RESIDUAL DNA ANALYSIS IN INFLUENZA VACCINE PROCESSING

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In cell-based influenza vaccine production, the European Pharmacopoeia demands a host cell residual DNA concentration of less than 10 ng per dose. To reliably measure residual DNA in both process samples and final vaccine using quantitative PCR, DNA preparation prior to analysis is a necessity. Samples from the vaccine purification process contain different buffers, salts, and cell-based compounds, and vary 3–4 logs in DNA concentration from harvest to the final product, which all put strain on the DNA preparation. For accurate determination of DNA concentration, recovery is of high importance. There are many commercially available DNA preparation kits that use different techniques to bind DNA, from spin columns with a DNA-binding membrane or medium (resin) to magnetic beads. However, these kits are mainly developed to purify DNA fragments from gel electrophoresis or genomic DNA from tissues such as blood or cultured cells, and do not have recovery as a priority. Few kits are intended for residual DNA determination in samples with high concentration of a protein or virus product. In this study, prototype media for DNA preparation, in bind-elute and batch mode, were evaluated for recovery, hands-on time, and throughput. In batch mode, recoveries of > 80% were achieved, but the technique exhibited matrix effects on real process samples. In bind-elute mode, recoveries of 40%–60% were achieved after elution. However, recovery could be improved by determination of DNA concentration, while keeping DNA bound to the medium.