations, for example, if there were any drug-drug interactions that might mean a treatment would be contraindicated for a significant proportion of the higher risk population. When discussing treatments with strong enough evidence to warrant consideration for rapid access, the Oversight Group was cognisant of any issues that might adversely affect certain patient groups and the need for alternative options for these groups (especially in the outpatient setting, for example, nirmatrelvir plus ritonavir, sotrovimab, molnupiravir, and remdesivir).

Vulnerable Patient Groups

141. RAPID C-19's assessment of the use of therapeutics for COVID-19 and their potential for rapid access was dependent on the clinical evidence available from the trials being undertaken. Clinical trial participants rarely included vulnerable groups such as those on the SPL (a general point not specific to COVID-19 trials).

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[18] "Defining the highest-risk clinical subgroups upon community infection with SARS-CoV-2 when considering the use of neutralising monoclonal antibodies (nMABBs) and antiviral drugs: independent advisory group report" – published 30 May 2022

142. As noted above, RAPID C-19 was aware that people on the SPL did not receive the same protection from vaccination as the general population, but there was little evidence on which to consider the effectiveness of specific treatments in these specific groups or any other specifically defined groups. For example, in the key trial of Evusheld (tixagevimab plus cilgavimab) for treating COVID-19, only 5% of trial participants were described as immunocompromised; for the key trial of remdesivir for pre-hospital treatment, 4%. It was unknown if the key trial results would be generalisable to the people at highest risk of severe outcomes from COVID-19, but RAPID C-19 acknowledged that these were the people most likely to benefit from COVID-19 treatments. Indeed, the continued need for treatment options to prevent disease progression once the vaccination programme was rolled out was because of the continued risk of severe outcomes from COVID for vulnerable population groups.

143. The DHSC had commissioned an independent advisory group for the purpose of identifying the cohort of patients who were at highest risk and therefore most likely to benefit from treatment, and the Oversight Group took account of the group's recommendations during its considerations about whether the clinical evidence warranted consideration for rapid access.

144. In hindsight, the system as a whole would need to do more to develop therapeutics for this group in the event of another pandemic. However, NICE's role within this process is limited as NICE's TA programme can only make recommendations on a licensed product and a product can only be licensed if there is available evidence of effectiveness.

Data and Data Security

145. It was not the responsibility of NICE or RAPID C-19 to record data on adverse events or to manage adverse events. RAPID C-19 also did not collect, process or verify data as such. It utilised information about the clinical trials of potential treatments for COVID-19 and their results, which were recorded in the relevant topic briefing documents. RAPID C-19 evaluated data in the sense that it assessed the quality of emerging evidence and the robustness of the results. Trial results were prioritised in the sense that the results from key trials were presented to the Oversight Group. Trial results

that were unlikely to impact on decision-making were recorded in the topic briefing documents. All documentation related to RAPID C-19 is saved on the NICE network drives.

146. RAPID C-19 did not undertake statistical analysis. It reviewed statistical analyses undertaken by trial investigators as part of its assessment of trial results.

147. All papers for the Oversight Group and other papers shared with members considered confidential (for example when trial investigators shared draft manuscripts with the secretariat), were circulated via 'NICEDocs', a secure data sharing platform. Furthermore, all members of the Oversight Group were asked to sign and return a confidentiality acknowledgement and undertaking form to the secretariat. The terms of reference state that confidential papers and confidential information such as academic or commercial-in-confidence material disclosed in group deliberations should not be discussed with colleagues who are not either members of the group or the NICE secretariat.

Public Communication and Transparency

148. A RAPID C-19 webpage was established on the NICE website at the end of August 2020 which provided information about the initiative. The RAPID C-19 interim process guide and Oversight Group membership were available to download from the webpage. The webpage also signposted to NICE's guidance and advice on COVID-19, and the NIHRIO online dashboard of therapeutics in trials for treating COVID-19.

149. Given the emergency pandemic circumstances and quick turnaround of documentation needed to enable the Oversight Group to consider as many potential treatments as possible, the provision of publicly available information could not be prioritised. Consideration was given as to whether it would be possible to publish topic briefings on the webpage. However, given that these were living documents continually maintained and updated by the secretariat, the resource needed to produce and maintain public content of an acceptable standard would have been significant. It was therefore not considered to be the best use of the limited resources available and would hamper the activity needed for the operation of RAPID C-19 itself, which was the main priority.

150. To mitigate the limited amount of publicly available information, a list of topics that had been considered by RAPID C-19 was included on the webpages and kept updated.

151. RAPID C-19 did not have a role in public engagement and communication, other than the information made publicly available as outlined above. Information regarding the operation of RAPID C-19 was shared in professional forums, for example:

a. **Posters**: These were developed by the secretariat and exhibited in the Health Technology Assessment international ["HTAi"] 2021 conference (held virtually on 19-23 June 2021) and the International Society for Pharmacoeconomics and Outcomes Research ["ISPOR"] 2022 conference (held on 16-18 May 2022). The audiences of these conferences included researchers, policymakers, regulatory and health technology assessment agencies, healthcare practitioners, technology developers and patients. Both these posters described the RAPID C-19 process and the achievements so far, in terms of the number of therapeutics considered and the number of therapeutics with patient access, with the ISPOR poster including some reflection on the challenges. Copies of these posters are attached to the statement at **Exhibit HK4-17/INQ000316257** and **Exhibit HK4-18/INQ000316258**.

b. **Presentations**: A member of the secretariat also contributed a presentation to a NIHRIO workshop held at HTAi 2021.

c. **Articles**: An article on the initiative drafted by members of RAPID C-19 and the secretariat was published in the Health Service Journal on 10 September 2021. A copy of this article is attached to the statement at **Exhibit HK4-19/INQ000316259.** The article highlights that a key achievement of RAPID C-19 was its ability to facilitate patient access to treatments within 10-15 days of significant trials reporting positive signals, without compromising quality, compared with the normal timeframe of about 9 months. It did however identify challenges that had been faced, including:
    i. Prioritising which therapeutics to focus on considering the uncertainty around disease pathogenesis and the emergence of new variants;

ii. Having to assess evidence and make recommendations based on pre-prints and press releases that present selective information, in the absence of accumulated robust evidence.

Areas of public concern

152. RAPID C-19 was aware of public concern about the availability of therapeutics for COVID-19, through the volume of enquiries received (by NICE and the other partner organisations involved) as well as the news and other media. It was aware of the volume of misinformation and of interest in specific treatments endorsed and promoted by activist groups and others, which was not supported by the evidence. RAPID C-19 members strived to be consistent in its messaging to ensure an aligned cross-system response to these enquiries.

153. NICE received many enquiries and freedom of information requests about a small number of specific treatments, and about the general RAPID C-19 process. The RAPID C-19 secretariat at NICE was also aware of public interest in therapeutics via the ATTF, who on occasion asked for information about the current evidence base for particular therapeutics that had been flagged by ministers, or by MPs' constituents.

154. RAPID C-19 members were also aware of public concern about a perceived lack of transparency, particularly in relation to Evusheld, during 2022. As explained in paragraph 173 below, it had not been possible to prioritise external communication due to the extraordinary circumstances in which it was operating, and so transparency was not of the standard expected of routine business as usual operations. In October 2022 RAPID C-19 worked with the DHSC ATTF to publish the Evusheld CMO reports on the ATTF website, to ensure that there was clarity on the evidence that had been considered for Evusheld, which was all in the public domain. It was also to help aid understanding about the consideration of evidence, strengths and limitations of different types of evidence, and the difficulties with linkage (lack thereof) of laboratory assessment data with clinical outcomes.

155. RAPID C-19 also shared the public concern about the health inequalities experienced by vulnerable groups such as those on the SPL and was cognisant of the

remaining unmet need for these groups. RAPID C-19 undertook further work in relation to Evusheld that was outside of its original remit (for example considering non-clinical and real-world evidence), in order to explore every avenue in relation to this therapeutic.

156. RAPID C-19 was aware that there may have been some misunderstanding about its role, with regard to incorrect assumptions about its responsibility for overall decision-making on interim access to therapeutics. While information was publicly available on the NICE website, it is acknowledged that the nuance of RAPID C-19's advisory role within the wider governance framework and decision-making responsibilities of the DHSC may not have been clear and that greater transparency earlier on may have helped increase public confidence and understanding.

Lessons Learned

Introduction

157. On 29 March 2022, the ET at NICE made a decision to undertake an organisational lessons learnt exercise. While the experience was still fresh in the memory, NICE wanted to take the opportunity to capture the lessons learnt from the pandemic response. The purpose of this was to inform the wider health care system, build on any positive changes, and ensure as effective a response as possible to any future public health emergencies and pandemics.

158. This statement will focus specifically on the lessons learnt relating to RAPID C-19. The statement of my colleague Dr Paul Chrisp addresses wider learnings identified by NICE.

159. The RAPID C-19 lessons learned exercise was undertaken in the summer of 2022. It included:

- an internal review within the secretariat (NICE staff only),
- an independent externally facilitated survey and a face-to-face workshop (NICE and RAPID C-19 partners).

160. In the internal secretariat review NICE staff reflected on what worked well, considered what could have been done differently, and thought about whether there were ways of working in RAPID C-19 that could be applied to other programmes of work in the team.

161. Impact Psychology for Business were commissioned to undertake the independent facilitation of the survey and workshop and produce a summary report.

162. They undertook a diagnostic survey to highlight the experience and lessons learned by those involved in the pathway and received 30 responses. The survey responses included representation from all RAPID C-19 partner organisations, with the aim of capturing the experience of the individuals involved.

163. The face-to-face workshop included a subset of RAPID C-19 participants and discussed the results of the survey and considered how the lessons learned could be applied in the system as a whole. It took place on 14 July 2022 in the NICE offices in Manchester and included representatives from NICE, NHSE, NIHR, MHRA, ATTF and the devolved administrations.

164. The report was finalised in October 2022 and disseminated to the RAPID C-19 members. A copy of the RAPID C-19 Pathway Lessons Learned Review is attached at **Exhibit HK4-20/INQ000252460.**

Findings, Recommendations and Implementation.

Internal RAPID C-19 secretariat review

165. In the internal secretariat review, there was consensus that the horizon scanning element of the process had worked well; it underpinned the operation of RAPID C-19, and regular interaction and collaboration strengthened the relationship between NICE, the NIHRIO, and the others involved. Previous multi-agency initiatives had underlined the importance of having what has been described as 'one version of the truth', that is, a trusted source of horizon scanning information on which all organisations involved rely on to inform activities, to avoid any duplication of effort. This was essential in RAPID C-

19 where time was of the essence and there was a huge amount of 'noise' (for example, in the media) to cut through in order to identify treatments with actual potential.

166. There was also a clear prioritisation method that all RAPID C-19 partners were signed up to and a clear rationale for the order in which the topics had been considered. The fact that the early topics considered had progressed to rapid access suggested that the method was reasonable and appropriate. The regular interaction had also enabled the process to be adaptive, for example by iterating the prioritisation criteria to ensure we could look beyond repurposed therapeutics to new treatments in development.

167. Other positives identified included the internal support from the NICE Information Services team in their responsiveness and flexibility, the timing of the Oversight Group meetings which facilitated regular full attendance, the establishment of a facilitator-style role in the meetings (rather than a chair), and the use of concise action and decision logs. It was felt that the briefing documents had become somewhat repetitive and unwieldy over time and were hugely resource intensive to produce. However, it was acknowledged that at the start of the pandemic there was a huge need to find effective treatments and it was imperative to include all the information and log all the ongoing trials as there was so little evidence of effective treatments at that time.

Survey

168. The survey results included representation from all the organisations involved in RAPID C-19 and were overwhelmingly positive, with particular aspects highlighted in the comments such as the quality of the co-ordination, secretariat and facilitation, the quality of the documentation, the commitment of those involved and the friendly and supportive environment in which the initiative operated.

Face-to-Face Workshop

169. During the workshop discussions the themes that emerged with regards to the key enablers of the initiative were the shared vision and perception of a common purpose, resulting in full commitment and engagement and a willingness to truly collaborate, which helped to ensure effective communication, a consistent approach and unified

delivery of agreed actions. The environment in which the Oversight Group conducted its business was also considered important – the feeling that it was an open forum or safe space for open dialogue, with all members being highly supportive and respectful as well as professional and responsive, which helped with the adaptive and flexible approach needed as the pandemic evolved. Information sharing was felt to overall be positive in terms of starting to break down the barriers between organisations, there was a willingness to engage in an open exchange of information, and empowerment for contribution and decision-making. The senior membership and cross-agency expertise also meant that all were empowered to contribute to discussion and decision-making – essentially having the right people involved with the right expertise was key to enabling rapid decision-making. Non-NICE members also commented on the high-quality co-ordination and briefing documents provided by the secretariat as a key enabler.

Key barriers and challenges

170. The lessons learned exercise identified key barriers and challenges to the optimal operation of the RAPID C-19 initiative. The main themes identified by members are detailed below.

171. In terms of challenges, the main and obvious challenge was the continuously changing landscape, which meant that it felt like the initiative was constantly playing catch-up, with published information quickly becoming irrelevant, together with 'information overload' and work pressure that at times felt unsustainable. The regular emergence of new variants was a significant issue and led to occasional lack of clarity about the role of RAPID C-19 in that it was not constituted to provide expert opinion on the likely or actual activity of the neutralising antibody technologies against new variants, or to review non-clinical evidence. The relevant expertise was sought to support the Oversight Group to understand the issues and interpret the data.

172. Some people noted an occasional lack of clarity about governance and roles which became more acute as the Oversight Group was being asked its opinion on whether certain treatments would work against the currently dominant variant, and the Oversight Group needed to guard against its remit expanding into other areas which the Oversight Group was not set up to address.

173. External communication was also identified as a challenge. It was not possible to dedicate resource to providing publicly available information about the operation of RAPID C-19 and its conclusions about specific therapeutics. Many felt that RAPID C-19 could have been more proactive and transparent which may have helped improve trust in the system, particularly at a time when there was much misinformation leading to a perceived lack of transparency. Each member organisation received a large volume of enquiries, including freedom of information requests. Ideally, the initiative could have been more proactively transparent. It was acknowledged however that it is unknown whether more information about the initiative in the public domain would have led to fewer enquiries and freedom of information requests.

174. While the information sharing that occurred between partners was felt to be a key enabler, there were issues identified which occasionally slowed things down, particularly around sensitive or confidential commercial information. For example, on occasions where the DHSC ATTF had engaged with companies and invited RAPID C-19 members to meetings, each member had to sign an individual non-disclosure agreement. It was felt it might have been helpful if it could have been clear that engagement with one RAPID C-19 partner constituted engagement with all. Members also suggested a more systematic in confidence feed of information on the progress of products through licensing would have been helpful.

175. An agreed standard of acceptable evidence was also raised as a point for consideration given there were sometimes different interpretations amongst partners of the relative value of preprints and press releases, and some levels of discomfort about any actions to progress to patient access based on results from these sources. The source of evidence available to RAPID C-19 during the pandemic ranged from press releases, preprints, draft manuscripts, submitted manuscripts, and published peer-reviewed papers. There was an inherent tension between the need to act quickly on positive signals from trial results and the desire to increase confidence in those results through the peer-review process. It presented a challenge to the usual approach and some discomfort at times with differing interpretations of the value of such sources.

- **Press releases**[19] – supported rapid response to potentially important results, but often lacking key data[20] and issued by companies with stakeholder/commercial motivations.
- **Preprints** – supported rapid response to potentially important results, but paper had not been peer-reviewed. While trusted sources (e.g. the RECOVERY trial) utilised this method, there were also some very poor papers and/or studies made available on preprint servers (some studies were later discredited entirely).
- **Draft manuscripts shared in confidence** – supported rapid response to potentially important results before they were publicly available – were shared by both companies and UK platform trial investigators – useful for early consideration but data often not yet validated or peer-reviewed.
- **Submitted manuscripts shared in confidence** – supported rapid response to potentially important results before they were publicly available – were shared by both companies and UK platform trial investigators – useful for early consideration but paper not yet peer-reviewed.
- **Published papers** – high confidence in quality of the trial and robustness of the results but could often not be waited for in the context of the pandemic and the need for rapid access to effective treatments.

However, given the emergency nature of the pandemic and urgent need for treatments, a more pragmatic approach to assessing evidence in the context of uncertainty was necessary. It is unlikely that this approach would be appropriate in non-pandemic circumstances, particularly as it was not possible to consider cost-effectiveness, which is key to ensuring value for the taxpayer and the sustainability of the NHS.

Outcome

[19] The type of data provided in a press release of trial results tends to include the top line results only, that is, the basic design of the trial (e.g. randomised, controlled), the number of participants included in the trial, the proportion of events (e.g. hospital admission or death) in the intervention and control groups and relative risk change for the primary outcome (e.g. hospital admission or death) between the groups and whether this change was statistically significant.

[20] The type of data that would typically be missing from a press release would be detailed information on the methodology of the trial (e.g. randomisation method, inclusion and exclusion criteria, power calculations and statistical analysis plan), trial sites, trial oversight and governance, data on baseline clinical and demographic characteristics of trial participants, detailed safety data, results for secondary outcomes and discussion around the interpretation of the findings in the context of existing evidence, and the limitations of the trial.

176. The outcome of the lessons learned review did not result in tangible, specific recommendations for implementation either in RAPID C-19 (as the initiative was coming to an end), or in business-as-usual practices. This was due to the unique circumstances of the pandemic and the unique pressure that put upon all the activity related to RAPID C-19.

177. In relation to what learning can inform whether similar bodies to RAPID C-19 and the ATTF should be set up in the future and what the threshold should be for instigation, NICE offers the following observations.

178. NICE's experience of RAPID C-19 underlined the importance of closer relationships with partner organisations and the value of a flexible and adaptive approach to effectively respond to specific circumstances. The collaborative multi-agency approach exemplified by the RAPID C-19 initiative helped enable the health system to organise and respond quickly to the immediate and significant need represented by the pandemic. This system-wide approach to therapeutics access has the potential to be evolved further to benefit outside of a pandemic scenario (see below).

179. The pandemic experience helped establish when deviation from standard processes was necessary, with an understanding of the risks involved and the need to mitigate these where possible, in recognition of the pandemic situation and driving imperative to enable access to therapeutics that could help patients, and the system. For NICE, the issues posed by the evolution of the virus in terms of its impact on existing evidence and the general challenge of linkage of non-clinical data to clinical outcomes[21], has resulted in much greater awareness and understanding that can be leveraged in business-as-usual activities, as well as a future viral pandemic. However, the fundamental challenge for decision making in the context of developing guidance around use of monoclonal antibodies for COVID-19 is around how in-vitro data translates into clinical and health economic outcomes.

[21] Linkage of non-clinical data to clinical outcomes refers to the use of in vitro (laboratory) data for determining the neutralising activity of a monoclonal antibody. In this case, neutralising activity is a measure of the effectiveness of a treatment for COVID-19 in a laboratory test. Reduced neutralising activity refers to a decrease in the ability of monoclonal antibodies to effectively prevent a virus from entering host cells. It is hypothesised that the lower the neutralising activity in the laboratory test, the less likely a treatment is to be effective in clinical practice.

180. RAPID C-19 was instigated by health system partners reaching out, utilising existing links and being cognisant of the need for a co-ordinated approach to therapeutics access in a pandemic that would need to be designed and supported by all the key organisations involved in the development to access pathway for therapeutics. It was set up within 4 weeks of the initial contact from the National Medical Director for Specialised Commissioning (the day of the announcement of a nationwide lockdown). While its processes and procedures iterated over time, due to the immediate need to focus on potential treatments, the routine operation and main order of business for the Oversight Group, in terms of using the time to consider potentially effective therapeutics, was established from that first meeting. The success of the initiative, and the maintenance of cross-system links in business-as-usual activities, suggests that a similar body could be established just as quickly in a future pandemic situation.

181. While it may not be appropriate for elements of the RAPID C-19 process itself to remain in place outside of pandemic circumstances, some aspects, in their broadest sense, can support business-as-usual activities. For example, having an appropriate governance framework to facilitate information sharing, cross-system collaboration, breaking down barriers between organisations, continuous improvement and empowered decision-making.

182. From the NICE perspective, the general concepts described above have been borne in mind with the set up and operation of other multi-agency collaborative initiatives such as the Innovative Licensing and Access Pathway (an initiative between the MHRA and NICE). Furthermore, the horizon scanning approach used in RAPID C-19 (the 'one version of the truth' concept), has informed the view of how cross-system horizon scanning could potentially work in future.

Further research regarding COVID-19 therapeutics

183. NICE does not play a role in the initiation and delivery of clinical research, however one important area identified for methods research is related to the emergence of COVID-19 variants. Clinical trial data for some therapeutics may not be valid where the dominant variant changes. It would often not be timely or economically viable to undertake new trials as new dominant variants emerge. In-vitro activity against new variants provides key evidence, but there is little consensus on how this should be

translated to predict clinical effectiveness and patient outcomes. NICE was in a leading position here through taking account of in-vitro activity profiles in COVID-19 guidance and through a major project to capture the full public health value of antimicrobials, where relevant clinical trial data was scant and there was high dependency on in-vitro evidence.

184. NICE also incorporates in-vitro evidence into health technology assessments. The MTA on COVID-19 treatments, first published in March 2023 (TA873), includes the consideration of in-vitro evidence. NICE commissioned an 'in-vitro expert advisory group' made up of experts in infectious disease, virology, vaccine epidemiology, immunology and pharmacology to support this work. This model could be deployed again in the event of future infectious disease with rapidly emerging variants. Key sources of in-vitro evidence and expertise to support NICE include UKHSA, MHRA and the Royal College of Pathologists.

185. Another area worthy of careful consideration is the application of health economic approaches. During the COVID-19 pandemic, there was a strong focus on detecting signals of therapeutic clinical effectiveness and acting on these. In responding to this unprecedented public health emergency, the focus on therapeutics' clinical effectiveness and not cost effectiveness was appropriate. In learning from the COVID-19 pandemic and preparing for future public health emergencies, there may be a case for developing rapid and pragmatic approaches to the health economic evaluation of therapeutics, using company early economic models[22] for example, such that the financial sustainability of the health and care systems are protected, even during public health emergencies.

186. More research to develop best practice and reach international consensus on how to incorporate in-vitro evidence in health technology assessment is needed both in the context of COVID-19 therapeutics and more broadly in the management of future pathogens.

[22] Companies often develop health economic models at a very early stage of product development to inform likely product value and development decisions. Such models could potentially be useful to NICE and other health technology appraisal agencies in evaluating value for money, even in the context of public health emergencies.

Statement of Truth

I believe that the facts stated in this witness statement are true. I understand that proceedings may be brought against anyone who makes, or causes to be made, a false statement in a document verified by a statement of truth without an honest belief of its truth.

Signed: Personal Data

Dated: 18 November 2024

Appendix 1 – RAPID C-19 Briefings and Reports to the CMO

2020

Date	Document	Exhibit Reference
29.04.2020	Briefing Paper - Cytokine adsorption technologies for treatment of respiratory failure in people with COVID-19	**HK4-22 / INQ000315850**
29.04.2020	Briefing paper and Rapid Action Plan (RAP): C19-001; remdesivir (Gilead)	**HK4-23/ INQ000315877**
29.04.2020	Briefing paper and Rapid Action Plan (RAP): C19-002; tocilizumab (Roche):	**HK4-24/ INQ000315904**
06.05.2020	RAPID-C19 Oversight Group Rapid Action Plan (RAP) and Briefing paper Hydroxychloroquine (generic) [C19-003]	**HK4-25/ INQ000315946**
06.05.2020	Outcomes reporting for decision-making by the RAPID C-19 Oversight Group	**HK4-26/ INQ000315947**
06.05.2020	RAPID-C19 Oversight Group Rapid Action Plan (RAP) and Briefing paper Lopinavir-Ritonavir (generic) [C19-004]	**HK4-27/ INQ000315948**
06.05.2020	RAPID-C19 Oversight Group Rapid Action Plan (RAP) and Briefing paper Remdesivir (Gilead) [C19-001]	**HK4-28/ INQ000315949**
06.05.2020	RAPID-C19 Oversight Group Briefing paper and Rapid Action Plan (RAP): C19-002; tocilizumab (Roche)	**HK4-29/ INQ000315950**
06.05.2020	Rapid Action Plan (RAP) and Briefing paper Anakinra, Kineret® (Swedish Orphan Biovitrum) [C19-005]	**HK4-30/ INQ000315951**
13.05.2020	Rapid Action Plan (RAP) and Briefing paper Azithromycin (generic) [C19-006]	**HK4-31/INQ000315953**
13.05.2020	Rapid Action Plan (RAP) and Briefing paper Methylprednisolone (generic) [C19-008]	**HK4-32/INQ000315954**
13.05.2020	Rapid Action Plan (RAP) and Briefing paperAzithromycin (generic) [C19-006]	**HK4-33/INQ000315955**
13.05.2020	Rapid Action Plan (RAP) and Briefing paper Mesenchymal stem cells [C19-007]	**HK4-34/INQ000315956**
20.05.2020	Rapid Action Plan (RAP) and Briefing paper Remdesivir (Gilead) [C19-001]	**HK4-35/INQ000315958**
20.05.2020	Rapid Action Plan (RAP) and Briefing paper Dexamethasone (generic) [C19-009]	**HK4-36/INQ000315959**
20.05.2020	Rapid Action Plan (RAP) and Briefing paper Favipiravir (Fujifilm Toyama) [C19-010]	**HK4-37/INQ000315960**
27.05.2020	Rapid Action Plan (RAP) and Briefing paper Hydroxychloroquine (generic) [C19-003]	**HK4-38/INQ000315962**

27.05.2020	Rapid Action Plan (RAP) and Briefing paper Remdesivir (Gilead) [C19-001]	**HK4-39/INQ000315963**
27.05.2020	Rapid Action Plan (RAP) and Briefing paper Ruxolitinib [C19-011] (Novartis Pharmaceuticals)	**HK4-40/INQ000315964**
27.05.2020	Rapid Action Plan (RAP) and Briefing paper Colchicine (generic) [C19-012]	**HK4-41/INQ000315965**
03.06.2020	Rapid Action Plan (RAP): C19-008; methylprednisolone (generic)	**HK4-42/INQ000315824**
10.06.2020	Rapid Action Plan (RAP) and Briefing Sarilumab (Sanofi) [C19-013]	**HK4-43/INQ000315826**
10.06.2020	Rapid Action Plan (RAP) and Briefing note Ravulizumab (Alexion Pharma UK Ltd) [C19-015]	**HK4-44/INQ000315827**
17.06.2020	Rapid Action Plan (RAP) and Briefing paper Dexamethasone (generic) [C19-009]	**HK4-45/INQ000315830**
17.06.2020	Rapid Action Plan (RAP): C19-018; prednisolone (generic)	**HK4-46/ INQ000315831**
17.06.2020	Rapid Action Plan (RAP) and Briefing Hydrocortisone (generic) [C19-014]	**HK4-47/INQ000315832**
17.06.2020	Rapid Action Plan (RAP) and Briefing Baricitinib (Eli Lilly and Company Limited) [C19-016]	**HK4-48/INQ000315833**
24.06.2020	Briefing Convalescent Plasma	**HK4-49/INQ000315836**
24.06.2020	Briefing Dornase alfa (Roche Products Limited)	**HK4-50/INQ000315837**
07.07.2020	Rapid Action Plan (RAP) and Briefing Colchicine (generic) [C19-012]	**HK4-51/ INQ000315840**
15.07.2020	Rapid Action Plan (RAP) and Briefing Heparin & enoxaparin (generics) [C19-022]	**HK4-52/ INQ000315843**
22.07.2020	Rapid Action Plan (RAP) and Briefing Sofosbuvir-daclatasvir (no sponsor) [C19-023]	**HK4-53/INQ000315846**
29.07.2020	Briefing Tocilizumab	**HK4-54/INQ000315849**
29.07.2020	Rapid Action Plan (RAP) and Briefing Interferon beta-1a (generic and unlicensed formulations) [C19-021]	**HK4-55/INQ000315851**
29.07.2020	Rapid Action Plan (RAP) and Briefing Interferon beta-1b (generic and unlicensed formulations) [C19-024]	**HK4-56/INQ000315852**
05.08.2020	Favipiravir (generic) Briefing	**HK4-57/INQ000315855**
05.08.2020	Rapid Action Plan (RAP) and Briefing Canakinumab (Novartis) [C19-025]	**HK4-58/INQ000315856**
12.08.2020	Rapid Action Plan (RAP) and Briefing Ivermectin (generic) [C19-026]	**HK4-59/INQ000315859**
12.08.2020	Rapid Action Plan (RAP) and Briefing Convalescent plasma [C19-020]	**HK4-60/INQ000315860**
12.08.2020	Rapid Action Plan (RAP) and Briefing Oseltamivir (Roche) [C19-017]	**HK4-61/INQ000315861**
19.08.2020	RAP and Briefing Doxycycine (generic)	**HK4-62/INQ000315864**

19.08.2020	RAP and Briefing Hydrocortisone (generic)	**HK4-63/ INQ000494651**
19.08.2020	Rapid Action Plan (RAP) and Briefing Ciclesonide (AstraZeneca UK) [C19-028]	**HK4-64/INQ000315866**
26.08.2020	Rapid Action Plan (RAP) and Briefing Hydrocortisone (generic) [C19-014]	**HK4-65/INQ000315869**
26.08.2020	Rapid Action Plan (RAP) and Briefing Ciclesonide (AstraZeneca UK) [C19-028]	**HK4-66/INQ000315866**
26.08.2020	Doxycycline (generic) briefing	**HK4-67/INQ000315864**
02.09.2020	RAPID C-19 RAP Briefing Vitamin D	**HK4-68/INQ000315873**
02.09.2020	RAPID C-19 briefing canakinumab	**HK4-69/INQ000315874**
02.09.2020	RAPID C-19 RAP Briefing Losartan	**HK4-70/INQ000315875**
09.09.2020	Rapid Action Plan (RAP) and Briefing Vitamin C (generic) [C19-031]	**HK4-71/INQ000315879**
09.09.2020	Rapid Action Plan (RAP) and Briefing Melatonin (generic) [C19-032]	**HK4-72/INQ000315880**
15.09.2020	Rapid Action Plan (RAP) Azithromycin (generic) [C19-006]	**HK4-73/INQ000315883**
30.09.2020	Rapid Action Plan (RAP) and Briefing Ciclosporin [C19-034]	**HK4-74/INQ000315888**
07.10.2020	Rapid Action Plan (RAP) and Briefing Povidone-iodine (Generic) [C19-035]	**HK4-75/INQ000315891**
07.10.2020	Rapid Action Plan (RAP) and Briefing Acetylcysteine (Generic) [C19-033]	**HK4-76/INQ000315892**
14.10.2020	Rapid Action Plan (RAP) and Briefing LY-CoV555 (bamlanivimab) monotherapy and combination with LY-CoV016 (etesevimab) (Eli Lilly and Company) [C19-040]	**HK4-77/INQ000315895**
14.10.2020	Rapid Action Plan (RAP) and Briefing Baricitinib (Eli Lilly and Company Limited) [C19-016]	**HK4-78/INQ000315896**
14.10.2020	Rapid Action Plan (RAP) and Briefing Zinc (Generic) [C19-037]	**HK4-79/INQ000315897**
21.10.2020	Ivermectin (generic) Briefing	**HK4-80/INQ000315900**
21.10.2020	REGN-COV2 (Regeneron) Briefing	**HK4-81/INQ000315901**
21.10.2020	Remdesivir (Gilead) Briefing	**HK4-82/INQ000315902**
21.10.2020	NSAIDs (generic) Briefing	**HK4-83/INQ000315903**
28.10.2020	Human Immunoglobulin (various sponsors) [C19-038] Briefing	**HK4-84/INQ000315907**
11.11.2020	Rapid Action Plan (RAP) and Briefing nitazoxanide (Romark Pharmaceuticals) [C19-042]	**HK4-85/INQ000315912**
18.11.2020	Convalescent Plasma Briefing	**HK4-86/INQ000315915**

18.11.2020	Rapid Action Plan (RAP) and Briefing Bamlanivimab (LY-CoV555) monotherapy and combination with etesevimab (LY-CoV016)	**HK4-87/INQ000315916**
25.11.2020	REGN-COV2 (casirivimab and imdevimab) (Regeneron) Briefing	**HK4-88/INQ000315919**
25.11.2020	Rapid Action Plan (RAP) and Briefing acalabrutinib (AstraZeneca) [C19-043]	**HK4-89/INQ000315920**
25.11.2020	Rapid Action Plan (RAP) and Briefing Tocilizumab (Roche) [C19-002]	**HK4-90/INQ000315921**
25.11.2020	Rapid Action Plan (RAP) and Briefing Baricitinib (Eli Lilly and Company Limited) [C19-016]	**HK4-91/INQ000315922**
25.11.2020	Radid Action Plan (RAP) and Briefing Emtricitabine/tenofovir (Generic) [C19-044]	**HK4-92/INQ000315923**
02.12.2020 0	Rapid Action Plan (RAP) and Briefing Tocilizumab (Roche) [C19-002]	**HK4-93/INQ000315921**
02.12.2020	Rapid Action Plan (RAP) and Briefing Baricitinib (Eli Lilly and Company Limited) [C19-016]	**HK4-94/INQ000315927**
02.12.2020	Rapid Action Plan (RAP) and Briefing rivaroxaban (Bayer) [C19-046]	**HK4-95/INQ000315928**
02.12.2020	Rapid Action Plan (RAP) and Briefing aspirin (generic) [C19-045]	**HK4-96/INQ000315929**
02.12.2020	Convalescent Plasma Briefing	**HK4-97/INQ000315930**
09.12.2020	Rapid Action Plan (RAP) and Briefing mesenchymal stem cells [C19-007]	**HK4-98/INQ000315934**
16.12.2020	RAPID-C19 Oversight Group Briefing azithromycin, generic [C19-006]	**HK4-99/INQ000315937**
16.12.2020	RAPID-C19 Oversight Group Briefing: ruxolitinib (Novartis Pharmaceuticals) [C19-011]	**HK4-100/INQ000315938**
16.12.2020	RAPID-C19 Oversight Group Briefing Doxycycline (generic) [C19-027]	**HK4-101/INQ000315939**
21.12.2020	Report to CMO on Baricitinib	**HK4-102/INQ000315940**
23.12.2020	RAPID-C19 Oversight Group Briefing otilimab (GlaxoSmithKline) [C19-050]	**HK4-103/INQ000315943**
23.12.2020	Briefing Mesenchymal stem cells [C19-007]	**HK4-104/INQ000315944**
23.12.2020	RAPID-C19 Oversight Group Briefing: heparin & enoxaparin (generics) [C19-022]	**HK4-105/INQ000315945**

2021

Date	**Document**	**Exhibit Reference**
06.01.2021	RAPID-C19 Oversight Group Briefing sarilumab (Sanofi) [C19-013]	**HK4-106/INQ000316020**
06.01.2021	RAPID-C19 Oversight Group Briefing: Tocilizumab (Roche) [C19-002]	**HK4-107/INQ000316047**
06.01.2021	RAPID-C19 Oversight Group Briefing Ivermectin (generic) [C19-026]	**HK4-108/INQ000316074**

06.01.2021	RAPID-C19 Report to CMO tocilizumab (Roche) and sarilumab (Sanofi)	**HK4-109/INQ000494427**
13.01.2021	Briefing: siltuximab (EUSA Pharma UK) [C19-056]	**HK4-110/INQ000316182**
13.01.2021	Briefing: CD24Fc (OncoImmune) [C19-055	**HK4-111/INQ000316183**
15.01.2021	RAPID-C19 Report to CMO hydroxychloroquine	**HK4-112/INQ000316184**
20.01.2021	Briefing: Convalescent plasma [C19-020]	**HK4-113/INQ000315991**
20.01.2021	Briefing: Ravulizumab (Alexion Pharma UK Ltd) [C19-015]	**HK4-114/INQ000316188**
20.01.2021	Briefing: GM-CSF drugs [C19-051]	**HK4-115/INQ000316189**
27.01.2021	RAPID-C19 Oversight Group Briefing Bamlanivimab (LY-CoV555) monotherapy and combination with etesevimab (LY-CoV016) (Eli Lilly and Company) [C19-040]	**HK4-116/INQ000316192**
27.01.2021	RAPID-C19 Oversight Group Briefing: heparin & enoxaparin (generics) [C19-022]	**HK4-117/INQ000316193**
27.01.2021	RAPID-C19 Oversight Group Briefing azithromycin, generic [C19-006]	**HK4-118/INQ000316194**
27.01.2021	RAPID-C19 Oversight Group Briefing anakinra, Kineret (Swedish Orphan Biovitrum) [C19-005]	**HK4-119/INQ000316195**
27.01.2021	Briefing - Doxycycline (generic) [C19-027]	**HK4-120/INQ000316196**
27.01.2021	RAPID-C19 Oversight Group Briefing colchicine (generic) [C19-012]	**HK4-121/INQ000316197**
29.01.2021	RAPID-C19 Report to CMO colchicine	**HK4-122/INQ000316198**
03.02.2021	RAPID-C19 Oversight Group Briefing: niclosamide (generic and unlicensed formulations) [C19-049]	**HK4-123/INQ000315969**
03.02.2021	RAPID-C19 Oversight Group Briefing: CT-P59 (Celltrion) [C19-048]	**HK4-124/INQ000315970**
03.02.2021	RAPID-C19 Oversight Group Briefing: favipiravir (generic) [C19-010]	**HK4-125/INQ000315971**
03.02.2021	RAPID-C19 Oversight Group Briefing: AZD7442 (AZD8895 + AZD1061) (AstraZeneca) [C19-053]	**HK4-126/INQ000315972**
10.02.2021	RAPID-C19 Oversight Group Briefing: Sarilumab (Sanofi) [C19-013]	**HK4-127/INQ000315975**
10.02.2021	RAPID-C19 Oversight Group Briefing Budesonide [C19-052]	**HK4-128/INQ000315976**
10.02.2021	RAPID-C19 Oversight Group Briefing TNF inhibitors (biosimilar) [C19-054]	**HK4-129/INQ000315977**
12.02.2021	RAPID C-19 Report to CMO Tocilizumab	**HK4-130/INQ000494448**
17.02.2021	Rapid Action Plan (RAP) and Briefing Vitamin D (generic) [C19-029]	**HK4-131/INQ000315980**

24.02.2021	RAPID-C19 Oversight Group Briefing: serotonin specific reuptake inhibitors (SSRIs) (fluvoxamine, fluoxetine) (generic) [C19-058]	**HK4-132/INQ000315983**
24.02.2021	RAPID-C19 Oversight Group Briefing: VIR-7831 and VIR-7832 (Vir Biotechnology Inc. and GSK) [C19-060]	**HK4-133/INQ000315984**
03.03.2021	Oversight Group Briefing: GM-CSF drugs	**HK4-134/INQ000315987**
10.03.2021	Briefing - Ivermectin (generic) [C19-026]	**HK4-135/INQ000315990**
10.03.2021	Briefing: Convalescent Plasma	**HK4-136/INQ000315991**
10.03.2021	RAPID-C19 Oversight Group Briefing Bamlanivimab (LY-CoV555) monotherapy and combination with etesevimab (LY-CoV016) (Eli Lilly and Company) [C19-040]	**HK4-137/INQ000316029**
10.03.2021	Briefing: colchicine (generic) [C19-012]	**HK4-138/INQ000315993**
17.03.2021	RAPID C-19 Briefing Ivermectin	**HK4-139/INQ000315997**
17.03.2021	RAPID-C19 briefing VIR-7831 & VIR-7832	**HK4-140/INQ000315998**
17.03.2021	RAPID-C19 briefing Statins	**HK4-141/INQ000315999**
24.03.2021	RAPID-C19 briefing ruxolitinib	**HK4-142/INQ000316002**
24.03.2021	RAPID-C19 briefing proxalutamide, enzalutamide and bicalutamide	**HK4-143/INQ000316003**
24.03.2021	RAPID-C19 Briefing REGN-COV2	**HK4-144/INQ000316004**
24.03.2021	RAPID-C19 briefing budesonide	**HK4-145/INQ000316005**
31.03.2021	RAPID-C19 briefing CT-P59	**HK4-146/INQ000315970**
31.03.2021	RAPID-C19 briefing P2Y12 antiplatelets CIC	**HK4-147/INQ000316009**
31.03.2021	RAPID-C19 briefing VIR-7831 & VIR-7832	**HK4-148/INQ000316010**
31.03.2021	RAPID-C19 briefing GM-CSFs [CIC]	**HK4-149/INQ000316011**
31.03.2021	RAPID-C19 Briefing Bamlanivimab (LY-CoV555)	**HK4-150/INQ000316012**
31.03.2021	RAPID-C19 briefing Dapagliflozin [CIC]	**HK4-151/INQ000316013**
07.04.2021	RAPID-C19 briefing budesonide	**HK4-152/INQ000316016**
07.04.2021	RAPID-C19 briefing nitric oxide	**HK4-153/INQ000316017**
07.04.2021	RAPID-C19 briefing Human Immunoglobulin	**HK4-154/INQ000316018**

08.04.2021	RAPID-C19 Report to CMO Budesonide	**HK4-155/INQ000316019**
14.04.2021	RAPID-C19 briefing GM-CSFs	**HK4-156/INQ000316011**
14.04.2021	RAPID-C19 Briefing REGN-COV2 [CIC]	**HK4-157/INQ000316024**
14.04.2021	RAPID-C19 briefing aviptadil	**HK4-158/INQ000316025**
14.04.2021	RAPID-C19 briefing anakinra	**HK4-159/INQ000316026**
14.04.2021	RAPID-C19 briefing Dapagliflozin	**HK4-160/INQ000316027**
14.04.2021	RAPID-C19 briefing sarilumab	**HK4-161/INQ000315975**
14.04.2021	RAPID-C19 Briefing Bamlanivimab (LY-CoV555)	**HK4-162/INQ000316029**
14.04.2021	RAPID-C19 briefing CCR5 inhibitors	**HK4-163/INQ000316030**
14.04.2021	RAPID C-19 briefing baricitinib	**HK4-164/INQ000316031**
21.04.2021	RAPID-C19 briefing molnupiravir	**HK4-165/INQ000316034**
21.04.2021	RAPID-C19 briefing CD24Fc	**HK4-166/INQ000316035**
21.04.2021	RAPID-C19 Briefing Bamlanivimab (LY-CoV555)	**HK4-167/INQ000316029**
21.04.2021	RAPID-C19 briefing sargramostim molgramostim	**HK4-168/INQ000316037**
21.04.2021	RAPID-C19 Briefing Ciclesonide	**HK4-169/INQ000316038**
28.04.2021	RAPID-C19 briefing montelukast	**HK4-170/INQ000316041**
28.04.2021	RAPID C-19 Briefing Ivermectin	**HK4-171/INQ000315997**
05.05.2021	RAPID-C19 briefing interferon beta	**HK4-172/INQ000316045**
05.05.2021	RAPID-C19 briefing CT-P59 v1.1	**HK4-173/INQ000494491**
05.05.2021	RAPID-C19 briefing BRII-196 and BRII-198	**HK4-174/INQ000316048**
05.05.2021	RAPID C-19 briefing baricitinib	**HK4-175/INQ000316049**
12.05.2021	RAPID-C19 briefing GM-CSFs	**HK4-176/INQ000316052**
12.05.2021	RAPID-C19 Briefing Povidone-iodine	**HK4-177/INQ000316053**
12.05.2021	RAPID-C19 briefing BI 767551 (DZIF-10c)	**HK4-178/INQ000316054**

12.05.2021	RAPID-C19 briefing BGB-DXP593 and BGB-DXP604	**HK4-179/INQ000316055**
19.05.2021	RAPID-C19 briefing anakinra	**HK4-180/INQ000316058**
19.05.2021	RAPID-C19 briefing molnupiravir	**HK4-181/INQ000316059**
19.05.2021	RAPID-C19 briefing Dapagliflozin	**HK4-182/INQ000316060**
26.05.2021	RAPID-C19 briefing colchicine	**HK4-183/INQ000316063**
26.05.2021	RAPID-C19 Briefing REGN-COV	**HK4-184/INQ000316064**
26.05.2021	RAPID-C19 briefing anakinra	**HK4-185/INQ000316058**
02.06.2021	RAPID C-19 briefing baricitinib	**HK4-186/INQ000316068**
02.06.2021	RAPID C-19 RAP Briefing Ivermectin	**HK4-187/INQ000316069**
02.06.2021	RAPID C-19 Briefing Ciclesonide	**HK4-188/INQ000316070**
02.06.2021	RAPID-C19 briefing budesonide	**HK4-189/INQ000316071**
02.06.2021	RAPID-C19 briefing pulmonary antifibrotics	**HK4-190/INQ000316072**
02.06.2021	RAPID-C19 briefing RDRP inhibitors	**HK4-191/INQ000316073**
18.06.2021	RAPID-C19 report to CMO budesonide	**HK4-192/INQ000494510**
09.06.2021	RAPID-C19 briefing aspirin	**HK4-193/INQ000316078**
09.06.2021	RAPID-C19 briefing VIR-7831 & VIR-7832	**HK4-194 /INQ000316079**
09.06.2021	RAPID-C19 RAP Briefing Bamlanivimab (LY-CoV555)	**HK4-195/INQ000316080**
09.06.2021	RAPID-C19 briefing Statins	**HK4-196/INQ000316081**
09.06.2021	RAPID-C19 briefing anakinra	**HK4-197/INQ000316082**
09.06.2021	RAPID-C19 ACE inhibitors	**HK4-198/INQ000316083**
16.06.2021	RAPID-C19 Briefing REGN-COV	**HK4-199/INQ000316086**
16.06.2021	RAPID-C19 briefing budesonide	**HK4-200/INQ000316087**
16.06.2021	RAPID-C19 briefing GM-CSF inhibitors	**HK4-201/INQ000316088**
16.06.2021	RAPID-C19 briefing VIR-7831 & VIR-7832	**HK4-202/INQ000316079**

16.06.2021	RAPID-C19 Briefing Bamlanivimab (LY-CoV555)	**HK4-203/INQ000316090**
16.06.2021	RAPID C-19 briefing baricitinib	**HK4-204/INQ000316091**
16.06.2021	RAPID-C19 briefing anakinra	**HK4-205/INQ000316092**
18.06.2021	RAPID C19 Report to CMO Sotrovimab	**HK4-206/INQ000494524**
18.06.2021	RAPID C19 Report to CMO Casirivimab and imdevimab	**HK4-207/INQ000316094**
23.06.2021	RAPID-C19 Briefing REGN-COV	**HK4-208/INQ000316097**
23.06.2021	RAPID C-19 briefing anakinra	**HK4-209/INQ000316098**
23.06.2021	RAPID C19 Briefing Bamlanivimab (LY-CoV555)	**HK4-210/INQ000316090**
29.06.2021	RAPID C-19 report to CMO Anakinra	**HK4-211/INQ000316100**
30.06.2021	RAPID C-19 briefing proxalutamide, enzalutamide and bicalutamide	**HK4-212/INQ000316104**
30.06.2021	RAPID-C19 briefing sarilumab	**HK4-213/INQ000316105**
30.06.2021	RAPID-C19 briefing budesonide	**HK4-214/INQ000316087**
30.06.2021	RAPID-C19 briefing VIR-7831 & VIR-7832	**HK4-215/INQ000494534**
07.07.2021	RAPID C-19 briefing baricitinib	**HK4-216/INQ000316091**
14.07.2021	RAPID C-19 Briefing REGN-COV	**HK4-217/INQ000494536**
14.07.2021	RAPID C-19 Briefing Bamlanivimab	**HK4-218/INQ000316114**
21.07.2021	RAPID C-19 Briefing Bamlanivimab (LY-CoV555)	**HK4-219/INQ000316117**
14.07.2021	RAPID C-19 Report to CMO Casirivimab and imdevimab (prophylaxis)	**HK4-220/INQ000316118**
21.07.2021	RAPID C-19 Report to CMO Bamlanivimab and etesevimab	**HK4-221/INQ000316121**
11.08.2021	RAPID-C19 briefing budesonide CiC	**HK4-222/INQ000316124**
11.08.2021	RAPID C-19 Briefing Ivermectin	**HK4-223/INQ000316125**
11.08.2021	RAPID C-19 Briefing REGN-COV	**HK4-224/INQ000316126**
20.08.2021	RAPID C-19 Publishing proposal	**HK4-225/INQ000316130**
08.09.2021	RAPID C-19 Briefing Baricitinib (Eli Lilly) [C19-016]	**HK4-226/INQ000316132**

08.09.2021	RAPID C-19 briefing update MSC	**HK4-227/INQ000316133**
17.09.2021	RACPID C-19 Summary briefing Budesonide	**HK4-228/INQ000316134**
22.09.2021	RAPID C-19 briefing imatinib and dasatinib	**HK4-229/INQ000316137**
22.09.2021	RAPID C-19 briefing SSRIs	**HK4-230/INQ000316138**
01.10.2021	RAPID C-19 summary briefing Casirivimab and imdevimab	**HK4-231/INQ000316139**
06.10.2021	RAPID-C19 briefing aviptadil	**HK4-232/INQ000316142**
06.10.2021	RAPID-C19 briefing molnupiravir	**HK4-233/INQ000316143**
06.10.2021	RAPID C-19 briefing remdesivir	**HK4-234/INQ000316144**
13.10.2021	RAPID-C19 briefing AZD7442	**HK4-235/INQ000316147**
13.10.2021	RAPID C-19 briefing remdesivir	**HK4-236/INQ000316144**
06.10.2021	Briefing: Molnupiravir (MSD/Ridgeback) [C19-039]	**HK4-237/INQ000316149**
06.10.2021	RAPID C-19 report to CMO molnupiravir	**HK4-238/INQ000316150**
27.10.2021	RAPID-C19 briefing aspirin	**HK4-239/INQ000316153**
27.10.2021	RAPID C-19 briefing remdesivir	**HK4-240/INQ000316154**
27.10.2021	RAPID C-19 Briefing Dexamethasone	**HK4-241/INQ000316156**
27.10.2021	RAPID C-19 briefing anakinra	**HK4-242/INQ000316157**
27.10.2021	RAPID C-19 briefing siltuximab	**HK4-243/INQ000316158**
22.09.2021	RAPID C-19 report to CMO Fluvoxamine	**HK4-244/INQ000316159**
10.11.2021	RAPID C-19 briefing aviptadil	**HK4-245/INQ000316162**
24.11.2021	RAPID C-19 briefing sotrovimab	**HK4-246/INQ000316165**
13.10.2021	RAPID-C19 Briefing REGN-COV	**HK4-247/INQ000316166**
24.11.2021	RAPID C-19 briefing AZD7442	**HK4-248/INQ000316167**
08.12.2021	RAPID-C19 briefing AZD7442	**HK4-249/INQ000316170**
08.12.2021	RAPID-C19 briefing molnupiravir	**HK4-250/INQ000316171**

08.12.2021	RAPID C-19 briefing baricitinib	**HK4-251/INQ000316172**
24.11.2021	RAPID-C19 briefing CT-P59	**HK4-252/INQ000316175**
22.12.2021	RAPID C-19 briefing PF-07321332	**HK4-253/INQ000316176**
22.12.2021	RAPID-C19 briefing molnupiravir	**HK4-254/INQ000316177**
22.12.2021	RAPID-C19 briefing AZD7442	**HK4-255/INQ000316170**
23.12.2021	RAPID C-19 Report to CMO AZD7442	**HK4-256/INQ000316179**
24.12.2021	RAPID C-19 summary briefing sotrovimab	**HK4-257/INQ000316180**
24.12.2021	RAPID C-19 summary briefing molnupiravir	**HK4-258/INQ000316181**

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Date	Document	Exhibit Reference
22.12.2021	RAPID C-19 Report to CMO Nirmatrelvir plus ritonavir (Paxlovid; Pfizer)	**HK4-259/INQ000316200**
12.01.2022	RAPID-C19 briefing ensovibep	**HK4-260/INQ000316217**
22.12.2021	RAPID C-19 Report to CMO Regdanvimab (Regkirona;Celltrion)	**HK4-261/INQ000316218**
31.01.2022	RAPID C-19 Summary Briefing: PF-07321332 plus ritonavir	**HK4-262/INQ000316219**
09.02.2022	RAPID C-19 briefing AZD7442	**HK4-263/INQ000316222**
16.02.2022	RAPID C-19 briefing opaganib	**HK4-264/INQ000316225**
16.02.2022	RAPID C-19 briefing AZD7442	**HK4-265/INQ000316222**
02.03.2022	RAPID C-19 briefing baricitinib	**HK4-266/INQ000316172**
02.03.2022	RAPID C-19 briefing sotrovimab	**HK4-267/INQ000316230**
02.03.2022	RAPID-C19 briefing interferon beta	**HK4-268/INQ000316231**
02.03.2022	RAPID C-19 Report to CMO baricitinib	**HK4-269/INQ000316232**
23.03.2022	RAPID-C19 briefing nitric oxide	**HK4-270/INQ000316235**
06.04.2022	RAPID C-19 briefing Adintrevimab	**HK4-271/INQ000316202**
20.04.2022	RAPID C-19 briefing Adintrevimab	**HK4-272/INQ000316202**
04.05.2022	RAPID C-19 Briefing Ensitrelvir	**HK4-273/INQ000316204**

04.05.2022	RAPID C-19 - Briefing Ensitrelvir (Duplicate)	**HK4-274/INQ000316204**
18.05.2022	RAPID C-19 Briefing AZD7442	**HK4-275/INQ000316209**
18.05.2022	RAPID C-19 Report to CMO - Tixagevimab plus cilgavimab (Evusheld, AZD7442; Astraxeneca) in pre-exposure prophylacxis	**HK4-276/INQ000316210**
15.06.2022	RAPID C-19 Briefing AZD7442	**HK4-277/INQ000316211**
15.06.2022	Report to CMO on Tixagevimab plus cilgavimab (Evusheld, AZD7442; Astrazeneca)	**HK4-278/INQ000316214**