UPSTREAM CONTROL STRATEGY DEVELOPMENT FOR AFUCOSYLATED SPECIES IN MAB BIOMANUFACTURING

Jianlin Xu, Bristol Myers Squibb, USA
jianlin.xu@bms.com
Khandaker Siddiquee, Bristol Myers Squibb, USA
Adam Rish, Bristol Myers Squibb, USA
Zhuangrong Huang, Bristol Myers Squibb, USA
Yashika Singh, Bristol Myers Squibb, USA
Johanna Santos, Bristol Myers Squibb, USA
Jianfa Ou, Bristol Myers Squibb, USA
Emily Rittershaus, Bristol Myers Squibb, USA
Xuankuo Xu, Bristol Myers Squibb, USA
Grace Yao, Bristol Myers Squibb, USA
Melissa Holstein, Bristol Myers Squibb, USA
Kitty Agarwal, Bristol Myers Squibb, USA
Gregory Keil, Bristol Myers Squibb, USA
Linda Hoshan, Bristol Myers Squibb, USA
May Ou, Bristol Myers Squibb, USA
Lakshmi Kandari, Bristol Myers Squibb, USA
Ji Zheng, Bristol Myers Squibb, USA
Dan Huang, Bristol Myers Squibb, USA
Gabi Tremml, Bristol Myers Squibb, USA
Michael Borys, Bristol Myers Squibb, USA
Sanchayita Ghose, Bristol Myers Squibb, USA
Anurag Khetan, Bristol Myers Squibb, USA

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Afucosylated species consist of N glycans lacking the fucose residue, i.e., G0, G0-GN, G1, G2, Man5, and all other high mannose species. Afucosylation is one of the key quality attributes for those monoclonal antibodies (mAb) where effector function is mediated through CD16a such as antibody dependent cellular cytotoxicity which determines product efficacy or potency. A small change in afucosylation may cause a big change in CD16a binding activity and product potency. Biomanufacturing consists of upstream and downstream portions. Many upstream parameters, e.g., cell line, media, and bioreactor conditions, may have an impact on afucosylation levels in the final drug substance, while downstream processing has minimal impact. To maintain consistent product quality and potency, controlling afucosylated species via upstream process and analytical strategies is important throughout the entire product and process development phases for mAb products. In this study, we compiled thousands of upstream parameters and afucosylation data points for 10 different mAb products at various clinical stages. Empirical and PLS model-based data analyses were performed to identify key upstream parameters that impacted afucosylation levels. Some of those parameters applied to all different cell line and mAb products, while other parameters are cell line dependent. As a resource for future projects, upstream process levers for controlling afucosylation were summarized, which can be used for effective control of afucosylation levels from early to late upstream process development and biomanufacturing.