Witness Name: Helen Knight
Statement No: 1
Exhibits: 17
Dated: 19 February 2024

**UK COVID-19 PUBLIC INQUIRY**

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**WITNESS STATEMENT OF HELEN KNIGHT (Module 3)**

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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 [“CE”] of the National Institute for Health and Care Excellence ["NICE"] dated 02 June 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. As requested, this statement will focus on the period between 01 March 2020 and 28 June 2022 ["the relevant period”] and should be read in conjunction with witness statements provided by NICE colleague Dr Paul Chrisp (Head of Publishing and Products at NICE) and the witness statement provided by the current CE, Dr Samantha Roberts.

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 Appraisal Programme and for the line management of a group of health technology assessment analysts.

4. In May 2011, I became Associate Director, providing support to the Programme Director and Centre Director in all aspects of the management and delivery of both the Technology Appraisal and Highly Specialised Technologies ["TA&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 Programme) 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 two sites (London and Manchester), directing a portfolio of complex projects, including the recent review of the methods used for health technology evaluation.

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. In July 2020, I was also appointed as one of two deputy directors for CHTE.

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 CE. During these absences, both myself and Jeanette Kusel, Director of Scientific Advice within CHTE (as Deputy Directors), 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 output.

8. In March 2022, the director role was more permanently split in two, with myself taking on the role of Acting Director of Medicines Evaluation, and Jeanette Kusel taking on the role of Acting Director of Medical Technology and Digital Evaluation. Mark Chapman then replaced Jeanette as Acting Director of Medical Technology and Digital Evaluation in May 2022. I produce an organogram for CHTE for the period January to December 2020, as **Exhibit HK01 - INQ000316242.**

9. A copy of the Senior Leadership Organogram is produced as **Exhibit HK02 – INQ000252455** This shows the NICE management structure between March 2020 and June 2022 and provides details of the changes of leadership within CHTE during the relevant period.

**Personal Background and Experience**

10. 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.

11. 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.

**Centre for Health Technology Evaluation – Role and Function during the pandemic**

12. NICE is an arm's length body of the Department of Health and Social Care ["DHSC"]. NICE was established to help ensure that people had equal access to clinically and cost-effective treatments, wherever they live. NICE helps practitioners and commissioners get the best care to patients, fast, while ensuring value for the taxpayer. CHTE is one of the eight (now ten) directorates at NICE.

13. CHTE's role is to develop 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.

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

15. CHTE also produced Medtech Innovation Briefings ["MIB's"] until 31 March 2023. These contained advice that supported the National Health Service ["NHS"] and social care commissioners and staff who were considering using new medical devices and other medical or diagnostic technologies. CHTE also produces advice and early engagement for the life sciences industry, providing a service that assists in preparation for evidence generation and NICE guidance development.

16. NICE operates in an environment that by its very nature has 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 recognized as a world-leading organization 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 needs for speedy and trusted guidance and advice.

17. 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 HK03 - INQ000087317** - NICE's Senior Management Team ["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 DHSC. The SMT agreed prioritisation criteria and the CHTE work programme, including Technology Appraisal ["TA"], Highly Specialised Technologies ["HST"], Interventional Procedures ["IP"], Medtech ['MT"] and, Diagnostic Assessments [DAP"], was reviewed in line with the following:

    - Guidance that was therapeutically critical.
    - Guidance that addressed COVID-19 diagnostic or therapeutic interventions.

- Guidance that was post consultation and could be completed by developers without engagement of stakeholders and/or committee members.
- 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.

18. 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.

19. 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. The full details of the outcome of this work can be found within two reports prepared for the NICE Guidance Executive ["GE"] titled "Adjustments to publication proposals due to COVID-19 in the Medical Technologies, Diagnostics and Interventional Procedures programmes" and "Adjustments to publication proposals due to COVID-19 in the Technology Appraisal and Highly Specialised Technologies programmes". These reports are exhibited as **Exhibit HK04 - INQ000252466** and **Exhibit HK05 - INQ000252467**. On 20 March 2020, GE approved this approach.

20. In summary, the following guidance was selected as therapeutically critical to continue for the health technology evaluation programmes:

    a. **Diagnostics guidance:**

        - High-sensitivity troponin for the early rule out of acute myocardial infarction. This was a fast-track request from NHS England ["NHSE"], enabling efficient management of A&E capacity by ruling out heart attacks.
        - Quantitative faecal immunochemical tests to guide colorectal cancer pathway referral for people with a change in bowel habit or abdominal pain. This was also a fast-track request from NHS, enabling efficient management of patients who may avoid the need for colonoscopy.

**b. Interventional procedures guidance:**

- Intravascular lithotripsy for calcified coronary arteries during percutaneous coronary intervention. This potentially allowed day case percutaneous coronary intervention in a group who otherwise might need a coronary artery bypass graft and Intensive Therapy Unit stay.

**c. Medical devices guidance:**

- PneuX for preventing ventilator-associated pneumonia in intensive care.
- Chest Imaging AI Technologies (publication of MIB)
- The MAGEC system for spinal lengthening in children with scoliosis. This related to serious safety concerns about the device that had been in the public domain for a significant period.

**d. Medicines guidance:**

- All technology appraisals 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 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. NHSE supported this approach.
- Phenylketonuria - sapropterin dihydrochlorid. 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.

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

21. During the pandemic CHTE took the lead on the development and implementation of The Research to Access Pathway for Investigational Drugs in COVID-19 ["RAPID C-19"]. This was a multi-agency initiative aimed at ensuring safe and timely patient access to therapeutics that showed evidence of benefit in preventing and treating COVID-19. Its role was to provide advice to the Chief Medical Officer ["CMO"] on the strength of the clinical effectiveness evidence of the therapeutics proposed for treating COVID-19. See below for further details.

Medtech Innovation Briefings

21. During the relevant period CHTE produced and published six COVID-19 related MIBs on:

    - Lifelight First for monitoring vital signs.
    - Cytokine adsorption devices for treating respiratory failure in people with COVID-19.
    - CFHealthHub for managing cystic fibrosis during the COVID-19 pandemic.
    - FebriDx for C-reactive protein and myxovirus resistance protein A testing.
    - URO17 for detecting bladder cancer.
    - SYNE-COV for predicting COVID-19 outcomes.

**22.** These briefings were NICE advice, designed to support NHS and staff when they considered using new medical devices and other medical or diagnostic technologies

to treat COVID-19, or to support NHS services during the pandemic. A summary of these briefings can be found at **Exhibit HK06 - INQ000252468.**

23. In addition to the above, CHTE were also involved in and/or produced the following during the pandemic:

    a. **Commissioning support briefing:** A commissioning support briefing on remdesivir for COVID-19 aimed to provide evidence for policy makers. The request, by colleagues in the DHSC responsible for the Therapeutics Taskforce acting for the CMO, asked whether NICE could provide an assessment of the clinical effectiveness of remdesivir in treating COVID-19. It was not NICE guidance or advice, so was not published. Its aim was to assist the DHSC and NHSE in procurement decisions on the drug.

    b. **Diagnostic evidence standards framework ["ESF"]:** NICE had limited involvement in COVID-19 test diagnostic work, but in June 2020, NICE produced an ESF: Diagnostic testing for SARS-CoV-2 and anti-SARS-CoV-2 antibodies to help manufacturers gather the best possible data and evidence while diagnostics were developed and validated at speed. There were additional requests from NHSE to produce economic modelling of hospital point-of-care SARS-CoV-2 viral detection tests guidance and MIBs on SARS-CoV2 viral detection and antibody tests to support COVID-19 testing strategy. The ESF was published on the NICE website. The MIBs and economic modelling developed in relation to SARS-CoV-2 were not subsequently approved for publication.

    c. **Advice service:** NICE provided a free fast track advice service for researchers developing novel diagnostics or therapeutics for COVID-19, to help expedite breakthroughs in care and support the life sciences industry. This assisted researchers from around the world optimise their approach to generating the essential evidence required to inform decision-making.

**Standard Methods and Processes**

**24.** 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 relevant time period the majority of CHTE evaluations of medicines followed the single technology appraisal ["STA"] process. This process is set out in the "Guide to the Processes of Technology Appraisal (2018)" produced as **Exhibit HK07 - INQ000316244.**

25. 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. Medicines are formally referred to the TA programme by the DHSC. NICE can only produce TA guidance on medicines that have a marketing authorisation for use in Great Britian.

26. The STA process has 4 broad phases:

- **Scoping:** The scope defines the key parameters of an evaluation such as the population, intervention, comparators and outcomes. Stakeholders are invited to comment on the scope before it is finalised.

- **Evidence submission**: Stakeholders are invited to submit an evidence submission once an evaluation has started. The company that manufactures the technology is also asked to submit a cost-effectiveness model.

- **Evidence review**: An independent academic group reviews the submitted evidence and provides a critique in the form of a report. This report is shared with stakeholders to respond to the key issues identified.

- **Appraisal of the evidence:** The stakeholder submissions and independent critique are considered by the independent advisory committee in a public meeting. Topic specific clinical, patient and commissioning experts are invited to attend and input to the committee meeting, but are not decision-making members.

27. Following the committee meeting, a consultation may be held on the committee's draft recommendations. Stakeholders may submit additional evidence as part of the consultation response, which is considered at a second committee meeting. The committee's final recommendations are published and subject to appeal. Once any appeals are resolved, final guidance is published. From this point, the clock starts on the mandatory funding timeframe stated in the implementation section of the guidance. In total, from initiating an STA to publishing final guidance, it takes approximately 40 weeks.

28. At the scoping, submission and draft guidance consultation stage, stakeholders are asked to highlight any equality issues. The committee considers these, and those considerations are documented in an equality impact assessment form published with the final guidance.

29. Medicines for the treatment of very rare conditions can be evaluated through the NICE HST programme. The HST programme also evaluates the clinical and cost-effectiveness of the medicine under question and the process of the HST guidance production broadly mirrors that of the STA process. During the relevant time period, the HST process was set out in the Interim Process and Methods of the HST Programme.

30. The evaluations of IPs follow the process and methods set out in the IP programme manual. The evaluations of diagnostics technologies started during the relevant time period followed the DAP manual. The evaluations of MTs started during the relevant time period followed the MT evaluation programme methods guide and the MT evaluation programme process guide.

31. IP, diagnostic and MT evaluations include similar main phases included in the STA process. However, the final recommendations are not subject to appeal. As a final quality assurance step in the relevant time period, the final recommendations were opened to resolution as a final quality assurance step. Resolution requests from stakeholders are considered on the grounds of breach of NICE's published process for the development of the guidance or factual errors in the proposed guidance.

32. The standard process for MIB development is set out in the Interim process and methods statement for the production of MIBs. A copy of this document is attached as **Exhibit HK08 - INQ000252470**.

33. Any guidance or advice produced by CHTE, including updates to guidance, is approved by NICE GE.

34. Any problems (adverse events) relating to a medicine or medical device used for treatment, or in a procedure, is reported to the Medicines and Healthcare products Regulatory Agency ["MHRA"] using the Yellow Card Scheme.

**Changes to NICE's approach during the pandemic**

Research to Access Pathway for Investigational Drugs for COVID-19 ["RAPID C-19"]

35. As stated above, RAPID C-19 was a pandemic-specific multi-agency initiative that was established on 29 April 2020 and was stood down at the end of March 2023. On 06 April 2020, following discussions between Meindert Boysen, NICE CHTE Director 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. On 29 April 2020, RAPID C-19 was established.

36. In normal circumstances it would take time for NICE to produce a full clinical and cost effectiveness analysis of a new therapeutic being licensed. For example, a standard single TA usually takes about 40 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 role of RAPID C-19 was to consider the potential therapeutics for treating COVID-19 and emerging evidence to inform system-wide preparations for patient access that could be accelerated and implemented as soon as there was robust evidence of clinical benefit.

37. RAPID C-19 operated within the governance framework of the DHSC Antivirals and Therapeutics Taskforce ["DHSC ATTF"]. It was made up of a range of key health care system partners including NICE, NHSE, MHRA, National Institute for Health and Care Research ["NIHR"] and the devolved administrations. NHSE had overall responsibility for RAPID C-19, while NICE's role was to provide the secretariat function, along with supplementing the horizon scanning information, provided by National Institute of Health and Care Research Innovation Observatory ["NIHRIO"], and evidence synthesis when identifying medicines showing promise in clinical trials, which could be prioritised for rapid regulatory consideration, interim clinical policy development and access.

38. It is important to note that RAPID C-19 did not formulate or provide clinical guidelines, guidance, advice or recommendations for clinicians. 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.

39. Decision-making on interim therapeutic access arrangements rested with the CMO and DHSC, and RAPID C-19's view was one of several sources of information and advice that informed this decision. Where interim access was agreed, this was taken forward by NHSE through development of interim access policies.

**40.** In August 2020, a guide relating to the RAPID C-19 process was developed, titled 'Research to Access Pathway for Investigational Drugs in COVID-19: interim process for NICE activities'. 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 HK09** - **INQ000315554**

RAPID C-19 Oversight Group

41. The RAPID C-19 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. Advisory members included DHSC ATTF and health technology assessment representatives from the devolved nations, as well as other staff from the key four organisations. From NICE, this included NICE staff from CHTE and the Science, Evidence and Analytics Directorate.

42. The RAPID C-19 Oversight Group was responsible for considering potential COVID-19 medicines in development and to identify and prioritise those likely to be expedited for patient access in the NHS. The group had a Terms of Reference, which was updated over time; a copy of the first iteration is exhibited as **Exhibit HK10** - **INQ000471160**

43. The designated RAPID C-19 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.

**44.** The RAPID C-19 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. A copy of the RAPID C-19 Nice Secretariat Organogram April 2020 – June 2022, is attached at **Exhibit HK11 - INQ000316250.**

45. The group's considerations were informed by briefings prepared 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 action and decision logs were maintained. The group functioned well as a collaborative, with all involved demonstrating a clear commitment to enabling rapid access to therapeutics with a potential for clinical benefit.

46. The RAPID C-19 Oversight Group agreed the next steps for each therapeutic, also called 'topic's', considering the emerging evidence. Options included:

    a. **Progress:** Where good evidence of efficacy is sufficient for further action to be taken by the CMO. The Oversight Group's assessment of the evidence and suggested next steps were summarised in a report to the CMO. This was often produced a day after the recommendation was made.
    b. **Monitor:** Where good evidence of efficacy was currently insufficient, but there are other ongoing trials. The topic would remain in the enrichment and monitoring stage and would be brought back to the RAPID C-19 Oversight Group when results from the identified key trial(s) were due.
    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 RAPID C-19 Oversight Group if new evidence emerged.

Life Sciences Team

47. The Life Sciences Team within CHTE provided the RAPID C-19 secretariat. The secretariat function comprised the coordination and development of the initiative. The Life Sciences Team's objectives and activities in relation to RAPID C-19 were to:

    - Provide the RAPID C-19 Oversight Group with the most accurate and up to date information on potential COVID therapeutics in ongoing trials, in the form of topic briefings (also supported by analysts from the Scottish Medicines Consortium ["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 NICE was aware of any developments regarding these therapeutics such as new evidence and regulatory plans.
- Co-ordinate partner agency involvement.

RAPID C-19 horizon scanning and prioritisation.

48. A central horizon scanning function identified potential therapeutics for consideration by RAPID C-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 MS Excel spreadsheet sent directly to those involved in the oversight and development of the horizon scanning. 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.

49. The NIHRIO scan identified all registered trials for COVID-19 therapeutics worldwide. The identified therapeutics were then ranked against a set of criteria, to which a scoring matrix was applied, as set out in **figure 1** below. The scoring matrix was amended in October 2020 to ensure that any COVID-19 therapeutics in development were not missed – as set out in **figure 2** below. The regulatory status criterion had been initially included because the access pathway for treatments with a UK licence (that is, existing drugs that had potential to be repurposed for COVID-19) was likely to be tweaked so that therapeutics in non-UK international trial were not disadvantaged by the criteria. The therapeutics with the highest scores were prioritised for consideration by RAPID C-19.

**Figure 1: 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/generalisable to NHS clinical practice. |
| | EU/US/Canada/Australia | 2 | |
| | UK | 4 | |
| **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. |

**Figure 2: RAPID C-19 horizon scanning scoring matrix from 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. |
| | US/Canada/Australia | 2 | |
| | UK/EU | 3 | |

| | | | |
|---|---|---|---|
| **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 | |
| **Special populations** | Active paediatric trials | 1 | To address the gap in trial activities in paediatric patients. |

50. 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 NICE or insight from members of the Oversight Group or the DHSC ATTF and included considerations such as biological plausibility, UK platform trial activity and/or regulatory intentions of sponsors. Furthermore, the prioritised list did not remain static as the trial landscape evolved.

Surveillance and monitoring

51. NICE staff would collate and interpret the horizon-scanning outputs from NIHRIO and supplement with additional information and monitoring, to develop briefings on priority topics for the RAPID C-19 Oversight Group to consider. Each briefing took up to 5 working days to develop. RAPID C-19 briefings were 'living documents', kept up to date by NICE with emerging evidence and other related information that could inform the potential for rapid access.

52. Supplemental information considered by NICE included:

- A NICE weekly literature search. This included new published papers, conference abstracts, preprints and international guideline developments.

The results from the broad search were triaged to specific therapeutics for detailed consideration.

- A dashboard was established that automatically checked for progress of ongoing trials listed on trial registries or likely to report on PubMed. While largely used by the NICE COVID-19 rapid guidelines team, an element of this 'trial tracking' was also utilised by RAPID C-19, alongside the additional intelligence provided by the DHSC ATTF or directly from trial investigators contacted by the team.

53. In addition, RAPID C-19 identified key trials to monitor that were considered likely to provide robust, generalisable and timely results that would be a strong enough signal of clinical benefit to consider rapid access. The NICE RAPID C-19 secretariat directly contacted the lead investigators of these trials, which included both academic sponsors and companies. This enabled the team to be prepared for when results were likely to become available, or to secure agreement with the investigators to share the results before they were publicly available. For example, the investigators of the REMAP-CAP trial provided RAPID C-19 with a full paper detailing the results of the tocilizumab and sarilumab arm of the trial before it was submitted for publication, which enabled the Oversight Group to review the evidence on 5 January 2021 and submit a report to CMO on 08 January 2021 recommending patient access. Subsequently, the paper was published on a preprint server on 9 January 2021 and later published in a peer-reviewed journal on 25 February 2021. Further details regarding key trials can be found at paragraph 69 below.

54. RAPID C-19 facilitated intelligence sharing between key health care system partners which could also be utilised by the COVID-19 rapid guidelines team. This included regulatory developments and anticipated timings for approval, updates on the progress of interim access policy development, and ongoing research developments, for example relating to the UK platform trials (inclusion of a new therapeutic, anticipated timing of readouts or early indication of results).

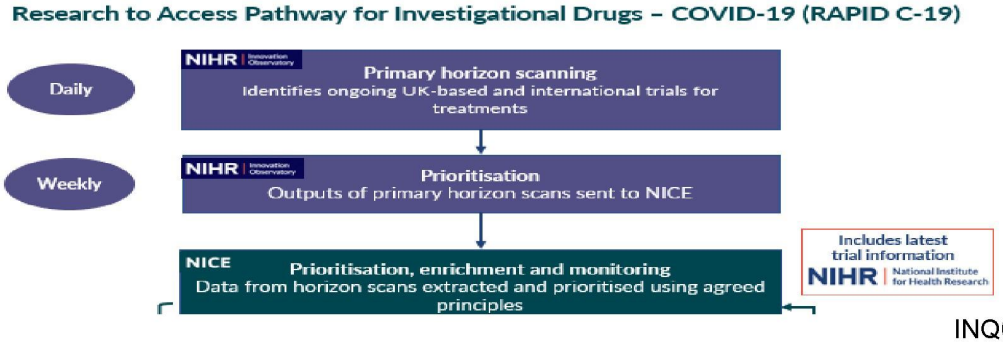
55. A weekly NICE COVID delivery group meeting was established in Autumn 2021 to enable internal consideration of the intelligence and subsequent co-ordination and alignment of NICE activity between CHTE and the Centre for Guidelines.

56. RAPID C-19 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 affect the group's considerations around potential rapid access. This included when:

    - There was a significant readout (high priority topic, UK platform trial, key trial) and substantive new trial data to review.
    - There was a development that could potentially change the position or take forward the current thinking with regard to potential for rapid access.
    - Advice on the next steps was needed.

57. A summary of the standard process of RAPID C-19 is summarised in **figure 3 below:**

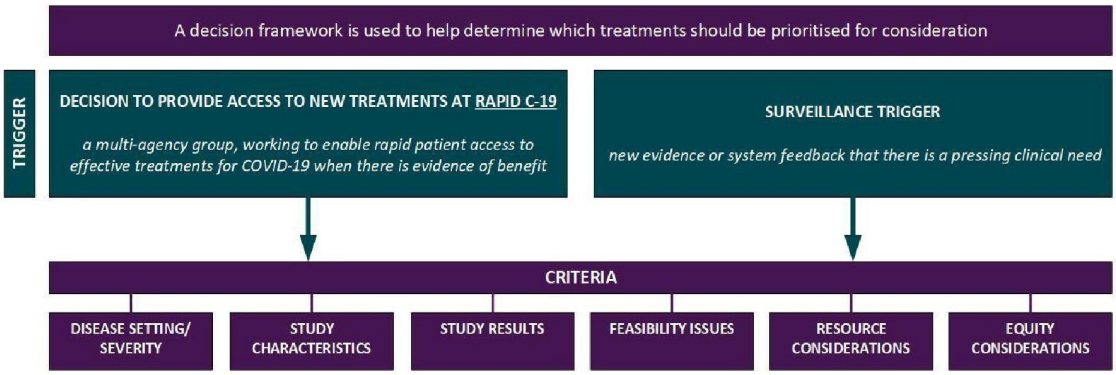
**Figure 3: RAPID C-19 Process Diagram**



Relationship with COVID-19 Rapid Guidelines

58. The relationship between RAPID C-19 and the COVID-19 rapid guidelines is illustrated in the "RAPID C-19 and COVID guidelines: therapeutics for COVID-19 process map" which is attached at **Exhibit HK12 -** **INQ000316255**. A positive signal from the RAPID C-19 Oversight Group would form a trigger within the COVID-19 rapid guidelines programme and if it met the required criteria, the therapeutic would be progressed for recommendation development. This process is set out in **figure 4:** COVID-19 rapid guidelines prioritisation criteria for COVID-19 therapeutics, below:

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




59. If a therapeutic with a positive signal was recommended by the RAPID C-19 Oversight Group for rapid access and rapid guideline recommendation development, a 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 rapid guideline team.

60. Once recommendations on that therapeutic were published in a COVID-19 rapid guideline, the RAPID C-19 topic briefing would be replaced by signposts to the rapid guideline. The rapid guideline content superseded all documentation rapidly developed to support the RAPID C-19 oversight group's considerations, and the rapid guideline evidence review took precedence over any versions of RAPID C-19

briefing documents. For further information, please see the statement of Dr Paul Chrisp.

MedTech Innovation Briefings Process

61. As a result of the pandemic, the process for the timeline and production of MIBs was shortened to 3 weeks instead of 12-15 weeks. This was achieved by changing working practices and working solidly on one topic rather than multiple topics at one time. Clinical experts were contacted earlier to allow more time for a response and they were only contacted once rather than twice to inform the briefing development.

62. No new interim process or statement was published during the pandemic. The production of MIBs was brought in-house to NICE staff rather than contracted out to external assessment groups during this period. All key steps in the MIB development process remained as in the published standard process but timelines were condensed due to in-house production.

**CHTE advice produced during the relevant period**

**63.** A spreadsheet, which provides a chronological list of all RAPID C-19 outputs for COVID-19 therapeutics during the relevant period is exhibited as **Exhibit HK13 - INQ000252475**

**Medicines Recommended**

64. A table summarising the list of medicines 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 HK14 - INQ000252476.**

65. For some therapeutics a topic briefing describing the publicly available evidence for a therapeutic was published on the NICE website. These summary briefings related to the following therapeutics.

- Budesonide.
- Casirivimab plus imdevimab.
- Sotrovimab.
- Molnupiravir.
- Nirmatrelvir plus ritonavir.

**NICE's use of key trial information and research information**

Key Trials

66. RAPID C-19 did not commission or design any clinical trials or research. As stated above, for all topics considered by RAPID C-19, key trials were identified, that is, trials that were considered likely to provide robust, generalisable and timely results. While the secretariat monitored all emerging evidence and kept the topic briefings up to date with the results of any new studies, it was the results from these key trials that were considered in detail by the Oversight Group.

67. The Oversight Group reviewed the results of key trials as soon as they became available and considered whether the strength of the evidence of benefit warranted consideration for patient access. Its opinion on next steps in light of the new evidence also took into account the existing evidence base (where previous studies were available) and other factors, for example the regulatory status of the product and any considerations around its potential use in clinical practice.

68. RAPID C-19 provided a report to the CMO when it considered that the evidence of clinical benefit was sufficient to warrant consideration for rapid interim patient access, but also when there was high interest (for example from government ministers, the public or the media) in a positive trial result and RAPID C-19's opinion was requested.

69. CMO reports were compiled for 20 topics. Patient access to repurposed treatments was facilitated within 10 days of the key trial readout (for example, dexamethasone, hydrocortisone, and tocilizumab in 2020), and access to new treatments facilitated within 14 – 42 days of marketing authorisation (for example, sotrovimab and molnupiravir in 2021). RAPID C-19 helped deliver treatments for NHS use across all 4 nations of the UK, with more than 200,000 (as of the end of October 2022) people having treatments as a result of rapid interim access arrangements (note that this figure includes non-hospitalised and hospitalised patients, but does not include dexamethasone, which very quickly became standard of care from June 2020).

70. Details of the key trials whose results prompted a RAPID C-19 response in the form of a CMO report, are detailed within the table at **Exhibit HK15 - INQ000252477**. As an example, one report sent to the CMO dated 6 January 2021 related to a trial of Tocilizumab and Sarilumab, in which the RAPID C-19 Oversight Group recommended consideration of rapid interim patient access (ICU patients).

71. Within this table are also details of those key trials whose results prompted rapid interim patient access prior to the CMO report being included in RAPID C-19 processes. 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).

**International Collaboration**

72. NICE had a lead role in developing best-practice guidance for the health technology assessment of tests and treatments for COVID-19, conducted as part of the external grant-funded Horizon 2020 HTx project. This was led by NICE's Science Policy and Research Team and was attended and informed by expert representatives from more than 22 countries globally. This focussed on country progress updates, review of

health technology assessment and regulatory methods, construction of disease pathways and review of economic methods.

73. NICE's Scientific Advice Team and Science Policy and Research Team also held meetings with Health Technology Assessment counterparts in Scotland (SMC), Wales (All Wales Therapeutics and Toxicology Centre), Canada (Canadian Agency for Drugs and Technologies in Health) and Australian Health Technology Assessment agencies to exchange on scientific issues and challenges of mutual interest relating to COVID 19 identifying opportunities for collaboration.

74. A full list of international collaborations is provided at **Exhibit HK16 - INQ000252478.**

75. RAPID C-19 did not formulate or provide clinical guidelines, guidance, advice or recommendations for clinicians, and did not collaborate with international bodies. However, in its role in monitoring for emerging evidence for therapeutics for COVID-19, it took account of international guidance (for example from the World Health Organisation, United States National Institute of Health), and synthesised evidence (for example systematic reviews, meta-analyses) that may have been conducted by international bodies. The secretariat function also contacted principal investigators of clinical trials being conducted outside of the UK to obtain information about when the results of those trials were anticipated to be available.

**Formulation / publication of clinical tools for healthcare workers**

76. CHTE did not have any direct involvement in the original formulation, publication or updating of clinical tools for healthcare workers during the pandemic, however NICE and NHSE worked with clinical experts and patient groups to develop statements about non-cancer managed access agreements ["MAAs"] during the pandemic. MAA refers to an arrangement that addresses a significant area of uncertainty in the evidence base identified by the technology evaluation committee within NICE. The statements set out general information about access to the treatments and suggested adjustments to the monitoring and assessment that are integral to collecting evidence to support NICE's decision on whether or not to recommend the drug.

77. The five MAAs were:

- Nusinersen for spinal muscular atrophy.
- Cerliponase alfa for ceroid lipofuscinosis type 2.
- Asfotase alfa for hypophosphatasia.
- Ataluren for Duchenne muscular dystrophy.
- Elosulfase alfa for mucopolysaccharidosis type Iva.

**78.** A summary of the five MAAs, including details of the providers that deliver these services is included at **Exhibit HK17 - INQ000252479.**

**Equality and Health Inequalities**

79. RAPID C-19 were aware of the disproportionate impact of COVID-19 amongst different population groups and the continuing need for treatment options to prevent disease progression despite the widespread roll out of vaccination, due to the continued risk of severe outcomes from COVID-19 for particular population groups. 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 did not receive the same protection from vaccination as the general population.

80. A key element of the Oversight Group's deliberations on specific treatments was the demographic characteristics of the people included in the trials, and consideration of vulnerable groups. When discussing treatments with strong enough evidence to warrant consideration for rapid access, it was cognisant of any issues that might adversely affect certain patient groups and the need for alternative options for these groups.

81. In November 2021, NICE became aware of a potential racial bias in pulse oximeters to measure oxygen saturation levels. Reports in the media identified that the Secretary of State for DHSC had ordered a review into racial bias in medical devices.

82. Equalities were addressed as a specific section within each MIB, titled 'equality considerations', therefore the following wording was included in the equalities section of Medtech Innovation Briefings on pulse oximeter technologies:

*The US Food and Drug Administration (FDA) has highlighted differences in precision of SpO2 monitors across different skin colours which may result in risk of inaccuracy for individuals with darker skin pigmentations. It reports that further evaluation on this association is needed (FDA safety communication, 2021).*

83. The MHRA highlighted a number of factors that can affect the accuracy of pulse oximeters, including skin pigmentation ('*MHRA use and regulation of pulse oximeters, 2021*'). It reports that darker skin pigmentation may cause an overestimation of oxygen saturation levels, so the relative changes in an individual person's reading should be considered as well as the numerical value.

**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**: 19/02/2024