Accelerated Capillary Electrophoreses Methods for Process Development and Clone Selection as a Medium Throughput Approach

Speeding up analyses while keeping resolution

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The development and production of recombinant biopharmaceuticals is a challenging field due to their structural complexity. When implementing a manufacturing process for new biopharmaceuticals or biosimilars, variations in the protein structure or post-translational modifications are likely to occur. Therefore, a characterization program is required.

Capillary electrophoreses methods such as cGE (capillary gel electrophoresis) or cIEF (capillary isoelectric focusing) support the characterization of physicochemical properties. While cGE provides information on purity, impurity and size distribution, cIEF is applied to investigate the characteristic charge profile or the specific isoelectric point of charged isoforms of biopharmaceuticals.

To support the fast development timelines of biopharmaceuticals, the throughput of analytical methods for protein characterization needs to be increased. In terms of sustainability and costs, high throughput methods are desirable, especially in early stages of process development or clone selection. High throughput CE methods (e.g. based on chip technology) however often result in drastic loss in resolution and thus, potentially in loss of information. A compromise in terms of speed and resolution is therefore required to rapidly have access to important physicochemical information on early stage biopharmaceutical products.

Here we present data for two complex mAb market products (IgG4 and IgG1), obtained with medium throughput methods for cGE and cIEF. Compared to results acquired with the respective methods optimized for high peak resolution, no significant differences are observed. The optimized methods can be performed in at least half of the time and with less sample material, making them less cost-intensive but qualitatively comparable. These medium throughput CE methods thus are convenient for the analysis of quality attributes such as purity, impurity and charge variant characterization in early stage development.