

VALIDATION OF THE MODEL-BASED CELL CULTURE MEDIA DESIGN PLATFORM “CELIA” FOR BIOMASS AND PRODUCT OPTIMIZATION IN A BIOREACTOR SETTING

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Key Words: Mammalian Cell Culture, Media optimization, Metabolic model.

The relevance of establishing local biopharmaceutical manufacture processes for human use products has become patent in recent years. To ensure the competitiveness of these processes, tools for increased productivity and robust process scale-up are required.

A key aspect for obtaining a good product yield in mammalian cell-based production processes is to keep operation conditions necessary for cell growth and maintenance throughout the process. In this context, the use of culture and feeding media that specifically provides the requirements of the production system are essential. Guaranteeing these conditions since process design stages to ensure a stable yield from a small-scale process design stage to a manufacture can still be a challenge. To address this problem the model-based cell culture media design platform for biomass and product optimization, CELIA (CELL culture media optimization), was developed. By integrating cell and product composition and characteristic process parameters, in a platform based on a detailed dynamic metabolic model with optimizable parameters, we are able to predict the specific nutritional requirements of a given cell line in a specific production process in order to design a specific media composition and feeding strategy customized for each production system. From this, an optimized fed-batch process design is obtained where the feed is based on nutritional requirements of the cells for maintenance, growth, and production.

Results obtained at a laboratory scale showed a significant increase in biomass for the model cells considered PK15, HEK293 CHO-tPA, ranging from 151% to 355% with respect to batch cultures. These findings are validated in a semi-industrial setting before transferring them to the industrial productive set-up. In addition, other industrially relevant cell lines are considered in the validation process.

The platform CELIA has high potential for contributing the development of biopharmaceutical and biosimilar production processes by increasing productivity and robustness of the process from its design stage.

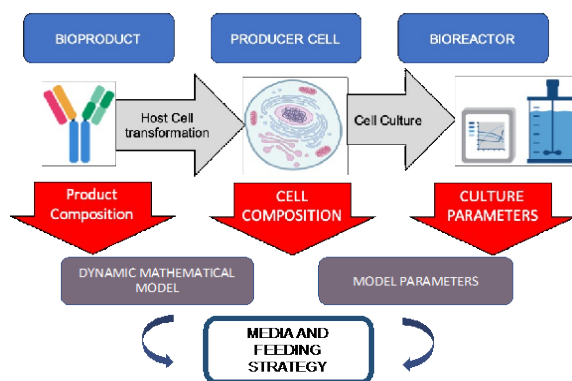


Figure1: Diagram for the operation of the CELIA Platform