Getting a Grip on Covid-19 Test Samples

In early 2020, the world of pathology and infectious disease testing was thrown into chaos by the Covid-19 pandemic. One of the key challenges in the global testing programmes for Covid-19 is how to track very large numbers of patient samples passing through inexperienced or under-staffed laboratories that have been asked to increase their daily throughput by as much as 10 times their normal workload.

Over the last 20 years sample management has totally changed from its origins in the laboratory that were quite basic and rudimentary. In the beginning, clinical sample management worked by storing the samples in tubes. At this time many labs, even in large hospitals & pharmaceutical companies, stored their tubes in standard chest freezers either unlabelled or at best with handwritten labels on the rack or on the outside of the storage tube. If a clinical lab was particularly advanced, their samples might have a barcode, a 1D barcode, labelled on to the side of the rack. The databases of samples stored, if they existed, were quite often just Word documents or Excel documents, although patient samples in Pathology were tracked more effectively from the start.

More advanced sample management really began when 2D barcoded tubes were introduced. We have evolved today to sophisticated tube and sample tracking applications. Sample management is now thought of as a genuine, serious discipline, as organisations realised that their samples were highly valuable.

The biggest issue for sample tracking during the current crisis is the availability of suitable consumables, followed by the available instruments for testing. With some countries in Europe looking to test more than 100,000 samples per day it is not hard to see why. If a lab uses 96-well PCR plates for this testing they will need over a 1000 plates per day. Typically, these are sold in cases of 100 plates so that's 10 cases per day, 50 cases per week. If all 27 EU states did that it would be 1350 cases of PCR plates per week. Now add in the USA & Canada, Australia, South East Asia... trying to mould, sterilise, pack and ship that many plates, even distributed across, say, 10 different manufacturers is a major logistical problem. Add to that the liquid handling tips and the RT-PCR and RNA extraction reagents which are also in short supply and the scale of the problem becomes apparent. There are now shortages of the very 2D-barcoded tubes which are so desperately needed to help track large numbers of samples.

In the short-term, if 2D-barcoded tubes are not available, the next best option is to use linear barcodes. These can be laser printed or inkjet printed onto tubes for short-term disposable use, but perhaps the quickest way to use them is a print-and-apply self-adhesive label. Suppliers in the lab field can offer the printers software to design the label and the consumables. Typically, a sample receipt form should be generated and attached to this should be multiple copies of a unique barcode on labels. This allows for both the documents and the tubes to carry identical copies of the bar code and for samples to be split further downstream.

To achieve some level of high-throughput, samples could be grouped into solid polypropylene blocks or deep well microplates, each holding 96 wells. These can have a linear barcode label applied to one end or side that can be read on most available automation platforms, but it is important that ALL the plates in a batch have the barcodes applied to the SAME end or side panel relative to the A1 position. This will prevent the plate being loaded the wrong way around on the robot deck. Because of their wide availability and use in agri-bio, compound storage, biosynthesis and sample storage, there is currently no shortage of 2ml deep well storage plates. These can be used for the RNA clean-up step in conjunction with 96 well filter plate technology. Alternatively, magnetic bead separation can be used if the liquid handling robot is equipped for this technique. Transfer to a 96 well PCR plate is still required, although 384-well PCR plates can also be used to speed up the throughput if the liquid-handling in use can support such small aliquots. All of these blocks and plates can carry 1D linear barcode labels. Tracking the samples within the plates relies on the A-H, 1-8 well location co-ordinates being accurately recorded; less error-proof than 2D barcoded vials, but cheaper and currently easier to set up.

The issue of RT-PCR reagents is a thorny one, as is the RNA extraction kit. Currently, the Francis Crick Institute in the UK is testing using home-made reagents reverse-engineered from proprietary solutions by Qiagen, Merck and Roche. This can be risky and obviously, there are no quality controls or manufacturers' guarantees that it will work in the same way that an off-the-shelf kit should. However, the Crick Covid-19 Consortium have published their SOPs for these tests on their website https://www.crick.ac.uk/research/covid-19/covid19-consortium which are optimised for Hamilton Star and Starlet robots for the clean up and Beckman FX robots for the extraction. These would need to be adapted to any other or smaller pipetting station in order to replicate the Crick Covid-19 Consortium protocol. Although the Francis Crick Institute already had 2D-barcode rack scanners from Ziath and others, they were hampered by the lack of available tubes.

The Covid-19 testing protocol followed by the Francis Crick Institute involves collection of sample swabs at hospital sites in 15ml Falcon tubes. The swabs are then transferred to uncoded 2ml screw cap plastic vials and linear barcodes received with the sample from each hospital are applied to these, such that the robot's 1D linear bar code readers can scan them on the deck. For less sophisticated automation, it should be possible to use commercially available wired, wireless or Bluetooth linear scanners such as those from Opticon for this step. The robot then transfers the digested contents of each 2ml vial to one well of a 2ml deep well plate which is already bar-coded on the short edge.

Of course, all that vital sample location data needs to be entered into a LIMS or database of some sort so that the RT-PCR results

can be tied directly to the correct patient samples. There are many systems and software available for this. One of the simplest and most cost-effective is the Samples software from Ziath. This basic "What is it? Where is it?" programme is an easy-to-use relational database that can be customised to track samples by any number of user-defined tracking tags, making it easy to find. For example, "all patients with positive RT-PCR result, over 50, who live in Cambridge, UK".

These are some of the ways that Sample Management issues are and will be tackled during the Covid-19 crisis and into the future. You can keep up to date with Neil Benn's thoughts on this subject via his blog posts on the Ziath website at www.ziath.com/index.php/blog

Neil Benn

Neil Benn graduated from Leeds with a BSc in Biotechnology and then an MSc from Hertfordshire University in Computer Science. His distinguished career in Laboratory Automation encompasses GlaxoSmithKline, CAT and the Max Plank Institute before setting up Ziath in 2005. He is a recognized authority on sample management in the laboratory.