

TARGETED MODULATION OF BIOCHEMICAL PATHWAYS TO OPTIMIZE THE BALANCE BETWEEN PRODUCTIVITY AND PRODUCT QUALITY IN BIOSIMILARS

Rama Bhupal Reddy Kandula, Upstream Process development, Biologics, Dr. Reddy's Laboratories Limited, Hyderabad, India.

ramabhupal@drreddys.com

Vikas Chandrawanshi, Upstream Process development, Biologics, Dr. Reddy's Laboratories Limited, Hyderabad, India.

Sampath Kumar Veeramally, Upstream Process development, Biologics, Dr. Reddy's Laboratories Limited, Hyderabad, India.

Suman Bandyopadhyay, Product Development, Biologics, Dr. Reddy's Laboratories Limited, Hyderabad, India.

C Nirmala Raju, Product Development, Biologics, Dr. Reddy's Laboratories Limited, Hyderabad, India.

Key Words: Process optimization, Targeted modulation, Biochemical pathways, CQA, Biosimilars

Process development for therapeutic protein production by maintaining desired quality attributes along with good productivity is a major challenge in today's competitive market of Biosimilar industry. The rapid growth in product demand has triggered for improvement in cell culture processes, in order to improve product titers, which often lead to undesired impact on critical product quality attributes (CQAs). Controlling the charge heterogeneity of monoclonal antibodies is essential due to its potential impact on structure, stability and function. There is enough evidence in literature to recommend that acidic species variants in the CDR of Fab region has a substantial effect on antigen binding and thereby on potency. In this study, we modulated product quality through targeting specific biochemical pathways, such as, oxidation, deamidation and glycation, to control charge variants species within the desired ranges, along with balancing the strategy that have been adopted to increase the protein productivity. In another instance, we were able to create a design space by altering the redox environment of the cell culture process to optimize a specific type of size variant, i.e., non-covalent dimers (Monomer), for a therapeutic fusion protein.