

Targeted Quantitation of Host Cell Protein Impurities

Use of High Resolution Mass Spectrometry for Targeted Quantitation of Protein Impurities



Effective control of host cell protein (HCP) is crucial in biopharmaceutical production to ensure safety and regulatory compliance. Specific host cell protein impurities can be targeted and accurately quantified by TOF-MRM.



Identify HCP targets at sub-ppm levels during HCP screening or process clearance monitoring



Stable isotope labeled versions of the proteotypic peptides are synthesized as internal standards for quantitation



Batch to batch monitoring of impurity levels as a critical quality attribute (CQA)



Method development using proteotypic peptides for quantitation and LC/MS optimization enhances sensitivity and specificity

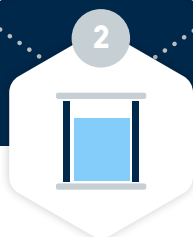
Workflow for HCP Quantitation Using Advanced Mass Spectrometry

Clarified Harvest

Viral Inactivation

CEX Based Polishing

UF/DF



Protein A



AEX Based Polishing

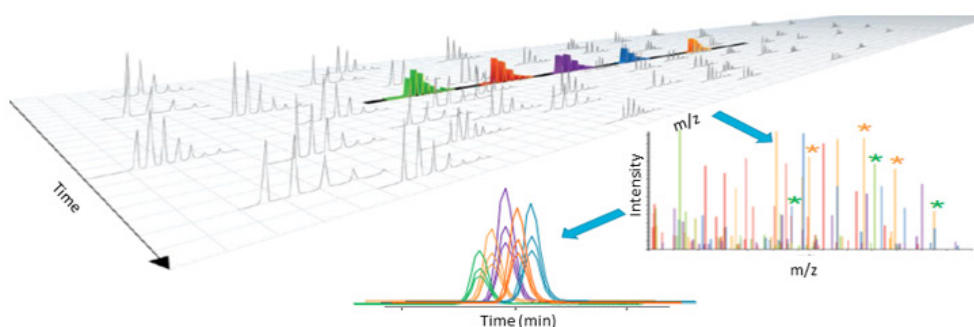


Viral Filtration



Final DP

● Applicable Step in the Workflow

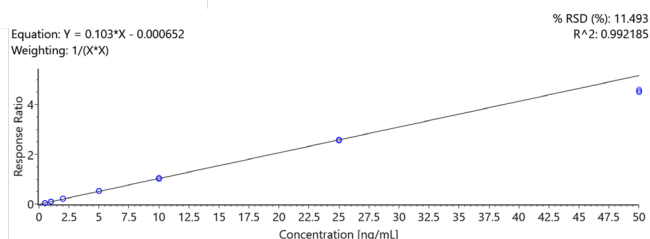
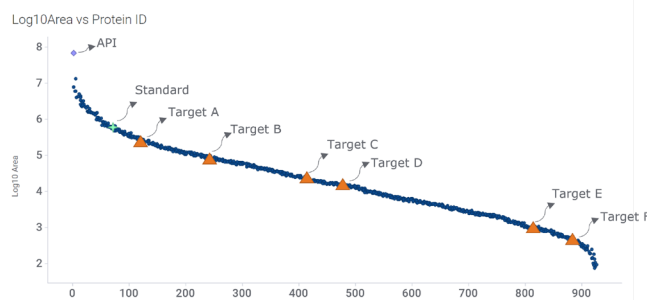


Target Quantitation

Dynamic Range of Impurity Proteins

Simultaneously monitor low abundance HCP risks by building on the HCP discovery.

Fig. 1: Levels of targeted protein impurities can vary greatly across the purification process. Downstream column eluates typically contains HCP levels that are several logs lower than the therapeutic drug.



	Concentration (ng/mL)						
	0.5	1.0	2.0	5.0	10.0	25.0	50.0
Inj 1	0.048	0.102	0.223	0.532	1.054	2.591	4.491
Inj 2	0.045	0.112	0.221	0.543	1.010	2.548	4.601
Inj 3	0.053	0.109	0.221	0.532	1.054	2.588	4.539
%RSD	8.3%	4.8%	0.5%	1.2%	2.4%	0.9%	1.2%

Linearity and Reproducibility

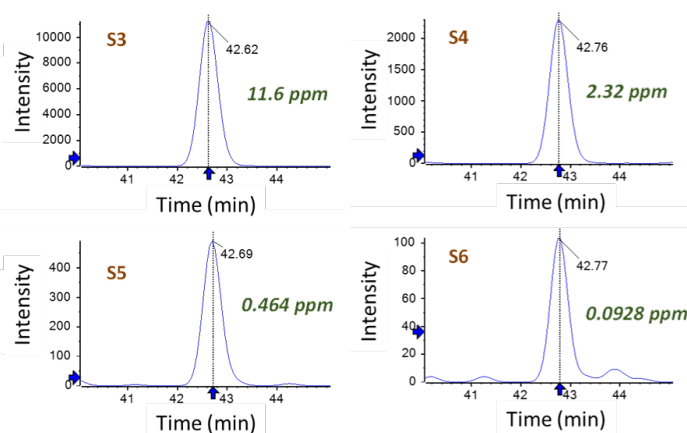
Make confident release decisions with consistent, reproducible, quantitative results

Fig. 2 - Linear regression analysis using $1/X^2$ weighting was performed and the slope, y-intercept, and R^2 are shown. Reproducibility from triplicate injections of each calibration curve point is shown as the coefficient of variation (%CV) and was less than 5% for all points greater than the LLOQ, and less than 10% at the LLOQ.

Signal to Noise for Target Proteins

Protect patient safety by detecting HCPs at the sensitivity levels that matter.

Fig. 3 – Signal to noise for surrogate peptides of various target proteins shows the ability to quantitate across a broad dynamic range.



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