

## TIMELINE

# Viral Safety

Why are viral safety practices the way they are today? What risks, scientific discoveries, and regulatory updates caused them to develop as they have?

This timeline highlights the milestones that created the viral safety standards used today. Throughout that evolution, Minaris Advanced Testing has been at the forefront, advancing the methods that make viral safety reliable, repeatable, and trusted.



Risks



Science



Regulatory

## 1960 SV40 contamination identified in polio vaccines.

Sweet & Hilleman (1960) and subsequent analyses document simian virus 40 (SV40) contamination of poliovirus vaccine lots produced in primary monkey kidney cells, driving early awareness of adventitious -agent risks in cell-substrate-derived medical products.<sup>1</sup>

## 1973 Endogenous retrovirus-like particles (RVLPS) discovered in CHO cells.

CHO cells, which later became the dominant host for recombinant biologics, are shown to secrete C-type and A-type retrovirus-like particles. Although non-infectious, their presence establishes the need for viral-clearance steps in recombinant biologics.<sup>2</sup>

## EARLY 1980s Solvent/Detergent (S/D) viral inactivation developed and adopted.

S/D treatment (e.g., TnBP + detergents) is developed in the early 1980s and fully adopted by 1985 for plasma-derived products, transforming safety against lipid-enveloped viruses (HIV, HBV, HCV) and influencing viral-inactivation strategy in biologics more broadly.<sup>3</sup>

## LATE 1980s (-1988) Low-pH incubation validated for viral inactivation in IVIG; later adopted for mAbs.

Studies show pH -4 incubation (with or without pepsin) inactivates enveloped viruses including HIV, HSV, VSV, and CMV. Low-pH hold becomes a canonical viral-inactivation step in recombinant protein processes, especially monoclonal antibodies.<sup>4</sup>

## 1982 ViroMed Founded

Pioneer in early viral safety testing and clinical virology, including the use of qPCR to detect viral contamination.

## 1989 Virus-filtration (nanofiltration) commercialized (e.g., Planova filters).

Asahi Kasei introduces Planova virus-removal filters (-1989), enabling robust size-based removal of small viruses. Filtration becomes a core orthogonal viral-clearance unit operation.<sup>5</sup>

## 1990s Real-world failures reveal limits of single-step inactivation.

Transmission events involving non-enveloped and acid-resistant viruses in plasma-derived immunoglobulins highlight the inadequacy of relying on a single inactivation step, driving industry toward multilayered removal/inactivation strategies.<sup>6</sup>

## 24 SEPTEMBER 1998 ICH Q5A (original) published.

ICH Q5A establishes harmonized global expectations for biotechnology products produced in mammalian cells, including cell-bank testing, adventitious-agent testing, and validation of viral-clearance studies (removal + inactivation).<sup>7</sup>

## 2000s Viral-clearance frameworks extended to CHO-derived recombinant proteins.

As CHO endogenous RVLPS remains a known intrinsic risk, recombinant-mAb and protein processes standardized pH hold, virus filtration, chromatography depyrogenation steps, and validated multistep viral-clearance packages.

## 2001 ViroMed acquires Axios and Quality Biotech

A new testing site is opened in St. Paul, MN, expanding the company's viral safety expertise, bringing to three the total number of sites in the company.

## 2001 ViroMed Reorganized as AppTec

## 2008 AppTec acquired by WuXi Pharmtech, becomes WuXi AppTec

Scales into leading provider of viral safety studies for the industry.

## 15 MARCH 2010 Porcine circovirus (PCV) DNA detected in Rotarix vaccine.

PCV-1 DNA is identified via deep sequencing in Rotarix and later PCV sequences are found in Rotateq. Regulators and manufacturers re-evaluate raw materials, cell substrates, and modern molecular detection methods.<sup>8</sup>

## 25 OCTOBER 2012 EMA approves Glybera, the first gene therapy in the EU.

Glybera's AAV vector marks the first marketed viral-vector gene therapy. AAV new regulatory considerations around replication-competent AAV (rcAAV), helpers, producer-cell contamination, and viral clearance for vectors.<sup>9</sup>

## 2016 USP (1050.1) published

The United States Pharmacopeia introduces General Chapter 1050.1 to provide detailed, practical guidance on the design, execution, and interpretation of viral clearance studies, complementing ICH Q5A by standardizing approaches to virus selection, study controls, and data evaluation in biologics manufacturing.<sup>10</sup>

## 19 DECEMBER 2017 FDA approves LUXTURN A (AAV).

First U.S. approval of an AAV gene therapy. Places additional regulatory focus on vector-production systems (triple transfection, helper viruses, baculovirus/Sf9 systems) and appropriate viral-safety testing strategies.<sup>11</sup>

## 2018 WuXi AppTec spins out WuXi Advanced Therapies.

This spinout creates a standalone manufacturing and testing business focused on cell and gene therapies.

## 24 MAY 2019 FDA approves ZOLGENSMA (AAV).

Large-scale viral-vector manufacturing highlights the limits of classical clearance approaches and increases attention to testing for helper viruses, producer-cell impurities, and adventitious agents in high-titer AAV processes.<sup>12</sup>

## 2020 WuXi Advanced Therapies assists with COVID-19 response.

Wuxi Advanced Therapies partners to support several antibody treatments for SARS-COV2, ensuring viral safety along with other aspects of development.

## 1 NOVEMBER 2023 ICH Q5A(R2) final text published.

Major update to viral-safety expectations: expands virus-selection guidance, platform/prior-knowledge use, considerations for viral-vector products, continuous manufacturing, and endorsement of modern molecular assays (e.g., NGS, PCR-based methods).<sup>13</sup>

## 10 JANUARY 2024 FDA issues Q5A(R2)-aligned final guidance.

FDA harmonizes with ICH Q5A(R2), emphasizing risk-based approaches, advanced detection methods, and updated expectations for viral-vector and continuous-manufacturing platforms.<sup>14</sup>

## 14 JUNE 2024 Q5A(R2) becomes effective in the EU.<sup>15</sup>

## 2025 WuXi AppTec / Advanced Therapies merges with Minaris Regenerative Medicine, becomes Minaris

Wholly US-owned business headquartered in Philadelphia combines CDMO for advanced therapies with Advanced Testing organization focused on biologics (protein therapeutics, cell therapies, viral vectors, and vaccines).

## 2026 and beyond

As biologic therapies become more advanced and ICH Q5A(R2) reshapes regulatory expectations, viral safety continues to evolve. Minaris Advanced Testing continues to advance the science of viral detection and clearance, serving the biotechnology industry to ensure the latest techniques are applied efficiently in safety studies. Find out how we do it and start a conversation at [minaris.com/all-testing-services/viral-clearance/](https://minaris.com/all-testing-services/viral-clearance/)

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