SARS-CoV-2 and Viral Respiratory Testing Strategy, Winter 2020

Purpose

Public Health England (PHE)and NHS laboratories will provide a service for the laboratory investigation of respiratory samples during the winter season 2020/21. A strategy is required to include clinical requirement alongside diagnostic capability and capacity. The strategy must ensure that the service can be maintained alongside testing for SARS-CoV-2 and that government, clinical and public health requirements are met. This document describes the proposed strategy according to the following assumptions a) SARS-CoV-2 testing capacity will remain at the current level b) adequate staffing resources will be available c) the commercially agreed supply chain for reagents and platforms will be sustained.

Background

The WHO Director-General declared the novel coronavirus SARS-CoV-2 an outbreak a public health emergency of international concern (PHEIC) on 30 January 2020. In the United Kingdom, a testing service for SARS-CoV-2 was established at pace. The initial capacity of healthcare providers including laboratory facilities has been increased to meet the government strategy and predicted worst-case scenarios. As the 2020 winter season in the approaches, PHE and NHS must develop a strategy to align with that of the government: to prepare the healthcare systems including laboratory capacity according to the worst-case scenario whilst hoping for the least case scenario.

Routine Seasonal Respiratory testing

Seasonal respiratory testing for viral causes of influenza-like illness is long established. A spectrum of laboratory tests is available that meet clinical and public health needs. Guidelines for routine respiratory testing can be accessed via the national standard methods for investigations (SMI) https://www.gov.uk/government/collections/standards-for-microbiology-investigations-smi .
Influenza pandemics are a natural phenomenon that have occurred from time to time for centuries – including 3 times during the 20th century. They alone present a challenge to the economic and social wellbeing of any country, as well as a serious risk to the health of its population. The current SARS-CoV-2 pandemic and seasonal influenza-like illness must be managed in tandem and laboratories must have capability to address the possibility of concurrent pandemics.

Respiratory symptoms and COVID19

Many people without COVID-19 are likely to have symptoms that resemble COVID-19 during the usual winter respiratory virus season in the United Kingdom. The winter respiratory season occurs during the months of October to March. It will be vital to rapidly diagnose patients with respiratory symptoms and provide the appropriate healthcare. In the worst-case scenario, an influenza pandemic may occur concomitantly with a second or third wave of COVID-19 cases. It will be essential to differentiate the cause of infection, cohort patients and use NHS resources appropriately and efficiently. The role of laboratory diagnosis is integral to strategic healthcare planning for winter 2020 in the United Kingdom.

Respiratory Cohorts

We have assessed that there should be four patient cohorts requiring different levels of minimum testing. The rationale is presented below. A proportion of diagnostic testing may be available within NHS trusts as near patient point-of-care tests (POCT). POCT testing can improve patient flow and lead to a reduction in hospital acquired infection (HAI) and improve admission and discharge rates. It is important to note that any rapid test with a sensitivity, specificity or limit of detection that is significantly less than that of laboratory based tests may require secondary laboratory testing. Rapid COVID-19 only tests will be of limited use for assessing patients with respiratory illness for admission cohorting during the winter respiratory season. Other seasonal viruses including influenza will need investigating for clinical cohorting and minimising the risk of nosocomial and secondary infections.

Rationale for patient cohorts and proposed test panels

Group 1

SARS-CoV-2 testing only (minimum requirement)

This patient group will include contacts of confirmed COVID-19 cases including outbreaks, contact tracing, discharge planning, screening programs in schools and hospitals and care homes

Group 2

SARS-COV-2, influenza A/B and RSV (minimum requirement)

This patient group will include symptomatic low-risk respiratory patients requiring admission. Negative results will enable patient cohorting but may require additional testing (group 3 or 4) as clinically directed.

Group 3

SARS-COV-2, influenza A/B, RSV, Adenovirus, parainfluenza virus (1-4), human metapneumovirus, Rhinovirus (minimum requirement)

This patient group will include high-risk patients (e.g. immunosuppressed, chronic lung conditions), surveillance programs and public health outbreak investigations.

Group 4

SARS-COV-2, influenza A/B, RSV, Adenovirus, parainfluenza virus, human metapneumovirus, Rhinovirus, Enterovirus, Mycoplasma, legionella (minimum requirement),

This patient group will include ICU/PICU/ECMO admissions and those with non-resolving or escalating symptoms and already testing in the workstreams above

Note on rationale

The rationale is a minimum requirement for each patient and is intended to complement upper and lower respiratory bacteriology culture methods for organisms.

The actual tests performed on specific platforms in each laboratory may exceed the minimum requirement. This will be influenced by existing diagnostic platforms, managed service contracts, local trust agreements and operational practicalities. Solutions that meet clinical and public health needs while addressing supply chain risks must be established in each laboratory.

Workload modelling

The number of tests required in each patient group will be determined by

1. Previous number respiratory tests (in-house and referred) per site (winter 2018/19) plus contingency. Statistics from two winter seasons are necessary to account for fluctuations in annual incidence of infections.
2. Agreed laboratory capacity for COVID-19 based on pillar 1 workflow and the assumptions below
3. The calculated percentages of each patient group according to the proposed four cohorts using the data obtained locally

Based on modelling, every regional and commissioned PHE testing laboratory will seek to achieve capability to meet the required capacity per patient group with the options of a) end-end, b) in-house and c) rapid testing platforms. The capacity and required test panels of existing platforms will measured against the required capacity and capability to identify gaps. The resultant needs identified will be met through acquisition of addtional equipment and laboratory assays as indicated in the gap analysis. It is proposed that NHS laboratories will work to this model with the additional consideration of referral of samples to other testing laboratories where ability or capacity cannot be met locally. The turnaround time of results for referred samples may be delayed.

Workflow modelling

The workflow must be modelled to include social distancing requirements, turn-around times, equipment capacity (including business as usual activities), sample receipt (courier delivery schedules throughout the day and into the evening), urgent samples (e.g. transplant patients), logistics of staff travel arrangements (rural areas, travel restrictions), management of shift patterns. It is anticipated that 24-7 working will be required to fulfil requirements, however actual requirements will be determined by the platforms and processes in each laboratory.

Turnaround times

- <24 hours for each workstream, rapid tests will be available in each lab with a TAT of <4 hours
- TAT will be measured daily as the average number of hours from receipt to verified result
- Outliers will be investigated and managed accordingly
- Laboratory solutions will be procured with time to result in mind

Assumptions

- Staffing will be available for planned capacity and shift patterns to enable 24-7 workflow processes where required
- A turnaround time of <24 hours will be required for all workstreams
- Addition equipment and laboratory assays can be procured if required
- The government strategy will not mandate a respiratory strategy that is unmanageable within this strategy
- The majority clinical and public health investigations will take place in NHS or PHE clinical laboratories.

- Clinicians, Laboratories and POCT teams will have the ability to select the most appropriate minimal level of testing for the patient groups and will not risk supplies by "over-testing" with broad-spectrum respiratory assays.
- Screening and contact tracing testing will take place in pillar 2
- Community cases of mild respiratory illness will be investigated for COVID-19 only
- Symptomatic respiratory illness in the community will be investigated for SARS-CoV-2 only.
- Laboratories will continue to investigate bacterial respiratory investigations by culture techniques
- Business as usual laboratory activities will be at 80%
- Continual review of the pandemic situation, overall viral respiratory test requirements and laboratory capacity will take place throughout the winter season and reasonable adjustments made to meet service needs

Risks

- Supply chains for suitable and sufficient multiplex assays cannot be assured
- Many laboratories may not be able to provide the required tests equipment/capacity/technical expertise)
- Age of existing equipment
- Commercial Multiplex respiratory assays that include SARS-CoV-2 are in developmental stages and performance characteristics of new assays cannot be assured
- Pace of pandemic does not allow for normal tendering and procurement processes
- Incidence of SARS-COV-2 and other respiratory infections cannot be accurately predicted there is a risk of over or under estimating with associated risk to service and with financial implications.
- If POCT testing is not aligned with laboratory based strategy, inefficiencies in testing, resources, finances and patient management may occur
- Selection of clinically inappropriate broad-spectrum tests for patients will risk supply for those who need it.

Current respiratory testing in laboratories

The current routine viral respiratory assays and platforms used in testing laboratories are stated in the embedded file below.

INPUT DATA HERE

The anticipated division of total workload into the 4 work streams will need to be verified by each site. The data set below will be utilised to estimate the percentage of each cohort from the total tests performed. The data will contain some inherent inaccuracies because of regional distribution of testing arrangements which have evolved and will continue to evolve for the duration of the pandemic and the winter respiratory season.

- Total number of SARS-COV-2 tests
- Number of community request tests
- Number of outbreak investigation
- Number of inpatient tests
- Number of ICU admissions
- Number of routine (Non-COVID-19) viral respiratory tests

Table 1. Predicted workload per laboratory Winter (Oct-Mar) 2020

Laboratory	Average daily routine viral respiratory tests (winter 2019*)	Average daily routine viral respiratory tests (winter 2018*)	SAR-COV-2 daily test numbers (agreed capacity)		Average Daily total (Average) of Column 2-4)	*Group 1 (30% of column 4)	*Group 2 (50% of column 4)	*Group 3 (15% of column 4)	*Group 4 (5% of column 4, divided by 13 to account for ICU LOS)

*October to March

Table 2. Existing platforms, daily requirement and existing capacity

Laboratory	**Platform/s group 1**	**a) requirement b) capacity**	**Platform/s group 2**	**a) requirement b) capacity**	**Platform/s group 3**	**a) requirement b) capacity**	**Platform/s group 4**	**a) requirement b) capacity**
e.g. Leeds	e.g. Cobas 8880, Panther	e.g. a) 100 tests b) 2000	Cepheid infinity And Cobas	a)500 b)50	NeuMoDx	a)50 b)100	NeuMoDx	a)1 b)100

Table 3 Gap analysis: Required platforms and test options based on table 2

Laboratory	Platform/s group 1	Platform and assay group 2	Platform/s group 3	Platform/s group 4
e.g. Leeds	None, capacity met	Additional Cepheid or multiplex Cobas 8800	None, capacity met	None capacity met

Key,green = capacity met, red= platform or assay reagent deficit

Proposed equipment per lab

Table four indicates the additional requirements per laboratory to meet the predicted need. For maximum efficiency, TAT requirements and post COVID-19 and legacy, laboratories should use high throughput end-to-end systems for high volume workload. End-to-end systems can reduce the need

for technical grade staff. Multiplex low throughput systems may be suitable for POCT testing in hospitals at points of entry such as the emergency department and admissions/discharge units. In-house assays for multiplex testing require multiple reactions per patient and are reliant on separate extraction, liquid handling, amplification and analysis. In-house assays require technical expertise to operate and interpret results and adds risk to service capability. The throughput of existing in-house assays can be increased by utilisation of liquid handlers and 384 well amplification platforms to replace lower throughput formats. This will require local assay development and validation. For contingency, laboratories will require at least two test options for each workstream. This may include a contingency of referring samples to other laboratories.

Commercial strategy

Where possible testing will be performed using existing platforms and assays if analytical performance and supply chain can be assured. Where new platforms or assays are required the strategy will be to explore the existing framework for suitable solutions. Where neither option meets the need, the open market will be approached and assessed for evidence of assay performance characteristics, technology compatibility, lead delivery times and supply chain assurance. Where multiple commercial solutions meet the criteria, tender specification will be scored. The chosen solutions must be in place by September 2020. To mitigate against the risk of unacceptable assay performance, more than one supplier will be considered for each solution and it is recommended that no commitment to procure is made prior to assay validation against the manufacturers performance characteristics. Where two or more suppliers perform equivalently, the solutions may be deployed across testing laboratories. Any contracts will be agreed for a period of no longer than 12 months in the first instance. This is to mitigate against the rapid pace of technological developments in multiplex testing and the risk in subsequent seasons of the emergence of a novel pathogen that is not included in the chosen solution.

The overall choice and use of platforms and assay across the UK should be coordinated so that supply chains are sustainable.

Assay performance

When selecting assays the performance characteristics of sensitivity, specificity and limit of detection (LOD) will be defined prior to selection and evaluation. The manufacturers performance characteristics must be demonstrably equivalent or greater than existing assays. This must be demonstrated by validation and/or verification in the laboratory. Where there is mitigation and justification, a lesser performing assay may be selected for example, a confirmatory assay may be a pragmatic solution for a positive result obtained using assay where specificity is lower than an existing assay but the sensitivity and LOD are equivalent or greater than the existing assay.

Next steps

The number of tests required and turnaround times per workstream will be calculated per laboratory. The capacity of existing platforms and assays to include SARS-CoV-2 and business as usual testing must be considered. Any gaps in requirements will be resolved through the acquisition of appropriate platforms and/or assays. PHE, NHS and DHSC will collaborate to ensure that approaches are complimentary and address supply chain restrictions.