



**MAXIMUM VIRUS SAFETY FOR  
BIOPHARMACEUTICAL PRODUCTION**

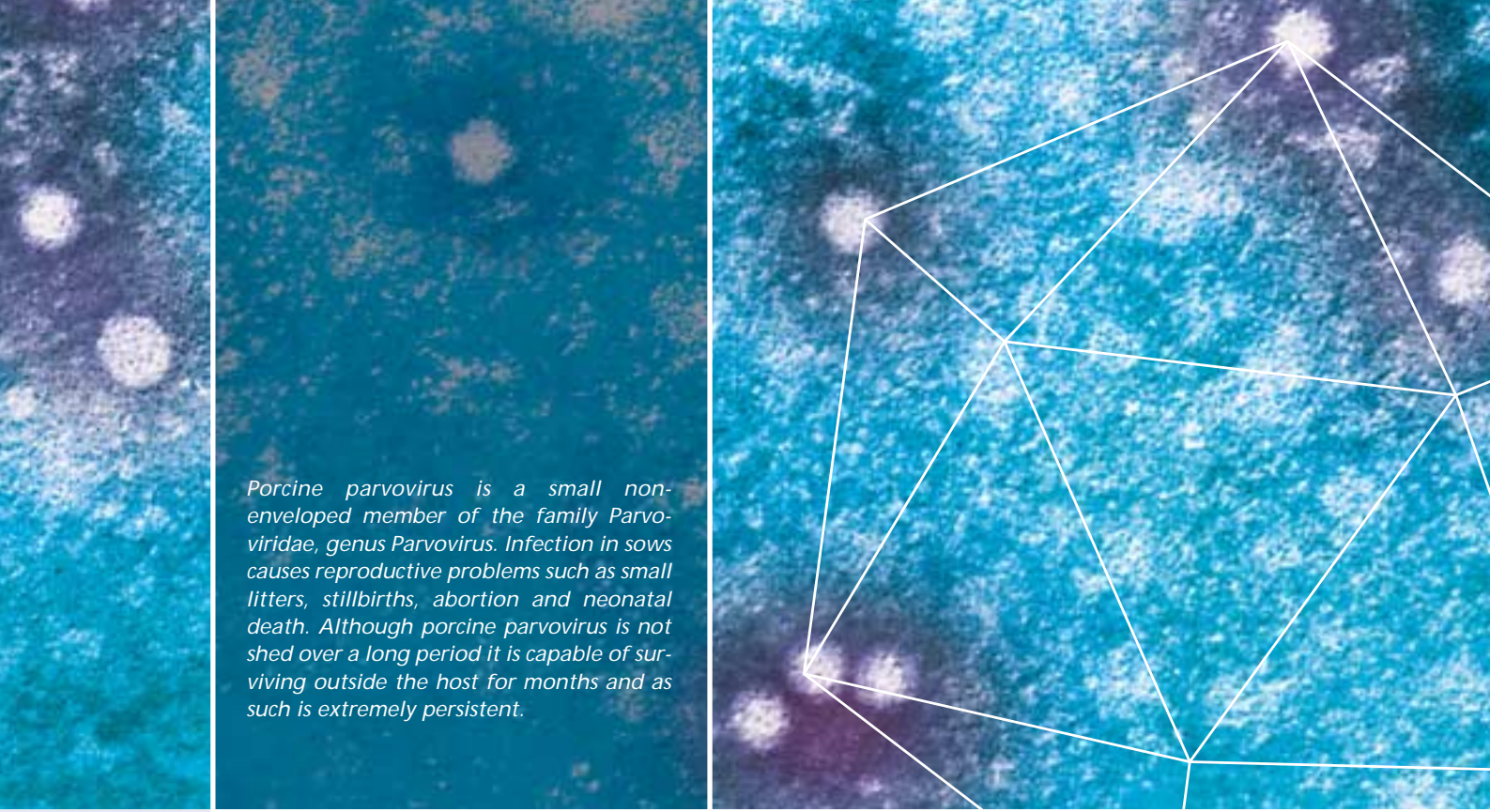
# Trypsin UV Inactivated

Parvovirus Contaminations in Trypsin <

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*Porcine parvovirus is a small non-enveloped member of the family Parvoviridae, genus Parvovirus. Infection in sows causes reproductive problems such as small litters, stillbirths, abortion and neonatal death. Although porcine parvovirus is not shed over a long period it is capable of surviving outside the host for months and as such is extremely persistent.*

## Virus safety – we look after your concerns

### Porcine Parvovirus contaminations in Trypsin

Trypsin solutions are widely used as cell dissociation reagents for continuous cell culture of adherent growing cells. Trypsin is extracted from porcine pancreas. Although trypsin is purified during production the enzyme can be contaminated with viruses such as porcine parvovirus.

In studies Trypsin from 10 different suppliers was tested with molecular beacon real-time PCR and conventional PCR assay on porcine parvoviruses. 4 out of 10 samples were tested positive. Although porcine parvovirus is not regarded as a human pathogen, parvovirus positive trypsin can contaminate cell cultures of vaccine producers.

### Increased safety requirements of biopharmaceutical products

Parallel to the rapid development of biologically derived products, analytical demands and capabilities have rapidly expanded as well. Sophisticated and sensitive techniques, like the "Polymerase Chain Reaction" (PCR), detect an increasing number of potentially harmful pathogenic contaminants in the manufacturing process, which may have previously passed Quality Control. As a result, regulatory agencies started to substantially increase the safety standards of biopharmaceutical products and introduced stringent guidelines for manufacture and Quality Control.

### Standard virus inactivation

Different viral inactivation and removal methods are available. However most of them e.g. chemical methods or filtration methods have their limitations. Gamma irradiation and heat inactivation are officially recognized by regulators. Both treatments can be quite aggressive and may have an impact on the yield of the active compound: It can be loss of protein by denaturation and therefore loss of biological activity.





*PAA's validated UV-C irradiation method is capable to destroy smallest, non-enveloped viruses (e.g. porcine parvovirus) without harming the quality or the shelf life of the products.*

## Irradiation with ultraviolet light – the validated method

Different to Gamma irradiation short wavelength ultraviolet light (UV-C) at 254 nm targets nucleic acids rather than proteins. The photons are emitted directly into the viral nucleic acids (RNA and DNA) and induce photochemical modifications. Photodimers, photohydrates and other adducts are formed, which destroy the nucleic acids of the viruses. Therefore non-enveloped viruses are very effectively destroyed by UV-C irradiation.

### The Instrument

"Viralator™" is a patented, computer-controlled UV-C thin film irradiator, which pumps a continuous flow of Trypsin or Serum through a stainless steel cylinder, rotating around a set of four mercury lamps. Experiments have shown that the highest clearance rates (up to 8 logs with viruses and 11 logs with mycoplasma) was achieved by utilizing low pressure germicidal lamps with >90% emission at 254 nm. This equipment is currently the only instrument to irradiate sensitive biological substances without either decreasing its biological activity or cell growth stimulation capacity.

### Validation

Over a period of three years a validated inactivation process which is consistent and reproducible according to cGMP was developed. Four virus validation studies were performed. A representative panel of viruses and mycoplasma was chosen that should demonstrate the ability of UV-C irradiation to efficiently inactivate particles different in their nucleic acid composition, their envelope and their sizes. It could be demonstrated that the inactivation capacity of UV-irradiation is equal (in the case of enveloped viruses) and superior (in the case of non-enveloped viruses) compared to other treatment methods e.g. Gamma irradiation. Furthermore the new UV-inactivation process retains enzymatic activity of components used in cell culture systems.

### Inactivation capacity of porcine parvovirus in Trypsin with UV-C Irradiation

The validation study, carried out by Tektagen-Charles River, Inc., USA (study number 22887), tested the inactivation capacity of porcine parvovirus in Trypsin. UV-C light was capable of inactivating this virus at a log reduction of >6 logs, which cannot be achieved with other treatments without inactivating the substance and thus limiting its use in a cell culture system. It was proven that the enzymatic activity of trypsin remains at normal level after irradiation with UV-C light at 254 nm.

Parvovirus, was chosen as it has a known resistance to Gamma-irradiation and is therefore an important challenger for the evaluation of PAA Laboratories proprietary UV-irradiation process.

### UV-C irradiation at 254 nm...

- > reduces the level of mycoplasma, enveloped and non-enveloped viruses significantly
- > reduces virus contamination more effective than Gamma-irradiation
- > remains enzymatic activity unaffected
- > is a fully validated process
- > results in a higher level of bio-product safety



# Trypsin

## UV Inactivated

### General

Trypsin is an essential reagent for routine cell culture work. It is commonly used for detaching cells from the culture substrate. PAA offers a trypsin that is treated by a validated UV inactivation process to destroy viruses and mycoplasma. Any potential contamination is completely eliminated for maximum safety in biopharmaceutical production. This process does not effect the enzymatic activity in any way.

### Benefits

- > Highly efficient detachment
- > Virus safe
- > Mycoplasma safe
- > Ready to use solution
- > Produced according to cGMP

### Order Information

Trypsin EDTA (1:250) UV Inactivated (10x)	L11-659
Trypsin EDTA (1:250) UV Inactivated (1x)	L11-660
Trypsin (1:250) UV Inactivated (1x)	L11-658

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