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Title- Development of an Enriched CHO Feed Media for Quality Therapeutic Antibody Production from High Performing Clones

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Abstract-

The use of feed media during protein production is essential to sustain viable cell densities and facilitate high productivity for modern high performing clones. However, the introduction of feed media can also have a significant impact on product quality attributes, such as glycosylation for therapeutic antibodies, which can ultimately impact therapeutic efficacy. For certain antibodies, the absence of fucose on the Nglycan at Asparagine 297 of the Fc domain has been shown to significantly increase binding to the FcgammaRIII receptor on NK cells and results in increased ADCC activity. Here we have incorporated product quality analysis including N-glycan analysis into our product development process for a new CHO feed media. Since ADCC is a critical part of the mechanism of action for our antibody of interest, we monitored the impact of feed media optimization on the N-glycan profile during development. Through optimizations to the feed media, we increased antibody titers by 3-fold compared to batch conditions and 10% compared to a benchmark feed. Whereas the benchmark feed significantly changed overall N-glycan profile compared to batch, optimization of our feed media allowed the overall N-glycan profile to remain similar to the batch. However, the percent fucosylation was similar across these conditions. The ADCC functional activity of these antibodies was then compared using an *in vitro* reporter assay. Antibody produced using our new feed media maintained the potency (EC_{50}) and efficacy (maximal fold-induction) in ADCC activity compared to batch and the benchmark feed conditions. By monitoring the impact of Nglycosylation on ADCC activity during our feed development process, we were able to ensure that our lead feed media maintained a critical quality attribute while successfully improving antibody titer.