

# Optimization and Control of Monoclonal Antibody Product Quality Using a Media and Process Toolbox Approach

Min Zhang, Meghan McCann, Stewart McNaull, Tim Hill

Upstream Process Development, FUJIFILM Diosynth Biotechnologies, U.S.A., Inc.

3000 Weston Parkway, Cary, NC 27513. Email: [min.zhang@fujifilmdb.com](mailto:min.zhang@fujifilmdb.com). Phone: 919-388-5672

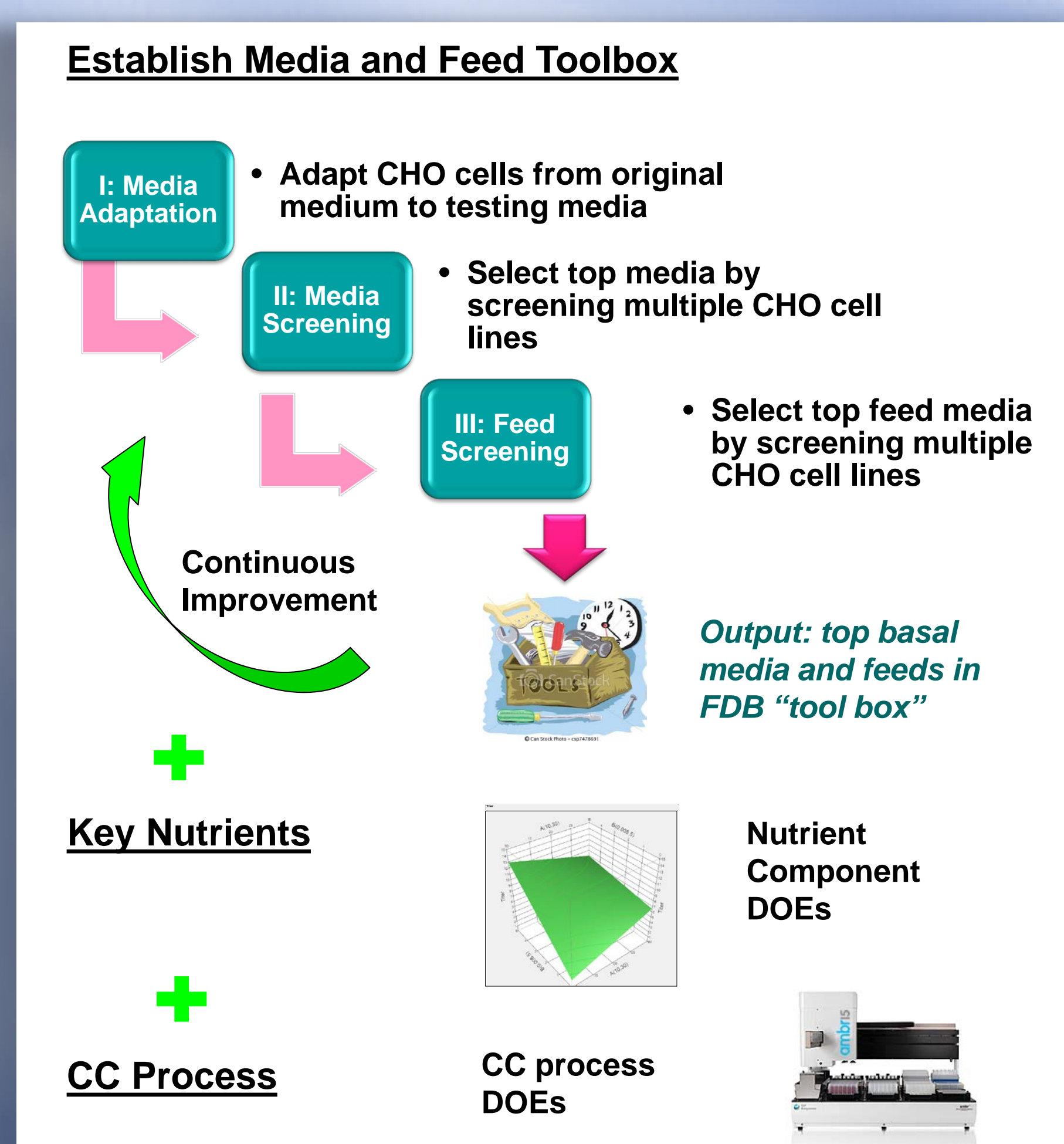
## Introduction

The complexity of cell culture processes, including media chemistry and process conditions, presents significant challenges to achieving desired monoclonal antibody (mAb) product quality optimization and control during process development, and scale up to manufacturing. To address these challenges, we present a development strategy targeting media, feeds, and process conditions using an established "tool box" approach. With this strategy, a variety of recombinant CHO cell lines were screened using a panel of basal media and feeds representing proven best of class commercially available and custom formulations. CHO cell lines studied cover a broad diversity with varied host genetic background (i.e. DG44, DXB11, GS-CHO, CHO-S). The toolbox approach generated strong improvement in cell culture performance including titer and cell growth with significantly reduced development time, and clearly showed that different media and feed combinations dramatically impact product quality profiles. A number of nutrient components were identified with clear linkage with selected product quality attributes (e.g. N-glycans) in nutrient component DOE studies, which adds more flexibility and capability to optimize and control product quality to the desired ranges by using the toolbox strategy along with cell culture process condition optimization.

## Cell Culture Toolbox Approach

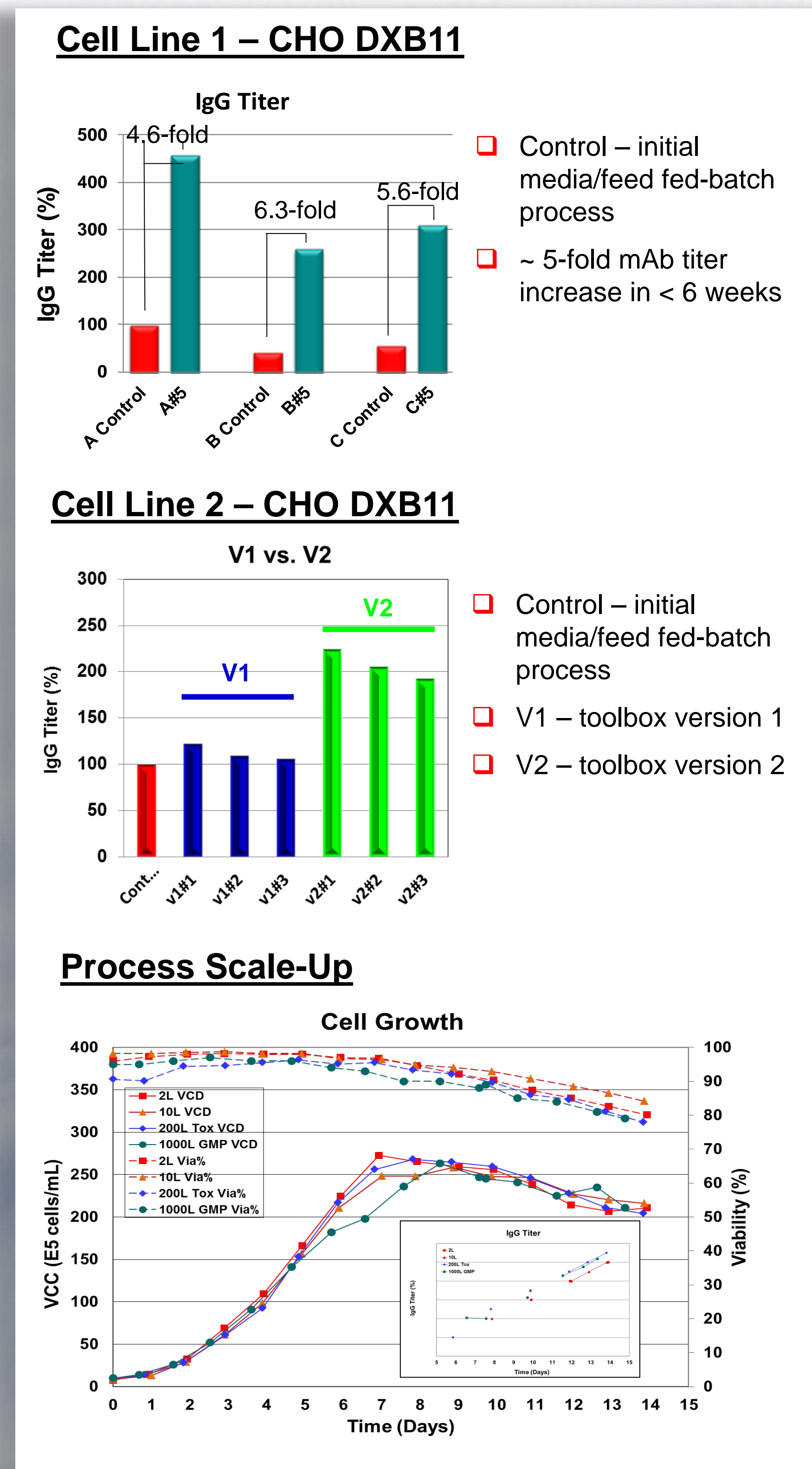
- GREAT DIVERSITY** – Establish a high-performance media and feed tool box by screening a panel of good quality basal media and feeds in wide variety of CHO mAb-producing cell lines with varied genetic background (DG44, DXB11, GS-CHO, CHO-S)
- EXTRA CAPABILITY** – Identify nutrient components with significant impacts on cell culture performance and product quality by Nutrient Component DOEs
- CELL CULTURE ENTITY** – Establish an effective "tool" as an intact development package along with cell culture process knowledge to optimize and control cell culture and product quality, with reduced development time. The toolbox knowledge would possibly save significant development time (weeks to months) for clients

## Development Strategy



## Demonstration in Cell Culture

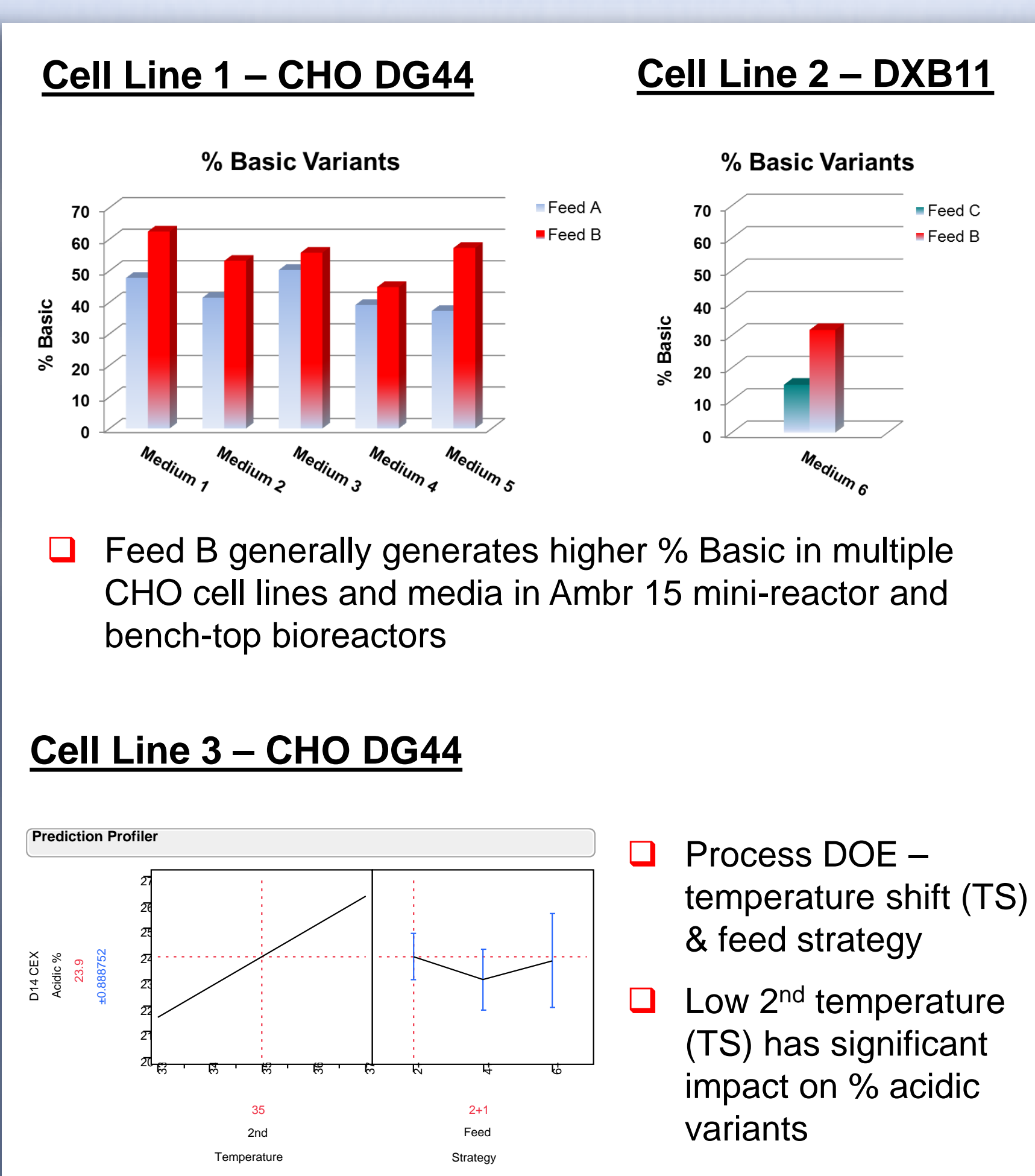
- Efficacy and efficiency of media and feed toolbox on cell culture performance improvement have been well demonstrated in multiple CHO cell lines
- Continuous improvement – advanced versions, toolbox version 1 to toolbox version 2
- Great process scale-up demonstration



## Product Quality Optimization

Toolbox Media/Feed/Process

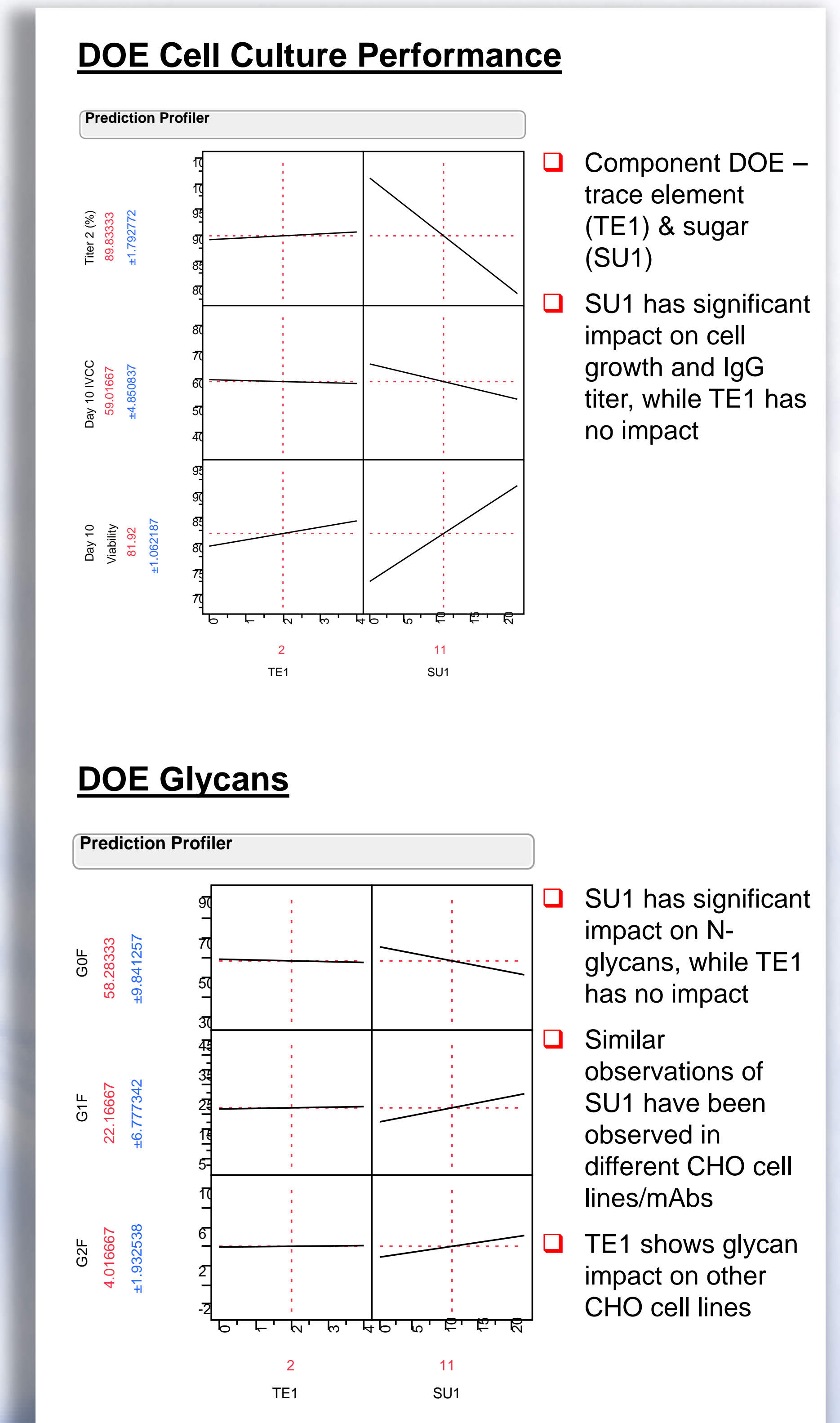
- Identify media/feed with common impact on product quality attributes
- Temperature shift has significant impact on mAb charge variants



## Product Quality Optimization

Nutrient components

- Component DOE – identify nutrient components impacting product quality
- Diversity check – multiple cell lines and processes



## Conclusion

- Fujifilm Diosynth Biotechnologies (FDB) has established a media/feed toolbox approach to target cell culture optimization and product quality optimization
- The superior cell culture performance including cell growth, titer, and process scalability has been demonstrated in multiple CHO cell lines, with a "continuous improvement" strategy
- The toolbox knowledge including media, feeds, cell culture process, and nutrient components provides flexibility and feasibility to optimize and control product quality to the desired range

## Acknowledgement

- FDBU Upstream team
- FDBU Analytical team
- FDBK Cell Line Development team
- FDB management