

VAC_20 - Optimizing downstream process conditions and anticipating scale up step of inactivated yellow fever vaccine for Bio-Manguinhos pilot plant implementation

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Introduction: The study of reproducibility conditions for downstream process of an inactivated yellow fever vaccine in small scale started in 2020. The adjustment of chromatographic parameters was necessary to allow the process execution in a volume scale compatible with operational conditions of a pilot plant facility in Bio- Manguinhos.

Objectives: Optimize the process conditions of chromatography processes in the downstream stage during the scaling up from bench to pilot plant scale.

Methodology: The clarified viral harvest produced in a bioreactor was submitted to endonuclease digestion followed by two purifications steps. The first step was performed by ion exchange chromatography with capture column, where viruses were eluted in two different conditions comparing to a specific NaCl concentration previously standardized. To reduce salt concentration from the first chromatography step and avoid virus precipitation, dilutions in the range of 0.02 to 0.2M NaCl final concentration were performed before submission to a multimodal chromatography step. Collected samples were analyzed according to the viral infectivity, residual DNA and Host Cell Proteins (HCP).

Results: Results from three independent experiments revealed an excellent condition of NaCl that was able to elute viruses from a capture column successfully. The final concentration of NaCl was selected to dilute the sample before submission to polishing column maintaining viral viability. These optimized conditions lead to 99% of virus recovery when tested by viral titration assay. Likewise, the purified material shown a reduction of 81% residual DNA and reduction of 99% HCP contaminants, after the second chromatography step.

Conclusion: Our results supported the potential use in the downstream process, due to reduction of 40% in the final volume of the material when compared to the previously established process, maintaining viral viability and efficient removal of contaminants, which makes the process compatible with the Bio-Manguinhos pilot plant capacity.

Keywords: yellow fever vaccine, downstream, process optimization