# Vaccine development: Covid-19 and beyond

With Covid-19 vaccines being developed at a rapid pace, **Josh Loeb** and **Julienne Wooster** ask why the most sought-after vaccines for animal diseases cannot be developed as quickly

WHY are there now multiple safe and effective Covid-19 vaccines – all developed at record speed – but still no vaccine for African swine fever (ASF), despite the disease causing a decimating pandemic in pigs?

How is it that some vaccines can be developed very quickly to combat certain diseases but not others?

Put simply, because not all infective agents are created equal.

Vaccines for people have traditionally taken longer to develop than those for animals, not least because the bar set by regulators to approve medicines for people is set that bit higher.

But the speedy development of the Covid-19 vaccines has less to do with the fact that this is a disease affecting people rather than 'just' animals than it does with the structure of the virus itself.

'Lucky' might seem a strange word to use in this context, but in many ways humanity really did get lucky in the fact that, on this occasion, a pandemic was occasioned by SARS-CoV-2 (the virus that causes Covid-19) rather than a different type of virus. This is because this particular virus presented scientists with a relatively easy target – and one they were already fairly familiar with.

First, some history: before the authorisation of the Covid-19 vaccines, the shortest production time for a human vaccine was four years – from 1963 to 1967 – for the mumps vaccine (one of the Ms in the MMR jab). By contrast, the Covid-19 vaccine was produced much faster – in part, it's true, because of a combination of urgent need and simple good fortune, but, most importantly, owing to the now notorious coronavirus 'spike protein'.

The prospect of global economic devastation spurred many wealthy countries to cooperate, contributing billions of pounds towards the creation of vaccines. And, due to the scale of the task at hand, new Covid-19-specific vaccine manufacturing facilities were created – in normal circumstances a financially risky strategy that manufacturers would prefer to avoid.

**African swine fever (ASF) has decimated pig populations around the world, but the complexity of the ASF virus means a vaccine could still be a long way off**

However, Mike Francis, a scientist with over 40 years' experience in vaccine development, cautions that money can only get you so far when it comes to vaccine success.

'We need to manage people's expectations, because it's not simply a case of throwing money at a disease,' he warns.

Speaking at a One Health Poultry Hub event earlier this year, Francis, the managing director of BioVacc Consulting and a member of the UK Vaccine Network, said that now people had seen how fast a suite of vaccines had been developed to combat a human pandemic, some might start wondering if the development of vaccines for diseases affecting livestock was comparatively slow simply because these diseases are typically lower down politicians' list of priorities.

But making such comparisons would be overly simplistic, he was quick to tell *Vet Record* in an interview after the event, explaining: 'The point I was trying to make is that the very rapid Covid-19 vaccine development has been based on known technologies and platform technologies which have already been applied to some extent...but I think people's expectations shouldn't be that we can automatically turn these around and bring new veterinary vaccines onto the market within a year.'

Essentially, he says, the viral enemy fate dealt humanity on this occasion had some key weaknesses that scientists could exploit.

'Coronaviruses themselves give a fairly clear target in the spike protein and there was previous knowledge that (a) we could develop coronavirus vaccines and (b) the spike protein would elicit an immune response,' he explains. 'We knew this from work we'd already done with other human coronaviruses.

'I think a lot of things were working in our favour with Covid-19, and I do feel that a lot of people's expectations, perhaps in the future – both for human and for veterinary vaccines – could be changed as a result of this, that they might think

> **It's not simply a case of throwing money at a disease**

it's just a matter of throwing money at something and the result will be a very rapid vaccine development programme. But that's not the case.'

He cites ASF as an example of a disease where the target has been much more challenging.

'There's a lot of research being thrown at it but it's a very difficult vaccine to develop,' he says. 'We've seen the same thing with HIV/AIDS – the disease has been around for a long time and a lot of money's been thrown at it, and while we can control it now with antiviral drugs, there's still no really effective vaccine, although there are promising signs on that front.

'So I think Covid-19 has been a sort of special case – but a very important example of some of these new vaccine technologies being applied very rapidly, and by the looks of it very successfully – I think we can all learn from that.'

Chris Netherton, who leads the ASF vaccinology group at the Pirbright Institute, agrees.

'Some viruses are very difficult to generate vaccines for,' he says. 'The ASF virus is a very complex virus. Its genome is over five times the size of SARS-CoV-2, the virus that causes Covid-19. Locating and understanding the function of its genes to then use in vaccines is therefore extremely challenging, and this is something that groups at the Pirbright Institute are currently researching.

'[Some] Covid-19 vaccines contain either subunits of the virus or inactivated viruses. For the ASF virus, the former are technically challenging to create owing to the difficulties in locating genes that generate protective responses. Inactivated ASF viruses have already been tried but do not work effectively. Work on live attenuated – weakened – virus vaccines is ongoing in Linda Dixon's group at Pirbright, research which is further ahead than the subunit vaccines.'

Covid-19 vaccine approaches have been able to follow blueprints laid out for other coronaviruses, he adds, whereas the ASF virus is the only virus in its group (Asfarviridae), and as such there are no closely related vaccines that could be used as blueprints in the same way.

'There are also other control measures available that can be applied to animal populations [to combat disease spread/prevalence],' he points out. 'For example, biosecurity can play a major role in controlling ASF, measures which are easier to implement in modern farm production systems rather than the human population.'

However, he also thinks the world's experience of the Covid-19 pandemic could have a silver lining in helping boost the development of a vaccine for ASF going forward.

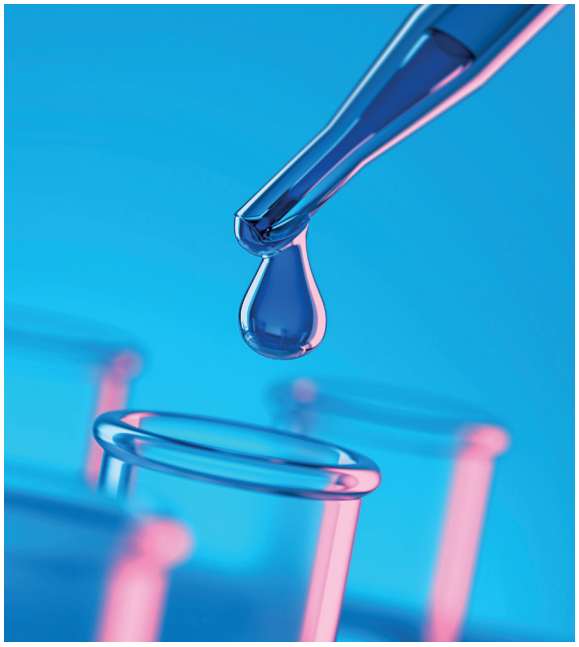
'The ongoing research to tackle the Covid-19 pandemic may mean the cost of some of the technology may come down,' he says, 'which in turn could make an ASF subunit vaccine more commercially attractive.'

The speed at which the Covid-19 vaccines have been rolled out may also raise questions about the failure to develop a deployable vaccine for bovine TB (bTB), despite more than 20 years of research.

A contributory factor is that bTB is caused by a bacterium, not a virus. *Mycobacterium bovis* hides from the immune system within macrophages, making it hard to target. A further complication is the need to differentiate between an infected animal and a vaccinated animal – although hope is on the horizon in the form of *Vet Record*'s 2021 Innovation Award winner, Actiphage, which uses new technology to distinguish vaccinated from infected animals.

'It's not comparing apples and apples to compare bTB with Covid-19,' says James Russell, president of the BVA and an expert in bTB.

'I'd mention two factors – one would be the level of investment in it, and that is not to denigrate the people who are working on the "DIVA" test [the test to differentiate infected and vaccinated animals] and the vaccine at the moment – they're doing amazing work...whereas the Covid-19 vaccine has broken all world records and has been rolled out in a way which isn't how a normal licensing system works.



**The ongoing research to tackle the Covid-19 pandemic may mean the cost of some technologies could reduce, which in turn could make other vaccines more commercially attractive**

> **Covid-19 has been a special case, but I think we can all learn from that**

'Mycobacteria are slippery customers. You're talking about a bacterium here which lives inside a white blood cell. That's pretty mega when it comes to defending yourself from any other kind of immune response, whether that's vaccine generated or body generated.'

When asked about the potential for unrealistic raised expectations in the veterinary world in light of the fast rollout of the Covid-19 jabs, Russell says: 'That's part of our job, isn't it, as vets, to manage expectations?

'I'd just point out that, [in regards to TB] this is something great minds have been working on for many, many decades and if there was a simple fix it'd been found by now – in both human TB and animal TB.'

It is clear that valuable lessons have been learned from this pandemic, and while we shouldn't expect the rollout of every vaccine to go as smoothly or as swiftly, the technology and processes that have been developed should positively impact vaccine development in veterinary as well as human medicine.

But, at the same time, we must also remember that vaccination alone is not the only way to prevent disease.