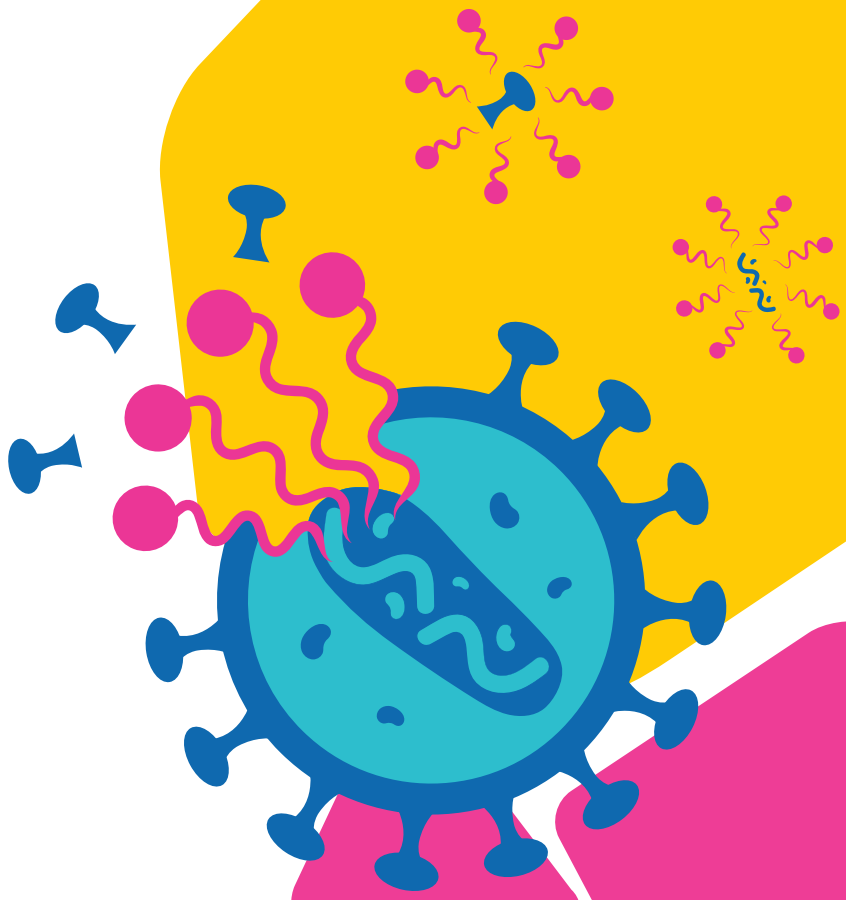
# The Deviron® Detergent Portfolio

## Greener Alternatives to Triton™ X-100 for Biopharmaceutical Applications





SAFC®

Pharma & Biopharma Raw Material Solutions

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# 1. The Detergent Landscape

Several critical steps in biologics production, including viral inactivation and cell lysis are performed with detergents.

Triton™ X-100 detergent (4-tert-octylphenol polyethoxylate) is the primary detergent templated in biomanufacturing processes. As of January 2021, its unauthorized use has been prohibited in the European Union by the European Commission, due to its listing on REACH (Registration, Evaluation, Authorization and Restriction of Chemicals).

The endocrine disruption and mutagenic effects of Triton™ X-100 degradation product have been pointed out as a potential danger to patients and the environment, leading to strict guidelines regarding its usage.

To address the need for alternatives to Triton™ X-100, we have launched the Deviron® C16 Emprove® Evolve detergent and the Deviron® 13-S9 Emprove® Expert detergent.

Our Deviron® portfolio of detergents is a best-in-class alternative to Triton™ X-100 detergent used for biomanufacturing applications.

## Key properties of Detergents

Surfactants are “surface active molecules” and have a characteristic amphiphilic nature, namely they present simultaneously a hydrophobic and a hydrophilic moiety. The adsorption of surfactants at interfaces is energetically favored, and at concentrations higher than the critical micelle concentration (CMC), surfactant molecules aggregate to form micelles, entities with a hydrophobic core and hydrophilic shell facing toward the solvent. Micelle formation is an equilibrium, and micelles can disassemble, interact, and solubilize lipid membranes, including virus envelopes or cell membranes. A detergent is defined as a surfactant or a mixture containing one or more surfactants having cleaning properties in dilute solutions. Detergents especially can permeabilize lipid membranes.

### The challenge of finding greener alternatives to Triton™ X-100

A wide variety of surfactant categories exist on the market. It is important to note that the surfactant molecule itself can be ionic, non-ionic, or zwitterionic.

With a deep knowledge of the detergent field, we screened more than 30 detergent molecules, looking for the best alternatives to Triton™ X-100.

### Key criteria:

- Readily biodegradable
- REACH compliance
- Viral inactivation (4-5 Log Reduction Value)
- Cell lysis efficiency
- Minimal impact on product functionality or quality
- Lack of process interference
- Effective removal by downstream operations
- Sensitive detection of trace amounts
- Manufacturability of IPEC-PQG-GMP quality material
- High volume manufacturing line

One of the main pain points for the biopharma industry is the purity level and relevant documentation available for detergents. Our Deviron® detergents, part of our EMPROVE® program, are a unique offering meeting purity, regulatory and efficacy needs.

This brochure will provide detailed application results for viral inactivation and cell lysis for Deviron® detergents.

## Deviron® Detergent portfolio

### Key features:

| Cat. No. | Deviron® C16 Emprove® Evolve Detergent | Deviron® 13-S9 Emprove® Expert Detergent |
|---|---|---|
| **Chemical name** | N, N-Dimethyltetradecylamin-N-oxide | Alcohols, C11-15-secondary, ethoxylated |
| **CAS** | 3332-27-2 | 68131-40-8 |
| **Quality Marker** | ISO9001, MQ400 | IPEC-PQG-GMP EXCiPACT, MQ500 |
| **REACH Compliance** | Yes | Yes |
| **Readily Biodegradable (>60 % within 28 days, OECD 301B)** | Yes, 88 % degradation | Yes, 74 % degradation |
| **Critical micelle concentration** | 0.002-0.003 % wt (24 °C) | 0.005 % wt (24 °C) |
| **Form** | Liquid, 30 % aqueous solution | Liquid, pure substance (100 %) |
| **Storage temperature** | 15-25 °C | 15-25 °C |
| **Documentation package** | Emprove® Evolve | Emprove® Expert |
| **Detection method** | Available (HPLC-ELSD) | |
| **Toxicology report** | Available | |
| **Efficiency for Viral Inactivation** | LRV ≥ 4, data available | |
| **Efficiency for Cell Lysis** | Yes, data available | |
| **Efficiency for Endotoxin removal for plasmid purification** | Yes, data available | |

# 2. Viral Inactivation with Deviron® Detergents

Viral safety is a major concern for biotherapeutic manufacturers. Cell-based processes may produce endogenous retroviral particles, and adventitious viruses can be introduced from contaminated source materials or during the manufacturing process. Human plasma-derived products are at risk of containing viruses, despite extensive screening of donation material. Detergent-mediated viral inactivation is widely used in multiple biotherapeutic production processes to achieve total virus clearance targets in a process.

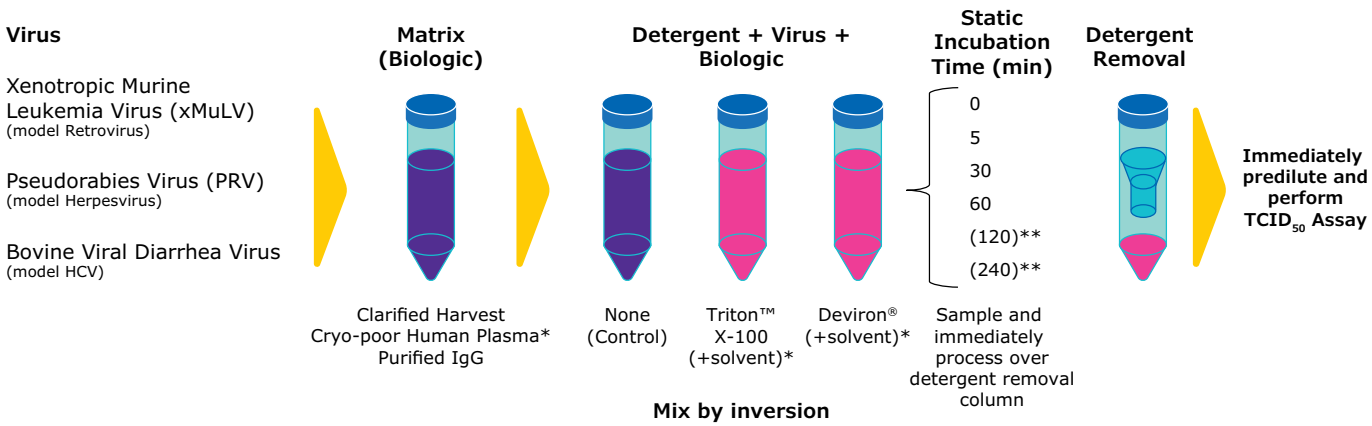
## Method

Detergent-mediated viral inactivation was evaluated in IgG, cryo-poor plasma and clarified CHO-derived cell culture fluid harvest matrices. Viruses including Xenotropic Murine Leukemia Virus (XMuLV), Pseudorabies virus (PRV), and Bovine Viral Diarrhea Virus (BVDV) were used to model endogenous retrovirus-like particles and/or rodent retrovirus, Herpesvirus and Hepatitis C, respectively. Triton™ X- 100 detergent and Deviron® detergents were prepared at target weight by volume (w/v) concentration. Solvent tri-n-butyl phosphate (TnBP) was added to a final concentration of 0.3 % for studies in the cryo-poor plasma matrix.

Feed and hold samples were collected from the no-detergent control. Samples collected at each time point are subjected to detergent removal using a Pierce™ Detergent Removal Spin Column (Thermo Scientific, Waltham, MA) according to manufacturer instructions.

Virus titers are measured using the Tissue Culture Infectious Dose 50% ($TCID_{50}$) assay, which determines infectious titer by measuring frequency of viral infection of sample dilutions in 96-well plates, and virus titers are expressed as $\log_{10}$ $TCID_{50}$/mL. Post-infection, 96-well plates were incubated at 37 °C for an interval required to observe cytopathic effects and visually scored. When virus is undetectable following detergent treatment, the LRV is limited by the assay limit of detection, which depends on the starting virus concentration, dilution performed to negate any cytotoxic effects and the volume assayed and is indicated numerically as a minimum value or graphically with an upward arrow or other symbol.

### Testing Method for Detergent-based Inactivation of Enveloped Viruses

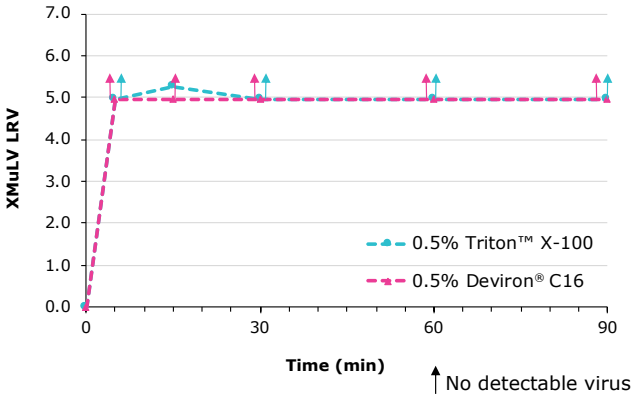



*the solvent TnBP, tri-n-butyl-phosphate, is added to the detergent only for experiments in plasma matrix.
**longer incubation times only for experiments in plasma matrices.

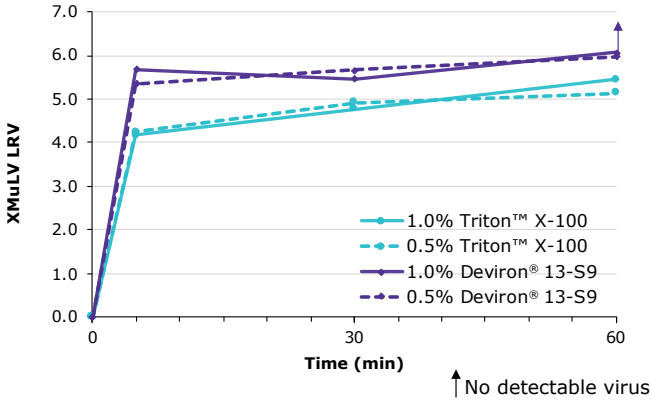
**Figure 1**. Detergent efficacy to inactivate enveloped viruses in different matrices. Triton™ X-100 detergent is the benchmark.

## Viral Inactivation in CHO Clarified Harvest

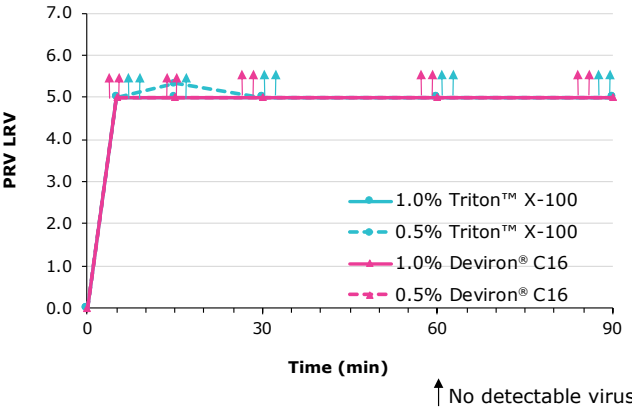
### Deviron® C16 in CHO clarified harvest at 22°C



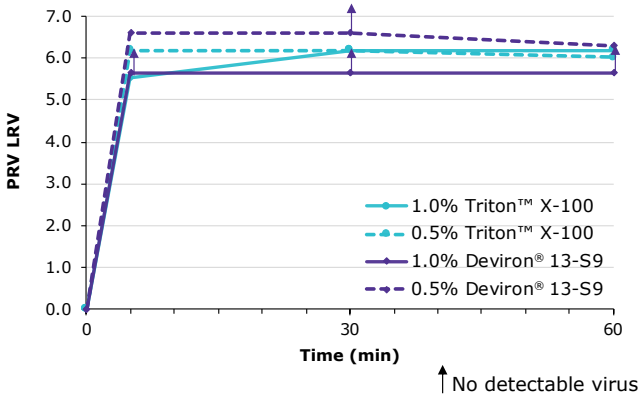

### Deviron® 13-S9 in CHO clarified harvest at 15°C




### Deviron® C16 in CHO clarified harvest at 22°C

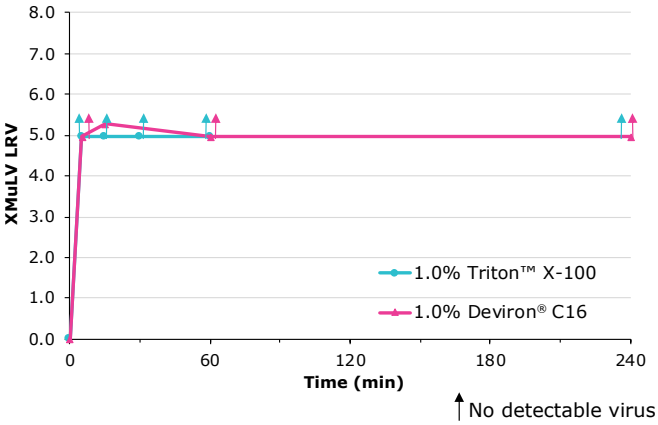



### Deviron® 13-S9 in CHO clarified harvest at 15°C

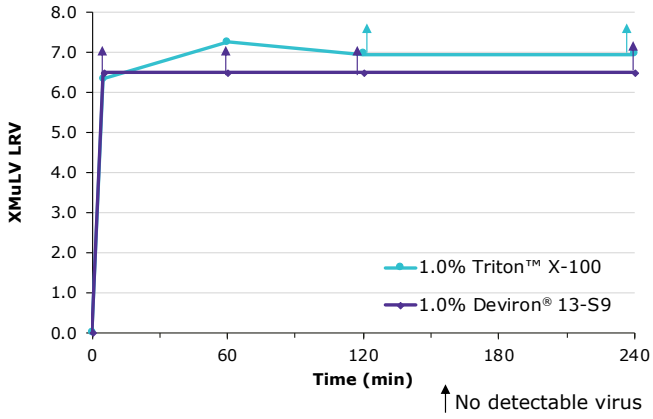


## Viral Inactivation in Plasma

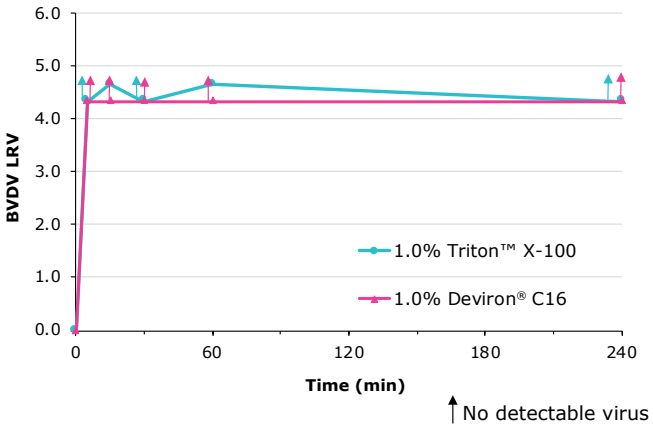
**Deviron® C16 in neat plasma with 0.3% TnBP at 22°C**



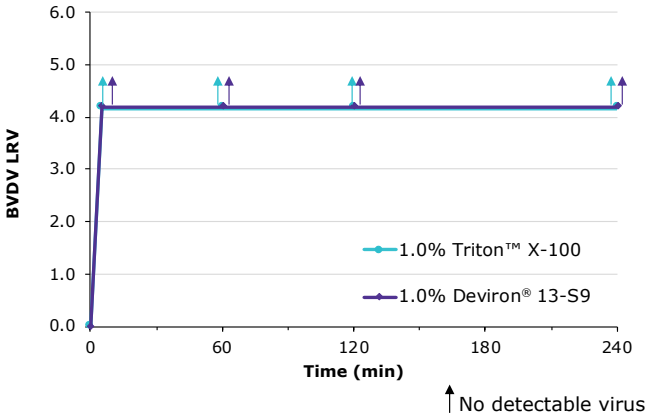

**Deviron® 13-S9 in Cryo-poor plasma with 0.3% TnBP at 22°C**



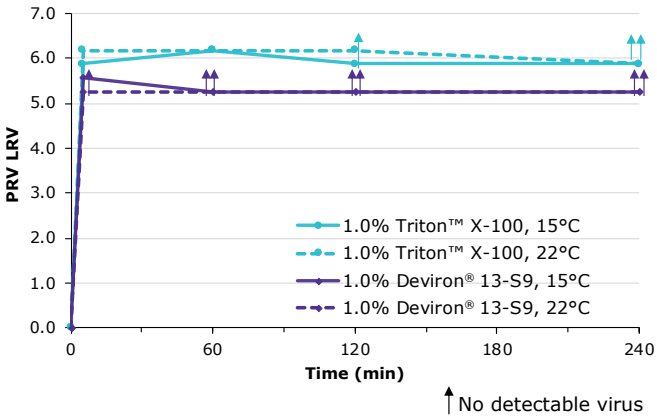

**Deviron® C16 in neat plasma with 0.3% TnBP at 22°C**



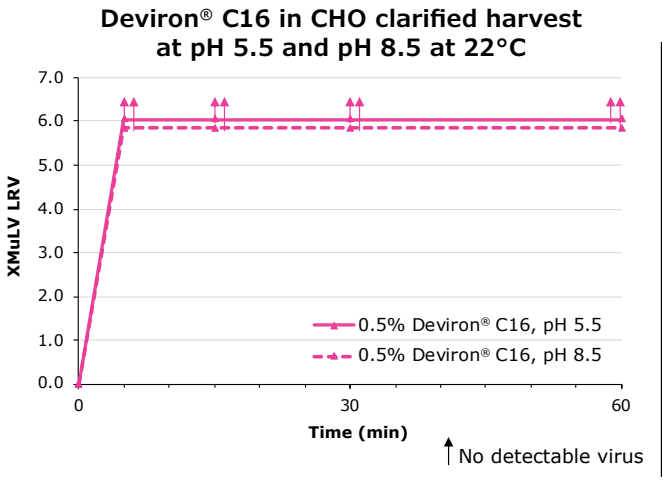

**Deviron® 13-S9 in Cryo-poor plasma with 0.3% TnBP at 15°C**

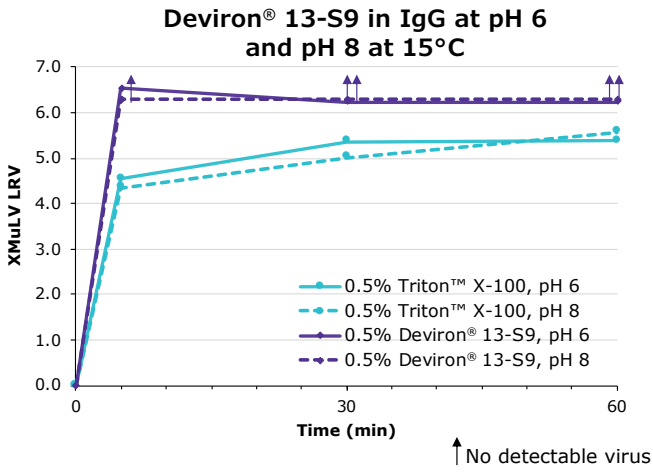



**Deviron® 13-S9 in Cryo-poor plasma with 0.3% TnBP with 15°C and 22°C**



## Viral Inactivation in CHO Clarified Harvest at Different pH Conditions




## Results

- Viral inactivation was demonstrated to be >4LRV for all the matrices tested with different model viruses.
- In most cases, the virus was below detection limit by 60 minutes post addition of Deviron® detergent.
- The viral clearance performance of Deviron® detergents was equivalent or better than Triton™ X-100 detergent for all matrices and model viruses.

# 3. Cell Lysis with Deviron® Detergents

The biomanufacturing of viral vectors as therapeutics often requires a cell lysis step to release the viral particles of interest. The host cells, HEK293 mammalian cells or Sf-RVN® insect cells, commonly employed to produce Adeno-associated virus (AAV) vectors, are typically lysed using detergents such as Triton™ X-100 or Polysorbate 20 (Tween™ 20).

We introduce two new options for cell lysis with our Deviron® detergents.

Cell lysis efficiency of the two Deviron® detergents was demonstrated with two different AAV serotypes produced by HEK293 and Sf-RVN® cells. The infectivity of the AAV after lysis was evaluated to assure no interference of Deviron® detergents with the final product efficacy.

## Method

HEK293 cells were cultivated according to their type, suspension or adherent, and transfected with the selected plasmid polyethylenimine (PEI) complex.

After 72 hours of cultivation, cells were harvested and lysed with the following procedure:

- Detergent concentration: 0.5 % wt/vol.
- Detergents: Tween™ 20 and Triton™ X-100 (benchmarks), Deviron® C16 and Deviron® 13-S9
- Nuclease: 25 U/mL Benzonase® endonuclease with 2 mM $MgCl_2$
- Lysis time: 2 h
- Temperature: 37 °C
- 5 % $CO_2$

Following incubation, total cell count and viability were determined with the Vi-CELL (model XR 2.06.3 Beckman Coulter).

After cell viability quantification, virus-containing supernatant was clarified by centrifugation.

The supernatant was analyzed to determine physical titer (capsid/mL) by enzyme-linked immunosorbent assay (ELISA) and genome titer (viral genome copies/mL) by digital PCR.

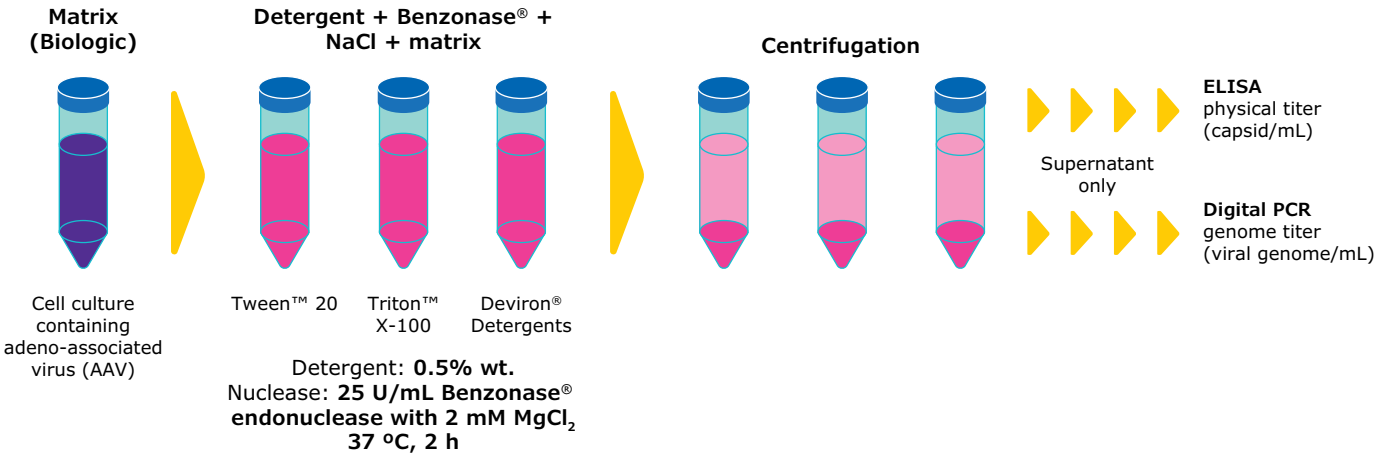



**Figure 2**. Assay to evaluate the efficacy of the detergents to lyse cells and release AAV. Triton™ X-100 and Polysorbate 20 (Tween™ 20) are the benchmark detergents.

Before the infectivity evaluation, the detergent was removed from the samples using a detergent removal column (Pierce), and infectivity was determined with the transduction unit assay.

Sf-RVN® cells were cultivated according to manufacturer instructions and infected with Baculovirus vectors. Cells were cultivated for 4 days and harvested. The lysis procedure was as described above. After cell viability quantification, AAV virus-containing supernatant was clarified by centrifugation.

## Results

The cell lysis efficacy of the detergents was evaluated by counting the total and live cells in each sample. This determination was performed automatically with the Vi-CELL for HEK293 cells and manually evaluating microscope images for the Sf-RVN® cells. With both cell lines, lysis of most of the cells was evident from the microscope images, confirming the effective lysis performance of the two Deviron® detergents, comparable to or better than the benchmarks, Triton™ X-100 and Polysorbate 20.

The viability of HEK293 cells (adherent and suspension) after lysis are shown below. The percentage is calculated based on the automated counting performed by the software, so should be considered as a trend with the actual viable percentage likely to be lower.

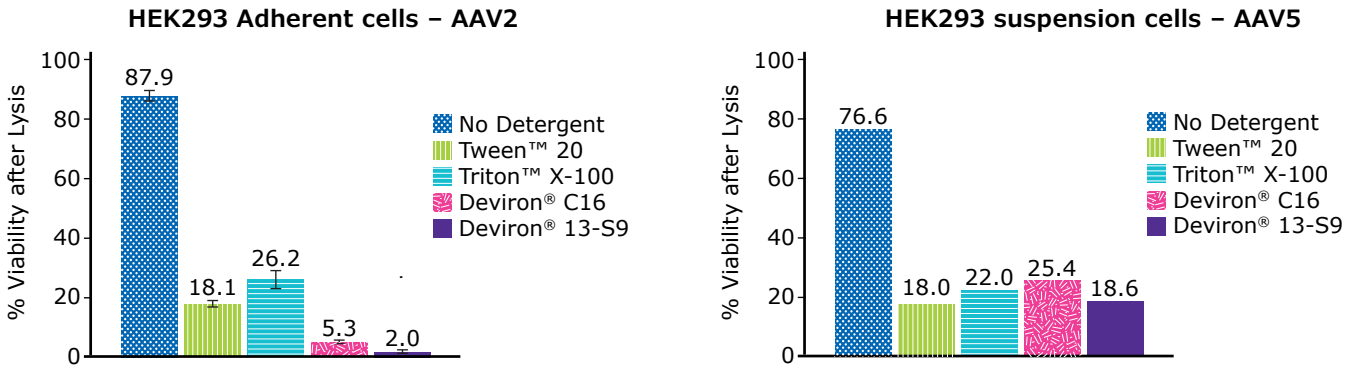



**Figure 3**. Percentage of viable cells after the lysis. The values were calculated based on the total and viable cells counted by the Vi-CELL (Beckmann Coulter).

Figure 3 shows that the two Deviron® detergents lyse the cells comparably well if not better than the benchmarks, Triton™ X-100 and Tween™ 20.

The genome titer was determined with digital PCR. Both Deviron® detergents were as efficient as the benchmarks in releasing capsids (data not shown) and the viral genome titers were comparably high.

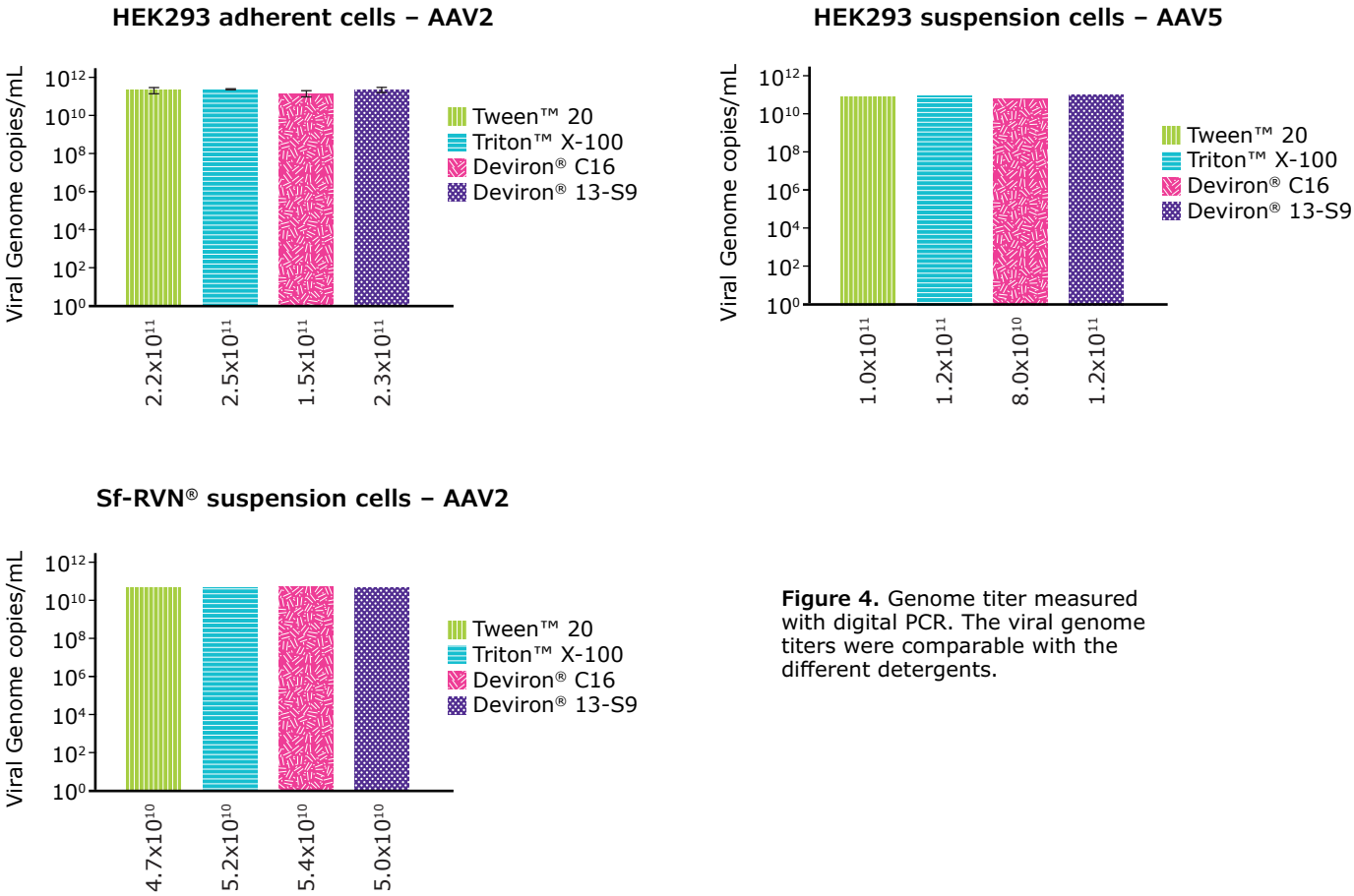



**Figure 4.** Genome titer measured with digital PCR. The viral genome titers were comparable with the different detergents.

Following cellular release and purification, the AAV must be functional to be an effective product. The infectivity of the AAV is a critical quality requirement. The infectivity was determined with a transduction unit assay and the results demonstrate that Deviron® detergents preserve the infectivity of the AAV (Figure 5).

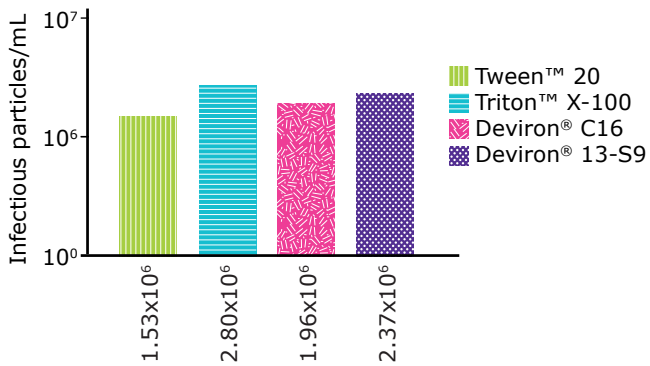



**Figure 5.** Infectivity of AAV after cell lysis of HEK293 adherent cells with detergents. The infectivity was determined with the transduction unit assay.

These results demonstrate that Deviron® detergents do not cause harm to non-enveloped target virus vector product. The data shows that there is no difference in functional virus titer between the different detergents.

## Cell Lysis with Deviron® detergents and Benzonase® endonuclease

In the cell lysis experiments, Deviron® detergents were employed together with the Benzonase® endonuclease. Typically, both cell lysis and host cell DNA digestion are performed simultaneously to maximize process efficiency, so demonstration of Benzonase® endonuclease activity in the presence of detergents is important. Enzyme activity of the Benzonase® endonuclease was calculated from the DNA content, measured using the Qubit device. The results demonstrate that Deviron® C16 and Deviron® 13-S9 do not interfere with the enzyme activity, even at a higher concentration than what is generally used in AAV manufacturing.

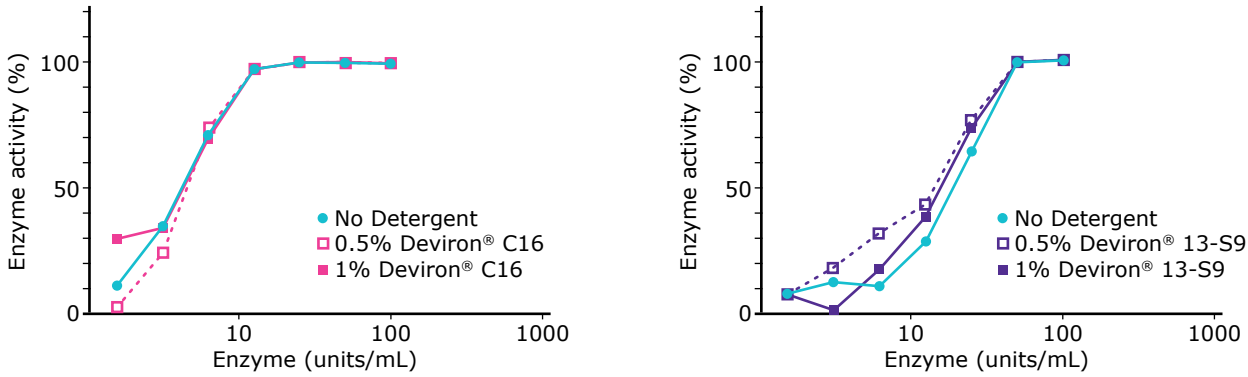



**Figure 6**. Enzyme activity of the Benzonase® endonuclease determined in samples containing Deviron® detergents.

# 4. Detection and Removal of Deviron® Detergents

Detergents are crucial for bioprocesses; however, they must be removed from the process stream by the downstream steps and detergent traces must be quantified to ensure patient safety.

According to WHO Technical Report Series 924 Annex 4 (“Guidelines on viral inactivation and removal procedures intended to assure the viral safety of human blood plasma products”), the permitted level of Triton™ X-100 detergent in the final product must be below 25 µg/mL, depending on volume and frequency of infusion. This limit refers to Triton™ X-100 and we can assume this as “worst case scenario”.

## Detergent removal in downstream processing: feasibility study

We performed feasibility studies for the removal of detergent in downstream process steps with three chromatography resins selected as models. The buffers for each chromatographic step are selected based on the manufacturer recommendations.

| | | |
|---|---|---|
| **Protein A (Affinity) Eshmuno® A, 120089** | Binding & washing | 25 mM Tris pH 7 |
| | Elution | 50 mM glycine, pH 2.8 |
| | CIP (clean-in-place) | 150 mM $H_3PO_4$ |
| **Cation Exchange (CEX) Eshmuno® S, 1200780** | Binding & washing | 20 mM phosphate, pH 6 |
| | Elution | 20 mM phosphate, 1 M NaCl, pH 6 |
| | CIP | 1 M NaOH |
| **Anion Exchange (AEX) Fractogel® EMD TMAE Hicap, 110316** | Binding & washing | 50 mM Tris, pH 9 |
| | Elution | 50 mM Tris, 1 M NaCl, pH 9 |
| | CIP | 1 M NaOH |

Feasibility studies are performed with a Scout column packed with resin.

The detergent solutions are prepared in binding and washing buffer. The concentration tested is ~1% wt. (~10,000 µg/g).

Fractions from each of the three steps (Binding & Washing, Elution, and CIP) are analyzed with the quantitative HPLC method described below.

The removal studies were performed in absence of matrix proteins, to directly assess detergent binding to the resins.

The results of the removal studies for Deviron® C16 detergent are reported in the table below.

| Columns tested | Type of resin | Removal |
|---|---|---|
| **Protein A** | Eshmuno® A | 99.6 % |
| **CEX (pH 6)** | Eshmuno® S | 43-64 % |
| **AEX (bind/elute mode, pH 9)** | Fractogel® EMD TMAE Hicap | 99.8 % |
| **AEX (flow-through mode, pH 9)** | Fractogel® EMD TMAE Hicap | Not suitable |

Deviron® C16 detergent is zwitterionic with an isoelectric point (pI) of 8.9, and thus the detergent charge depends on the solution pH:

**pH< 8.9 → net positive charge**

**pH> 8.9 → net negative charge**

In the case of CEX, Deviron® C16 detergent is positively charged at pH 6 and will bind to the resin; this is why the removal efficiency is low. Similarly with the AEX flow-through mode, Deviron® C16 detergent is negatively charged and binds to the resin.

The resin selection should be based on the unit operation pH, the charge of Deviron® C16 detergent, and on the isoelectric point of the purified protein. We recommend performing the virus inactivation with Deviron® C16 detergent prior to protein A affinity capture step to assure a complete Deviron® C16 detergent removal.

The results of the removal studies for Deviron® 13-S9 detergent are reported in the following table.

| Columns | Type of resin | Removal |
|---|---|---|
| **Protein A** | Eshmuno® A | 100 % |
| **CEX (pH 6)** | Eshmuno® S | 100 % |
| **AEX (pH 9)** | Fractogel® EMD TMAE Hicap | 100 % |

Deviron® 13-S9 detergent is non-ionic and does not bind to any of the resins tested. The detergent is present only in the flow through fractions; no detergent traces were detected in the eluate and CIP fractions.

For specific process and method development, reach out for technical support.

## Quantitative detection method of residual detergent

The quantitative method to detect residual detergent employs a HPLC (Agilent Technologies 1100 series) in combination with an evaporative light scattering detector (Agilent Technologies 1290 Infinity ELSD).

**Eluents employed in our method are the following:**

- Acetonitrile gradient grade for liquid chromatography LiChrosolv® (Supelco®)
- Ultrapure water (Milli-Q® Advantage A10 water purification system)
- Trifluoroacetic acid for spectroscopy Uvasol® (Supelco®)

## Chromatographic conditions:

| | Deviron® C16 detergent | Deviron® 13-S9 detergent |
|---|---|---|
| Column | **Purospher® STAR RP18e (Cat# 1.50252.0001)** | **BIOshell™ A400 Protein C4 (Cat# 66828-U)** |
| | 5 µm | 3.4 µm |
| | 250 x 4 mm | 10 cm x 4.6 mm |
| | Temperature: 75 °C | Temperature: 30 °C |
| Conditions | Eluent A: water + 0.1% TFA | |
| | Eluent B: acetonitrile | |
| | Flow rate: 0.8 mL/min | |
| | Injection volume: 100 µL | |

| ELSD parameters (Must be optimized for each device) | |
|---|---|
| Evaporation Temp (°C) | 80 |
| Nebulization Temp (°C) | 80 |
| Nitrogen gas flow (SLM, standard L/min) | 1.2 |
| Smoothing (SMT) | 30 (= 3 s) |
| Detector gain (PTM) | 5 |

## Gradient:

### Deviron® C16 detergent

| t (min) | % Acetonitrile | Column Outlet |
|---|---|---|
| 0 | 30 | Waste** |
| 3.5 | 30 | Waste-ELSD |
| 11 | 80 | ELSD |
| 13.5 | 80 | ELSD |
| 13.6 | 95 | ELSD |
| 15.5 | 95 | ELSD |
| 15.6 | 30 | ELSD |
| 22 | 30 | ELSD |

** protection of ELSD against high salt load

### Deviron® 13-S9 detergent

| t (min) | % Acetonitrile | Column Outlet |
|---|---|---|
| 0 | 30 | Waste** |
| 3.5 | 30 | Waste-ELSD |
| 12.50 | 80 | ELSD |
| 16.00 | 80 | ELSD |
| 16.10 | 30 | ELSD |
| 22.00 | 30 | ELSD |

This detection method was developed and optimized in the absence of protein. Samples with high protein concentration require sample preparation, to avoid column overloading with protein.

Calibration standards with the Deviron® detergents are prepared in water. Triplicate measurements are carried out for each sample. The calibration curve is log peak area vs log concentration because the ELSD signal is not linear.

## Calibration curve Deviron® C16 detergent

| Conc. (µg/mL) | Mean area[1] | Log conc.[2] | Log area[2] |
|---|---|---|---|
| 0.1* | 805 | -1 | 2.9 |
| 0.5** | 12653 | -0.3 | 4.1 |
| 1 | 43009 | 0 | 4.6 |
| 2 | 149114 | 0.3 | 5.2 |
| 5 | 759245 | 0.7 | 5.9 |
| 10 | 2350293 | 1 | 6.4 |

[1] Mean value of the triplicate measurements of each sample

[2] ELSD signals are not linear, logarithm calculated to obtain a linear calibration curve.

* LOD

**LOQ

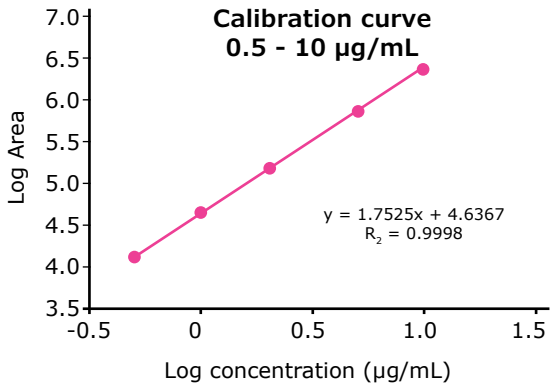
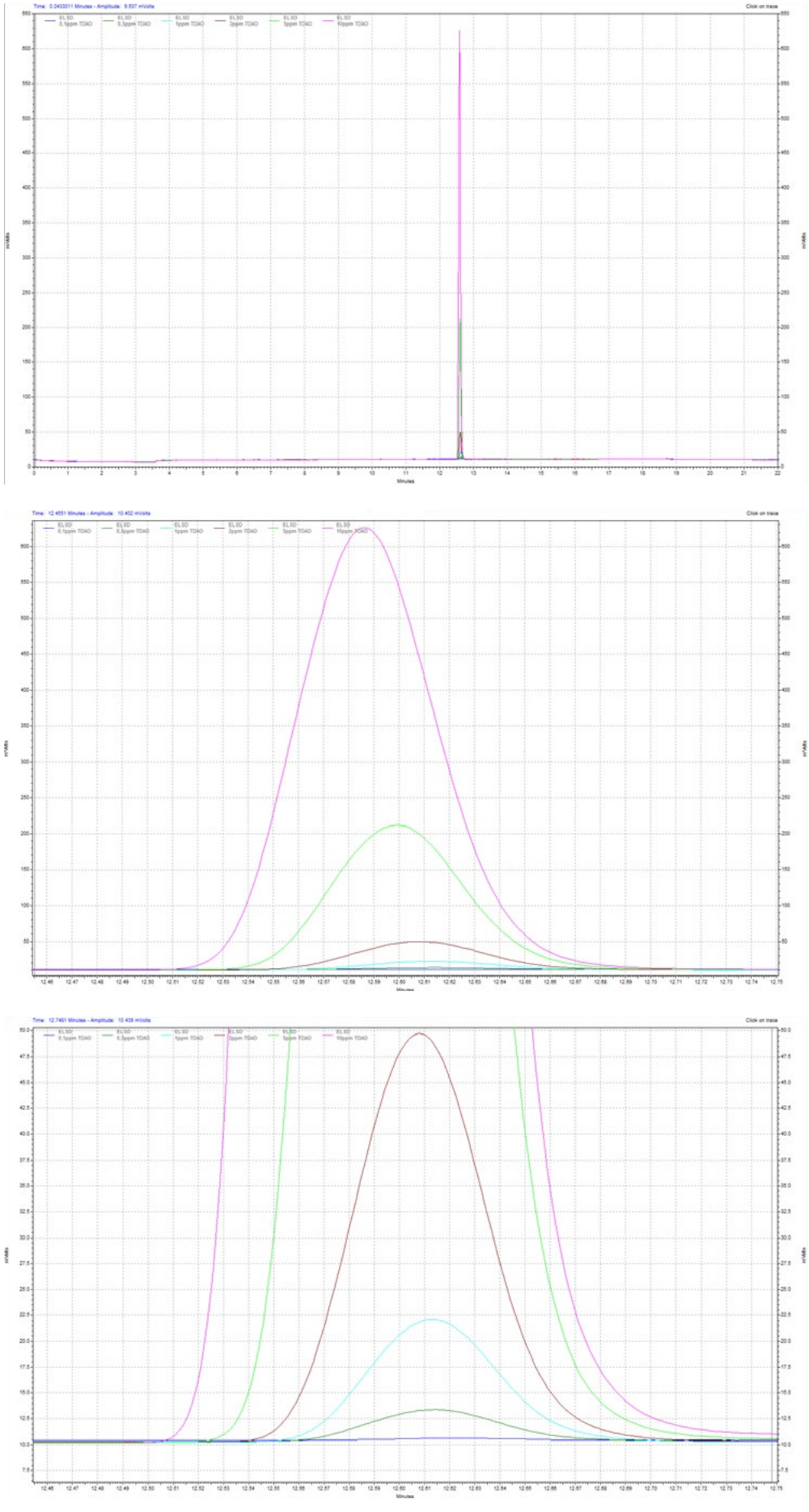



**Figure 7**. Calibration curve for Deviron® C16 detergent

**Figure 8**. Overlay of the sample chromatograms measured for the calibration curve of Deviron® C16, concentration range 0.1 to 10 µg/mL. Progressive magnification of the peaks to better observe lower concentration peaks.



## Calibration curve and chromatograms of Deviron® 13-S9 detergent

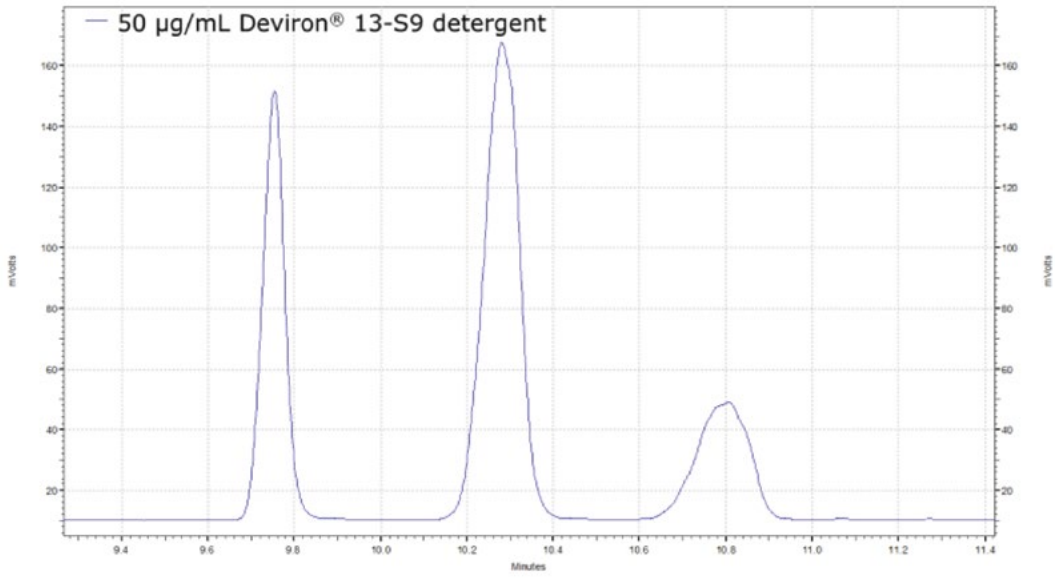



**Figure 9**. Deviron® 13-S9 chromatogram

Deviron® 13-S9 chromatogram presents three peaks. Only a single peak is used for the quantification. Generally, the most intense peak is used, however, the other peaks would be suitable if they are sufficiently intense.

| Conc. (µg/mL) | Mean area[1] | log conc.[2] | log area[2] |
|---|---|---|---|
| 2* | 4386 | 0.3 | 3.6 |
| 5** | 18496 | 0.7 | 4.3 |
| 10 | 62272 | 1.0 | 4.8 |
| 25 | 290982 | 1.4 | 5.5 |
| 50 | 926157 | 1.7 | 6.0 |
| 100 | 2652384 | 2.0 | 6.4 |

[1] Mean value of the triplicate measurements of each sample

[2] ELSD signals are not linear, logarithm calculated to obtain a linear calibration curve.

* LOD

**LOQ

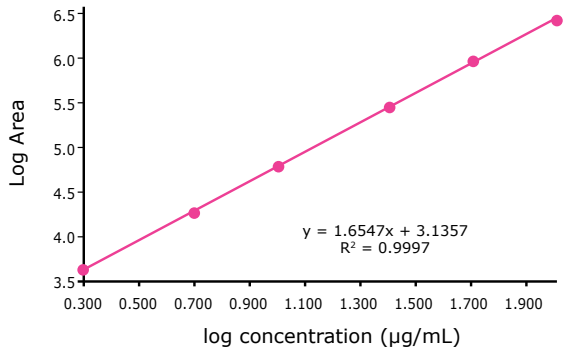
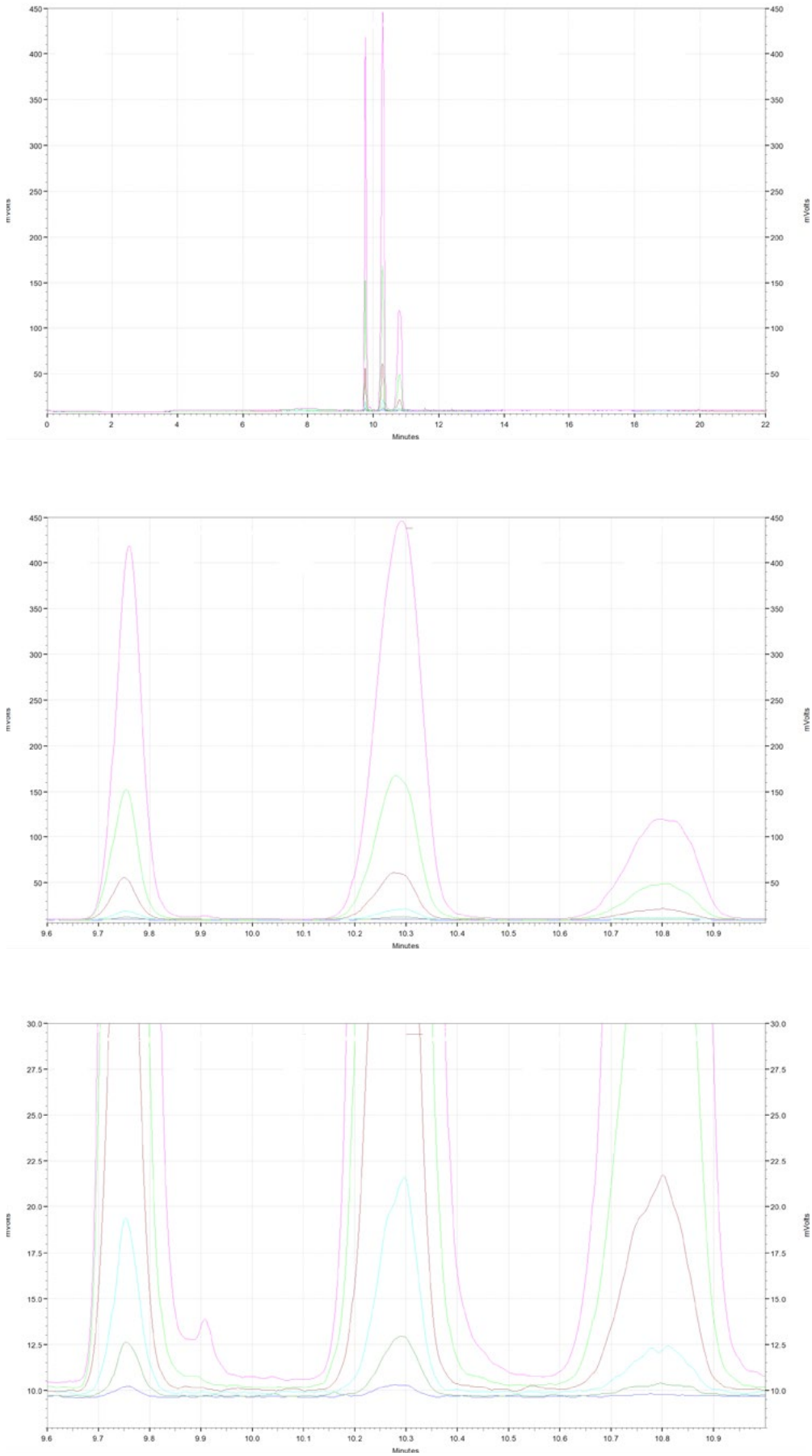



**Figure 10**. Calibration curve for Deviron® 13-S9 detergent

**Figure 11**. Overlay of the sample chromatograms measured for the calibration curve of Deviron® 13-S9, with range of 2 -100 µg/mL. Progressive magnification of the peaks to better observe lower concentration peaks.



# 5. Deviron® Detergents Frequently Asked Questions

**1. Can I continue to use Triton™ X-100 if I'm not located in the European Union?**

The Triton™ X-100 ban has been decided by the ECHA[1] under the REACH[2] regulation. The main driver was the high toxicity of the product for human health and environment. Therefore, removing this product from bioproduction is a significant desire in the industry. Non-EU regulatory agencies will also evaluate the product usage, likely leading to additional bans in other geographies.

**2. Can I use a research grade detergent for biomanufacturing?**

Detergents are generally manufactured in high volume with organic chemistry chain reactions. Often the raw material quality is low to minimize production costs and can lead to dangerous impurities in the end-product like dioxane or nitrosamine. Research grade detergents are intended for use for cleaning applications only and should not be used in drug manufacturing processes or formulation.

**3. What are the key steps to switch to Deviron®13-S9 detergent?**

Deviron® 13-S9 detergent comes with three lots available of IPEC-PQG-GMP EXCiPACT manufactured product. Samples of these lots can be requested currently for qualification purposes. The EMPROVE® dossiers available with our products contain all information needed to file with regulatory agencies. Toxicology information is also available.

**4. I want to evaluate Deviron® detergents but have no expertise, how can you support me?**

For application-related support, you can rely on our team of biomanufacturing experts to guide you through this change. Get in touch with your local contact for technical consultancy.

**5. What is the difference between MQ400/Emprove® Evolve and MQ500/Emprove® Expert (cGMP)?**

To help with your regulatory filing, we created different documentation and quality programs to help you get the right product for the right application. Click on the following links to learn more about the EMPROVE® and M-Clarity® programs. The Deviron® C16 EMPROVE® Evolve and the Deviron® 13- S9 EMPROVE® Expert are part of the highest quality levels we offer.

**6. What are the recommended concentrations for target applications?**

For viral inactivation in a mAb process, the ASTM[3] E3042-16 standard used for Triton™ X-100 can provide guidance on implementation of detergent alternatives. Concentrations used in the industry vary between 0.5 and 1%, with plasma being seen as the riskiest application due to the use of human derived blood product. Implementation of a new detergent will require generation of validation data to demonstrate viral inactivation efficacy in a specific customer process.

**7. Can you develop a cGMP detection method for Deviron® detergents**

Our R&D experts developed detection methods for our Deviron® detergents that can be transferred to our customers. However, for cGMP detection methods, our Bioreliance® laboratory is the partner of choice. Get in touch with us for any question.

**8. Are Deviron® detergents compatible with Benzonase® endonuclease for cell lysis applications?**

Benzonase® endonuclease is the gold standard for DNA digestion in AAV[4] biomanufacturing processes. Deviron® detergents are fully compatible with the Benzonase® endonuclease portfolio. There is no loss of enzymatic activity or detergent property with the use of both in combination.

**9. What is the manufacturing capacity of Deviron® detergents?**

Deviron® detergents are released from our Darmstadt, Germany site, with the capacity to provide more than 100 tons of product/year. Do not hesitate to provide us with a forecast to discuss case-specific lead times.

[1] European Chemicals Agency
[2] Registration, Evaluation, Authorization and Restriction of Chemicals*
[3] ASTM International
[4] Adeno Associated Virus
Triton™ is a trademark of The Dow Chemical Company or an affiliated company.

## Ordering information

| Description | Pack Size | Cat. No. |
|---|---|---|
| Deviron® C16 Detergent EMPROVE® Evolve solution | 1 L | 1086931000 |
| | 2.5 L | 1086932500 |
| | 25 L | 1086939025 |
| Deviron® 13-S9 Detergent EMPROVE® Expert | 1 L | 1086941000 |
| | 2.5 L | 1086942500 |
| | 25 L | 1086949025 |

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