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## NMR-BASED DESIGN OF CHEMICALLY-DEFINED PROTEIN-FREE FEED MEDIUM FOR THE CHO EXPRESSION SYSTEM

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Recombinant expression of antibodies and other biotherapeutics relies heavily on the use of CHO cell lines. The product expression levels in these cell lines are dependent on the feed medium, one of the most important components of the cell culture process. We have developed a systematic approach to designing a chemically-defined feed medium through collaboration between Merck's Process Development and Assay Development groups. Historically, feed media have been derived from non-chemically defined sources, such as bovine serum and yeast hydrolysate. While these media support robust cell growth and productivity, their chemically-complex nature has hindered efforts to increase the cells' productivity. It has also caused process performance variability at manufacturing scale because of the lack of controls used in the production of these complex raw materials. Merck's Nuclear Magnetic Resonance (NMR) capability has enabled us to identify the nutrients that yeast hydrolysate supplies and their consumption rate. We then used this information to iteratively design, test, and redesign a chemically defined feed medium. After three rounds of iteration, we were able to achieve 93% of the production reached with yeast hydrolysate. These results validate the NMR-based approach for feed design. Additional rounds of design are planned to continue increasing productivity, beyond the benchmark set by yeast hydrolysate.