Making the Medicines of Tomorrow

Lonza
Integrated Biologics

Article

Manufacturability and developability assessment as the technical foundation of a strong biologic candidate

A good therapeutic concept is not automatically a developable molecule

An article from **Early Development Services**,
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In early biologics development, attention often centers on biological function. If a molecule binds the right target, shows the desired activity, or generates promising efficacy signals, teams naturally want to advance it quickly. However, biological promise alone does not guarantee development success. A viable biologic candidate must also be manufacturable, stable, analytically tractable, and compatible with a realistic development path.

This is why manufacturability and developability assessments are so important at an early stage. These assessments are not secondary to discovery. They help determine whether a promising molecule can become a practical development candidate, before significant time, budget, and technical resources are committed.

What manufacturability and developability assessment are designed to reveal

In silico manufacturability assessment uses sequence analysis to identify potential high-risk areas in a molecule and highlight where sequence re-engineering may be needed. It can reveal liabilities that may influence stability, product quality, safety, and process performance, including:

- Non-standard or unpaired cysteines, glycosylation sites, and post-translational modification risks;
- Deamidation, isomerization, fragmentation, oxidation, N-terminal cyclization, and C-terminal clipping;
- Hydrophobicity, solvent accessibility, charge, molecular weight, extinction coefficient, absorbance, and pI;
- Aggregation risks that may affect manufacturability, stability, efficacy, or safety.

Developability assessment is therefore not a broad or vague quality screen. It is a structured evaluation of molecular and physicochemical attributes that can affect process fitness, product quality, scalability, and overall program feasibility. When these attributes are evaluated early, teams have a clearer basis for deciding whether to optimize, re-engineer, compare, or discontinue a candidate.

Why early identification of sequence liabilities matters

Sequence liabilities are especially important because they can drive downstream issues that typically only become visible later, such as expression instability, purification complexity, product-quality heterogeneity, or an altered safety profile. Identifying these risks late can create delays, rework, and avoidable pressure on development timelines and budgets.

The purpose of assessment is not simply to characterize a molecule. It is to determine whether the molecule is compatible with a credible manufacturing path. Early identification of liabilities enables teams to:

- Adjust or re-engineer the sequence before development progresses too far;
- Prioritize candidates with stronger technical profiles;
- Define where additional monitoring or testing will be required; and
- Make clearer go/no-go decisions before cell line development and manufacturing investment.

Lonza's decision-tree approach formalizes this logic by linking sequence analysis, advanced structural modeling workflow and *in silico* developability assessment to risk mitigation. Our risk evaluation is interpreted based on Lonza's manufacturing knowledge to help customers de-risk by the most suitable path – from additional testing to sequence re-engineering. This helps reduce uncertainty before candidates move into more resource-intensive stages.

How experimental expression and analytical characterization support developability

Although bioinformatics analysis is powerful, developability cannot be established by prediction alone – manufacturability is ultimately about a molecule's physiochemical properties. Expression and analytical characterization therefore provide a critical second layer of evidence – helping teams understand how a molecule behaves in practice rather than relying only on predicted risk.

Rapid expression of research-grade material can include vector design and construction, expression screening, stable pool expression, purification, and product-quality analysis. Analytical methods such as CE-SDS, cIEF, SE-HPLC, DLS, LC-MS, binding assays, and chromatography-based purification approaches can help confirm whether predicted risks translate into measurable product-quality or process challenges.

Why early manufacturability assessment improves outcomes

The technical value of early developability assessment lies in its effect on downstream decisions. Early de-risking supports informed decision-making, more realistic timelines and budgets. This translates into faster delivery later in development, lower total cost, and stronger long-term outcomes.

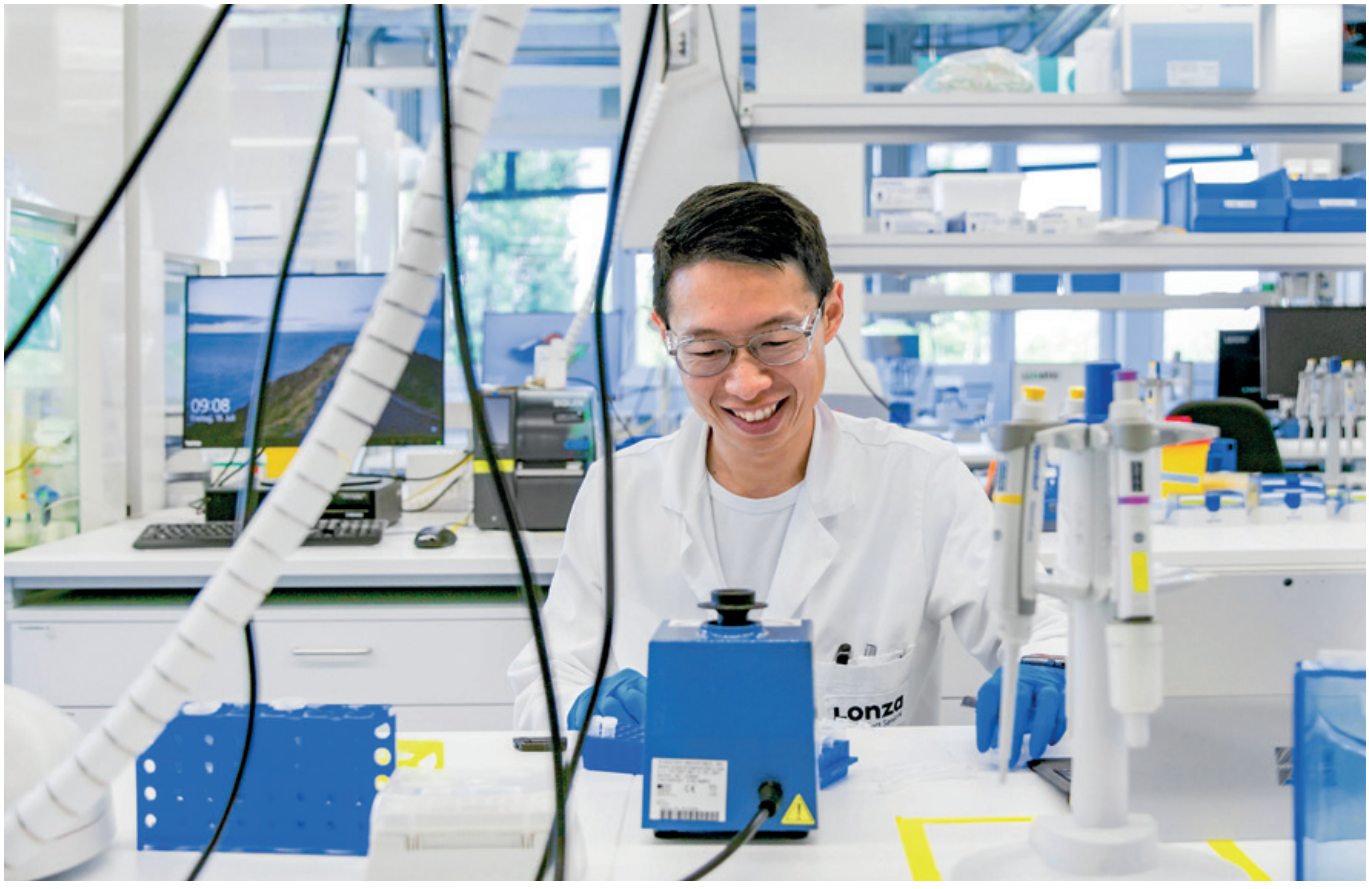
Lonza's Early De-Risking Package brings together *in silico* sequence analysis, non-GMP expression in a commercial expression system, *in vitro* analytics and immunogenicity safety profiling, delivered in a consolidated report designed to support development decisions and investor discussions. At a practical level, this type of assessment helps teams:

- Identify liabilities that may complicate purification, formulation, or product quality;
- Determine whether the molecule can be expressed at suitable levels in a relevant system;
- Clarify whether molecular design or vector configuration should be optimized before cell line development;
- Identify immunogenicity red flags that could compromise patient safety; and
- Generate stronger evidence for whether a candidate should progress, be re-engineered, or be deprioritized.

This is not an abstract exercise. It is a practical, data-rich approach to selecting stronger candidates and removing avoidable technical uncertainty before scale-up and later-stage investment.

Early manufacturability assessment helps turn promising molecules into stronger development candidates

Early development data packages, both *in silico* and *in vitro,* are foundational in biologics development because they help determine whether a molecule is merely promising or truly developable. Early assessment enables teams to base progression decisions on evidence about sequence risk, expression performance, product quality, and manufacturing relevance while there is still time to intervene. In a development landscape shaped by cost pressure, high attrition, and rising expectations for data quality, early assessment is one of the most effective ways to improve the probability that a biologic program can advance successfully.



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