Accelerating Cell Line Selection with Integrated Analytical Strategies

Cell line development is a critical determinant of success in biologics manufacturing. It lays the foundation for product yield, quality and long-term process stability. Yet, despite major advances in host engineering, vector systems and culture conditions, early-stage clone selection remains one of the least analytically supported stages of development.[1]

Therapeutic proteins, including monoclonal antibodies, enzymes and fusion proteins, are now central to modern treatment strategies for cancer, autoimmune conditions and genetic disorders. For each of these modalities, a well-characterised and scalable production cell line is essential. This makes cell line development not just a technical necessity, but a strategic priority for biopharmaceutical developers.

In practice, decisions about which clones to progress are often based on incomplete or delayed data, typically obtained only after expansion or purification. This not only introduces inefficiency but also increases the risk of overlooking high-performing candidates. As the pace of biologics development accelerates, the gap between biological complexity and analytical capability becomes harder to ignore. Speed and confidence in cell line selection can ultimately be the difference between a successful biologic and a stalled program. To address this, developers are increasingly turning to in-process analytical tools, such as rapid protein quantification platforms, to gain earlier insight and support more data-driven selection workflows.

This challenge is illustrated in Figure 1, which maps a typical cell line development process and highlights key decision points where data is often limited or delayed.

CHO Cell Line Development: Then and Now

Chinese hamster ovary (CHO) cells have long served as the preferred host for recombinant protein production due to their adaptability, capacity for human-like post-translational modifications and extensive regulatory track record. Over the last two decades, process yield and robustness have improved significantly through host engineering and upstream optimisation.[2] Despite these advances, the fundamental architecture of clone screening, from transfection to selection of the top clone, remains largely unchanged.[3]

This persistence reflects the extensive research that has shaped our understanding of recombinant protein production in CHO cells. Over several decades, studies have uncovered the molecular and metabolic mechanisms that influence expression outcomes, including chromatin accessibility, nutrient signalling and stress adaptation.[4,5] While molecular engineering and media optimisation have become increasingly sophisticated and streamlined, analytical methods at early screening stages have not kept pace. This disconnect continues to limit the ability to make timely and data-informed decisions during cell line development.

The need for more immediate and informative measurement tools is especially acute as developers pursue more complex formats. From bispecific antibodies to unstable or difficult-to-express fusion constructs, early insight into expression performance is critical to avoid costly delays or missed candidates.

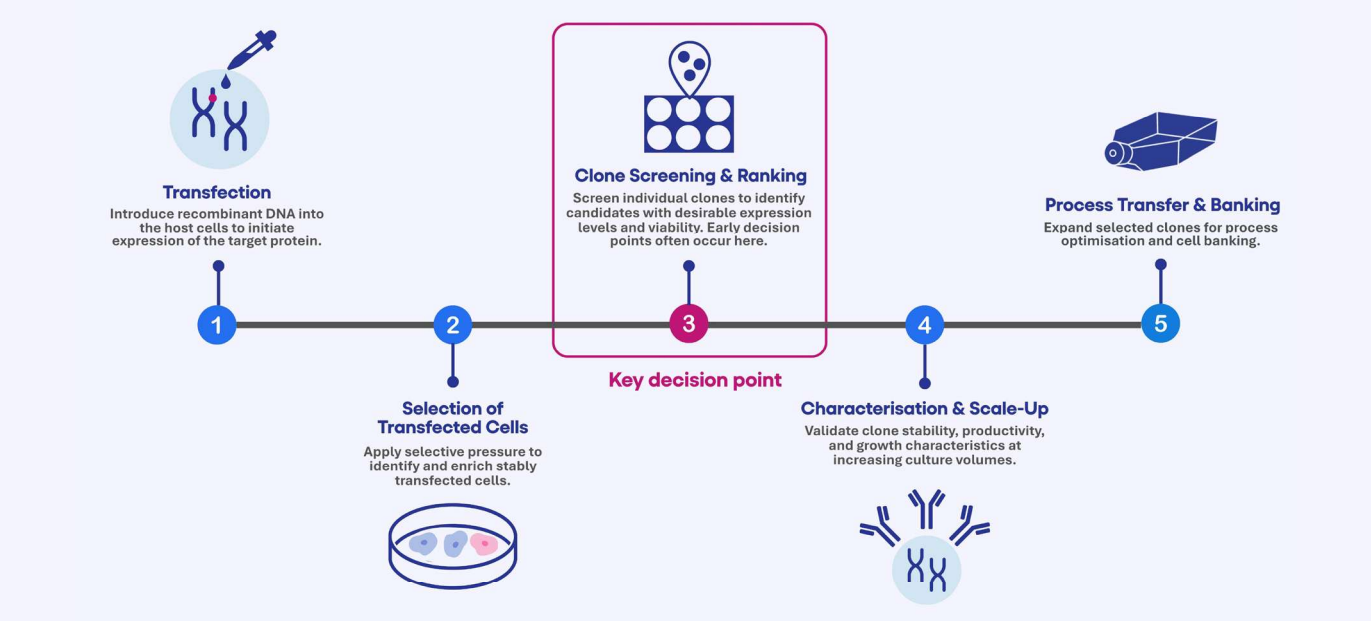

Figure 1: Cell line development workflow overview. High-level overview of the key stages in recombinant cell line development, highlighting where early analytical decisions are typically made.

Method	Time to Result	Crude Sample Compatible	Throughput	Ease of Use / Setup
ELISA	1 - 2 days	Low–Moderate	Low - Moderate	Standard protocols; moderate hands-on time
HPLC (e.g., SEC)	1 - 2 days	Low	Low	Requires dedicated instrumentation and trained users
Octet (BLI)	< 2 hours	Moderate	Moderate	Benchtop format; operator training required
Mass Spec (LC-MS)	1 - 2 days+	Yes (with prep)	Very Low	Complex setup; typically requires specialist lab infrastructure
Amperia™	< 2 hours	Yes	Low - Moderate	Benchtop system; designed for routine lab use

Note: This comparison is based on typical usage scenarios in non-GMP R&D settings. Performance and workflow may vary by construct, assay design, and lab environment.

Table 1: Comparison of protein quantification methods for early clone evaluation. A side-by-side comparison of commonly used analytical tools, showing trade-offs in speed, sample compatibility and infrastructure needs. ELISA: Enzyme-Linked Immunosorbent Assay; HPLC: High-Performance Liquid Chromatography; SEC: Size Exclusion Chromatography; BLI: Biolayer Interferometry; LC-MS: Liquid Chromatography–Mass Spectrometry.

Gaps in Clone Selection and Evaluation

Today's clone evaluation workflows still depend heavily on traditional protein assays such as enzyme-linked immunosorbent assay (ELISA), high-performance liquid chromatography (HPLC) and sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). These methods are robust but slow, batch-based and often decoupled from the point of decision.[6] They typically come into play only after significant expansion, requiring large amounts of product and delaying critical insights. As a result, early-stage agility is limited. The trade-offs between these commonly used analytical methods, including differences in speed, sample requirements and suitability for early-stage workflows, are shown in Table 1. These limitations help explain why developers often face challenges in generating timely and informative data to guide confident decision-making.

In the absence of fast and direct product measurements, developers frequently rely on proxy readouts such as cell growth or fluorescence. While these allow for higher screening throughput, they often fail to capture meaningful differences in cellular productivity, expression stability or stress response. Having worked extensively on CHO clone characterisation and bioreactor modelling, we have seen how subtle phenotypic differences at the screening stage can lead to significant downstream consequences. Yet tools capable of capturing these differences early in development, and at a scale suitable for exploratory workflows, remain limited. What is often missing is not a lack of metrics, but the ability to access meaningful data early enough to guide confident decisions.

Addressing this bottleneck does not require replacing existing assays. Instead, it calls for augmenting current workflows with tools that provide just enough information, just in time.

In-Process Quantification to Support Early Decisions

Bench-level protein quantification is gaining traction as a practical solution to support earlier clone triage and more efficient resource allocation. Whether during screening, scale-down optimisation or early vector assessment, having access to concentration data within the same lab and the same day offers a meaningful advantage.[7]

While not intended to replace gold-standard analytics, platforms such as Abselion's Amperia™ provide a pragmatic way to reduce uncertainty and close feedback loops earlier in the process. By delivering actionable data at the screening or early expansion stage, in-process quantification helps teams make better use of their time, incubator space and downstream capacity without disrupting existing workflows.

This approach complements established analytical strategies by enabling faster access to quantitative data during early development. While not a substitute for the detailed characterisation required later in the pipeline, early quantification supports more informed prioritisation and helps minimise delays during screening. The impact of this shift is illustrated in Figure 2, which contrasts traditional and integrated workflows to highlight how in-process quantification can streamline early decision-making.

Collaboration Highlight: University of Manchester Case Study

Professor Alan Dickson's group at the University of Manchester partnered with Abselion to evaluate whether benchtop quantification could provide practical support for early clone selection in a real-world setting. The study included samples from both the mini pool stage and individual clones, covering key points in the selection process where earlier data could support more informed decisions. The aim was to assess whether having access to protein concentration data at these stages could help prioritise candidates more effectively and reduce the risk of advancing underperformers.

Using crude culture supernatants, the team rapidly quantified antibody expression and observed clear ranking correlations

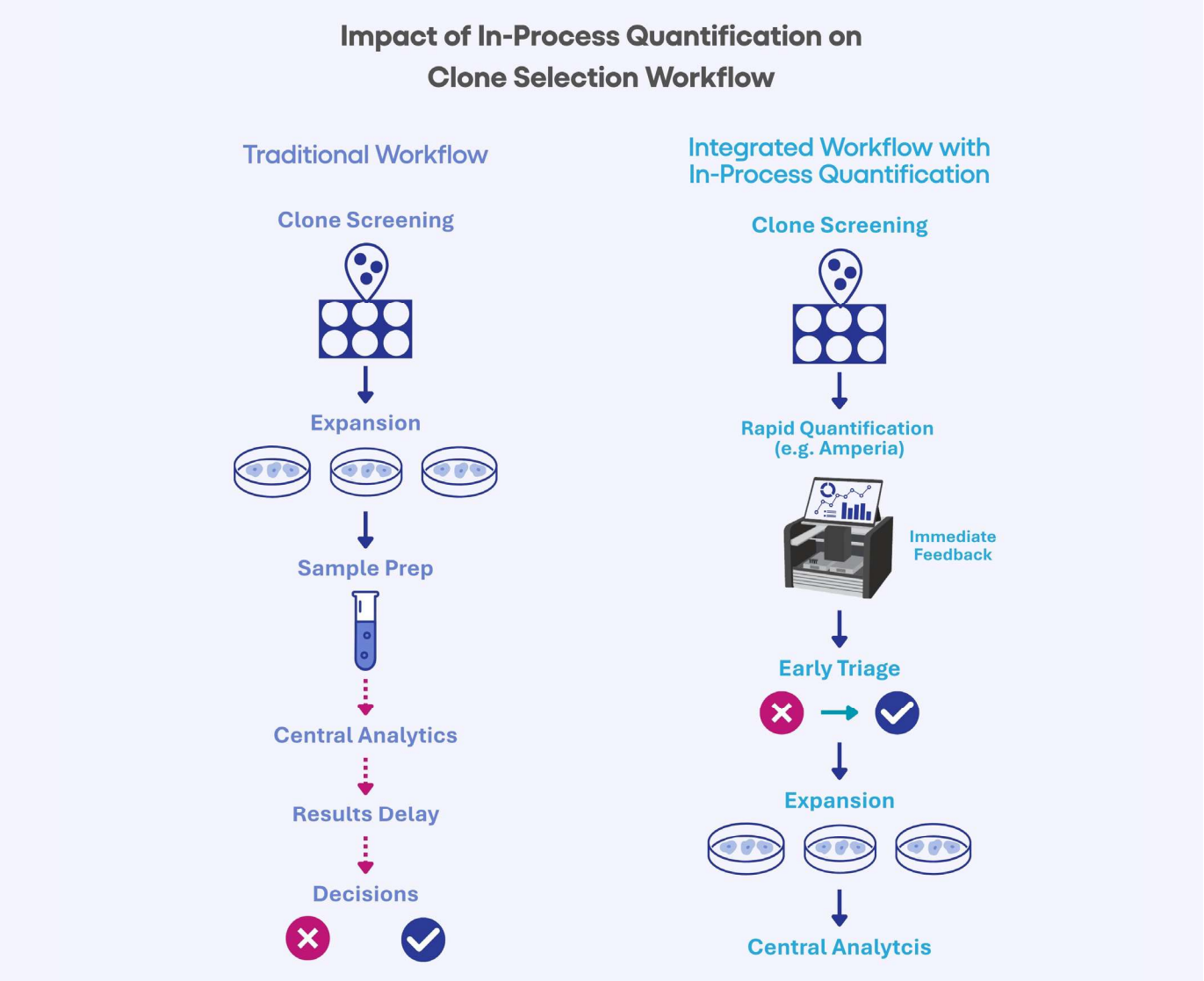

Figure 2: Impact of in-process quantification on clone selection workflow. A visual comparison of traditional and integrated workflows. In-process quantification enables earlier decision-making, reduces reliance on late-stage assays and helps prioritise productive clones faster.

with gold-standard ELISA results obtained later in the workflow. In-process benchtop quantification supported earlier triage of low-producing clones and streamlined the transition to bioreactor testing, helping to make these steps more efficient and responsive.

The impact of this approach is illustrated in Figure 3, which compares conventional and integrated workflows. Incorporating Amperia into the process helped reduce assay turnaround times and enabled faster progression through the study overall.

Looking Forward: Connecting Data, Decisions and Development

As biologics pipelines grow in both complexity and urgency, there is increasing recognition that upstream workflows must evolve beyond incremental improvements. The ability to make confident and data-driven decisions earlier in development will be key, not just to decreasing timelines, but also to improving the quality and manufacturability of molecules entering the pipeline.

In this context, the role of in-process analytics is shifting. Rather than being seen as standalone tools, benchtop quantification systems are becoming part of a more integrated strategy that connects clone selection, cell line optimisation and early process development within a tighter feedback loop.[7]

The goal has always been to help close the gap between academic insight and industrial application, whether through advanced cell line modelling, novel host engineering strategies, or now, more accessible analytical approaches. The ideal future is one in which every decision from clone to clinic is informed by timely and context-relevant data. Achieving this will require the integration of real-time analytics with data modelling, automation platforms and AI-driven decision tools. Just as importantly, it will require practical tools that empower researchers at the bench, not only in high-throughput labs, but across the diverse environments where biologics are designed, optimised and translated.

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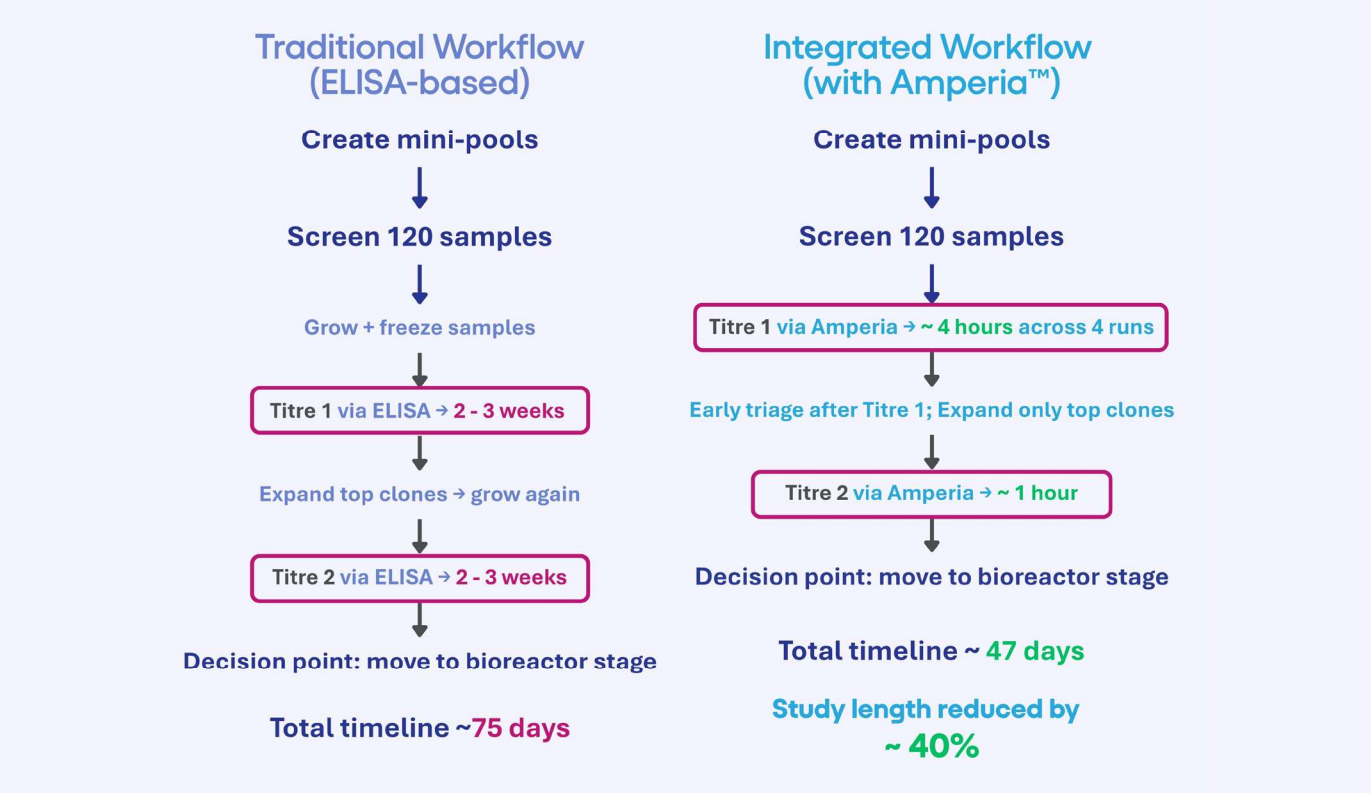

Figure 3: Case study: Integrated workflow enables faster clone selection. Workflow comparison of ELISA-based and Amperia-supported clone selection processes at the University of Manchester. Use of benchtop analytics reduced turnaround time and shortened total study duration by approximately 40%.

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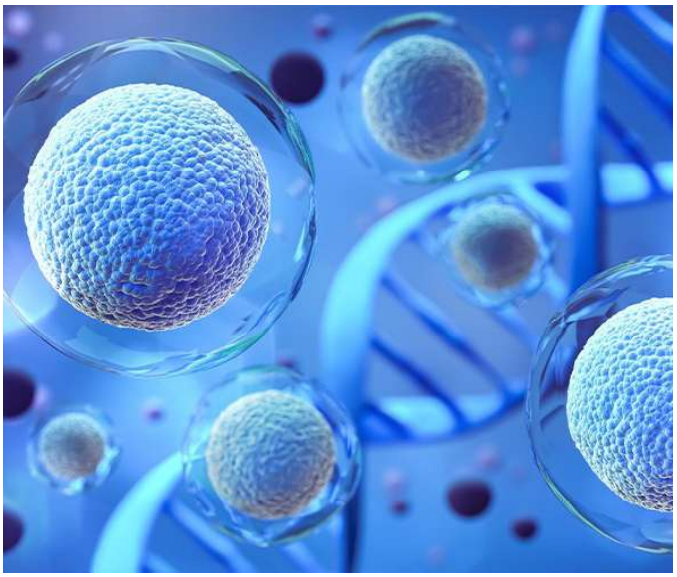

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