

Early protein expression assessment and the value of starting in a proven system

Expression is not just a supply activity;
it is an early development decision point

An article from Early Development Services,
Integrated Biologics, Lonza

In biologics development, early expression work is sometimes viewed mainly as a tool to produce material for screening or early testing. However, it is far more important than that. The expression stage is often the first point at which a molecule is challenged in a system that begins to reveal how it may behave as a real development candidate. It is where assumptions about productivity, assembly, stability, and scalability start to be tested experimentally rather than inferred conceptually.

At Lonza, early protein expression is one of our core pillars of Early Development Services because it is directly linked to de-risking and optimizing the path to the clinic. Expression performance is closely connected to broader developability. If a molecule expresses poorly, assembles incorrectly, shows instability in pools, or behaves unpredictably in a relevant CHO system, those findings may point to deeper issues that could affect cell line development, process performance, timelines, cost, and regulatory readiness. This is why early expression assessment should be treated as a technical evaluation step, not simply as a production step.

Why the choice of expression platform matters from the start

Using a commercially relevant and regulatory-familiar expression platform from the beginning provides greater clarity. The GS Gene Expression System® platform has powered the development of more than 100 commercial products and

provides a scalable, integrated system that combines host cells, vectors, enabling technologies, technical support, and an extensive regulatory track record.

Platform continuity matters because the value of early expression depends heavily on how relevant the resulting data

are to later development. If a molecule is first characterized in a non-representative system, the program may generate encouraging but misleading results. Lonza's case study on early work performed in HEK293 cells illustrates this point clearly. In that example, early expression and lead selection work had been performed in HEK293 cells, but a protease cleavage issue emerged later in CHO expression. An earlier CHO-based assessment could have identified the issue sooner and reduced the impact on resources and timelines.

Early development is not simply about generating data quickly. It is about generating technically relevant data in a system that reflects where the molecule is likely to go next. If early protein expression is conducted in a system that does not meaningfully model manufacturing conditions, a program may gain speed initially but lose time later when hidden liabilities emerge. By using a commercially relevant system such as Lonza's GS Gene Expression System® technology, teams can understand how a product performs in the expression platform intended for cell line development. This makes early expression assessment a practical de-risking tool, producing data aligned with the molecule's likely manufacturing path and improving the relevance of observations around yield, product quality, and molecular behavior.

How GS Ori-Go® vectors strengthen early expression work

GS Ori-Go® vectors are the latest innovation within the GS Gene Expression System® platform. They are designed to support higher titers, shorter timelines, and a simplified workflow with less hands-on complexity in the lab.

For early expression work, this innovation can make early-stage comparison among candidates more informative. Higher expression and improved clone or pool performance help

teams observe differences in productivity, pool stability, and product quality before major downstream investment is committed. A simplified process can also remove steps that would otherwise slow progression, enabling teams to generate decision-relevant data sooner in a workflow closer to the system intended for later development. In practical terms, GS Ori-Go® vectors can help early expression move beyond material supply and become a stronger technical screen for developability, scalability, and progression readiness. The vectors work with the LHP-1 promoter and GS piggyBac® transposon system to support improved titers, expression stability, product quality, and bulk-pool performance, including performance that can support scale-up for toxicology material and IND-related work.

Why early expression should be integrated with broader early development work

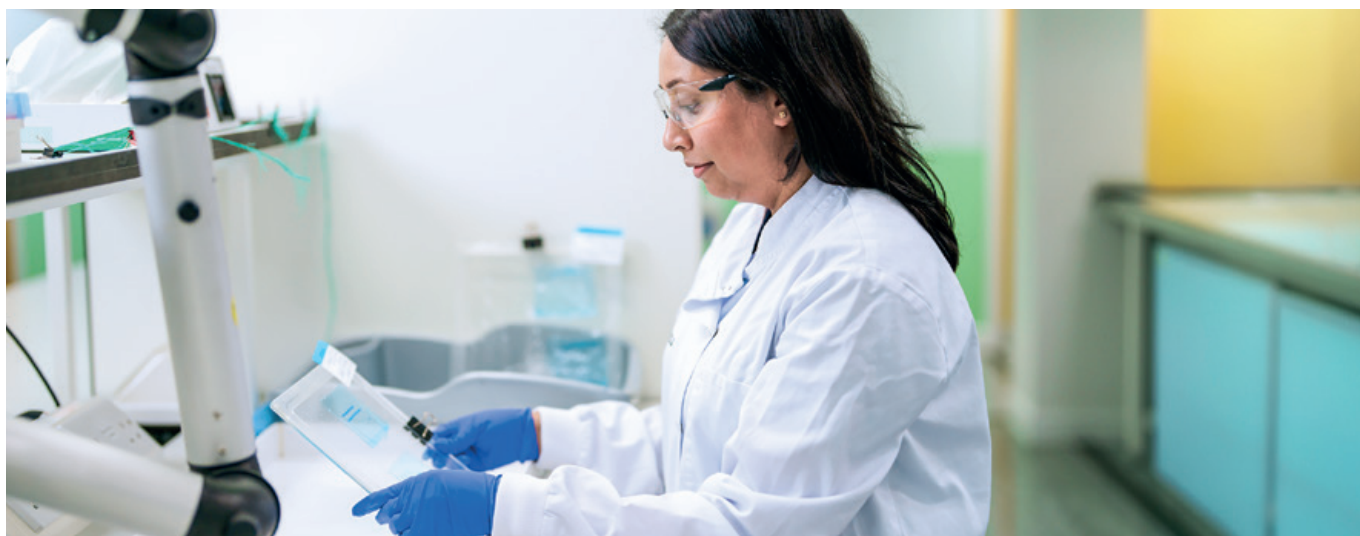
Protein expression should not be treated as a standalone service. Within Lonza's Early Development Services toolbox, expression sits alongside manufacturability assessment, immunogenicity assessment, humanization and deimmunization, and additional immunosafety capabilities. Together, these activities create a broader early workflow that can support candidate selection, material generation, and risk mitigation before a program moves deeper into development.

With an integrated approach, expression data become more powerful because they can be interpreted alongside other early development evidence. A molecule that expresses well but carries clear manufacturability liabilities still presents risk. A candidate that provides promising early material supply but raises immunosafety concerns may not be the right one to advance. Conversely, a candidate that performs well across expression, manufacturability, and safety-related assessments becomes a stronger technical choice for progression.

Table 1

Common customer challenges addressed by the EDS toolbox.

EDS toolbox	Typical problem to be solved
 Bioinformatics: manufacturability assessment and antibody humanization/deimmunization	Finding sequence liabilities late can cause significant delays and re-work
 Protein expression	Investment in an incorrect or non-optimized production platform results in high COGs and possibly non-competitiveness
 Immunosafety: immunogenicity and immunotoxicity assessment	Immunogenicity is the primary cause of clinical failure



Why expertise matters in early expression assessment

Early expression assessment is not just a matter of running a transfection and measuring a titer. Its value lies in designing the right vector strategy, selecting the right host system, interpreting expression data correctly, and understanding what the outputs imply for downstream development. For example, multiple vector designs and sequence variants were evaluated for a three-chain molecule, and the final design was selected based on the combination of high titer and high monomer level. Screening stable pools with small-scale affinity chromatography and product quality analysis provided early information on product assembly in the GS-KO system and supported selection of the vector that produced the highest levels of correctly assembled product.

This work shows that early protein expression requires more than material generation. It requires specialist expertise that connects molecular design, construct architecture, expression biology, and analytical data. When interpreted together, these insights turn early expression into a development science discipline that can support better downstream outcomes.

How early expression assessment improves technical outcomes

Early expression assessment is strongly connected to better downstream outcomes. It supports more informed decision-making, more realistic budgets and timelines, faster delivery later in development, and reduced overall cost. Lonza's early de-risking package combines *in silico* developability assessment, small-scale expression in the GS® expression system, and *in vitro* PBMC-based screening into an integrated package designed to generate meaningful data early. This helps teams support decision-making, investor discussions, and a clearer understanding of IND timelines and risks to monitor.

Early expression assessment also helps determine whether a molecule can be produced in a way that supports real development needs. It provides evidence on pool behavior, productivity, product quality, assembly, and system compatibility. When performed in a proven platform, it allows teams to interpret early findings with greater confidence because those findings are connected to the platform the program may use later. In this sense, early expression is one of the most practical ways to reduce technical uncertainty while the molecule and development path are still open to optimization.

Building a stronger development path with earlier and more relevant expression insight

Early expression assessment is a core technical part of biologics development because it provides the first meaningful evidence of whether a candidate can perform in a system relevant to future manufacturing. When this work is done in a proven platform such as the GS Gene Expression System® platform, and strengthened by innovations such as GS Ori-Go® vectors, it can generate stronger and more relevant data on productivity, stability, and product quality while reducing unnecessary workflow complexity and supporting faster progression.

Early expression assessment improves decision quality. It helps biologics developers compare candidates more intelligently, identify construct- or platform-related liabilities sooner, and integrate expression findings with manufacturability and immunosafety data to choose a stronger path forward. For programs aiming to reduce risk before major downstream investment, early expression assessment is not only useful; it is one of the most actionable ways to build a more developable biologic from the start.

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