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## ***Cell-Line Engineering Should Be Evaluated by Product Quality Robustness Rather Than Yield Alone***

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### **ABSTRACT**

Chinese hamster ovary cell-line engineering is often judged through productivity-centered endpoints because titer is easy to rank, economically visible, and strongly coupled to development timelines. Yet a high-producing clone is not necessarily the clone whose product attributes remain fit for purpose as genetic state, culture age, metabolic load, media composition, or bioreactor conditions change. This Perspective argues that cell-line evaluation should therefore shift from yield maximization alone to product-quality robustness: the capacity of an engineered production system to preserve predefined quality attributes and acceptable process performance across a relevant, explicitly bounded set of perturbations. The argument integrates evidence on genomic integration, epigenetic state, secretory and metabolic burden, glycosylation engineering, process-dependent quality variation, scale-down perturbations, and analytical forecasting. A proposed quality-robustness logic is developed without treating molecular change as failure, analytical prediction as mechanism, or a single perturbation study as proof of manufacturing generalizability. The practical implication is not that productivity becomes secondary, but that yield should be interpreted jointly with product quality, stability, perturbation response, and evidence strength when selecting engineered cell lines.

**Keywords:** CHO cells, Cell-line engineering, Product quality, Glycosylation, Process robustness, Biomanufacturing

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### **INTRODUCTION**

Chinese hamster ovary (CHO) cell-line development has long rewarded traits that accelerate recovery of high producers, but contemporary engineering increasingly recognizes that productivity, product quality, and long-term stability are distinct outputs rather than interchangeable measures of the same phenotype [1, 2]. This distinction matters because the therapeutic consequences of a recombinant protein are mediated by the product actually manufactured, not by volumetric titer alone. Glycosylation provides a clear example: specific glycan structures can influence stability and biological function, while the significance of a given shift remains molecule- and context-dependent [3]. At the same time, CRISPR-enabled targeted integration and other precise engineering strategies have expanded control over genomic architecture without demonstrating that precision alone guarantees stable quality across process conditions [4].

The inferential problem is therefore narrower than the familiar claim that “quality matters.” A clone can be genetically well characterized yet process-sensitive; highly productive yet burdened; glycoengineered toward a desired profile yet fragile to media or scale-related perturbations. Conversely, molecular drift need not imply

manufacturing failure if critical outputs remain acceptable. This Perspective proposes that cell-line success be evaluated through product-quality robustness: preservation of fit-for-purpose product attributes and acceptable production behavior over a predeclared challenge space. Yield remains essential, but it becomes one coordinate of the decision rather than the decision itself. This formulation does not assume a universal score, a fixed perturbation panel, or a regulator-endorsed threshold; the relevant attributes and challenges must remain product-, host-, and process-specific.

#### *The productivity-centred engineering paradigm*

Productivity-centered selection is scientifically rational when the immediate bottleneck is insufficient expression. Multiauxotrophic CHO engineering, for example, can intensify selection pressure and accelerate isolation of high-producing recombinant-protein populations [5]. Such approaches demonstrate that host design can move the productivity frontier, but they do not establish which high producer will retain acceptable critical quality attributes (CQAs) under later manufacturing conditions.

The same separation appears when the host itself is adapted. Long-term selection at subphysiological temperature produced CHO populations with increased biomass and productivity, while N-glycan processing remained broadly preserved for the tested model products [6]. That result is important precisely because it is not evidence that productivity gains are generally quality-neutral; it shows that the relationship can be favorable in a defined host, perturbation history, and product context.

Platform acceleration creates a similar interpretive risk. A scalable transient CHO system can deliver high titers while still requiring explicit assessment of product quality and scalability before its performance is extrapolated to stable commercial manufacture [7]. During stable-pool selection, suppressing expression of difficult-to-express proteins improved later productivity for many tested proteins, consistent with the idea that excessive expression during selection can reshape which cells survive the development bottleneck [8]. The effect was not identical across all products.

These observations motivate a proposed critique of productivity-centered ranking. Screening at one environment can preferentially select cells optimized for that environment and for the variable being measured. A robust cell line should therefore not be defined as “the highest titer clone with no obvious defect,” but as a high-performing candidate whose product and cellular phenotype remain acceptable when challenged along conditions that are plausibly encountered during development and manufacture.

#### *Product quality as the primary output*

Product quality is generated by the coupled cell-process system. Culture environment, accumulated host-cell proteins, and other upstream conditions can affect glycosylation, charge variants, aggregation, degradation, and related attributes, so sequence identity and high titer are insufficient proxies for the final product state [2]. The relevant question is not whether every CQA must remain numerically unchanged, but whether variation remains compatible with the product’s intended quality target and function.

This principle does not require assuming that faster or less conventional development architectures are inferior. For trimeric SARS-CoV-2 spike antigens, CHO stable pools produced material with measured quality characteristics similar to corresponding clonal lines in the studied development setting [9]. The appropriate inference is product-specific: measured comparability can justify development decisions in a defined context; pool status by itself cannot.

Process chemistry can also expose quality dependence that a yield-only screen would miss. In an Fc-fusion process, sodium chloride affected glycosylation and N- and O-glycan site occupancy, and mitigation improved recovery of the more highly glycosylated product forms [10]. The mechanism and magnitude are not transferable automatically to other molecules or media, but the study demonstrates why a cell line should be judged by the quality behavior of its product under relevant process conditions.

Quality risk is also selective rather than uniformly unstable. Extended CHO culture showed that most host-cell-protein expression was comparatively stable while a smaller subset changed with cell age and included impurities of manufacturing concern [11]. Thus, robustness should not be equated with absence of biological change. It should identify which changes reach attributes that matter. This is also the boundary between analytical difference and therapeutic significance: glycan variation can affect function, but an observed glycan shift does not by itself establish clinical inferiority or superiority [3].

#### *Genetic and epigenetic stability*

Cell-line instability is often discussed as declining expression, yet the manufacturing problem is broader. CHO instability can involve loss of productivity, altered product quality, or both, and the responsible mechanisms can include genomic rearrangement, silencing, production burden, and selection during prolonged culture [12]. A useful stability definition must therefore be longitudinal and output-linked rather than based only on a static genetic snapshot.

Epigenetic regulation adds a second layer. Chromatin state and DNA methylation can contribute to transgene expression and phenotype, but no single epigenetic pattern functions as a deterministic predictor of product-quality robustness [13]. Epigenomic information can nevertheless improve locus selection: genome-wide analyses have been used to nominate genomic regions with features consistent with stable expression [14]. Such safe-harbor or hotspot logic reduces uncertainty about integration context; it does not eliminate construct, product, or process dependence.

Observability is improving. Cas9-targeted nanopore sequencing can jointly resolve integration sites, integrated-sequence structure, and methylation state in recombinant CHO cells [15]. This makes structural and epigenetic risk easier to characterize, but analytical detection must remain separated from consequence. An integration rearrangement or methylation change is not automatically a failed manufacturing phenotype.

Long-term culture provides a direct warning against that collapse. Changes in growth, gene expression, and metabolism accumulated during extended culture yet were not synonymous with production instability in the tested CHO system [16]. A robustness framework should therefore ask whether a change persists, recovers, propagates to product attributes, or remains phenotypically tolerable.

Genomic engineering can still reduce identifiable sources of variability. High-throughput integration profiling has yielded candidate CHO hotspots that supported strong expression after retargeting [17-19]. Targeted integration can also alter clone-specific responses to environmental perturbation, showing that engineering architecture affects more than baseline expression [20]. Controlled landing-pad systems can reduce clonal variation under defined conditions [21]. Three-dimensional chromatin maps further show that integration context exists within a higher-order regulatory architecture rather than a simple linear sequence neighborhood [22]. Collectively, these findings support a narrower conclusion: rational genomic design can make the starting state more controlled, but quality robustness must still be demonstrated as a property of the engineered cell-process system.

Because genetic change, epigenetic drift, and manufacturing-relevant instability are not interchangeable, **Table 1** separates what is observed from what would justify an intervention or a product-level concern.

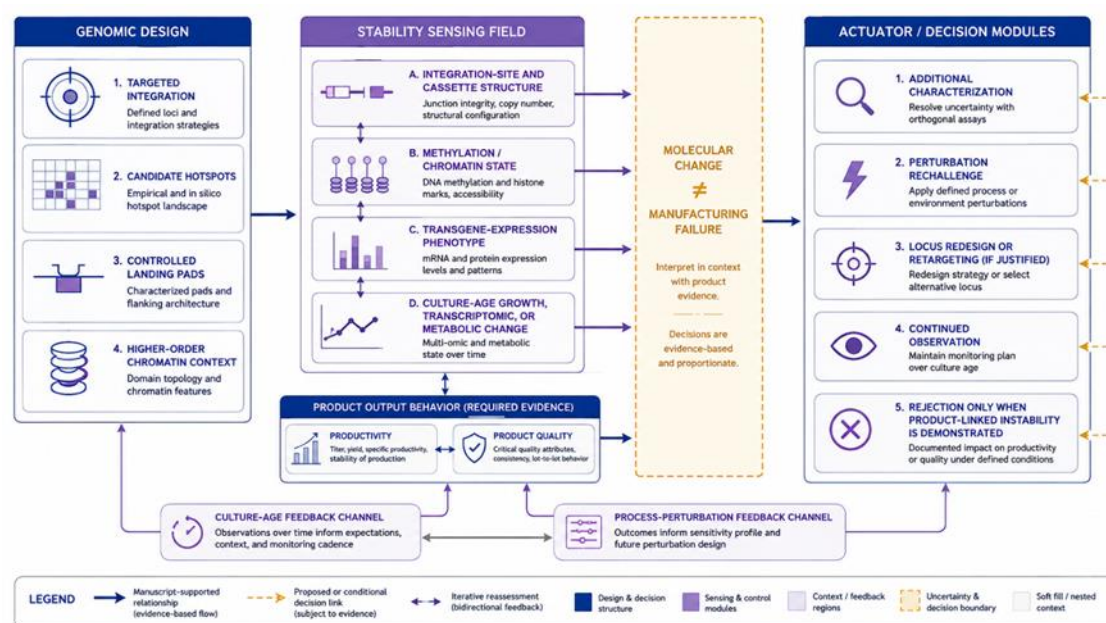
**Table 1.** Distinguishing molecular drift from manufacturing-relevant instability in engineered CHO cell lines

| Scenario family                       | Stability classification basis                                              | Observable evidence                                             | Control or diagnostic action                                                | Recovery behavior that discriminates interpretations                                                   | Cell-line engineering evaluated-product test                                        |
|---------------------------------------|-----------------------------------------------------------------------------|-----------------------------------------------------------------|-----------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Defined integration architecture      | Structural integrity and reproducible expression from a characterized locus | Integration-site structure, copy organization, expression state | Confirm locus and cassette integrity; compare expression over culture age   | Persistence of expression without new structural evidence strengthens a stability interpretation       | Advance only if the product-quality profile also remains acceptable                 |
| Epigenetic-state variation            | Change in chromatin or methylation with uncertain functional consequence    | Methylation, accessibility, transcriptional change              | Repeat state measurement and relate it to expression and product attributes | Reversible state change without output deterioration argues against classifying drift alone as failure | Treat epigenetic state as a risk descriptor, not a stand-alone rejection criterion  |
| Long-term phenotypic drift            | Time-dependent growth, transcriptomic, or metabolic change                  | Culture-age trajectories and production phenotype               | Compare early and late states under matched conditions                      | Persistent molecular change with preserved production can represent tolerated adaptation               | Reject only when drift reaches predefined performance or product-quality limits     |
| Perturbation-sensitive clone behavior | Clone response differs after an environmental shift                         | Condition-dependent transgene expression or growth response     | Rechallenge under the relevant process condition                            | Return toward baseline after disturbance indicates a different risk state from persistent divergence   | Evaluate the clone across the intended challenge space, not only at nominal culture |

|                             |                                                                              |                                                        |                                                                          |                                                                         |                                                                                                         |
|-----------------------------|------------------------------------------------------------------------------|--------------------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| Genomic-context uncertainty | Baseline expression is acceptable but locus context is incompletely resolved | Hotspot, landing-pad, or chromatin-context information | Improve genomic characterization or retarget integration where justified | Reproducibility across derived clones reduces one source of uncertainty | Proposed decision use: require product-level evidence before equating genomic precision with robustness |
|-----------------------------|------------------------------------------------------------------------------|--------------------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|

Note: The final column is a proposed article-level decision interpretation. The table does not define a universal score, threshold, or regulatory acceptance criterion.

The same distinction is visualized in **Figure 1** as a sensor-actuator network in which genomic and epigenetic measurements inform actions only after crossing an explicit interpretation boundary.



**Figure 1.** Genetic-state signals become manufacturing decisions only after product-linked interpretation

### Metabolic burden and cellular stress

A productivity phenotype is sustainable only if the cell can carry the associated biosynthetic load. Selection for difficult-to-express proteins can impose burdens that alter which cells survive the development process [8]. Cross-host comparison of CHO and HEK293 cells further showed that secretory-pathway demands differ among recombinant proteins and that selected pathway interventions improve production only for subsets of products [23]. The engineering target is therefore not a generic “high secretory capacity,” but a product-matched allocation of folding, trafficking, modification, and energetic resources.

Metabolic engineering can improve parts of that state. CRISPR-mediated rewiring of amino-acid catabolism reduced lactate or ammonium secretion and improved growth-associated phenotypes for selected edits [24]. Those outcomes are useful indicators of cellular efficiency, but they do not prove that product CQAs remain robust. Conversely, engineering can target a quality failure directly: expression of a bacterial pathway producing a peptide-aldehyde protease inhibitor reduced proteolysis and increased specific productivity for two model proteins without a detected growth or viability penalty in that system [25]. This is a quality-protective objective rather than a titer-only intervention.

The proposed robustness criterion is therefore conditional. A beneficial edit should improve or preserve the intended cellular function while being challenged for unintended CQA drift, altered impurity burden, or process sensitivity. Stress accommodation, not merely stress-marker suppression, is the relevant concept: the engineered cell must sustain an acceptable product under the conditions that expose its biosynthetic limits.

### Glycosylation and other critical quality attributes

Glycosylation illustrates why product quality must be defined before engineering success can be judged. Glycan composition can influence stability, receptor interactions, immune effector function, and other product-specific properties, but the same direction of glycan change is not universally desirable [3]. The evaluation target must therefore be a fit-for-purpose glycan profile rather than “more” or “less” glycosylation in the abstract.

CHO engineering can directly reshape these attributes. Multiplex disruption of B4Gal-T isoforms altered N-glycan galactosylation on secreted proteins and model therapeutics [26]. An intracellular anti-FUT8 strategy reduced Fc core fucosylation and enhanced an ADCC-related functional readout while supporting antibody production in the tested system [27]. MicroRNA engineering likewise produced bidirectional changes in monoclonal-antibody galactosylation, illustrating that regulatory as well as coding interventions can tune a CQA [28]. None of these results implies that one glycan target is optimal across all antibodies or therapeutic proteins. Genotype is only one determinant. Sodium chloride affected glycosylation and glycan-site occupancy in a specific Fc-fusion process [10], while cross-host secretory-pathway differences depended on recombinant-protein properties that included post-translational demands [23]. Thus, a successful glycoengineered clone at one nominal condition has demonstrated target-quality engineering, not necessarily target-quality robustness.

This Perspective therefore distinguishes two questions. First, did the engineering intervention move the product toward the intended quality state? Second, does that state remain acceptable across relevant culture age, media, metabolic, temperature, mixing, and scale-related disturbances? The second question is the robustness test and cannot be inferred from the first.

#### Cell-line–process interactions

A cell line does not express a fixed manufacturing phenotype independently of its environment. Targeted genomic designs can alter how recombinant CHO clones respond to hypothermic culture shifts [20], while controlled landing-pad systems can reduce baseline clonal variation when environmental conditions are held constant [21]. These observations support two separate inferences: engineering can reduce one source of baseline variability, and process response can remain conditional even after genomic control is improved.

The interaction becomes more consequential during scale translation. In a single multicompartiment bioreactor used to mimic large-scale heterogeneity, imposed conditions altered metabolism and growth, whereas the measured glycan-galactosylation response was more closely associated with power input than with the heterogeneity perturbation itself [29]. This is evidence against treating “scale-up stress” as one undifferentiated exposure. Mixing, oxygen, power input, substrate gradients, temperature, and other disturbances can affect different biological levels and need separate challenge logic.

Process analytical technology can increase observability without eliminating inference boundaries. Data-driven models have been used to forecast multistep mammalian cell-culture trajectories toward digital-twin applications [30]. Raman spectroscopy combined with convolutional neural networks has also been used to predict cell-culture quality-related variables within evaluated datasets [31]. Such tools can shorten the delay between state change and detection, but their predictions remain conditional on calibration, sensor quality, process regime, and domain similarity. Prediction is not mechanistic explanation, and model output is not itself a product-release decision.

The proposed consequence is to treat each candidate cell line as a response surface rather than a nominal-run point. Product quality and process performance should be observed over explicitly chosen conditions and time windows, with process measurements, cellular-state indicators, and CQAs kept analytically distinct. **Table 2** organizes that temporal logic without assuming that every disturbance must produce a measurable quality change.

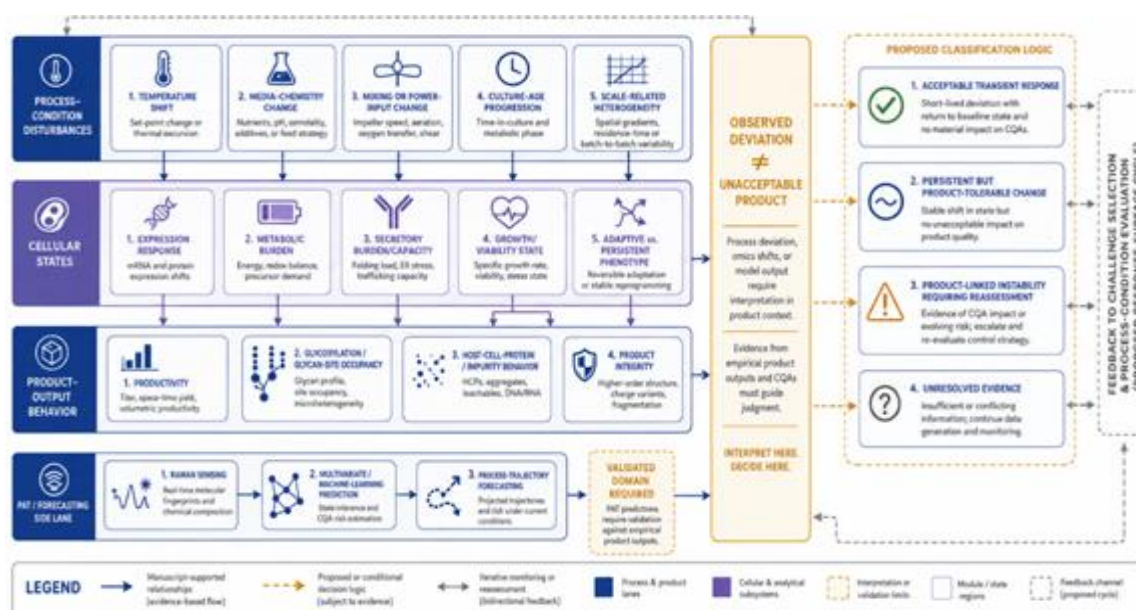
**Table 2.** Temporal windows for interpreting cell-line responses to process disturbance

| Evaluation window | Entry condition                               | Measured variable                                      | Hidden biological state that remains uncertain | Disturbance source                                       | Transition or persistence question                      | Time-dependent validation need                          | Product-quality robustness consequence                               |
|-------------------|-----------------------------------------------|--------------------------------------------------------|------------------------------------------------|----------------------------------------------------------|---------------------------------------------------------|---------------------------------------------------------|----------------------------------------------------------------------|
| Nominal baseline  | Qualified culture before deliberate challenge | Growth, productivity, selected CQAs, process variables | Latent sensitivity not expressed at baseline   | Normal operating variation                               | Is consistency maintained when the environment changes? | Establish repeatable baseline and measurement precision | Baseline excellence is necessary but does not demonstrate robustness |
| Early disturbance | Initial exposure to a defined process shift   | Immediate process and cellular responses               | Adaptive, transient, or destabilizing response | Temperature, media chemistry, mixing, or specified shift | Does deviation resolve, amplify, or reach               | Resolve onset rather than only end-point output         | Early cell-state change alone does not establish quality failure     |

|                           |                                                                 |                                                            |                                                 |                                                           |                                                                   |                                                         |                                                                                             |
|---------------------------|-----------------------------------------------------------------|------------------------------------------------------------|-------------------------------------------------|-----------------------------------------------------------|-------------------------------------------------------------------|---------------------------------------------------------|---------------------------------------------------------------------------------------------|
|                           |                                                                 |                                                            |                                                 |                                                           | product attributes?                                               |                                                         |                                                                                             |
| Sustained challenge       | Continued exposure after initial response                       | Persistent metabolic, expression, growth, and CQA behavior | Selection or adaptation during exposure         | Repeated or prolonged process stress                      | Does altered state persist while quality remains fit for purpose? | Compare trajectories rather than isolated measurements  | Persistent acceptable output supports a stronger robustness inference                       |
| Recovery window           | Return toward nominal conditions                                | Direction and completeness of recovery                     | Residual state memory or irreversible change    | Removal of disturbance                                    | Does the system recover to an acceptable production state?        | Distinguish delayed recovery from persistent divergence | Proposed evaluation window: recovery separates reversible response from durable instability |
| Scale-transfer window     | Process environment with different heterogeneity or power input | Process gradients, metabolism, productivity, selected CQAs | Adequacy of scale-down representation           | Mixing, mass transfer, power input, spatial heterogeneity | Is product quality preserved when disturbance structure changes?  | Validate scale-down relevance and model domain          | Scale-down evidence supports but does not prove commercial-scale robustness                 |
| Model-assisted monitoring | Sensor and historical data available during any window          | Spectral or multivariate predictions                       | Unmeasured mechanism and out-of-domain behavior | Sensor drift, domain shift, unrepresented states          | Does predictive validity persist in the current process state?    | Requalify calibration and external-domain performance   | Prediction supports detection but cannot replace empirical CQA qualification                |

Note: The recovery-window logic and response-surface interpretation are proposed synthesis elements. No row defines a regulatory hold point or universal acceptance threshold.

Because the same process signal can map differently onto cellular state and product quality, **Figure 2** places an explicit decision boundary between observed perturbation and an inference of unacceptable product performance.



**Figure 2.** Process disturbances reach product-quality decisions through separable cellular and analytical states

*Robustness across manufacturing perturbations*

Robustness is perturbation-specific rather than generic resistance to change. Cold-adapted CHO populations increased biomass and productivity while preserving the evaluated N-glycan processing for tested model products [6]. Extended culture showed a different pattern: most host-cell-protein expression remained comparatively stable while a smaller subset changed with cell age [11]. Long-term culture can also alter growth, transcription, and metabolism without corresponding production instability [16]. At bioreactor scale, imposed heterogeneity and power input produced different metabolic and glycan responses [29]. Temperature, culture age, mixing, media, and scale should therefore not be collapsed into one “stress” test.

Baseline consistency is also distinct from robustness. Targeted engineering can alter clone-specific responses to hypothermia [20], whereas controlled landing-pad integration can reduce clonal variation under a fixed environment [21]. Digital tools extend observability but retain domain limits: Raman soft sensing, machine-learning model-predictive control, and autonomous process analytical technology (PAT) can support quality-related monitoring or bounded intervention within evaluated process contexts [31-33]. Forecasting likewise anticipates trajectories only within its validated data domain [30].

This Perspective therefore defines robustness as preservation of predefined fit-for-purpose critical quality attributes (CQAs) and acceptable production behavior across a specified perturbation set. Because nominal performance, disturbance response, recovery, and model confidence can imply different actions, **Table 3** separates those decision states.

**Table 3.** Decision states for interpreting manufacturing perturbations during cell-line evaluation

| Decision state                           | Governing condition                                                    | Hidden state or uncertainty                              | Permissible action                               | Reassessment trigger                               | Unresolved product-level question                             |
|------------------------------------------|------------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------|----------------------------------------------------|---------------------------------------------------------------|
| Nominally strong, unchallenged           | High output and acceptable baseline CQAs                               | Latent process sensitivity                               | Apply predefined challenge set                   | Reproducible disturbance-linked drift              | Does performance persist outside the selection environment?   |
| Disturbed, product-stable                | Cellular or process variables deviate while CQAs remain acceptable     | Transient adaptation versus emerging instability         | Observe persistence and recovery                 | Product drift or impaired recovery                 | Is the altered state tolerable?                               |
| Persistently altered, product acceptable | New cellular state remains after challenge                             | Longer-term stability and second-disturbance sensitivity | Extend challenge coverage                        | CQA loss or progressive performance decline        | Can the altered state remain manufacturing-robust?            |
| Product-linked instability               | Disturbance accompanies unacceptable CQA or integrity change           | Causal mechanism may remain unresolved                   | Reassess clone, engineering, or process strategy | Reproducible recovery after justified intervention | Can remediation restore quality without another liability?    |
| Model/PAT warning outside domain         | Analytical prediction signals risk under poorly represented conditions | Calibration validity and true product state              | Verify empirically                               | Confirmed CQA deviation or external revalidation   | Does the warning reflect product, process, or model boundary? |

Note: These decision states are proposed synthesis, not regulatory categories, release criteria, or universal thresholds.

*A quality-robustness evaluation framework*

No selected evidence establishes a universal scalar score for cell-line quality robustness. Digital-twin scholarship instead describes integration of sensing, analytics, and process models while emphasizing implementation and validation challenges [34]. The framework advanced here is therefore proposed as a decision architecture, not a validated metric.

Five components are retained. First, define the baseline with productivity and product attributes; reduced clonal variability under controlled conditions does not establish perturbation resistance [21]. Second, specify plausible manufacturing challenges rather than an undifferentiated stress panel; distinct perturbation dimensions can produce distinct responses [29]. Third, measure product-quality response directly. Fourth, classify persistence and

recovery because molecular drift can occur without production instability [16]. Fifth, qualify confidence according to the evidence layer supporting the decision.

Those layers must remain separate. Epigenetic state supplies mechanistic context but is not a substitute for product challenge testing [13]. Higher-order chromatin structure likewise refines locus context without becoming a CQA readout [22]. Improved metabolic phenotype after an edit does not establish robust product quality [24].

Measurement, prediction, intervention, and acceptance are also distinct. Forecasting can anticipate process trajectories [30]; Raman-based models can increase CQA observability within a calibrated domain [31]; model-predictive control can enforce specified process constraints [32]; and autonomous PAT can accelerate attribute-focused development [33]. Digital-twin integration may connect these functions, but it requires process-specific qualification [34]. The proposed framework therefore ends at a product-linked decision boundary: evidence must justify preservation of the intended quality state under the declared challenge space, rather than merely confidence in the measurement technology.

#### *Translation to cell-line development*

Translation begins before final clone ranking. CRISPR-enabled engineering can make integration more deliberate [4], epigenome-informed safe-harbor selection can reduce uncertainty about genomic context [14], and targeted long-read sequencing can characterize integration structure and methylation jointly [15]. Hotspot screening [17], high-fidelity recombinase-mediated cassette exchange [18], and site-specific integration strategies [19] further control starting architecture without proving downstream robustness.

Candidate ranking should then remain product-specific. Secretory bottlenecks vary among recombinant proteins [23], engineering can address proteolytic loss where relevant [25], and glycoengineering can alter galactosylation [26], fucosylation [27], or regulatory control of glycan processing [28]. Each intervention should therefore be judged against the intended product-quality target and its behavior across process conditions.

Development speed can remain an objective. High-titer transient production can support rapid material generation when scalability and quality are evaluated separately [7]. Stable pools can likewise be useful when measured comparability with clonal material is demonstrated for the intended product and development stage [9]. Attribute-focused PAT may accelerate evidence generation [33], while digital-twin concepts remain conditional on domain-specific validation [34].

The proposed advancement rule is to progress a high-yield candidate only when its relevant quality profile remains fit for purpose across a predeclared challenge set and no unresolved stability signal plausibly threatens a critical product attribute. The challenge set, CQAs, observation windows, and acceptable variability must remain molecule-, platform-, process-, and development-stage specific.

## CONCLUSION

Yield remains indispensable, but it is an incomplete definition of cell-line engineering success. Genomic control, metabolic and secretory engineering, glycan modulation, PAT, and computational control can improve individual production functions without eliminating the conditional relationship among cell state, process environment, and product quality. Product-quality robustness reframes selection around preservation of the intended product across relevant disturbances while distinguishing transient adaptation, persistent instability, analytical prediction, and demonstrated product consequence. The framework proposed here is not a validated score and prescribes no universal threshold; its purpose is to make high productivity necessary but insufficient for advancement.

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