



## Key Challenges in Cell Line Development: Aragen's Comprehensive solutions

Biologics are quickly becoming a crucial component of the healthcare industry due to their significant role in the treatment of numerous diseases, including cancer, auto immune, and inflammatory disorders. However, building a reliable and reproducible process for efficient biologics production is not only technically challenging, but also necessitates modern infrastructure, high throughput technology, and adherence to regulatory norms.

Cell Line development (CLD) is the foundation of biologics manufacturing, employing living cells as production centers. Technically the process is extremely sensitive, with specific obstacles associated with each phase of the process.

Identifying the obstacles associated with CLD during the project's inception and the results being anticipated is crucial for making informed decisions for the project's successful completion. Here we discuss the challenges that different pharmaceutical companies experience while developing cell lines for biopharmaceutical manufacturing, as well as how Aragen makes smart decisions to assist the clients in overcoming these challenges.

### Challenges associated with the Cell Line Development

The cell line development procedure comprises several steps, beginning with correct gene design to bioreactor assessment of the transfected host cell lines. It is critical for service providers to understand the difficulties that each stage may encounter and optimize each step so that the process being built is efficient and provides clinical quality biologics in sufficient yield. Furthermore, for regulatory clearances, the process must be scalable at different bioreactor levels without compromising the product quality.

## Selection of the right host cell Line

The selection of the appropriate cell line is crucial for the biopharmaceutical production, as its performance will eventually decide the performance of the entire production process. Selection of the poorly expressing cell line leads to multiple rounds of optimization increasing the cost of the production process. The selected cell line should be easy to transfect and express the anticipated biologic in its fully functional form.

Aragen provides range of host cell lines which acts as biological factories for range of biologics. All our platforms are well documented, approved by regulatory authorities and are free to own. Our platforms can be tested in parallel and depending on the performance of the minipools, we proceed with the platform best suiting the requirement of the sponsor. Details of some of our platforms are described below.

### 1. CHO-DG44

Aragen's DG44 platform is a royalty-free platform based on Chinese hamster ovary (CHO) technology using dihydrofolate reductase (DHFR) selection to mark cells that have successfully integrated the vector. DG44 is well-accepted by both sponsors and regulators and delivers high antibody titers in commercially available media and feeds. Titers obtained for standard antibodies are  $\leq 5$  g/L. These host cell lines are free to own, and already more than three engineered cell lines have been commercialized based on these platforms.

### 2. CHO K1 GS -/- knockout (MilliporeSigma CHOZN®)

Aragen's CHOZN is a glutamine synthetase (GS) knock-out using the Talon technology. These cell lines are royalty-free, established modern platforms with extensive regulatory acceptance and success with numerous biological formats, including difficult to express proteins (fusion proteins, high molecular weight proteins, bispecific antibodies, etc.). Standard titers for standard antibodies are around 5 g/L.

### 3. Asimov

Asimov is a more recent technology that, like CHOZN®, makes use of a CHO GS knockout. It employs proprietary transposase integration and artificial intelligence (AI) to optimize the expression cassette for improved productivity, particularly in the case of novel formats or proteins that are anticipated to be difficult to express. These, like our other platforms, are royalty free, with standard antibody titers of about 5 g/L.

Additionally, Aragen's proprietary expression vector systems are flexible tools carefully designed to facilitate enhanced, stable expression of the inserted genetic material while minimizing any secondary effects on the host cells. These vectors are designed by expert scientists with experience in dealing with expression platforms for large, complex molecules, which are often challenging to express.

## Clone Selection

Selection of the high performing clone from the transfected culture is a challenging and arduous process. The performance of the clones is unpredictable, so higher the number of clones screened, higher is the probability of achieving the most productive cell line. Designing the optimal screening strategies requires multiple rounds of optimization delaying the process development. Once, few efficient clones have been identified multiple assays should be performed to identify the features of each clone requiring scientific expertise and can be labor and time intensive.

At Aragen, screening of the clones can be carried out through traditional approaches such as, western blotting, enzyme-linked immunosorbent assay (ELISA) or advanced technologies like fluorescence-activated cell sorting (FACS), flow cytometry, utilizing high content imaging systems. Flow Cytometry Platform, provide deeper insights to facilitate the ranking and selection of production clones with rapid and simultaneous evaluation of titer, productivity, and cell viability. To identify the high performing clones, we adopt an approach in which we divide the bulkpool into multiple minipools such that each clone can be accessed for its quality.

## **Analytics and characterization**

once the appropriate clone is identified, it must be expanded and fully characterized. orthogonal characterization should be implemented to identify all the physio-chemical properties of the biologic and different assays should be performed to access its safety and efficacy. These analyses are likely to involve the use of multiple instruments, platforms, and methodologies. Additionally, evaluating the features and quality of the product requires analysis and integration of datasets from different technologies. This demands significant expertise across multiple disciplines, which might be unattainable for small biotech's.

Aragen provides optimal cell line characterization packages, comprehensively designed for detailed analysis of the cell lines in accordance with ICH regulatory guidelines. We efficiently carryout range of assays which can be customized to fit the clients need.

## **Scalability**

One of the most critical challenges in biologics production is scaling up procedures to achieve commercial manufacturing. Making judgments based on models that may not accurately depict conditions at larger scales can be an obstacle to commercialization success. Furthermore, scaling up typically entails shifting the process to intermediate scales and considerable optimization at each, which is costly and can cause significant delay.

At Aragen, once the few potential single cell clones are identified extensive bench scale and pilot scale strategies are designed to test the growth of the clones at different bioreactor levels. Initial testing is done on shaker flask and different culture parameters like media screening, feed screening, temperature shift, feeding strategy, shaking speed are extensively analyzed and then the parameters are tested for their scalability at different bioreactor levels.

## **Conclusion:**

There are various challenges associated with cell line development, but the vendors can explore various solutions to reduce the risks associated with biologics development. Aragen offers solutions to all the challenges associated with cell line development through its decades of experience in the biologic development, advanced infrastructure, and expert scientific personnel. Depending on the unique requirements, we provide global resources and excellent capabilities at every level of the cell line generation process. We believe that each of our client's ideas has the potential to change people's lives. Our goal is to deliver clients' products to clinics while minimizing risk and maximizing efficiency. Aragen is trusted by clients in a variety of industries, including biotech, agrochemicals, and veterinary medicine.

If you would like to learn more about our CLD capabilities, please contact our customer support team, and we'll be pleased to help you realize your vision.

Let's begin the  
conversation



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