Table of contents

2001

The first VC study was executed in the US.

1987, in France.

>14,000

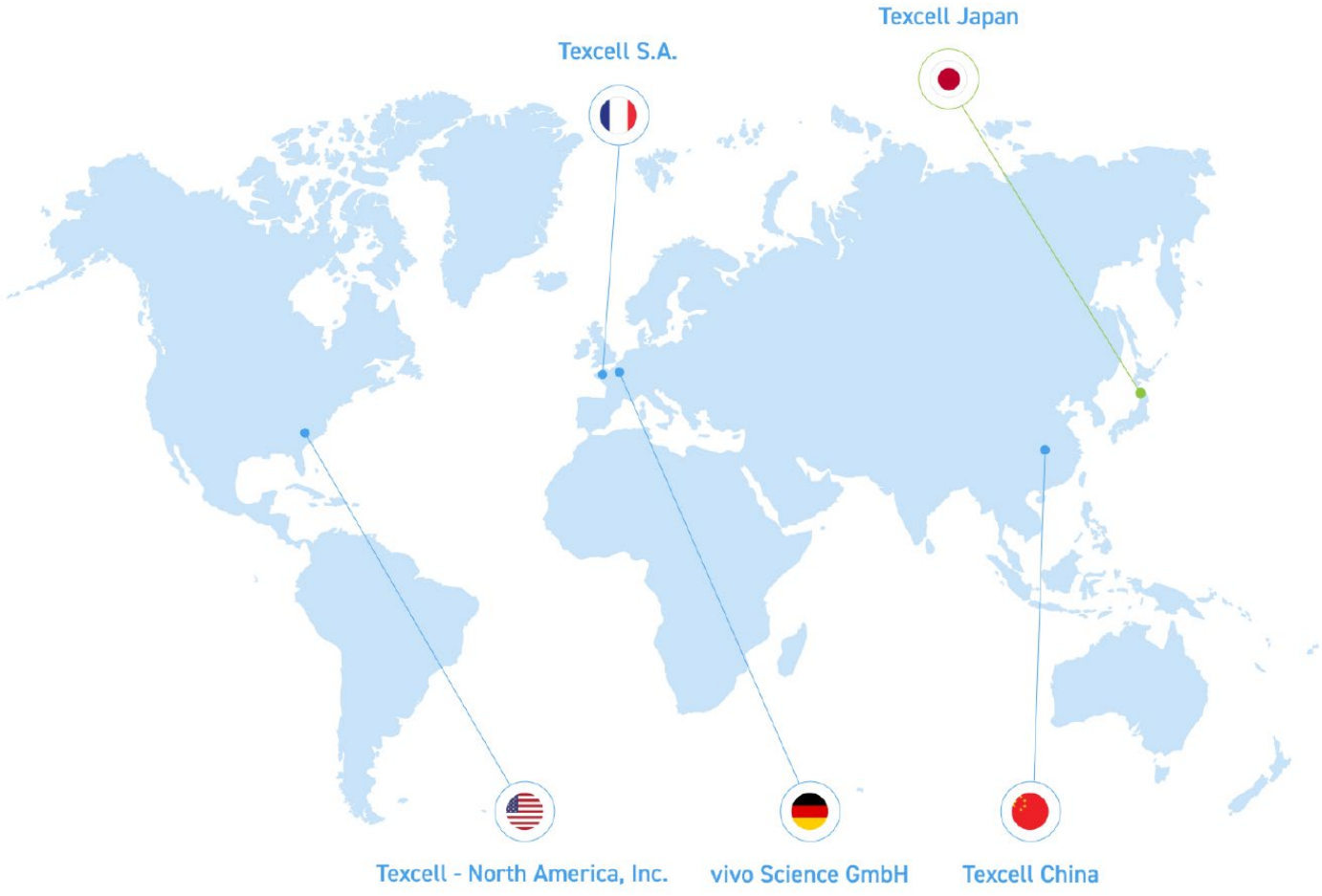
VC studies executed worldwide.

IND & BLA

3

VC Facilities.

USA, France, & China.



1- Quality Statement

☑ GLP (Good Laboratory Practices)

- Conducted under **GLP regulatory standards (21 CFR Part 58)**.
- Follows **ICH Q5A (R2)** guidelines for viral clearance practices.
- Complete **quality oversight** ensured by Texcell's internal QA department.
- Data from GLP studies **can be used for regulatory submissions**.

⚠ Non-GLP (For Information Only)

- Conducted under **GLP standards (21 CFR Part 58)** but lacks:
  - 📌 Study Protocol(s)
  - 📌 Quality Oversight
  - 📌 Final Report
- Designated as **'FIO' (For Information Only) studies**.
- Results **cannot be used alone for regulatory submissions** but may support GLP study data.

2- How to Define the Virus Panel?

The selection of viruses for **viral clearance evaluation** follows the **ICH Q5A (R2) guidelines** (Section 6). The recommended viruses should:

- ☑ **Potentially contaminate the product** – Represent real contamination risks.
- ☑ **Cover a wide range of properties** – Ensure robustness in clearance validation.
- ☑ **Test the manufacturing system's ability to eliminate viruses** – Verify process efficiency.

Virus Classification

The selected viruses fall into four categories:

1. **Relevant viruses** – Viruses known to be potential contaminants of the product.
2. **Specific model viruses** – Chosen for their similarities to potential contaminants.
3. **Non-specific model viruses** – Broad-spectrum viruses that challenge the system.
4. **Production viruses** – Viruses naturally associated with the production process.

Examples of commonly used virus combinations in viral clearance studies for gene therapy products or monoclonal antibodies (mAbs) produced in CHO cells, intended for IND or BLA applications:

Gene therapy		mAB produced in CHO cells	
IND study	BVDV & PPV	IND study	XMuLV & MVM
BLA study	BVDV, EMCV (=HAV), PRV, PPV	BLA study	XMuLV, PRV, Reo-3, MVM

Rationale for Virus Selection in Viral Clearance Studies:

Virus	Type	Purpose / Rationale
BVDV *(Bovine Viral Diarrhea Virus)*	Enveloped RNA	Model enveloped virus; evaluates the efficiency of inactivation and removal steps.
PPV *(Porcine Parvovirus)*	Non-enveloped DNA	Highly resistant small virus; challenges chemical inactivation and filtration robustness.
XMuLV *(Xenotropic Murine Leukemia Virus)*	Enveloped retrovirus	Represents potential retroviral contaminants from CHO cells; ensures effective retrovirus removal.
MVM *(Minute Virus of Mice)*	Non-enveloped DNA	Extremely small and resistant parvovirus; used to validate the robustness of virus filtration steps.
EMCV *(Encephalomyocarditis Virus)* / **HAV model**	Non-enveloped RNA	Picornavirus model; tests process capability against potential HAV-like contaminants.
PRV *(Pseudorabies Virus)*	Enveloped DNA	Large herpesvirus model; evaluates inactivation of enveloped viruses.
Reo-3 *(Reovirus Type 3)*	Non-enveloped RNA	Medium-sized robust virus; provides an additional challenge for clearance validation.

Summary:

The combination of these viruses provides a balanced panel that covers a **wide range of viral properties** (enveloped vs. non-enveloped, RNA vs. DNA, small vs. large, resistant vs. sensitive), ensuring a thorough assessment of the process's ability to remove or inactivate potential viral contaminants for **gene therapy products** and **CHO-derived monoclonal antibodies** in both **IND** and **BLA** submissions.

3- Levels of Service

Texcell offers **three service levels** to adapt to the specific needs of your **viral clearance project**.

Level 1 – Classic

- **Who does what?** The **Sponsor** executes all scaled-down process steps **except for virus filtration** (typically handled by the virus filter vendor).
- **Best for:** Sponsors who prefer full control over process execution.

We recommend Level 1 for a first project with us, as it allows you to visit our site, meet our teams, and become familiar with our facilities.

Level 2 – Collaborative

- **Who does what?** The **Sponsor leads the execution**, while Texcell provides **qualified technical support**.
- **Best for:** Sponsors needing expert **assistance** while maintaining control over the process.

Level 3 – Premium

- **Who does what?** The **Sponsor provides tech transfer**, and **Texcell personnel execute the scaled-down process steps** for virus inactivation or chromatography.
- **Best for:** Sponsors who want **Texcell's expertise** to handle critical steps of the process.

Details of levels of service described below:

Tasks	Level 1	Level 2	Level 3
	Classic	Collaborative	Premium
Determination of Scaled-Down Process	Sponsor	Sponsor	Sponsor
Procurement of Process Materials	Sponsor	Sponsor	Sponsor
Technology Transfer (Training)	Not Applicable	Not Applicable	Sponsor + Texcell
Creation of Data Capture Sheets	Sponsor	Sponsor	Texcell
Execution of Scale-Down Process	Sponsor	Sponsor + Texcell	Texcell
Execution of Spiking and Viral Assays	Texcell	Texcell	Texcell

4-Preliminary testing

1. Why is preliminary testing performed?

Preliminary testing assesses the compatibility of testing materials with Texcell assay systems and ensures accurate virus quantitation.

2. What tests are included in this evaluation?

The preliminary testing includes the following assessments:

- **Cytotoxicity to indicator cells:** Ensures the sample is not toxic to the cells used in the assays.
- **Interference with virus assays:** Determines if the sample affects virus detection and quantitation.
- **Inhibition in qPCR assays:** Verifies that the sample does not interfere with virus detection using quantitative PCR.
- **Hold control assessment of virus stability:** Evaluates virus stability under process conditions.
- **Threshold of inactivation** (for detergent/chemical treatments only): Determines the conditions required to neutralize the inactivation effect of detergents/chemicals to prevent underestimation of viral load.
- **Virus recovery** (only for solid viral clearance studies)**:** Develops methods to efficiently recover virus from the starting material to ensure accurate quantification in viral clearance samples.

These tests help ensure the reliability of virus detection and quantitation throughout the study.

3. What sample volume is required?

For each virus assay, **2 × 15 mL aliquots** per sample are required. This volume includes extra material in case retesting is needed. (See example below)

Example – Required Material Volumes for preliminary testing

- ***For 1 chromatography step with 1 virus****:*
  2 × 15 mL *of material are required.*
- ***For 1 pH treatment step with 2 viruses****:*
  2 × (2 × 15 mL) *of material are required.*

Virus recovery (For solid viral clearance studies **only):** The volume required for the recovery assay will depend on the project and will be communicated to you directly by our teams.