



CUSTOMER SPOTLIGHT



# From Vectors To Adventitious Agents: Tracking Viruses in Biologics

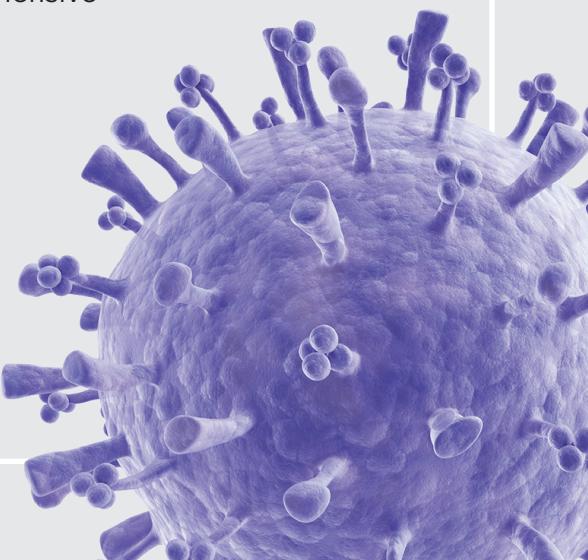
Learn how one lab is filling an industry need by using Twist's Comprehensive Viral Research Panel

Twist's Comprehensive Viral Research Panel is a powerful and versatile tool for researchers. The panel's breadth of coverage means researchers have the power to detect thousands of different viruses in a sample with the potential to discover novel, variant genomes. Such a panel can be valuable during biologics manufacturing.

**GenomeScan**, a provider of Next-Generation Sequencing (NGS) services in the research and clinical space, knows the importance of comprehensive viral testing. To meet the needs of their customers — particularly those developing biologics — GenomeScan has turned to Twist's Comprehensive Viral Research Panel.

We sat down with them to learn more about their work and how Twist's panel is being used.

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## How are you applying Twist's Comprehensive Viral Research Panel in your NGS workflows?

We're using Twist's panel for two distinct applications. First, we use the panel to survey samples for viral species that may be present in a biological matrix or specimen. Second, this same panel is also utilized for quality control testing for the detection of adventitious agents during the manufacturing of biologics, thereby ensuring safety, quality, and efficacy of the released biologics. In both applications, this panel allows us to detect a wide range of viruses making it suitable for what our customers require from a wide-ranging microbial test.

## Why is pathogen detection so critical to your work, and how are Twist products helping you deliver benefits to the public?

When there is a potential viral outbreak, public health officials must become investigators as they work to rule out potential causes and ultimately identify the viral culprit. This process includes the use of laboratory tests that help identify genetic elements from specific viruses. The results of such tests could then be used to inform public health decisions. The performance of the assay used to detect viruses is critical because we need to have confidence in the accuracy of the results, whether it's a negative finding or a positive identification. So, we rely on our vendors to supply us with quality materials and provide us technical support where needed. Twist's Comprehensive Viral Research Panel is a big part of that. We have also worked with Twist to create two proprietary custom spike-in panels to enable detection of our internal positive controls which contributes to our confidence in our assay's results.

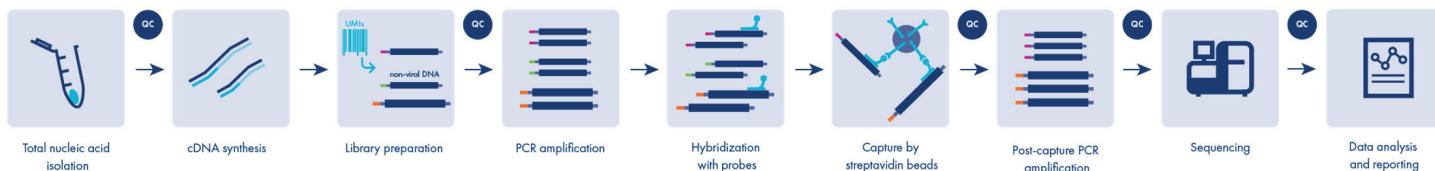
Similarly, when companies are producing materials that are derived from biological sources—such as engineered T cells or gene delivery vehicles—viral testing is critical. These types of materials are often used in therapeutic development. Because of that, it is very important that the final product be pure, containing only what is intended. If any contamination occurs by viruses or other microbes (so called adventitious agents), the result could be a very serious immune reaction in the patient (among other potential outcomes). Using a viral research panel to quality check manufactured biologics enables us to detect a wide range of potential adventitious agents and decrease the likelihood of unintended side effects.

Lastly, viral testing is helpful during the biologics manufacturing process when viral vectors are a necessary part of the therapeutic development process. Cell therapies, for example, are often manufactured by modifying cells using CRISPR or other genetic tools that are delivered through viral systems. However, the virus must be absent from the final therapeutic cell stock. To confirm that the virus is absent from the final therapeutic product, viral panels can be designed.

## Can you briefly describe how Twist reagents support and fit into your whole NGS workflow?

We have a proprietary NGS and data analysis workflow (**Figure 1**) in which we utilize Twist's Comprehensive Viral Research Panel. This workflow starts with total nucleic acid isolation, which can be from a variety of sample types. During our library preparation we also use several Twist products including their Library Preparation Enzymatic Fragmentation (EF) Kit 2.0, Unique Molecular Identifiers (UMIs) Adaptor System, and Standard Hybridization and Wash Kit v2. Finally, the sequencing is performed by using the Illumina NovaSeq sequencing platform and reagents. After obtaining the raw data, we can analyze the results with a customized proprietary pipeline and subsequently report the data to a customer.

Our workflow is also designed to detect a wide range of viruses and to monitor viral clearance during the biologics manufacturing process. In addition to the Comprehensive Viral Research Panel, here too we have two extra proprietary spike-in probes, synthesized by Twist, which are included to detect our internal positive controls. A custom QC tool is then used to assess the success of the experiment by determining the number of reads from the controls. After obtaining the raw data, we can analyze it with a customized proprietary pipeline and subsequently offer a certificate of analysis.



**Figure 1.** GenomeScan has built a proprietary NGS and data analysis workflow that utilizes Twist's Comprehensive Viral Research Panel.

### What key benefits do you find in Twist products?

We have chosen to work with the Comprehensive Viral Research Panel because of its breadth, high uniformity, and high on-target rate. This panel is not only capable of screening for >3,000 different viruses in a single reaction but is also modifiable, such that we can add custom panels targeted to additional viruses or controls as needed. All of this enables us to build a viral detection assay and workflow with excellent performance metrics for our processing of samples (**Table 1**).

### There are many potential viral sequencing solutions out there, what made Twist's stand out to you?

Because the panel's design is so complete in the breadth of coverage of viral pathogens, we can both save on resources and time while also testing for a broad range of potential pathogens in each sample. As a result, this targeted approach is a more cost-effective solution than metagenomic sequencing which detects all sequences irrespective of their relevance (e.g. detection of ubiquitous or non-pathological species which may use up a large portion of the available sequencing space). Conversely, if we had to test for viruses or viral families individually, it would be unwieldy and overly time consuming. Twist's target enrichment panels and NGS reagents create the ideal convergence of assay content to cast a broad net while saving us time and resources.

SAMPLE	VIRUS	GENOME TYPE	COPIES/REACTION	VIRAL NA	IDENTITY (%)	GENOME COVERED (%)
Influenza A Virus	Influenza A Virus	ssRNA	500	10%	95.96%	82.65%
SARS-CoV-2	SARS-CoV-2	ssRNA	500	10%	99.85%	97.51%
Flurona Mix	Influenza A Virus	ssRNA	25,000	10%	96.50%	98.72%
	SARS-CoV-2	ssRNA	500	0.2%	99.81%	97.55%
Flurona Mix	Influenza A Virus	ssRNA	500	0.2%	96.53%	98.56%
	SARS-CoV-2	ssRNA	25,000	10%	99.87%	97.64%
Virome Mix	Mastodeno Virus F	dsDNA		16.67%	99.88%	99.82%
	Herpesvirus 5	dsDNA		16.67%	99.86%	97.09%
	Respiratory Syncytial Virus	ssRNA		16.67%	96.44%	67.71%
	Influenza B Virus	ssRNA		16.67%	98.96%	100%
	Orthereo Virus 3	dsDNA		16.67%	98.27%	98.02%
	Zika Virus	ssRNA		16.67%	88.31%	88.40%

**Table 1: Specificity of GenomeScan's viral detection workflow was tested using 8 different spike-in controls including ssRNA, dsRNA and dsDNA viruses.** As vehicle control, either ctDNA or whole-cell nucleic acid (NA) extract was used as a background material, the latter containing ~10-15x as much RNA as DNA. Multiple virus combinations were tested to demonstrate sensitivity and specificity in more complex scenarios. Mourik et al <https://doi.org/10.1101/2023.08.23.23294459>

## Do you have any examples of how Twist's products and services changed your business or how you serve your clients?

Relative to other technologies, Twist's solutions enable higher throughput to process more samples and deliver results in the timeframe expected by our customers. Our ability to deliver consistently with our services has really helped us build strong relationships with our clients and scale our business.

## Beyond the product, why are you working with Twist?

We are at the beginning of a close collaboration with the highly enthusiastic team at Twist. On several occasions, Twist has supported us and offered expert advice regarding project design. They act not only as our product suppliers but also as our partners in our efforts to serve clinicians and bio-manufacturers.

## What is your outlook for the future of pathogen testing in this field?

In the future, we expect that NGS testing may potentially be used proactively for clinical samples. We are also seeing a large increase in requests for viral sequencing as a QC step in biologics manufacturing, so it is likely that this will become far more prevalent within the biologics space. It is becoming clear that NGS offers unparalleled sensitivity, specificity, and accuracy with affordable pricing for these applications. So, we expect these types of tests will be adopted more frequently.

## Linked documents

### PRODUCT SHEET

[https://www.twistbioscience.com/sites/default/files/resources/2020-11/ProductSheet\\_NGS\\_ComprehensiveViralResearchPanel\\_11Nov20\\_Rev1.0.pdf](https://www.twistbioscience.com/sites/default/files/resources/2020-11/ProductSheet_NGS_ComprehensiveViralResearchPanel_11Nov20_Rev1.0.pdf)

### APPLICATION NOTE

[https://www.twistbioscience.com/sites/default/files/resources/2023-02/DOC-001207\\_AppNote\\_CompViralResPanel-REV2-singles.pdf](https://www.twistbioscience.com/sites/default/files/resources/2023-02/DOC-001207_AppNote_CompViralResPanel-REV2-singles.pdf)

### TECHNICAL LEAFLETS

<https://www.genomescan.nl/adventitious-agents/#viralpanel>

### SPECIES LIST

<https://www.twistbioscience.com/resources/technical-document/twist-comprehensive-viral-research-panel-strain-and-species-list>

## Ordering information

**103545:** Twist Comprehensive Viral Research Panel with One Codex software, 2 Reactions, Kit

**103547:** Twist Comprehensive Viral Research Panel with One Codex software, 12 Reactions, Kit

**103548:** Twist Comprehensive Viral Research Panel with One Codex software, 96 Reactions, Kit



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