J.T.Baker® Viral Inactivation Solution (Detergent) Clearance by Purification Process

OBJECTIVE

J.T.Baker® Viral Inactivation Solution (VIS) is a ready-to-use, readily biodegradable[1], nonionic detergent-based solution for inactivation of virus in biomanufacturing processes. When using VIS, a final active detergent concentration of ≤0.1% in the harvested cell culture fluid (HCCF) or process intermediates is effective in achieving ≥6.5 log of viral inactivation. A study performed by an independent laboratory demonstrated VIS is capable of robust viral inactivation under typical manufacturing environmental temperatures ranging from 4°C to 24°C. VIS is compatible with typical bioprocessing steps of monoclonal antibody (mAb) and analogous proteins with no impact on product stability or process performance. Refer to Avantor Technical Note, *Stability of protein therapeutics with J.T.Baker® Viral Inactivation Solution 110*. However, one of the critical aspects of using detergent-mediated viral inactivation (DVI) is that the subsequent purification process is able to remove the detergent from product. Therefore, a comprehensive study has been performed to demonstrate the detergent removal capability of Protein A resin using J.T.Baker® BAKERBOND® PROchievA™ Protein A resin.

METHOD

To conduct a detergent clearance study, it is crucial to have a suitable analytical tool to trace the residual detergent in post-detergent treated sample processed over a subsequent purification step. For this reason, a High-performance liquid chromatography (HPLC)-based analytical method was developed and used to detect the active detergent in J.T. Baker® Viral Inactivation Solution (VIS) at a ppm level. J.T.Baker® Viral Inactivation Solution Analytical method for detection of active ingredient, method 100-300-1001, is available under an active Confidentiality/Non-disclosure Agreement.

The evaluation was executed using clarified HCCF from Chinese Hamster Ovary (CHO) cells producing IgG1 and typical Protein A chromatography methodology. Briefly, HCCF was incubated with VIS at 15 – 24°C for one hour and passed over J.T.Baker® BAKERBOND® PROchievA™ protein A column chromatography. The run parameters are summarized in **Table 1.** All the samples were analyzed by HPLC detection method.

Table 1: Protein A chromatography process parameters

Process parameters	Description
Column/resin	PROchievA (Protein A affinity resin)
Column volume (CV)	5 mL (5.3 cm B.H. X 1.1 cm I.D.)
Resin load density	45 mg/mL, IgG1
Residence time	8 min (flowrate: 0.625 mL/min)
Equilibration	PBS, pH 7.4, 10 CV
Load	Harvest (HCCF) with 1% VIS (1000 ppm detergent)
Wash 1	PBS, pH 7.4, 10 CV
Wash 2	25 mM Tris, pH 8.0, 5 CV

Elution	100 mM Acetic acid, pH 3.4, 5 CV
Sanitization	0.1 N NaOH, 5CV, 30 min hold

RESULTS AND DISCUSSION

The analytical data indicated excellent detergent clearance capability of protein A chromatography as the detergent amount in protein A eluate was below the limit of detection (<1 ppm) by the HPLC method. There was no visible detergent peak in analytical HPLC chromatogram. Fig. 1 represents the detergent clearance data by PROchievA column.

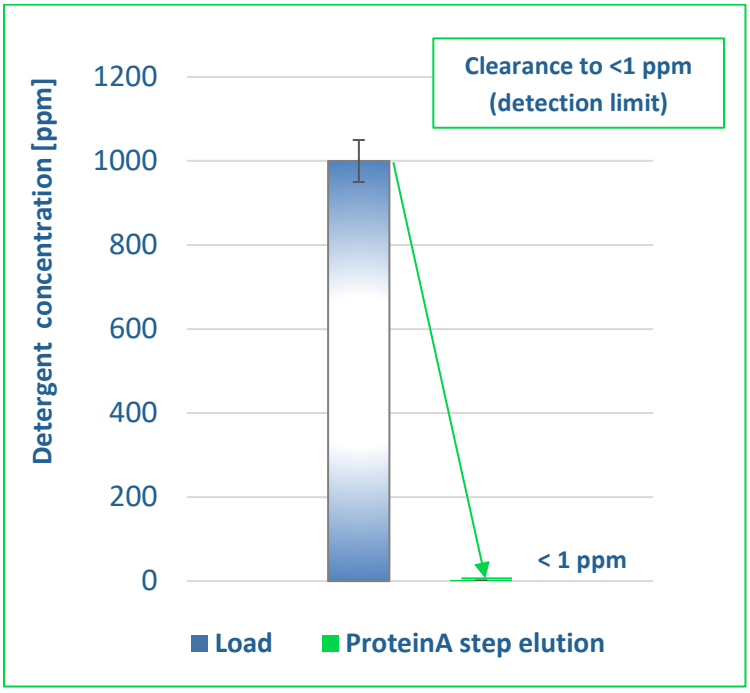

Fig. 1. Detergent clearance by Protein A chromatography

CONCLUSION

One of the critical factors in selecting an appropriate detergent for viral inactivation in biologic's manufacturing is that the subsequent process steps are able to remove the detergent from the process intermediates. The study data clearly demonstrates the detergent is cleared (<1 ppm) through protein A chromatography. It can be assumed from the detergent's physicochemical properties this detergent can simply be removed by any affinity or other process chromatography through bind-and-elute mode of operation.

1. ISO 7827:2010, OECD Test Guideline 301F (28d): >60% (10-day window met)