The Next Evolution of Raw Material Control for Cell and Gene Therapy Manufacturing

From Vague Certificates of Analysis to Analytical Verification

Executive Summary

Cell and gene therapies are reshaping modern medicine, enabling highly personalized treatments and new therapeutic modalities that were unimaginable only a decade ago. Yet while manufacturing technologies continue to evolve rapidly, one critical aspect of process control remains rooted in historical paradigms: the qualification and control of complex biological raw materials.

For decades, supplier qualification, vendor audits, and Certificates of Analysis (CoAs) have formed the foundation of raw material control strategies. These approaches remain highly effective for chemically defined components and well-characterized reagents. However, advanced therapies increasingly depend upon complex biological materials and proprietary formulations whose composition and performance cannot be fully described using traditional analytical approaches.

As the CGT industry matures, manufacturers are increasingly asking a new question:

How much analytical understanding of incoming materials is sufficient to support robust manufacturing and regulatory confidence?

The answer may define the next generation of raw material control strategies for advanced biomanufacturing.

Biothentix™

Biothentix™ proposes one possible approach to this challenge using encoded analytical Certificates of Analysis (CoAs): multiplex biological signatures capable of verifying the identity and consistency of complex materials without disclosing proprietary formulations or exact component concentrations.

By enabling analytical verification while preserving intellectual property, encoded CoAs may provide a new framework for harmonizing supplier release testing, incoming material verification, technology transfer, and lifecycle process control.

In many respects, an encoded analytical CoA functions as a digital signature for biological materials — authenticating identity and consistency without revealing the proprietary information used to create them.

The Historical Model Was Built for Simpler Inputs

Traditional biopharmaceutical manufacturing relied heavily on raw materials whose identity and composition could be verified using well-established analytical techniques.

Salts, amino acids, sugars, vitamins, and chemically defined media components can typically be confirmed using orthogonal methods including chromatography, spectroscopy, compendial tests, and supplier documentation.

Under these conditions, supplier qualification combined with incoming verification provides an effective quality framework.

Cell and gene therapy manufacturing increasingly operates in a different environment.

Modern manufacturing workflows often depend upon complex and highly engineered materials including: proprietary cell culture media, recombinant growth factor mixtures, cytokine cocktails, extracellular matrix preparations, conditioned media, feeder cell products, hydrolysates, and ancillary reagents specifically optimized for cellular performance.

These materials frequently derive their value not from a single constituent, but from the collective biological behavior of dozens or more interacting components.

Regulatory Expectations Continue to Evolve

Global regulatory agencies have consistently encouraged manufacturers to improve process understanding, strengthen control strategies, and adopt risk-based approaches throughout product lifecycles (e.g., ISO/AWI 20399-4:2025, USP<1043>, Ph.Eur. 5.2.12).

Quality by Design principles, comparability exercises, process characterization studies, and lifecycle management all reflect a common theme: **Greater process understanding enables more effective risk management and more robust control strategies.**

This trend is particularly relevant in cell and gene therapy manufacturing, where biological variability often exceeds that observed in traditional recombinant biologics.

Regulators have not prescribed specific analytical approaches for characterization of complex biological raw materials.

However, manufacturers that can demonstrate deeper understanding of incoming materials, stronger control strategies, and improved traceability are often better positioned to support:

- root cause investigations,
- comparability studies,
- multi-site manufacturing & technology transfer,
- process changes,
- and regulatory interactions.

Protecting Innovation While Building Trust

One of the most significant challenges associated with complex biological raw materials is the tension between transparency and intellectual property protection.

Suppliers invest substantial resources developing proprietary formulations that provide competitive differentiation and improve manufacturing performance. Manufacturers seek sufficient analytical understanding to establish robust control strategies and support product quality, which generally means greater visibility into incoming materials.

Historically, these objectives have often been viewed as competing priorities.

Emerging multiplex analytical approaches suggest a different model may be possible.

Biothentix was developed around the concept of an encoded analytical Certificate of Analysis enabled by a multiplex fingerprint — a multiplex biological signature capable of verifying the identity and consistency of a complex material without disclosing proprietary formulations or exact component concentrations.

Under this model, a supplier establishes an approved analytical fingerprint for a proprietary material using a panel of carefully selected biological markers. The resulting fingerprint becomes an encoded Certificate of Analysis that confirms identity and consistency while preserving confidentiality.

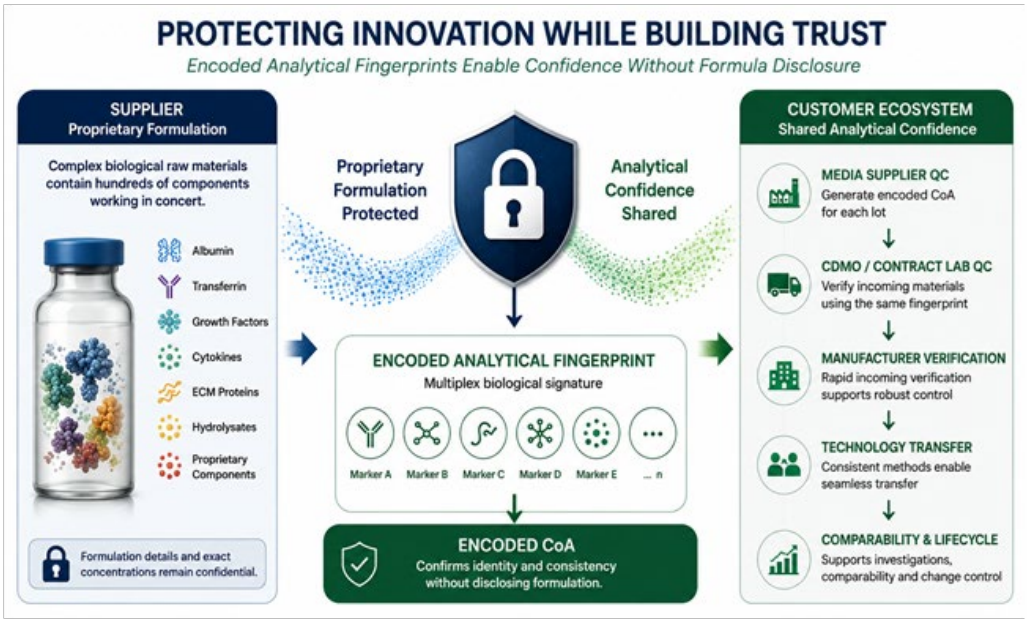
Customers, contract testing laboratories, CDMOs, and manufacturing sites can verify incoming materials against the same encoded standard using a harmonized analytical method without gaining access to formulation details.

The objective is not full compositional characterization.

The objective is analytical confirmation that the material received is consistent with the material intended.

In this model, analytical data becomes a mechanism for establishing trust while preserving innovation.

Rather than replacing mass spectrometry, chromatography, or orthogonal characterization methods, Biothentix serves a different purpose: Enabling rapid verification that a complex material is consistent with an established analytical standard.



Beyond Verification: The Opportunity for Ecosystem Harmonization:

One of the most powerful aspects of encoded analytical fingerprints is that they create value simultaneously for suppliers and manufacturers.

Suppliers benefit from the ability to differentiate complex products using objective analytical evidence while protecting proprietary formulations.

Manufacturers benefit from increased confidence in incoming materials, harmonized testing strategies, and improved comparability across sites and manufacturing partners.

The result is a naturally aligned ecosystem.

A supplier can release proprietary materials using an encoded analytical Certificate of Analysis generated from a standardized multiplex fingerprint.

Customers receiving those materials can perform incoming verification using the same analytical framework, generating confidence that the material received matches the material intended.

Contract testing laboratories and CDMOs can implement the same methods to support outsourced testing, investigations, and technology transfer activities.

A Strategic Opportunity for Raw Materials Suppliers

For organizations that both manufacture biological raw materials and support biopharmaceutical manufacturing workflows, the opportunity may be particularly compelling.

The same analytical platform used internally for supplier release and quality control can also be deployed externally to customers seeking harmonized incoming verification.

This creates a natural push-pull dynamic:

- suppliers generate encoded Certificates of Analysis using multiplex fingerprints,
- customers adopt the same analytical platform for incoming verification,
- contract laboratories implement harmonized workflows,
- and manufacturers gain confidence through shared analytical standards.

The same platform that enables supplier differentiation can therefore become the mechanism through which customers establish trust.

This alignment has the potential to create stronger customer relationships, improve supply chain transparency, and accelerate adoption of standardized analytical workflows across the cell and gene therapy ecosystem.

Looking Forward

The biopharmaceutical industry has repeatedly demonstrated that improved analytical understanding ultimately leads to improved manufacturing control. Host cell protein assays, residual DNA quantitation, rapid sterility methods, molecular contaminant detection, and advanced characterization technologies all followed similar trajectories from emerging capability to standard practice.

Complex biological raw materials may represent the next frontier in biomanufacturing control strategies.

As advanced therapies continue to rely on increasingly sophisticated biological inputs, analytical verification may increasingly complement supplier qualification as part of a modern framework for raw material control.

The question is not whether complexity exists within modern biological raw materials.

The question is whether the analytical frameworks used to establish trust in those materials will evolve alongside the therapies themselves.

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