SIGMA-ALDRICH®

NEXT GENERATION MEDIA SYSTEM

PERFORMANCE
CHO MEDIA

EX-CELL® ADVANCED™ CHO FED-BATCH SYSTEM

SAFC®

Introducing the newest cell culture product line by SAFC

EX-CELL® Advanced™

The performance you expect with the peace of mind needed in a world of increasing regulatory and supply pressures. EX-CELL Advanced products offer enhanced performance, assured regulatory compliance, and the security of supply required for today's biopharmaceutical environment.

NEXT GENERATION CHEMICALLY-DEFINED PRODUCTS

Developed from a leading scientific team supporting industrial biopharmaceutical applications for more than two decades:

- Elimination of all non-essential components
- Improved inter and intra lot to lot consistency
- Road-tested to ensure scalable bioreactor performance

PROVEN MANUFACTURABILITY AND CONSISTENCY

World-class supplier of cell culture media for clinical and commercial bio-manufactured products:

- Scalable GMP-ready product
- Stable dry and liquid media formats
- Multi-site manufacturing redundancy

ROBUST AND SUSTAINABLE SUPPLY CHAIN

Lower risk profile for improved business continuity:

- Single Global Supplier Quality Management program
- Well Characterized Critical Raw Materials
- Raw material transparency, traceability, and documentation

COMPREHENSIVE FORMULARY SUPPORT

A commitment to providing value beyond performance:

- Competitive pricing
- Unburdened Intellectual Property
- Collaborative regulatory support

EX-CELL Advanced CHO Fed-batch System

Cat. No.	Description	Format	Media Category	Composition									
				Amino Acids	Vitamins	Trace Elements	Lipids	Growth Factors	Glucose	Hydrolysates	Glutamine	Hypoxanthine / Thymidine	Phenol Red / 2-Mercaptoethanol
14366C	Fed-batch Medium	Liquid	ACF/Chemically Defined	•	•	•	•	•	•				
24366C	Fed-batch Medium	Powder	ACF/Chemically Defined	•	•	•	•	•	•				
24367C	Feed 1 w/glucose	Powder	ACF/Chemically Defined	•	•	•	•	•	•				
24368C	Feed 1 w/o glucose	Powder	ACF/Chemically Defined	•	•	•	•	•					

PRODUCT DESCRIPTION

EX-CELL Advanced CHO Fed-batch Medium and Feeds are chemically defined and contain no animal derived components. This newest system from SAFC has been specifically developed to support growth and productivity across a diverse set of Chinese Hamster Ovary (CHO) cells in fed-batch cultures while still allowing for flexibility in the adjustment of protein quality attributes.

SAFC Cell Sciences and Development Team developed a contemporary fed-batch system using applied mathematics (multivariate analysis, data mining) to establish correlations of characterized raw materials to critical process and product attributes such as doubling time, specific productivity, waste product formation, and charge variance.

EX-CELL Advanced CHO Fed-batch Media and Feed System

PERFORMANCE

STUDY 1 DESIGN

Three distinct model CHO cell lines (CHO S, CHO dhfr, CHOZN® GS) were selected for a comparative evaluation of the EX-CELL Advanced CHO Fed-batch System and leading commercially available CHO cell culture media and feed supplements from three different vendors. All cultures were monitored for viable cell density, metabolites, and antibody (IgG) titer up to day 14.

Culture Conditions

- TPP bioreactor tube cultures
- 200 rpm / 50 mm orbital diameter
- 37 °C, 80% RH, 5% CO_2 (Note: 8% CO_2 with CHO S)

Feed Strategy

- 5–10% (v/v) bolus addition on culture days 3, 5, 7, 9 and 11
- Glucose concentration maintained above 4 g/L

RESULTS

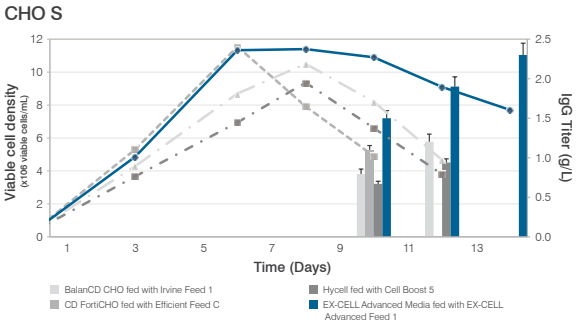


Figure 1: Viable cell density and productivity comparative at TPP tube scale

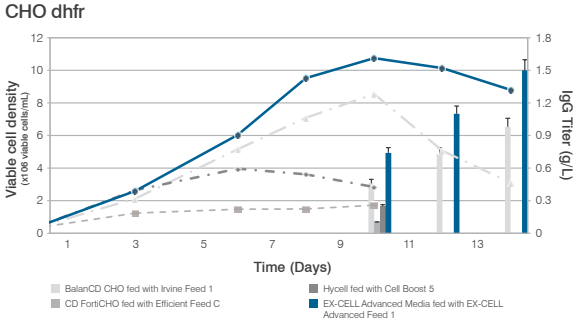


Figure 2: Viable cell density and productivity comparative at TPP tube scale

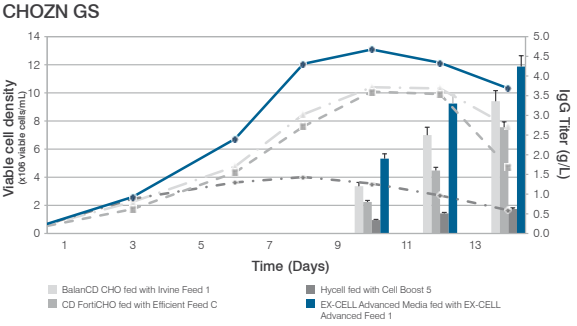


Figure 3: Viable cell density and productivity comparative at TPP tube scale

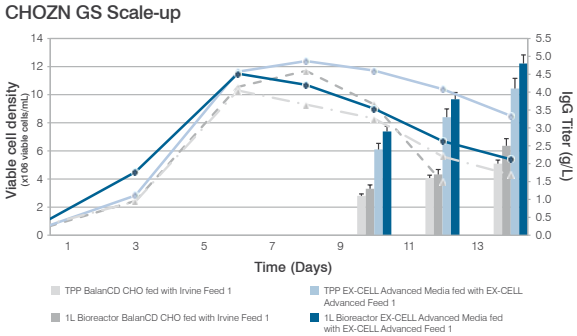


Figure 4: Demonstrates the scalability in the performance of the EX-CELL Advanced CHO Fed-batch System. Study comparison between SAFC's small scale model (TPP tubes) and 1 L benchtop bioreactor (BioStat Q+) using the top competitor media and feed products in the CHOZN cell line. Parameters were as follows: pH 6.9, DO 40%, and temperature 37 °C.

STUDY 1 CONCLUSION

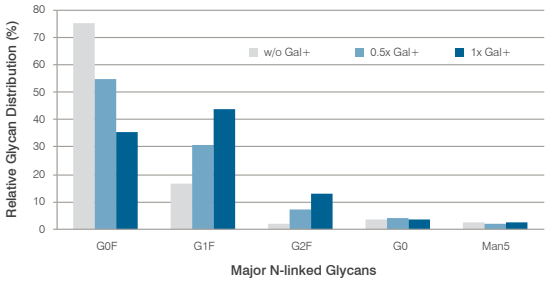
The EX-CELL Advanced CHO Fed-batch System demonstrated a sustained high biomass with maximum titers across all model cell lines. Moreover the optimized media and feed combination by SAFC outperformed other leading commercial fed-batch products with a 2–4 fold increase in titer. Scalability of the EX-CELL Advanced CHO Fed-batch System was also demonstrated in a direct comparative of performance from SAFC's validated fed-batch culture model in TPP to 1 liter bioreactor yielding >4.5 g/L IgG titer.

DIRECTING PROTEIN QUALITY

STUDY 2 DESIGN

EX-CELL® Advanced™ CHO Fed-Batch System in combination with our Protein Quality Supplement, (Cat. No. 14701C) was evaluated for impact on protein quality. CHO GS cells were banked, thawed, and passaged 3 times. Cultures were fed 7.5% (v/v) EX-CELL Advanced CHO Feed 1 on culture days 3, 5, 7, 9 and 11. Glucose concentration was maintained above 4 g/L. Additionally, EX-CELL Glycosylation Adjust (GAL+) was supplemented beginning on day 2 and every other day through day 10 of the 14 day fed-batch culture. Culture supernatants were harvested on Day 14 for purification and analysis. No differences were observed in Viable Cell Density, Viability, and Titer.

Directing Glycosylation in EXCELL®Advanced™ Fed-batch System



STUDY 2 CONCLUSION

The EX-CELL Advanced CHO Fed-batch system is responsive to simple and effective means for directing consistent product quality as demonstrated by the supplementation of the culture with EX-CELL Glycosylation Adjust (GAL+).

SAFC is proud to offer a set of contemporary media products that are easy-to-use and give a system performance to help achieve maximum titers and consistent product quality during development. Both media formulations have established stability profiles in both powder and liquid formats. Stability for the one-part low volume addition includes 30d stability after rehydration at room temperature to allow for flexibility and efficiency during production. The EX-CELL Advanced CHO Fed-batch System sets a new benchmark in fed-batch culture media for product consistency, productivity, and reliability you demand.

PRODUCT HANDLING AND STORAGE

Product handling using aseptic techniques is required to avoid contamination. Do not use if cloudy or if solution has precipitated. Other evidence of deterioration may include color change, pH shift or degradation of physical or performance characteristics.

Powder medium formats should be stored in the original container at 2 to 8 °C and protected from moisture. Evidence of deterioration may include clumping, color change, and/or consistency in powder. Liquid media may be stored for up to 1 year at 2 to 8 °C and protected from light. Storage of feed media after rehydration (Cat. No. 24367C and Cat. No. 24368C) at room temperature, protected from light for up to 30 days. Do not use after 30 days. Refer to product label for rehydration instructions and/or visit sigma-aldrich.com/CHOperformance.

INTENDED USE

This product is intended for Further Manufacturing Use in the bio-manufacturing industry. It is not intended or approved for *in-vitro* diagnostic use in the human or veterinary industries.

FORMULATION SUPPORT

SAFC is committed to providing all necessary support for proprietary products including EX-CELL Advanced CHO Fed-batch System. The disclosure process to support Regulatory Filing is simple and available upon request. Our team will rapidly respond and address any technical concerns with the media performance. Please contact Quality Services department for any support needed.

RELATED PRODUCTS

SAFC offers the following products which are intended for use with EX-CELL Advanced CHO Fed-batch Media System. EX-CELL Glycosylation Adjust (GAL+) allows developers to easily achieve desired N-linked glycosylation by increasing the galactose site occupancy on the oligosaccharide to a higher level.

Cat. No.	Description	Format	Size
14701C-100ML	EX-CELL® Glycosylation Adjust (GAL+)	Liquid	100 mL
14701C-1000ML	EX-CELL® Glycosylation Adjust (GAL+)	Liquid	1000 mL

For additional information, visit
sigma-aldrich.com/finishfaster

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