



# Vaccine and Biologics Development in an Emerging Post-Pandemic Landscape

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## What Role Will Analytical Testing Solutions Play in Supporting Safe, Speedy, and Successful Vaccine and Biologics Development in The Future?

It is clear within the global health science industry that analytical biosafety testing and advances in developing scientific technologies will play an important role in drug development's response to the next pandemic. The emergence of SARS-CoV-2 in December 2019, and the subsequent declaration of a global pandemic by the World Health Organisation in March 2020, had an unprecedented impact on drug development. Many sponsors – from emerging biotechs to big pharma - found themselves grappling with the need to assure supply to patients enrolled in existing studies while transforming R&D pipelines to accommodate the urgent need for safe and effective Covid-19 vaccines and treatments.

Pre-pandemic, the fastest vaccine ever developed (for mumps) took four years. The development and authorization of the first Covid-19 vaccines took just 326 days<sup>i</sup>, from the time viral sequencing became available: a previously inconceivable feat and an undisputed 'scientific triumph'.

Yet, during the time it took to develop the vaccines, more than 70 million Covid-19 cases and 1.6 million deaths were recorded worldwide<sup>ii</sup>. Rapid vaccine development in the event of the next pandemic is unsurprisingly viewed as essential to minimize future transmission, serious illness, and fatalities. The Coalition for Epidemic Preparedness Innovations (CEPI) has published a goal, supported by governments around the world, that in the event of another pandemic 'vaccines should be ready for initial authorization and manufacturing at scale within 100 days after the next pandemic pathogen is recognized'<sup>iii</sup>.

The scientific achievements associated with the rapid development of the Covid-19 vaccines will not only influence strategies for the next pandemic. Lessons learned will also play a critical role in future vaccine and biologics development spanning multiple disease types.

However, the increased volumes of vaccines in development, coupled with the expedited timelines associated with an emerging post-pandemic landscape, raises valid concerns about the short and long-term safety of vaccine candidates. Alleviating these concerns, and tackling vaccine hesitancy in some patient populations, is dependent on drug development's ability to overcome significant ethical, scientific, and regulatory hurdles. Analytical biosafety testing of vaccine candidates remains critical but how has Covid-19 enhanced the function? And how can the mission-critical compliance obligation be harnessed to support the rapid, compliant, and successful development of tomorrow's vaccines and biologics, today?

<sup>i</sup>[https://cepi.net/news\\_cepi/cepi-welcomes-us-fda-approval-of-pfizer-biontechs-covid-19-vaccine/](https://cepi.net/news_cepi/cepi-welcomes-us-fda-approval-of-pfizer-biontechs-covid-19-vaccine/)

<sup>ii</sup>World Health Organization. WHO Coronavirus (COVID-19) dashboard <https://covid19.who.int/>

<sup>iii</sup><https://www.nejm.org/doi/full/10.1056/NEJMp2202669>

# Analytical Biosafety Vaccine Testing 101

Before exploring analytical biosafety testing's future role in facilitating expedited, safe, and compliant vaccine development, it's important to understand

what it is and why it is an essential component of vaccine development and manufacturing.

## What is analytical biosafety testing and why do we do it?

Analytical biosafety testing is a process that safeguards the integrity of biological vaccine products by ensuring materials are free of microbial or viral contaminants, and that other impurities – introduced during the manufacturing process - have been appropriately characterized.

Precise, in-depth analytical biosafety testing, throughout a vaccine candidate's lifecycle from cell banks and viral seed stocks through to clinical and commercialization stages, plays an important role in delivering a safe supply to patients. It is also pivotal to upholding regulatory compliance and supporting expedited time to market (and return on investment).

Vaccine analytical biosafety testing for viral contaminants is critical because:

- Viruses replicate in all types of living organisms, which makes the biological systems used to create biological therapeutics, like vaccines, extremely vulnerable to contamination.
- Viruses have the potential to cause severe, chronic, and fatal illnesses in humans.

- The absence of consistent, effective testing can compromise the quality of the entire development process, with a failure to demonstrate consistent product purity jeopardizing regulatory approval.

While mitigating these risks is crucial, there have been several instances of virus transmission to humans through contaminated vaccines. A recent example occurred in 2010 when Porcine Circovirus type 1 (PCV1) DNA was unexpectedly detected, via Next Generation Sequencing, in the rotavirus vaccine products of some major pharmaceutical companies. At least one of these companies confirmed the PCV1 DNA was found in the cell bank and virus seed, indicating contamination was present during the early development stages. Fortunately, when tested in human cell lines, productive PCV1 infection was not observed<sup>iv</sup>.

However, this instance serves as a cautionary tale: a reminder of the importance of robust analytical biosafety vaccine testing processes through each development stage. It also highlights the importance of implementing appropriate methods to effectively test un-purified bulk harvest, drug substances, and drug products.

## The vaccine testing process

Testing of source materials and products is a fundamental step to screen for contaminants and assure vaccine purity. Creating an appropriate viral testing strategy calls for an assessment of how likely it is that, considering the starting materials and reagents used, contamination from endogenous and adventitious viruses will exist.

The strategy must also consider the nature and intended use of the final vaccine product and be mindful that all potential contaminants may not be predicted.

During the testing process, several approaches are employed: general assays, species-specific assays and assays that detect virus markers (virus DNA, RNA, protein, or particles).

## Testing methods – the technology for viral detection

Detecting viral contaminants in biological vaccines, and identifying their source, requires a holistic approach.

Potential test methods typically include adventitious agent tests, usually nonspecific tests capable of detecting a broad range of viruses; species-specific assays, designed to detect the presence of identified potential contaminants (e.g., specific bovine or porcine viruses in serum or trypsin, respectively, or murine viruses in mouse cells); and tests for retroviruses.

### TESTING METHODS AVAILABLE TO BIOPHARMACEUTICAL COMPANIES INCLUDE:

- Electron Microscopy (EM)
- Nucleic Acid Test (NAT)
- Quantitative Polymerase Chain Reaction (QPCR)
- Next Generation Sequencing (NGS)
- Cell-based infectivity assays



Download the SGS technical bulletin 'Control Viral Contaminants with Effective Testing' to learn more about the testing methods available to detect and identify the source of viral contaminants in biologics.

<sup>iv</sup> <https://pubmed.ncbi.nlm.nih.gov/24056737/>



## Close up on compliance

Regulatory authorities require testing to be carried out at every stage of the manufacturing process of the product, including cell-substrate banks, viral seed banks, raw materials of animal origin, bulk harvests, and batches of the final manufactured clinical product.

The samples must be tested to recognized international guidelines, including World Health Organization guidelines, the International Conference for Harmonization (ICH) guidelines, U.S. Food and Drug Administration (FDA) Vaccine 2010 guidelines (4), and/or European Pharmacopoeia (EP) guidelines, in addition to country-specific requirements, as appropriate.

- Key ICH guidelines include 'Q5A. Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin'

- Key guidelines from regulatory authorities in the USA, including the FDA and United States Pharmacopoeia (USP), include 'Characterization and Qualification of Cell Substrates and Other Biological Materials Used in the Production of Viral Vaccines for Infectious Disease' Indications (2010)
- Key guidelines for EU regulatory authorities, including the European Medicines Agency (EMA) and EP, include 'Production and Quality Control of Medicinal Products Derived by Recombinant DNA Technology' (December 1994) and the European Directorate for the Quality of Medicines & Health Care

## Covid-19 Vaccine Development & Analytical Biosafety Testing Under The Microscope

Covid-19 disrupted the compliance framework governing drug development, when – in April 2020 – members of the International Coalition of Medicines Regulatory Authorities (ICMRA) pledged to 'strengthen global collaborative efforts to align the facilitation of rapid development, approval and global roll-out of safe and effective medicines to prevent and treat Covid-19.'

While analytical biosafety testing has always been a pre-requisite to successfully enter a vaccine clinical trial and to obtain approval and commercialization, the pandemic brought the function into a much sharper focus. No longer viewed as a necessary cost center, through the pandemic's lens, analytical biosafety testing strategies became synonymous with a

sponsor's ability to deliver vital Covid-19 vaccines to market with a combination of speed and precision.

The primary challenge facing sponsors of Covid-19 vaccine trials, in relation to analytical biosafety testing, was operating with increased speed without cutting corners. The key to achieving this ideal was embracing rapidity and clear communication, through dedicated project management and the use of validated software to schedule and plan operations. Accuracy and compliance were two other behavioral cornerstones, prioritized by Covid-19 vaccine sponsors and supported using GMP validated methods and stringent quality assurance checks, to facilitate fast and effective testing operations.

<sup>4</sup><https://www.icmra.info/drupal/en/covid-19>



## Fast and effective analytical biosafety testing

As pioneers in the development of the analytical biosafety testing industry, our Biosafety Centre of Excellence has increased its capacity over the years for testing cell banks for vaccines, gene and cell therapies, monoclonal antibodies, and other recombinant protein-based biological medicines (including a vaccine testing solution suitable for coronavirus).

SGS is committed to rapidly delivering expert resources to safeguard patient safety, through fast and effective preclinical testing.

In early 2020 In a consortium led by the Jenner Institute, Oxford University, SGS has joined forces with specialists in infectious diseases, research and innovation, and pharmaceuticals to rapidly develop, scale up and produce a potential vaccine called ChAdOx1 nCov-19. With time of the essence, the consortium needed a 'right-first-time' approach to developing its biosafety vaccine testing program. This meant ensuring expert resource was available to both plan and execute the testing strategy, along with access to cutting-edge facilities.

SGS was committed to rapidly delivering expert resources during quarter 1 2020 to support the consortium with its objective to ensure the range of biological vaccine components were subjected to a robust viral risk assessment for discussion with the Medicines and Healthcare Regulatory Agency (MHRA)

By the end of April 2020, further fast-tracked batches delivered thousands of doses for the phase I/II clinical trial. To accommodate the increasing demand with speed and accuracy, in June 2020 SGS invested in bolstering its capability, hiring and training 35+ full-time employees, and delivering testing on cell, viral, bulk, and in-process drug components in the second half of 2020 ahead of MHRA's December 2020 approval of AZD 1222. The completion of testing as part of a global supply chain aided the rapid clinical vaccine planning and program.

In 2021, SGS increased investment and more staff allowing for an increase in testing output with a key OTD focus. By the end of 2021, 3 billion doses of the AZD 1222 vaccine had been administered to patients across 180 countries.

Commenting on the partnership with the consortium, Dr. Archie Lovatt, Scientific Operations Director (Biosafety), SGS said:



*"Being selected by the consortium to provide analytical testing solutions for this Covid-19 vaccine candidate is testament to the caliber of the expert people, robust processes and cutting-edge technology that combine to make SGS an industry leader in analytical biosafety testing – a position we've held for more than quarter of a century."*

*"With the world watching with bated breath, the pressure was on to develop a best practice strategy, scientific response, and viral risk assessment before rolling out an effective testing schedule with previously inconceivable rapidity. Unwilling to compromise on quality and dedicated to supporting the consortium to deliver on its mission to expedite the vaccine's time to market, we didn't hesitate to invest in scaling up our capabilities to accommodate increasing demand."*

*"We're incredibly proud of the role we have played in delivering a much-needed vaccine to market quickly and safely and in doing so helping to protect humanity from the devastating effects of Covid-19."*

## Archie's podcast



## Laying The Foundations For Future Breakthroughs with Best Practice Biosafety Testing

The positive impact of vaccines on global human health is substantial and recent examples are not just limited to drug development's response to the pandemic. Research published in December 2021 demonstrated the human papillomaviruses (HPV) vaccine, first introduced in the UK in 2008 and offered to girls (and boys since 2019) between the ages of 11 and 13, is cutting cervical cancer by almost 90%<sup>vi</sup> in people who receive the vaccine.

According to leading scientist Prof Peter Sasieni, the director of the clinical trials unit at King's College London, the vaccine is "leading to such dramatic reductions in cancer that the screening program would need to change soon"<sup>vii</sup>, with modelling suggesting between one and three checks during a person's lifetime would be appropriate for those who have been immunized. This is not only good news for patients, but it will support healthcare providers to operate more cost-effectively, with an emphasis on prevention vs. cure.

Nonetheless, it is true that the pandemic has focused the world's attention like never before on the power of vaccines. Not only have Covid-19 vaccines prevented susceptibility and transformed health outcomes for those who contract the virus, but Covid-19 vaccines have also been instrumental in supporting the recovery of economies around the world, with countries that were swift deployers of vaccines recording better macroeconomic outcomes compared to slower deployers<sup>viii</sup>.

As such, vaccine development is back at the forefront of drug development with 1700 candidates in preclinical analysis for a wide range of clinical conditions at the end of April 2022<sup>ix</sup>.

In turn, best practice analytical biosafety testing will remain paramount for sponsors keen to replicate the rapid product development and commercialization of Covid-19 vaccines, without compromising patient safety, quality, or regulatory compliance.

### Top tips for creating vaccine analytical biosafety testing best practice

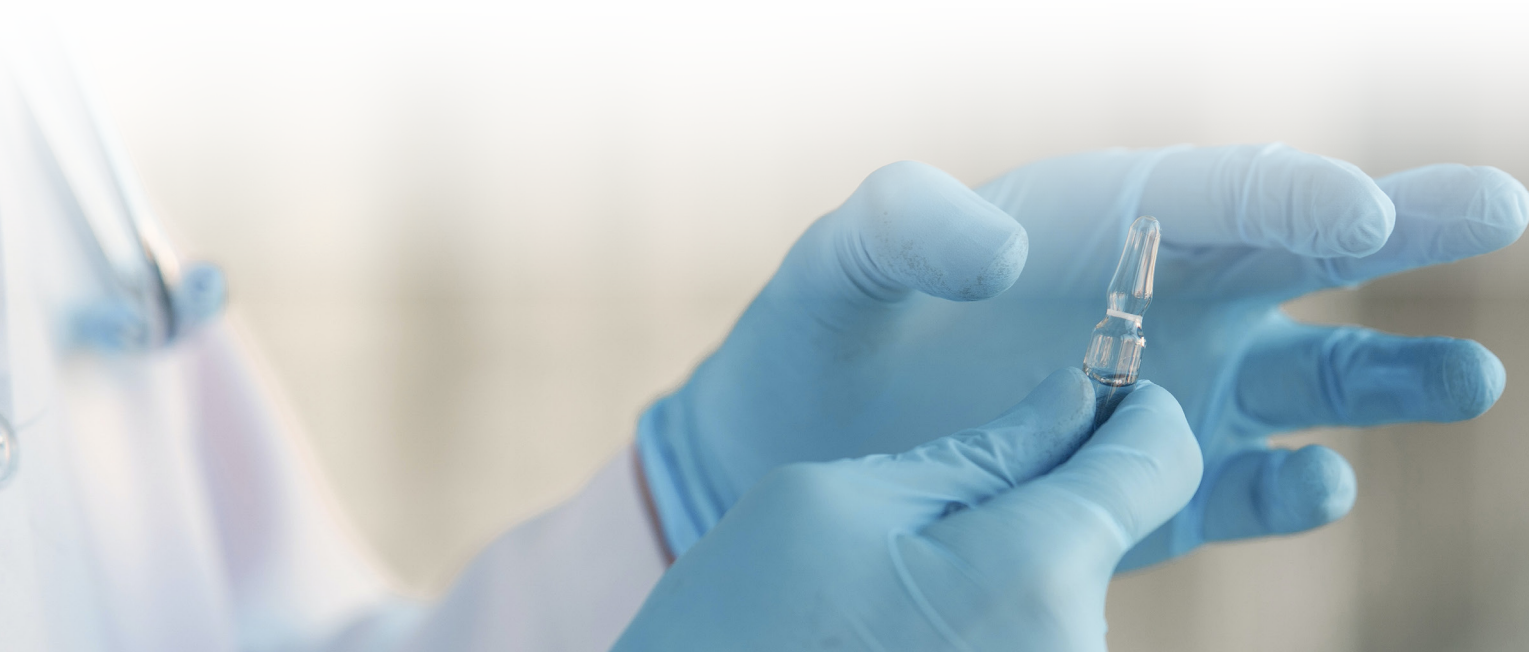
- Scope requirements during the pre-clinical stage
- Engage a specialist outsource partner with access to expert people, robust processes, and effective technology
- Ensure compliance with current ICH and/or FDA and/or European Pharmacopoeia guidelines
- Take a risk-based approach to execute a scientifically justified testing strategy
- Capture data from appropriate tests at different stages of development and manufacture
- Address highly product-specific requirements – for example, study designs for testing product that requires neutralisation
- Implement Good Manufacturing Practice (GMP) / Good Laboratory Practice (GLP) compliant testing
- Prioritise interaction and ongoing discussion, as appropriate, with key stakeholders

<sup>vi</sup>[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)02178-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02178-4/fulltext)

<sup>vii</sup><https://www.bbc.co.uk/programmes/m0014wvk>

<sup>viii</sup><https://voxeu.org/article/economic-effects-covid-19-vaccines>

<sup>ix</sup> GlobalData





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### The analytical biosafety testing of tomorrow

While all current testing methods have an important place in the creation of a holistic analytical biosafety testing strategy, Next Generation Sequencing (NGS) represents a rapid, scalable, and high throughput method of determining the order of nucleotides in complete genomes or targeted areas of RNA or DNA. Using NGS, a population of sequences in the sample can be surveyed, allowing the detection of unknown viruses, integrated retrovirus provirus, transcripts, and endogenous sequences. The benefits of utilizing this method are clear. Lower sample input is needed, NGS is highly accurate and can detect variants at lower allele frequencies, compared with other methods.

NGS can also enable studies to be performed quickly and cost-effectively.

While not fully embedded into today's drug development landscape, nor supported with full global regulatory approval, NGS represents a powerful tool with vast applicability that will likely continue to revolutionize vaccine development. With this in mind, vaccine developers should opt to partner with providers of analytical biosafety testing that not only provide a full range of testing methods to meet today's requirements but invest in and pioneer the use of testing methods of tomorrow.

### Preparing for the next pandemic

According to CEPI, five best practice strategies enabled the rapid vaccine development of Covid-19 vaccines.

These were:

- leveraging existing insights about new pathogens and development technologies
- Supporting innovation in the vaccine development process
- Using advanced analytics to inform development and manufacturing processes
- Promoting collaboration among stakeholders (including data and information sharing)
- Continuously reviewing evidence to support swift approval<sup>\*</sup>.

Analytical biosafety testing will play an important role in drug development's response to the next pandemic

<sup>\*</sup><https://www.nejm.org/doi/full/10.1056/NEJMp2202669>



## Summary

No amount of testing can ever definitively prove the absence of an infectious agent. Clearly, it is not possible to test all of a product, so if a contaminant is present at a low level, then there is a statistical chance that it will not be detected.

Additionally, it is important to note that not all viruses or all individual virus isolates will necessarily be detected in the assay systems used. Virus biosafety testing, therefore, requires a risk-based approach involving a combination of methods, dependent on factors such as the production parameters, the viral risk assessment of raw materials, and the clinical application of the product.

One thing is for certain, the pressure to develop and deliver safe and effective Covid-19 vaccines has irreparably transformed the way biotech sponsors approach drug development. Strategies and tactics used to expedite timelines, without compromising safety or compliance, will be finetuned in the years to come. Analytical biosafety testing will form a key part of this broader post-pandemic transformation. By investing in a best practice approach, complete with access to expert people, robust processes and cutting-edge technology, vaccine developers can operate future clinical trials with increased safety, rapidity, and success.

## About SGS

SGS is the world's leading inspection, verification, testing, and certification company. SGS is recognized as the global benchmark for quality and integrity. With more than 96,000 employees, SGS operates a network of over 2,700 offices and laboratories around the world.

SGS Health Science leverages its digitalized network of laboratories, present in North America, Europe, and Asia-Pacific, to deliver harmonized testing solutions for analytical development, biologics characterization, biosafety, and quality control, as well as clinical trial management to large pharmaceutical and biotechnology firms.

SGS provides a comprehensive range of biosafety services such as virology, cell and molecular biology, as well as microbiology and electron microscopy. Health Authorities, including the US FDA and the EMA, requires companies to undergo safety testing to demonstrate that all cell banks, viral banks, raw materials of animal origin, bulk harvests, and

batches of the clinical drug are free of bacteria, fungi, mycoplasma, viruses, and other potential contaminants.

We offer a comprehensive range of integrated solutions, including biosafety testing & characterization of raw materials, cell bank & virus seeds, unprocessed bulks/viral harvests, and drug substance/product.

For any of your biologics, we help you comply with the global regulatory guidelines and testing requirements. Our team of experienced scientists has over 20+ years' experience in GMP, FDA, EP, and ICH compliant validated assays.

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