

# Fusion of Enhanced Cell Performance with Improved Productivity: Development of a Robust Chemically Defined Formulation for Culture of Chinese Hamster Ovary Cells

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## Introduction

Undefined components, such as protein hydrolysates, have been routinely used in the biopharmaceutical industry to boost the growth and productivity of recombinant protein-producing Chinese Hamster Ovary (CHO) cells in culture. Due to regulatory concerns and the variability associated with these components, a need for chemically defined (CD) basal formulations has emerged. SAFC Biosciences (SAFC) has offered CD formulations in the past and has now expanded on that knowledge and expertise to develop a novel chemically defined formulation that yields both good growth and productivity for cultured CHO cells. This most recent medium, EX-CELL™ CD CHO Fusion, has shown enhanced performance in batch culture alongside legacy SAFC formulations as well as competitive performance against formulations available from external vendors. In addition, EX-CELL™ CD CHO Fusion shows good performance in fed-batch culture utilizing various plant hydrolysates as well as proprietary chemically defined feeds.

## Materials and Methods

### Cell lines and media:

Four recombinant IgG-producing test cell lines (Table 1) were initially maintained in EX-CELL™ CD CHO Fusion (SAFC Biosciences) and supplemented appropriately.

CELL LINE	PARENTAL	MEDIA SUPPLEMENT
1	CHO-S Derived	6mM L-Glutamine
2	CHO-S Derived	6mM L-Glutamine
3	CHOK1SV*	25µM methionine sulphoximine
4	CHOK1SV*	25µM methionine sulphoximine

\*Licensed from Lonza Biologics

All legacy SAFC Biosciences formulations compared to EX-CELL™ CD CHO Fusion (SAFC Biosciences) were chemically defined.

For competitor assays, five CD formulations were tested alongside EX-CELL™ CD CHO Fusion (SAFC Biosciences). All stocks were adapted over at least five passages in each test condition before initiation of growth and productivity assays.

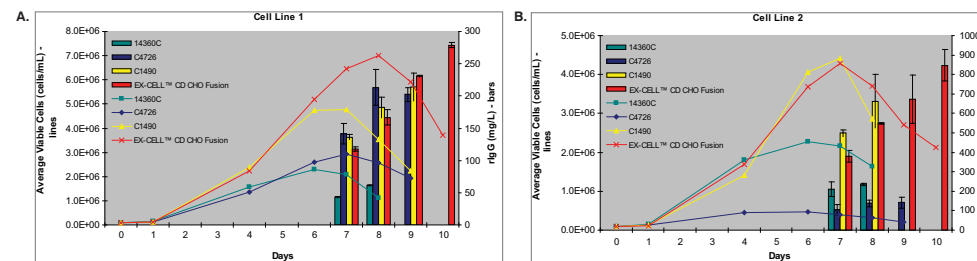
In the fed-batch assays, EX-CELL™ CD CHO Fusion (SAFC Biosciences) was supplemented on days two and four of culture with 3 g/L glucose and either 10% initial culture volume of proprietary chemically defined feed or 1g/L hydrolysates, where appropriate.

For each assay, cultures were inoculated directly from stocks into TPP® (Techno Plastic Products AG) 50ml bioreactor tubes and conditions were averaged after being evaluated in duplicate. Cultures were seeded at 2-3 E5 cells per milliliter and terminated when viabilities decreased to less than 70%.

### Productivity assay:

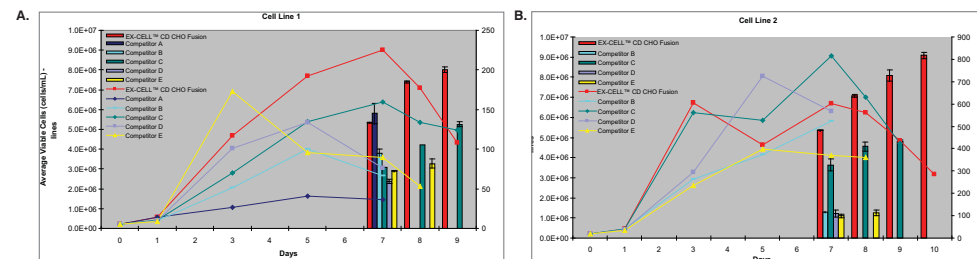
Human IgG: IgG concentrations were quantitated using the Octet QK Bio-Layer Interferometer (ForteBio).

## Results



**Figure 1. EX-CELL™ CD CHO Fusion compared to legacy SAFC Catalog formulations.**

A) Cell Line 1, B) Cell Line 2. CHO cells were screened with all the chemically defined catalog formulations currently available from SAFC Biosciences. As seen from improvements in both growth and productivity, EX-CELL™ CD CHO Fusion demonstrates the progress that has been made in the development of chemically defined formulations that can produce high cell densities and IgG titers.

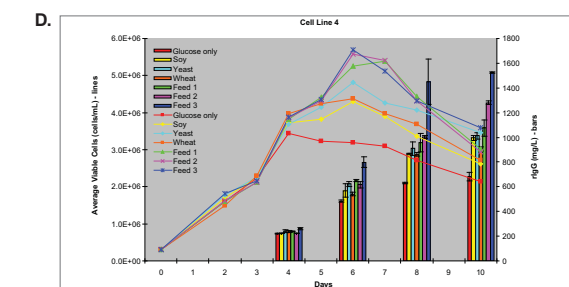
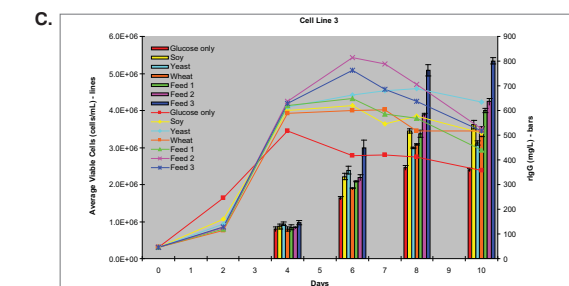
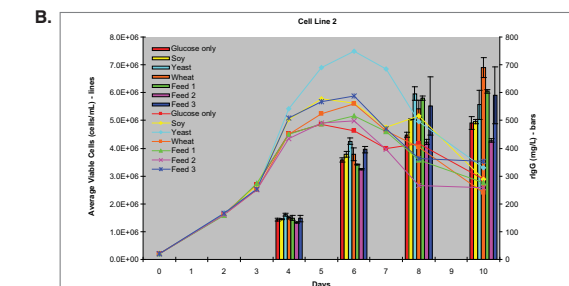
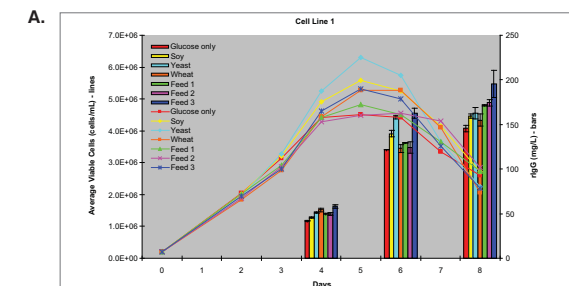


**Figure 2. EX-CELL™ CD CHO Fusion compared to five competitor formulations.**

A) Cell Line 1, B) Cell Line 2, C) Cell Line 3. Results show the differences in the viable cell densities and cumulative IgG productions of each cell line. In each experiment, EX-CELL™ CD CHO Fusion is competitive for cell growth and is superior for productivity. The overall performance of EX-CELL™ CD CHO Fusion demonstrates its versatility among cell lines and competitiveness with other formulations available for CHO cell culture. Note: Competitor A did not survive the adaptation process for Cell Line 2 so was not included in the assay.

## Conclusions

- SAFC Biosciences has developed a novel chemically defined formulation called EX-CELL™ CD CHO Fusion.
- EX-CELL™ CD CHO Fusion exceeds the overall performance of legacy SAFC chemically defined catalog offerings.
- When used alongside chemically defined competitor formulations, EX-CELL™ CD CHO Fusion achieves competitive growth and superior cumulative productivity.
- EX-CELL™ CD CHO Fusion can be used as a robust platform formulation that, when complimented with the appropriate CD feed, effectively replaces the need for undefined components to yield increased IgG production.



**Figure 3. Fed-batch comparison in EX-CELL™ CD CHO Fusion using three plant hydrolysates and three chemically defined feeds.**

A & B) Cell Lines 1 and 2, C & D) Cell Lines 3 and 4. While the degree to which feeds improve culture performance is cell line dependent, the data show that EX-CELL™ CD CHO Fusion can be used in combination with multiple defined and undefined feeds to enhance growth and productivity of CHO cells.