Custom traditional and multi-omics media development enhances antibody production in CHO cells
Achieving titer increase up to 4-fold while maintaining product quality

**Situation**
Antibody manufacturers using CHO cell lines often seek to improve productivity to support scale-up for clinical trials or commercial production. Manufacturers are also required to maintain strict critical-to-quality (CTQ) antibody product attributes with scale-up. In addition, efforts are continually underway to reduce manufacturing costs—with increased antibody titers per run, the manufacturing cost may potentially be reduced. Manufacturers may also realize cost savings by optimizing formulations to remove or reduce components or by implementing a platform formulation for multiple molecules. Furthermore, manufacturers may realize scale-up storage and cost benefits by converting formulations from liquids to dry formats.

Titer improvements of at least 1.5- to 2.0-fold are often required to gain manufacturing cost reductions. This is particularly difficult since media and feeds are relatively complex. Achieving multiple goals, combined with this complexity, can make it challenging to identify an effective path forward. Additionally, manufacturers may not have the required experience, equipment, personnel, or time to dedicate to productivity optimization projects in house.

**Solution**
Manufacturers engaged Gibco™ Media by Design™ Services (formerly Gibco™ PD-Express™ Services) for their productivity optimization projects. These service projects are led by a group of experienced bioproduction scientists who have in-depth knowledge of the approaches and methods required to increase antibody productivity. The team is also supported with a dedicated project manager. A review of recent antibody optimization service projects with CHO cells has demonstrated the success of the team in helping clients achieve their desired goals.

The projects included some of the following service options:
- Basal, feed, or clone selection media optimization
- Platform medium development
- Feeding strategy or process optimization
- Product quality assessments and modulation
- Bioreactor verification
- Non-cGMP pilot formulation for customer evaluation
- Liquid to dry format conversion

**Results**
Selected productivity optimization projects conducted by the Media by Design Services teams over the last 5 years with CHO-K1, CHO-S, and DG44 cell lines showed strong improvement in antibody titers, consistently meeting or exceeding project goals to achieve at least 1.5-fold titer enhancement (Figure 1).
- In CHO-K1 cell lines, an average 1.8-fold titer improvement was achieved, with increases ranging from 1.5- to 2.1-fold
- In CHO-S cell lines, an average 4.4-fold titer improvement was achieved, with increases ranging from 4.2- to 4.7-fold.
- In a DG44 cell line, an average 3.0-fold titer improvement was achieved.

![Figure 1. Strong increases in antibody titer productivity achieved with optimization services.](image-url)
For selected projects, product quality was evaluated for glycan structures, charge variants, and aggregation, and the results were found acceptable (data not shown). Additionally, some projects achieved success with development of platform formulations. Requests for liquid media format conversion to a Gibco™ Advanced Granulation Technology™ (AGT™) medium or a dry powder medium (DPM) were also developed. Finally, many of the projects were scaled up in bioreactors, and the manufacturing feasibility of the optimized formulation was determined with non-GMP pilot production.

Optimization projects are conducted in a phased approach that can use either a traditional or multi-omics workflow. A typical traditional workflow can evaluate up to 50 metabolites. As outlined in Figure 2, after technology transfer, additional phases are conducted with multiple rounds of design of experiment (DOE) to develop media and feeds, with potential later phases for process optimization, format conversion, and pilot non-GMP production.

A multi-omics workflow typically evaluates up to 1,000 metabolites and 7,000 proteins. Following technology transfer, the metabolic baseline is established, and multi-omics data are analyzed and interpreted. Based on results of the multi-omics phase, a basal medium and feed DOE is performed, followed by medium, feed, and process optimization. As with the traditional workflow, format conversion and non-GMP production may be conducted (Figure 3).

These service projects have successfully helped clients achieve their desired goals through customizable flexible options, taking into consideration the client’s timeline, budget, and capacity constraints. With advanced facilities and technologies for cell culture and analytics, Media by Design Services is well suited to support clients with their productivity challenges.

From a company with 60 years of media development experience and more than 150 service projects completed, Media by Design Services can help clients meet their optimization goals of enhanced antibody productivity, potentially reduce manufacturing costs, and ultimately boost their ROI.

### Summary and discussion

The results presented demonstrate that Media by Design Services can effectively design and execute customized CHO-based antibody optimization projects. The project outputs provided manufacturers the ability to achieve their desired scale-up goals, including enhancing productivity, maintaining product quality, and potentially improving return on investment (ROI).

The design of each service project is flexible and customized based on the client’s productivity improvement goals, budget, and timeline requirements. The project can be structured in either of two ways: as a “consultation” (with experiments conducted by the client) or as “in-house” (with experiments done by the services team). Depending on the specific project workflow and scope, an antibody productivity optimization project is usually completed within 9 to 12 months. However, due to their customizable nature, specific project timelines can vary.