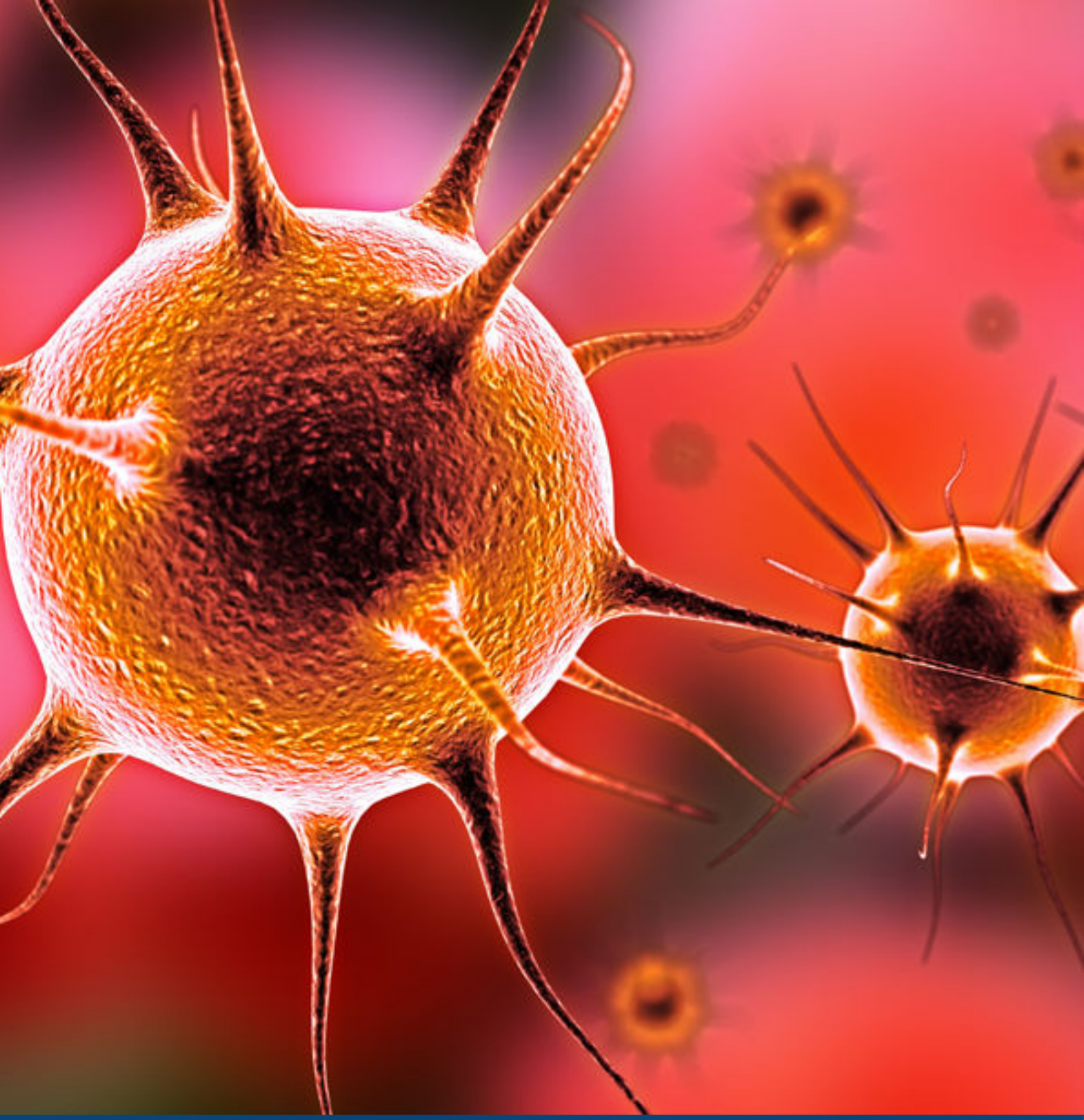

Viral Clearance

Ensure the biopharmaceuticals and medical devices safety

Mérieux NutriSciences

Control of the contamination

CONTROL OF THE CONTAMINATION AT 3 LEVELS

The combination of these 3 approaches is the most effective way to guarantee the **safety of a biopharmaceutical or medical devices**:

1. selecting and testing cell lines and other raw materials, including media components, for the absence of undesirable viruses which may be infectious and/or pathogenic for humans
2. assessing the capacity of the production processes to clear infectious viruses - **Viral Clearance Study**
3. testing the product at appropriate steps of production for absence of contaminating infectious viruses

The manufacturer is responsible
for investigating and ensuring viral safety at 3 levels

Our capabilities - The Viral Clearance Study

Our dedicated virology lab control the viral safety of your product by **assessing the capacity of the production processes to clear infectious viruses**.
The objective of viral clearance studies is to evaluate the ability of the manufacturing process to inactivate/remove known or even unknown viral contaminants, and to estimate process robustness by characterizing its ability to clear different model viruses.

Viral clearance study

It is extremely important that the design, planning and execution of the viral clearance study are discussed in details with the customer.

Process steps to be employed in the study

Only the process **steps considered to be able of inactivating/ removing viral agents are tested** in a viral clearance study. Critical steps need to be selected before starting the Viral Clearance testing. Among others some of the most commonly applied are:

- Treatment with strong acids and bases
- Heat treatment
- Filtration
- Treatment with solvents/detergents

Viruses selection

Viruses for clearance evaluation and process characterisation studies should be **model viruses** that can **resemble viruses which may contaminate** the product. The model viruses should also **cover a wide range of physical-chemical properties** in order to test the ability of the system to remove or inactivate viruses.

Thanks to the wide experience of Mérieux NutriSciences Specialists, we are able to assist you to control the viral safety of your product by **assessing the capacity of the production processes to clear infectious viruses**.

What kind of Virus?

- Virus that could contaminate the raw material
- Model viruses that can be easily propagated on cell cultures
- Viruses that can be propagated to high titers
- Resistant viruses
- Virus whose infection is easily recognizable in the laboratory
- Viruses that meet different biochemical characteristics:
  - viruses with DNA or RNA genome
  - viruses with or without a lipidic envelope
  - viruses of large or small dimensions

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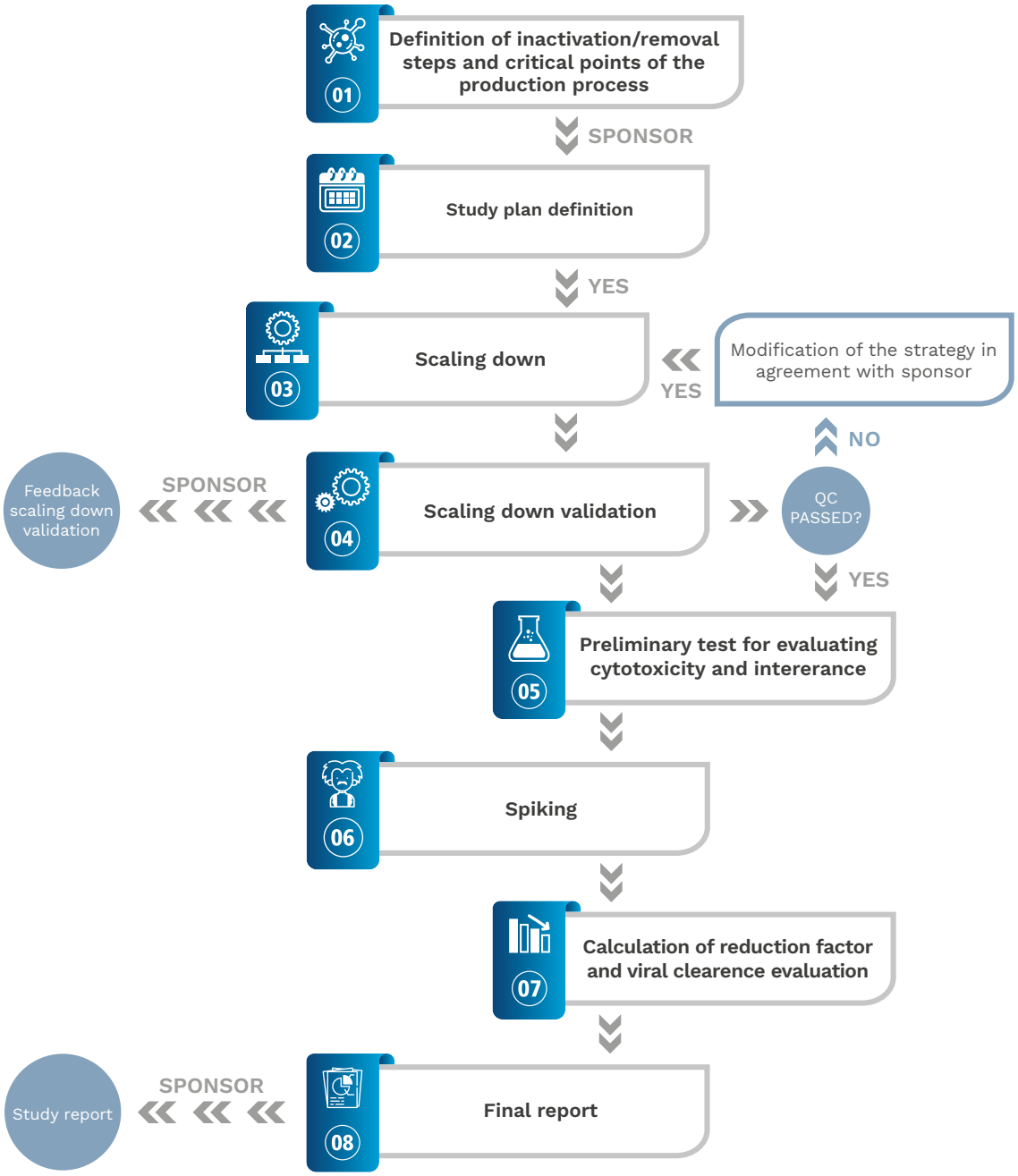
The objective of viral clearance studies is to evaluate the ability of the manufacturing process to **inactivate/remove known viral contaminants**, and to **estimate process robustness** by characterizing its ability to clear different model viruses.



Viral safety process

Viral safety of a manufacturing process can be ensured with an integrated approach thanks to multiple control and risk reduction strategies, but it is impossible to totally eliminate the risk. A high level of viral safety can be reached through:

- the careful control of raw materials
- the knowledge of the global reduction factor
- an effective monitoring system

Viral Clearance

Viral clearance studies are required to assess the safety of biopharmaceuticals, such as blood products, monoclonal antibodies, recombinant proteins, tissue derived products, prior to entering clinical trials and ahead of commercial launch.

Viral clearance studies are also needed for evaluating viral safety of certain types of medical devices, that utilize materials of animal origin, such as bovine/porcine heart valves, bone substitutes for use in dental applications, collagen, gelatine and heparin.

Contamination events in biomanufacturing **can be catastrophic** when they occur: consequences of such events can have impact on patient safety and drug shortages as well as legal, regulatory and financial implications. The impact on manufacturing operations is significant since follow up on contamination events include investigation management, decontamination and other corrective actions which are very expensive and time consuming.

Contamination events conseguences

- Impact on patient safety
- Drug restriction
- Implications at regulatory level
- Closure of production facilities
- Economic loss
- Legal consequences

Regulation and guidelines

The **International Conference on Harmonization ICHQ5A guidance as well as the EMEA/CPMP/ICH/295/95 guidance and the guideline ISO 22442-3**, discuss the risk of potential viral contamination and approaches to apply to ensure viral safety of products derived from cell lines or tissue of human or animal origin. Such contamination could arise at different production stages.

Potential sources of Viral Contamination

Viral contamination on cell cultures
could occur in Master Cell Bank (MCB) by several routes, as:

- derivation of cell lines from infected animals
- use of virus to establish the cell line
- used of contaminated biological reagents such as animal serum components
- contamination during cell handling

Adventitius viruses in raw materials
could occurs, as:

- blood and plasma derived products
- medical devices obtained from animal tissues
- proteins and recombinant proteins of animal origin or produced in animals

could be introduced during production by several routes, as:

- the use of contaminated biological reagents such as animal serum components
- the use of a virus for the induction of expression of specific genes encoding a desired protein
- the use of a contaminated reagent
- the use of a contaminated excipient during formulation

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A STRONG PRESENCE IN EUROPE AND WORLDWIDE

MÉRIEUX NUTRISCIENCES OFFERS ITS SCIENTIFIC EXCELLENCE IN PHARMACEUTICAL, FOOD, CHEMICAL, BIOCIDE AND COSMETIC PRODUCTS TESTING AND CONSULTING TO ENSURE SUPPORT, OPTIMAL REACTIVITY AND FLEXIBILITY TO ITS CUSTOMERS ALL OVER THE WORLD.

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Better Food. Better Health. Better World.

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