SWITCH PROGRAM

CELLiST™



Accelerate Your Success with Our 'Switch Program' – An End-to-End Media Transition Solution

What is the ‘Switch Program’?

Our end-to-end Switch Program supports the seamless transition to new CELLiST™ cell culture media, reducing production costs and ensuring optimal compatibility with your biopharmaceutical processes. Our dedicated team partners with you to ensure your goals are met seamlessly and efficiently.

Included in the service

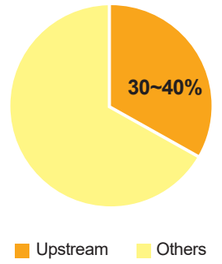
Comprehensive support for custom media development, achieving higher productivity and optimal protein quality, all aligned with your production goals and completed in a shorter timeframe.

Timeline

The timeline for the Switch Program ranges from 4 months to 1 year, depending on the selected approach, with ongoing support to ensure a seamless transition aligned with your production needs.

Benefit of ‘Switch Program’

[Breakdown of Cost of Goods Sold (COGs)]



Our Switch Program offers exceptional cost-efficiency by reducing a major component of upstream costs, which are media expenditures. Upstream process costs account for 30-40% of total bioprocess expenses. By switching to high-performance, cost-effective media and reducing batch numbers, our Switch Program can significantly lower labor, consumable, and operational costs. Additionally, it can help reduce downstream processing costs, further enhancing operational efficiency.

Seamless 'Switch Program'

Experience a hassle-free transition with our Switch Program. Our end-to-end service encompasses not only the development of optimized media but also comprehensive change control support, ensuring a smooth and efficient process throughout.

Switch Program

End-to-end Service

Project Initiation

- Receive and Acknowledge Customer Inquiries
- Execute Project Agreements (NDA, MTA)
- Establish Project Scope
- Initiate Material Transfer

"Media Switch"

- Media screening
- Spent Media Analysis
- Media optimization
- Process Optimization (optional)
- Prototype production
- Final Evaluation
- Reporting

*The details are described on the next page.

Support during PV and Regulatory Approval

- Data generation for change control (if required)
- Documentation support for regulatory approval

Media Switch: Full Media Development Service

Media Screening
- **Prerequisite:** Customer must provide cell line
- Media library screening
- Feed media selection
- Feeding strategy optimization

Media Optimization
- Spent media analysis to optimize critical components
- Media formulation adjustments
- Cell culture test for validation of optimized formulations

Advanced Optimization
- Critical process parameter (CPP) optimization
- Protein quality control

Prototype Production
- Prototype media production (non-GMP)

Final Evaluation
- Cell culture test for comprehensive evaluation of finalized media
- Deliverables transfer including prototype media
- (Optional) Cell culture test in benchtop bioreactor (2L)
- Continuous consultation on process development

Note: Workflows and service details are fully customizable to meet customer requirements.

Media Switch: Fast-Track Media Fine-tuning Service

Media Screening (at Customer Site)
- Panel media transfer
- Media library screening at customer site

Spent Media Analysis
- **Prerequisite:** Customer must provide spent media
- Spent media analysis of key metabolites and amino acids
- (Optional): Protein quality analysis

Media Optimization
- Media formulation fine-tuning

Prototype Production
- Prototype media production (non-GMP)

Final Evaluation (at Customer Site)
- Prototype media transfer
- Cell culture test for evaluation of finalized media at customer site

Is the Switch Program Effective?

Absolutely. Our Switch Program has a proven track record of successfully optimizing cell culture processes for various projects. As demonstrated in the case study below, we leveraged media development and a Quality by Design (QbD) approach to improve the cell culture process for a client's biosimilar pipeline. This effort contributed to the successful EMA approval of a biosimilar anti-cancer therapeutic, now advancing through commercialization.

Our program ensures smooth transitions with a focus on maintaining product quality and speeding up time-to-market.

[Case Study]

1. Media Development

Effort was put to maximize yield and match the glycosylation and charge variants (CV) profiles of the original drug. To develop the media, we created a starting medium from our in-house media library and utilized Ajinomoto Group's expertise in cell culture media to determine the final media composition. In addition, candidate components were tested for adjusting glycosylation and CV profiles. This process ensured not only consistent production of the target protein but also similarity of glycosylation and CV profiles to those of the original drug. Finally, subsequent process optimization led to a 27% increase in yield compared to the original media.

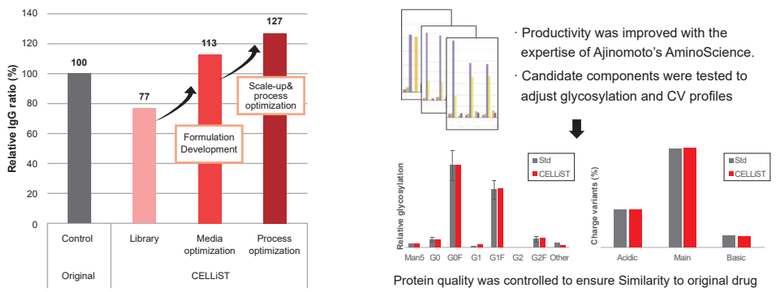


Figure 1. Process of media development for enhancing productivity and matching protein quality attributes.

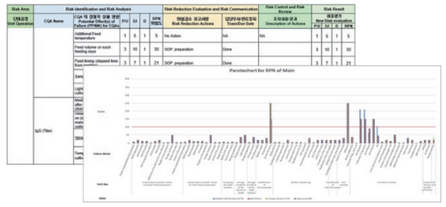
2. Process optimization using QbD approach

2.1 Risk assessment

Risk assessment involves procedures to ensure that the manufacturing process of pharmaceutical products does not compromise product quality and that the process consistently produces products meeting intended quality characteristics and specifications.

Failure Mode and Effects Analysis (FMEA) was employed to identify potential risk factors and critical process parameters (CPPs). The potential impact of critical quality attribute (CQA) failures was also evaluated, and prioritized CQAs were identified for subsequent experiments.

Unit operation risk assessment



Purpose

· Check potential risk factors
· Assess potential CPPs
· Discuss ways to reduce risks

Method

· Failure Mode Effects Analysis (FMEA)
· RPN = P/U x S/I x D

Figure 2. Unit operation risk assessment. Potential risk factors were assessed using FMEA method.

2.2 Design of Experiment (DoE) study

The objective of this stage was to conduct a DoE study of the main culture process as part of the QbD framework, within the process characterization studies of biopharmaceuticals. This study evaluated four different parameters: temperature, agitation, dissolved oxygen and pH, based on the results from the operational unit risk assessment of the main culture process. Cell cultures were performed accordingly, and CQAs were analyzed. This led to the development of a statistical model, investigating the relationship among CQAs, CPPs, and the identified design space. Finally, Monte Carlo simulations confirmed that the process is robust at the set point, along with the proven acceptable range (PAR) and normal operating range (NOR).

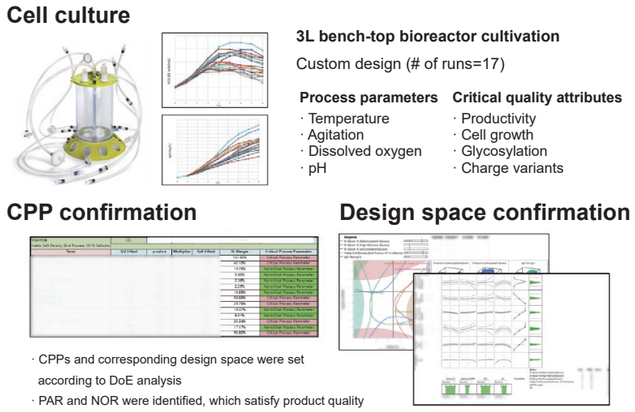


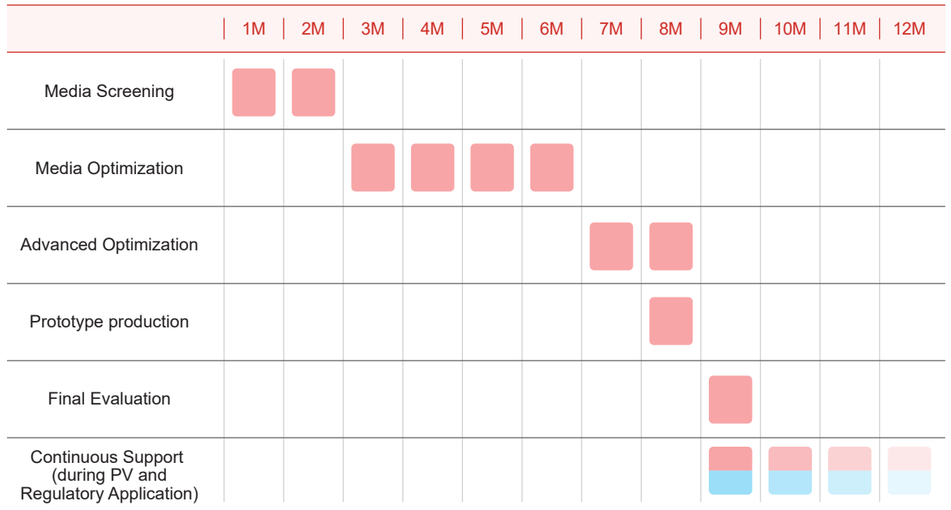
Figure 3. Design of Experiment (DoE) study conditions and analyzed entities including (1) CPPs confirmation and (2) Design space confirmation.

3. Conclusion

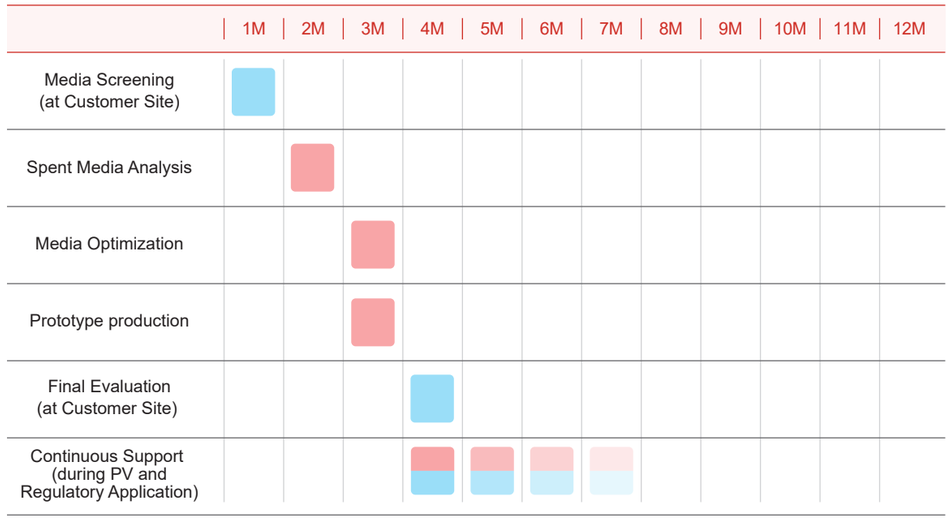
With the implementation of QbD approach and enhanced-performance customized media, this project not only achieved the optimization of the culture process but also ensured that the product consistently met its predefined quality criteria with greater predictability. As a result, production costs were reduced, and optimal compatibility was achieved, resulting in approval by the regulatory body.

Timeline

Media Switch by Full Media Development Service



Media Switch by Fast-Track Media Fine-tuning Service



**The timeline is dependent on customer requirements.

Blue color represents steps to be conducted at the customer site.

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For quoting, ordering, product sample request

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