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PII: S1570-0232(17)31040-1
DOI: https://doi.org/10.1016/j.jchromb.2017.11.043
Reference: CHROMB 20940

To appear in: *Journal of Chromatography B*

Received date: 12-6-2017
Revised date: 27-11-2017
Accepted date: 30-11-2017

Please cite this article as: Babita Saxena Parekh, Arvind Srivastava, Shanmuuga Sundaram, Ming Ching-Heish, Joel Goldstein, Michael Barry, Qinwei Zhou, Correlating Charge Heterogeneity Data Generated by Agarose Gel Isoelectric Focusing and Ion Exchange Chromatography Methods, Journal of Chromatography B https://doi.org/10.1016/j.jchromb.2017.11.043

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ABSTRACT

An isoelectric focusing method (IEF) has been used to assess the charge heterogeneity profile of a monoclonal antibody during the early stages of product development. A more precise and sensitive ion exchange chromatography (IEC/CEX) method was developed and implemented as development progressed and was used concurrently with IEF for lot release and to monitor charge heterogeneity. Charge variants resolved by both methods (IEC and IEF) were purified and characterized. Tryptic peptide mapping and N- linked oligosaccharide profile analyses of the IEC and IEF fractions indicated a structural correlation between the charge variants separated by these two methods. The major sources of molecular heterogeneity were due to the variation in the sialyated carbohydrate structure and heavy chain C-terminal lysine truncation. By monitoring the rates of change in the charge heterogeneity profiles of the monoclonal antibody stored at elevated temperatures by the IEC and IEF methods, a positive