

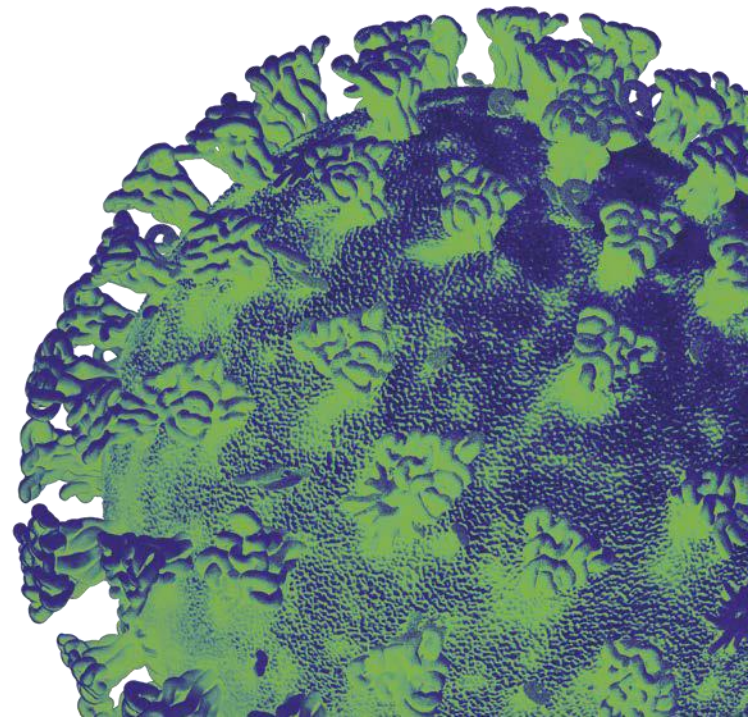
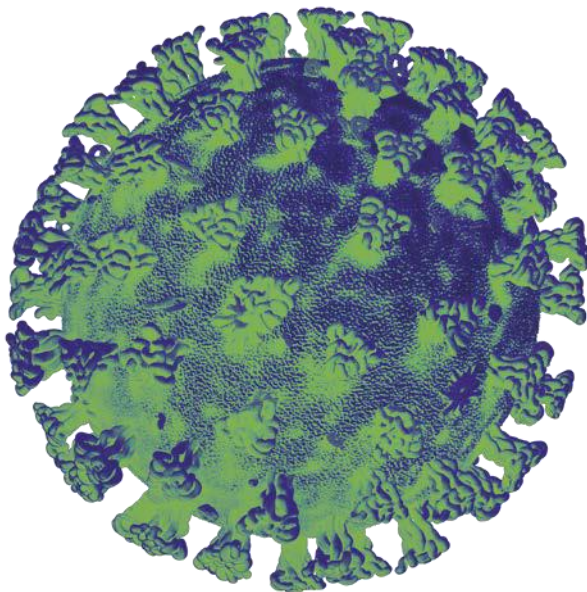
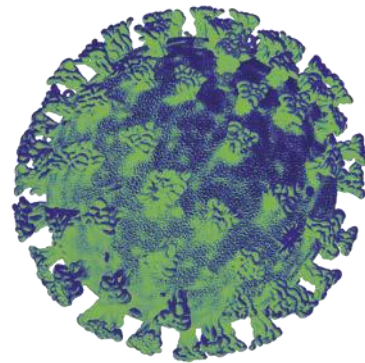


Llywodraeth Cymru
Welsh Government

Technical Advisory Group

Guidance for assessing the Potential for New
Technologies to improve SARS-CoV-2
diagnostic Testing

19 October 2020



Testing Sub-Group of the Welsh Government COVID-19 Technical Advisory Group: Guidance for assessing the potential for new technologies to improve SARS-CoV-2 diagnostic testing

Overview

There are a large number of commercial organisations that have developed, or are developing, products that are intended to support diagnostic testing of SARS-CoV-2. Many of these organisations employ lobbyists, public relations and salespeople whose job is to attempt to sell these products via any route possible.

This will include engagement with decision makers and government, as well as with staff within organisations undertaking diagnostic testing. Understanding the potential role of these new technologies and where they fit into laboratory diagnostic testing is critical to assess if these approaches offer benefits to the pandemic response in Wales.

This document provides outline guidance covering the laboratory diagnostic process, to enable the identification of where a new technology sits within the sample pathway, and from this to perform an initial, realistic, assessment of the likely impact of that technology on testing capacity. This document also outlines key bottlenecks, which should be kept in mind when considering new technology offerings.

Scope

This document is focused on providing guidance associated with technologies designed to detect the presence of an active infection of SARS-CoV-2 in an individual. Detection of individuals who have previously had an infection of SARS-CoV-2 is out of scope. Also please note that this document is focused on the laboratory phase of testing, and does not consider/include bottlenecks in the pre-laboratory stage (e.g. related to the physical collection or shipping of samples) or in the post-laboratory stage (e.g. related to reporting back results and acting on these for example as part of TTP). It is important to note that these bottlenecks can have a considerable impact on testing throughput.

Background

In the UK public discourse, there has been a considerable focus on the raw numbers of tests available to perform SARS-CoV-2 diagnostic tests. While understandable, this focus on testing numbers abstracts the laboratory process and infrastructure that is required to perform and report SARS-CoV-2 diagnostic tests. While tests should only be performed for clear medical reasons, with a clear clinical or public health objective, increasing testing capacity may be desirable or required for a number of reasons.

However, what is critical to understand is that the process of diagnostic testing is analogous to a production line in a factory. A number of processes (Figure 1) must be performed on each sample in a particular order to go from the swab taken from a patient to an actionable result that is ready to be communicated back to patients and medical/public health staff.

This set of processes or steps can be referred to as a sample's journey (the process for SARS-CoV-2 is outlined in Figure 1). Each process/step will have a capacity. It is the process/step with the smallest capacity which determines the overall 'capacity' for testing. Because processes must be carried out in order, the maximum capacity of the end-to-end process is dependent upon the step with the least capacity. Although necessarily occurring in series, each step is effectively independent. Consequently the fact that later steps may have more capacity than an earlier, rate limiting, step is effectively irrelevant when considering the capacity of the overall process.

By investigating and understanding our rate limiting steps we can optimise our testing system to

push as many samples through as possible. However, this must be understood as an end-to-end process, as the capacity of a given step is only meaningful in the context of the capacity of the preceding steps. This document seeks to provide an overview of the laboratory process, to flag key bottlenecks and to provide insight to evaluate the meaning or potential value of additional/new technologies. We calculated the theoretical capacity at each point of the sample journey for the PHW labs, to articulate the current situation and identify areas where potential improvements could provide the biggest impact on testing numbers.

End to end Sample Pathway with lab/staff capacity, requirements and bottlenecks

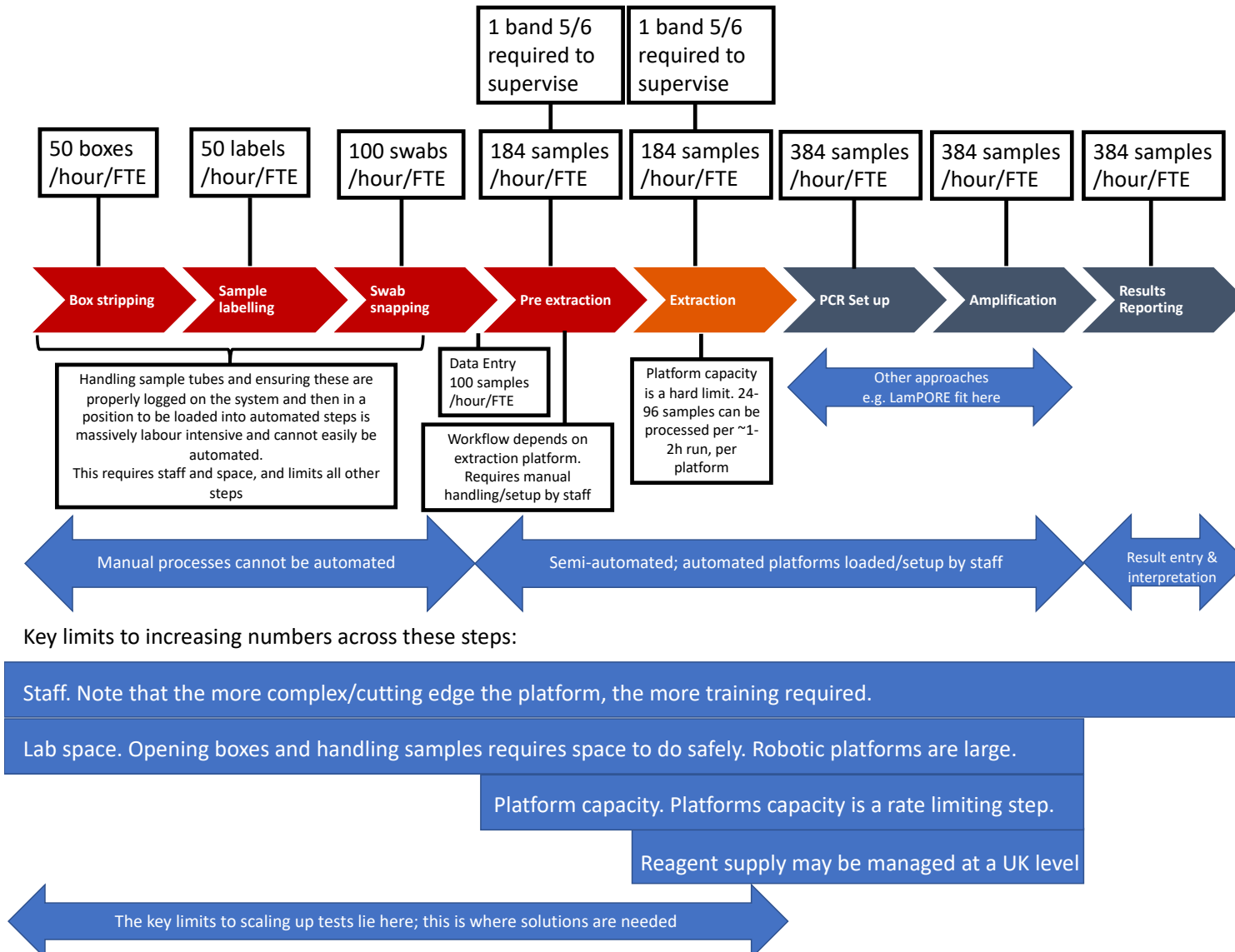


Figure 1 The laboratory process for SARS-CoV-2 testing. Steps are coloured by the extent to which they affect current total/final testing capacity within PHW. Red = Critical; Orange = Significant; Grey = Capacity not currently limiting.

We provide the time taken at each step, per hour, per member of full time staff to outline what staff capacity is available. The first three steps are wholly manual, and so wholly dependent upon staff. The following four steps depend both on staff and automated platforms. The final step is staff dependent to ensure high quality results are delivered. There are four key limits to increasing test numbers, which apply differently across the pipeline. Staff and space are key limitations, and are key current bottlenecks for the service. These cannot be rapidly ordered up, and are dependent upon a number of factors including training and provision of laboratory space. It should be noted that the more complex or cutting edge the analysis/extraction platforms, the more training and more highly qualified staff must be.

Platform capacity and reagent supply are principally issues for the high throughput elements of the activity, once the manual steps have been completed. These are limited by the fact that often platforms such as robotics or extraction platforms are physically large and expensive, and use

platform-specific reagents. This creates issues for hosting these in laboratories, training staff, and rapid ordering from suppliers. However, without these platforms, it is not feasible to run a high throughput laboratory. Processing thousands of extractions and sample preparations per day manually would result in tens of thousands of pipetting actions, which would rapidly cause RSI and other health issues for lab staff, as well as introducing testing errors. Therefore automation of these processes must be a cornerstone of providing diagnostic laboratory services.

Placing a technology into the sample pathway

The first step when examining the potential of a new technology is to identify where in the sample pathway the technology sits. This should be relatively obvious, although in some cases publicity material from companies has played down or ignored the front end process required to prepare a sample for testing using the indicated platform. Using the details in Figure 1, the first process undertaken should be to identify which step the technology will impact. It is important to remember that this is an end-to-end process, and so improvement at one step may not translate to an overall increase in capacity.

Understanding current capacity and bottlenecks

The available capacity at each step should be tracked and recorded by testing organisations/laboratories in Wales. This will then enable the identification of steps that are rate limiting, and enable colleagues from across the pandemic response to understand where innovations are needed. Using an up-to-date capacity report, it should be easy for staff to rapidly identify if an innovative technology may provide benefit to the testing programme. This may be provided in one of two ways;

1. The technology will increase capacity within a rate limiting step
2. The technology will improve sensitivity/specificity/speed of testing, and/or will free up staff time to enable more capacity to be bought to bear on a rate limiting step.

In the examination of a new technology it is important to understand key logistical elements, including;

- Staff requirements (including training/level and numbers)
- Space requirements

In addition to the potential number of samples that the technology could process.

The introduction of a new platform requires extensive validation and, if this is positive, the subsequent integration of the new technology into processes, potentially requiring significant staff retraining. The resource demand associated with this work must not be underestimated. In these cases, the benefit must outweigh this potential disruption to laboratory services.

Therefore, before attempting to progress the introduction of a new technology the following questions should be answered;

1. What step does the technology fit into?
2. Is this a step that needs additional capacity?
3. What are the implications of putting the technology into service?
4. How is the new technology better than what already exists?

And, if possible:

5. How will the new technology impact the existing sample pathway and processes?
6. Is there sufficient confidence that the resource 'cost' associated with the evaluation and potential subsequent integration of the new technology into existing testing ecosystem will yield sufficient benefits to make the investment worthwhile?

Challenges with the addition of platforms and increasing complexity

The consideration of the deployment of new technologies must also necessarily be informed by the number of platforms and processes already available to undertake a given step. Over the last 6-9 months additional platforms have been procured and put into service to support a number of the individual processes for SARS-CoV-2 testing. For example, there are in the region of 10-15 platforms in use within the PHW laboratory network that can be used to perform what is covered by the 'PCR setup' and 'Amplification' steps shown in figure 1.

Each platform has its own performance criteria (requiring specific guidance on report interpretation), and requires dedicated staff training and processes to deliver high quality results. Additionally, the more platforms in operation, the more considerable the logistical challenges (e.g. around supply management and storage).

Each new platform introduced therefore adds complexity to the delivery of testing and the interpretation of results, which must be offset by its utility and potential contribution to any increasing testing capacity.

Planning for the introduction of a new technology

Any planning for the introduction of a new technology must involve the laboratory teams who understand the full sample journey. The identification of new technologies for introduction into service by staff who do not have experience or understanding of the sample journey has the potential to create significant extra work, and unnecessarily raise expectations of other stakeholders.

The questions and considerations articulated above provide a basis by which staff can rapidly assess if a new technology might represent an opportunity worth pursuing. However, once this analysis has been performed, and if it appears as if the new technology may meet laboratory needs, further assessment must be undertaken by qualified personnel to ensure that the technology will fit with current operations and will offer benefit to the people and patients of Wales.

Impacts outside the sample journey through the lab

Finally it is important to emphasise that the sample journey through the laboratory is not the only place where bottlenecks exist, or could impact on the flow of samples for testing. The pre-laboratory phase includes a range of bottlenecks which impact the availability of samples to feed the laboratory process. The post-laboratory phase includes a number of bottlenecks that affect the rapidity and range of uses for test results. Furthermore it is important to note that innovations/changes elsewhere in related areas (e.g. the provision of point of care testing) may also have a knock on effect on the requirements and capacity of testing within the diagnostic testing process.