COVID-19 | SARS-COV-2 B.1.1.7 VARIANT

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NOTES	

What's New?

There's a new variant of the virus out there that appears more transmissible (infectious) but no more virulent (harmful) than the previous one. And because it seems to be a lot better at spreading it's rapidly becoming the most common strain out there. So what does this mean for productions?

- In terms of the Tier 4 restrictions announced on Saturday, Film and TV Production is listed as a business which can remain open but there may be operational hurdles: hotel availability in Tier 4 areas or for guests from Tier 4 areas, restrictions on international travel or quarantine exemptions etc.
- The effectiveness of **PCR testing** is unchanged (but see below).
- Effectiveness of the Pfizer and other **vaccines** will not be affected.
- **The principal change is that there is really no room for complacency.**

  Let's be honest. We're all sick of this virus and have had enough of it. Vaccines are coming, there's a light at the end of the tunnel, it's easy to get a bit complacent about masks and distancing and all that.

  Not any more. We all need to super-vigilant and doing more of the stuff we know works. And we need to be doing it more assiduously and more often.

As ever, this is a rapidly changing landscape – but we know a lot more about the virus than we did a year or so ago and while we don't know everything about this variant yet we're not helpless. Far from it.

As a rule, viruses mutate over time and tend to get better at transmission but less serious – they want to use you, not kill you – so this 'new' strain **isn't** going to spread in new ways or cause a different clinical syndrome.

Ideally a virus wants to replicate as much as possible while causing as few symptoms as possible so the host can stay mobile and mingle with lots of other people so the virus can keep spreading.

In this case it seems SARS-CoV-2 has had a software upgrade so it sticks to host cells better - which makes it better able to establish an infection.

What Productions Need to Do

Everything you're doing now but ***better*** and ***more of it***.

- **Distancing**. This is a *social* virus. Enforce distancing wherever possible. We recommend sticking to the 2m rule rather than falling back on the '1m plus with mitigations'.
- **Screening**. Ensure you're screening **all** production staff regularly and not creating any disincentive to declare symptoms or positive test results in the person or their close contacts outside the production.
- **Face coverings / masks**. Enforce the proper and assiduous wearing of high-quality face coverings or masks. Consider upgrading all face protection to FFP2/3 with face fitting - but remember masks are more about *source control* (stopping the virus escaping) than preventing it entering so no vents.
- **Ventilation**. Do everything possible to avoid creating crowded, stuffy spaces. Achieve some air circulation.

- Because this variant appears better at establishing an infection it has been suggested viral loads may be higher (which is plausible but we'd like some more data) – this makes the above points especially important.
- **Hygiene**. Although the evidence shows infection from surfaces is probably a lower risk, still enforce hand sanitising and sensible cleaning particularly of high touch areas.
- **Testing and isolation for close contact work**. Ensure everyone involved in close contact work is regularly tested using PCR or LAMP tests. Pay *particular* attention to SAs or other 'day players'.

  Back up testing with effective isolation.

  Use a UKAS-accredited lab because as part of their ISO they'll be alive to whether any mutations will affect their assays.

What's Happened?

Evolution, that's what's happened. SARS-CoV-2 lineage B.1.1.7 (also called VUI-202012/01, for the first 'variant under investigation', December 2020), appears to be spreading faster than other variants in the UK.

When a virus reproduces it's a bit messy. Often the daughter viruses aren't perfect copies. This means that some might be less able to propagate, some more so. Which is what's happened here.

With so many SARS-CoV-2 infections in the world it's entirely expected that new strains will occur and compete. It is thought this one happened during a long infection of a single patient that allowed the virus to go through an extended period of evolution with multiple variants competing for selective advantage - and possibly infection with two strains at the same time was involved too.

There have been a number of changes to this virus over the last year and different countries have been affected by different strains - but most importantly these strains have not resulted in any relevant clinical variations such as new symptoms.

But this variant **is** different. SARS-CoV-2 mutates at a rate of about 1 to 2 changes per month. Which is low – and that's in a genome 30,000 letters long.

What that means is if you sequence the genome of the virus today it will differ in around 20 places compared with the earliest genomes sequenced in China in January.

> **⚮ | What's in a Genome?**
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> A genome or genetic code really is just like computer software – it's a long sequence of a very few letters – 4, actually, A, C, U and G - so it's not quite binary like a computer but it's not far off. It's basically a long number that contains instructions that tell cells how to make stuff.

But B.1.1.7 has acquired more than 17 mutations seemingly all at once.

Among the 17 are 8 mutations in the gene that codes the spike protein of the viral coat, two of which are troubling.

> **⚮ | 17 or 23?**
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> There are 17 'non-synonymous' or coding, mutations. These change the protein sequence coded for by one of the viral genes. There's also a few 'synonymous (or 'silent') mutations that don't really do anything and are junk picked up over 3.8 billion years of evolution – which makes up the 23 to which Patrick Vallance referred.

One, N501Y, has previously been shown to increase how tightly the virus binds to its entry point into human cells, the ACE2 receptor. Another, 69-70del, leads to the loss of two amino acids in the spike protein and has been found in viruses that worked out how to evade the immune response in some immunocompromised patients.

N501Y has been around since at least April in Brazil and 69-70del since at least January / February in Thailand / Germany so both were already circulating globally prior to combining in this this new lineage.

Yet another, P681H is immediately adjacent to the furin cleavage site, a known location of biological significance [(1)].

How Infectious / Serious Is It?

In the press conference on Saturday Patrick Vallance said that B.1.1.7 accounted for about 26% of cases in mid-November but by early December it was over 60%. Boris Johnson added that the mutations (there are several) may have increased the virus's transmissibility by 70% - but that is premature; there are too many unknowns to put a number on it conclusively yet. But it's certainly high.

The 70% figure is arrived at in two main ways; by comparing the number of copies of this strain in an area compared with other strains, and by comparing the R number where the variant is present with the R number elsewhere. Neither is perfect; for example if large event takes place where a lot of people get infected with the new variant, against a backdrop of near-lockdown that will look the same as high transmissibility.

Also the rapid dominance of B.1.1.7 over other strains might be down to chance; a variant that spread rapidly from Spain to the rest of Europe—confusingly called B.1.177—was thought to be more transmissible but wasn't; it just got carried all over Europe by people who had taken holidays in Spain.

Another reason scientists are cautious is the new mutant also carries a deletion in another viral gene, ORF8, that previous studies suggest might reduce the virus's ability to spread.

One of the mutations - N501Y - is also present in a strain found in South Africa where cases are soaring in the Eastern Cape, Western Cape and KwaZulu Natal. There is anecdotal evidence that the South African variant may be causing more serious disease in young people and the otherwise healthy. But equally more young people may be getting sick because many more are getting infected.

PCR

The 69-70del deletes six letters in the viral genetic code that instruct the host cell to insert amino acids 69 and 70 into the spike protein.

Coincidentally (and rather interestingly) one of the most common PCR tests, TaqPath, looks for pieces of three genes – including the one with the 69-70 del mutation. This means that this 'channel' comes up negative when running a PCR on the new variant. The other two channels still come up positive so this doesn't mean PCR tests won't work any more - but it does mean we can track B.1.1.7 simply and accurately via the hundreds of thousands of PCRs performed daily.

Also all viruses mutate - which is why PCR tests used by diagnostic labs target more than one part of the viral genome. Also labs know which genes their tests target and are very vigilant about checking test performance.

The Vaccine(s)

The Pfizer and Moderna mRNA vaccines – to use the 'software' analogy above – basically deliver an email to your immune system containing some code telling it what the spike protein on the virus looks like and how to deal with it. Then the vaccine deletes itself like a Snapchat message.

Remember that genetic material like RNA is essentially a long number - so mRNA vaccines are *literally* antivirus software.

A recent paper [2] **looked at the possibility of a universally effective vaccine** – one that would take the inevitable mutations in its stride – and they analysed 18,514 SARS-CoV-2 sequences sampled since December 2019.

They found that principally because the mutation rate in SARS-CoV-2 is low, any vaccine targeted against the spike glycoprotein (which all current candidates are) would be impervious to mutations in the virus.

References

1. **Rambaut, Andrew, et al.** *Preliminary genomic characterisation of an emergent SARS-CoV-2 lineage in the UK defined by a novel set of spike mutations.* OVID-19 Genomics Consortium UK (CoG-UK). s.l. : ARTIC Network, 2020.

2. *A SARS-CoV-2 vaccine candidate would likely match all currently circulating variants.* **Dearlove, Betahny, et al.** Boston MA : s.n., 31 August 2020, PNAS.