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Quality and Analytics

Technologies Evolve To Provide Insight into New Processes and Products

by Gal Haase; Jonathan Dharamraj; and Ludwig Macko and Valentina Armiento



Quality and Analytics

Technologies Evolve To Provide Insight into New Processes and Products

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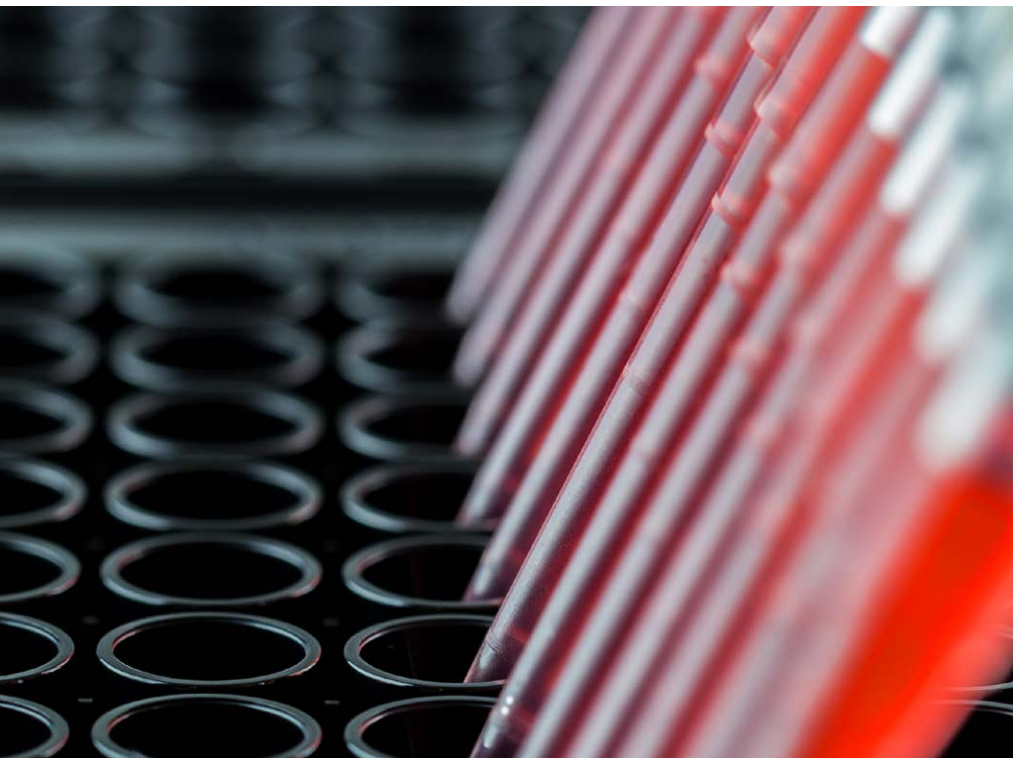

In an era of increasingly complex biological products, analytical excellence forms the foundation for competitive advantage. Process analytics and complex assay development come into play earlier in a product life cycle than ever before. Quality assurance and control (QA/QC) strategies are evolving along with available technologies. The authors in this eBook explore aspects of the quality and analytics in the contexts of laboratory digitization, raw-materials monitoring, and modern analytical methods. Together these articles present a picture of operational evolution driven by advancing science and technology.

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Get Ready for the Future of Digital Operations

AI Integration Requires Laboratories To Focus on Processes and Data First

by Gal Haase

Artificial intelligence (AI) tools already are integrated into many software and hardware products that biopharmaceutical laboratories are buying today. But how soon will organizations be able to leverage and maximize AI for long-term value? The answer is simple: as soon as their laboratories are running smoothly in all other respects.

Recently, my company surveyed more than 150 laboratory scientists to investigate the trends and innovations that matter most for their operations. AI continues to be a leading catalyst for change, but it was not our survey respondents' primary concern. Over half (54%) of them said that "data overload/data management" was their biggest current issue. Nearly as many (53%) cited funding and cost pressures, and 49% said that automation of manual processes was a key concern. Nearly two-thirds (65%) cited adoption of technology for "fixing inventory management" as the top priority ahead of AI and automation.

According to those scientists, only 15% of their laboratories are fully digitized at present. Among large pharmaceutical and biotechnology companies, just under half (48%) of respondents told us that their laboratories were fully digitized. In this case, we use *digitization* to mean adoption of advanced automation and sophisticated data-analytics platforms. However, over a quarter (28%) of large companies are only partly digitized at this stage, which points to the fact that even within well-funded organizations, laboratories aren't as efficient as they could be. Most start-up companies and academic institutions (83% of those surveyed) remain in the initial stages of digitization.

Overall, digital maturity, inventory management, and disconnected systems present significant challenges. Ultimately, though, progress will be unstoppable. When asked about trends that will transform laboratory operations, 77% of respondents said that automation will drive the most change, and 75% also pointed to AI. However, siloed platforms — e.g., electronic laboratory

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notebooks (ELNs), laboratory information management systems (LIMS), substance-registration software, workflow-management tools, and screening data analytics — and fragmented data make laboratory personnel spend much of their time manually collating, collecting, and recording data.

Doing It by Hand

Automation is critical to the journey toward AI in biomanufacturing and analytics. Automating repetitive and manual tasks, especially data capture and sample tracking, is key to the future. Over half (58%) of our survey respondents plan to automate repetitive tasks, and 57% expect to automate sample workflow tracking as well. Neary half (48%) are focusing on automating data capture and recording.

However, over 50% of our survey participants say that their laboratories still rely on manual processes, with digital maturity far from being fully achieved. Within that half, 39% of midsized and 38% of small biopharmaceutical companies rely on manual processes. Acquiring data from multiple instruments and applications takes time and creates potential for errors, especially when people must process raw, clumsy, comma-separated values (CSV) data for inclusion into ELN or LIMS platform.

At some organizations, test equipment is not integrated directly into any laboratory-management platform, although instruments and software are available to do it. Even when such basic equipment is implemented into a platform, however, that is only one step toward automating a laboratory.

Inventory and Automation

Many laboratory processes can be automated, with inventory management providing an obvious example. When supplies are low, experiments will be delayed. Laboratories need to manage their inventories efficiently so that critical materials will be on hand while overstock is minimized. Over half (55%) of our survey participants report already using inventory-management software, and nearly two-thirds (65%) plan to adopt a new system for that purpose. Those results signal a rising demand for more sophisticated and integrated solutions.

Automation can also accelerate sample and compound management. Robot arms can take materials directly from automated stores and liquid handlers and introduce them directly into testing equipment. If such automation is beyond an organization's budget, then using barcodes can help to ensure that samples and compounds will be tracked every step of the way.

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At some organizations, test equipment is not integrated directly into any laboratory-management platform. Even when such basic equipment is implemented, that is only **ONE STEP** toward automating a laboratory.

However, that requires diligence in scanning materials during every step, or human error will prevail.

Too Much of Everything

Life-science experiments can generate from tens to hundreds of thousands of data points. Managing those data becomes a challenge, beginning with collecting and managing results from multiple instruments, formats, and locations and extending to processing those results for comprehensive analysis. Just transforming unstructured data to structured form can require great effort toward simplifying analysis.

Furthermore, when multiple scientists use different databases, their data can take different forms across different "benches" with no single source of "truth." Scattered data can impair an organization's ability to generate high-level analyses. If you are simply performing one assay, then it's easy to analyze the results using general statistical methods. But when analyzing multiple assays to generate insights about processes or make biopharmaceutical discoveries, you need to collect every datum — including instrument metadata and perhaps even some environmental data. Information scattering makes it all too easy to miss critical elements and thus misinterpret the overall meaning. Furthermore, scattered data limits replicability of results and can compromise the documentation necessary to ensure good research and development (R&D), manufacturing, and testing practices from certification to process validation.

AI Isn't an Easy Fix

Although AI can accelerate discovery in biotechnology laboratories, its adoption creates challenges along the way. Data must be secured within an AI infrastructure; many platforms are offered in the form of software as a service (SaaS), so cloud security must be addressed. "Regular" data-storage regulations also need to be enforced.

Meanwhile, regulatory frameworks regarding the use of AI in R&D, manufacturing, and testing are under development. Their progress will need to be tracked for organizations to ensure ongoing compliance. Nearly half (48%) of scientists that we surveyed believe that implementation and oversight of AI tools will bring enforced changes from regulatory and market pressures. Ethical perspectives related to adopting AI for certain processes and analyses also need consideration.

Disparate AI tools can create problems based on their software infrastructure, so users will need low- and no-code solutions and easy integrations through built-in application programming interfaces

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When **MULTIPLE** scientists use different databases, their data can take different forms across different "benches" with no single source of "truth."

(APIs) that ease the burden on laboratory scientists and their organizations' information technology (IT) teams. When adopting any form of AI, researchers will need to ensure that it is analyzed for the "FAIR" data principles of findability, accessibility, interoperability, and reusability. Human oversight of AI always will be critical. It can project idiosyncratic results, for example, because of how scientists phrase their queries. Scientists must be the final decision-makers, especially when drug quality, safety, and efficacy are at stake.

Moving Forward

AI adoption will add significant value to R&D, manufacturing, and testing in the near future. By analyzing massive data volumes, such technology will bring faster, more effective results than ever have been possible before. Building AI into ELNs and LIMS will simplify data documentation.

One often-overlooked benefit is AI's ability to bridge the past and future. Laboratory scientists will be able to upload legacy protocols from portable document format (PDF), image, text, and word-processing software form into usable and reusable digital data. Historical results from a breadth of formats can be integrated into a new single source of organizational truth, creating opportunities for further discovery.

Connections between people and data will simplify when researchers can use AI chatbots to query databases directly rather than spending days waiting for their turn in programmer queues. Creative scientists will be able to combine their knowledge with AI's ability to optimize experiments and design fast, effective assays that will accelerate results.

And AI will streamline basic processes across entire laboratories. It can facilitate inventory management by analyzing consumption patterns and using predictive analytics to ensure that supplies will be ordered on time. Laboratory systems could have longer service lives than in the past once built-in or after-purchase predictive analytics can notify laboratory managers when maintenance is necessary. Meanwhile, instrument use will be streamlined as AI provides for increasingly effective planning and scheduling.

Finally, once AI has been integrated into all processes across a given laboratory, quality and analytical groups will be able to do much more with the same financial investments. If and when budget cuts come or grants are rejected, a laboratory should be able to continue operating efficiently.

What Researchers Want

According to our survey, life-science researchers have specific ideas about what AI can do for their laboratories and research.

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HUMAN oversight of AI always will be critical. It can project idiosyncratic results, for example, because of how scientists phrase their queries. **SCIENTISTS** must be the final decision makers, especially when drug quality, safety, and efficacy are at stake.

Only 17% of those surveyed expect AI to improve their data documentation and integration, whereas nearly a quarter (24%) say that it will allow them to manage massive data volumes from experiments, instruments, and other sources. About 19% speculate that AI will accelerate drug discovery.

Most professionals that we surveyed plan to implement AI in their laboratories within the next two to five years, with current plans for augmenting rather than replacing existing systems. By eliminating manual operations and speeding analyses over time, life scientists will be able to focus increasingly on the creative parts of their jobs rather than rote tasks that can sap their energy otherwise.

By eliminating manual operations and speeding analyses over time, life scientists will be able to focus increasingly on the **CREATIVE** parts of their jobs rather than rote tasks that can sap their energy otherwise.

A Must-Have for the Long Term

Early technology adopters most often have a competitive advantage over those who are slower on the uptake. Comprehensive AI infrastructure will enable laboratories to reduce costs, optimize resources, and accelerate discoveries. However, such gains will be offset if other challenges related to automation and inventory management aren't addressed during the implementation process. Without addressing those concerns, life science will continue to operate at its current pace, preventing AI from delivering on its full promise for advancing transformative cures.

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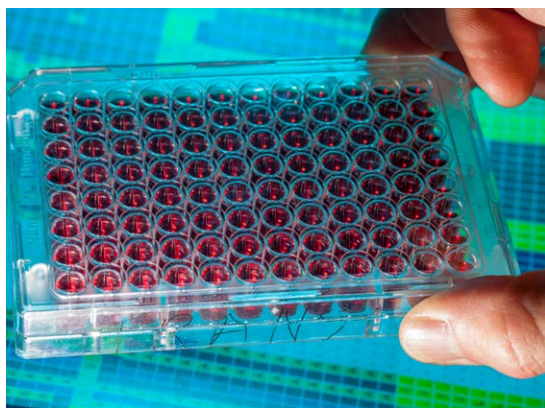
Rethink Raw-Material Analytics for Biomanufacturing

Next-Generation Therapies Demand Next-Generation Inputs

by Jonathan Dharamraj

As biologics and novel drug modalities increase in complexity, raw-material quality has emerged as a pivotal factor in ensuring product safety, efficacy, and consistency. The shift from classical small-molecule therapies through genetically engineered biologics to advanced modalities such as RNA-based drugs and cell/gene therapies (CGTs) has introduced new dependencies on materials of both biological and synthetic origin, each bringing its own characteristic analytical challenges.

Regulators now expect comprehensive material characterization, traceability, and control strategies that extend deep into company supply chains. As a result, drug developers are reevaluating how raw-material assays fit within their quality by design (QbD) frameworks and risk-management programs. A renewed focus on analytical rigor, supplier qualification, and phase-appropriate assay validation is reshaping how biomanufacturers and their analytical partners approach material testing and regulatory readiness.



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Expanding Complexity in Chemistry, Manufacturing, and Controls

The raw-material landscape for biologics and advanced therapies is evolving faster now than ever before. Traditional pharmaceutical manufacturing relied primarily on well-characterized materials such as buffers, amino acids, and growth factors. Today's biotherapeutic pipelines, however, incorporate increasingly diverse and sensitive components such as lipid nanoparticles, viral vectors, plasmids, chemically modified nucleotides, human cells and tissues, and novel excipients — each of which presents specific analytical and regulatory challenges. Such raw materials profoundly affect product quality attributes (PQAs), process consistency, and ultimately patient safety.

For monoclonal antibodies (mAbs) and other recombinant proteins, even trace impurities in a single excipient or reagent can

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alter glycosylation profiles, potency, or aggregation tendencies. For example, trace metals such as manganese, copper, zinc, and iron are known to influence mAb N-glycosylation profiles, altering the balance of glycan species within a given batch (**1**).

In CGT manufacturing, the stakes can be even higher. Materials such as transfection reagents, serum supplements, and plasmids are inherently variable and often sourced through complex global supply chains, making process reproducibility difficult. Endotoxin contamination in plasmid DNA and residual solvents in polymer transfection reagents have caused batch inconsistencies, for example (**2**). Without robust control strategies, such variabilities can translate directly into inconsistent transduction efficiencies, vector potencies, and cell viabilities.

Adding further complexity, many next-generation materials are biologically derived, multicomponent systems with limited historical reference data. Their characterization often requires advanced analytical techniques — e.g., liquid chromatography with mass spectrometry (LC-MS) for molecular fingerprinting, quantitative polymerase chain reaction (qPCR) for vector integrity, and nuclear magnetic resonance (NMR) spectroscopy for compositional profiling — combined with statistical modeling to understand performance consistency.

Regulators have responded accordingly. Agencies around the world now expect drug developers to establish risk-based raw-material qualification programs that include deep analytical insight, supplier oversight, and traceability to ensure end-to-end quality control. Such expectations no longer are limited to late-phase programs, with many investigational new drug (IND) application–enabling and early development stages now requiring data-driven justification of material suitability. As a result, some drug developers are turning to specialized contract research organization (CRO) partners with expertise in complex material analysis and method development to fill related capability gaps and accelerate regulatory readiness.

Many next-generation materials are **BIOLOGICALLY** derived, multicomponent systems with limited historical reference data. Their characterization often requires advanced analytical techniques combined with statistical modeling to understand performance consistency.

Analytical Innovation and Phase-Appropriate Strategies

As biologics and novel modalities progress, analytical innovation has become central to effective raw-material control. The biopharmaceutical industry is shifting away from one-size-fits-all testing toward phase-appropriate assay strategies that balance scientific rigor, speed, and regulatory alignment. Established analytical technologies such as high-performance liquid chromatography with ultraviolet spectroscopy (HPLC-UV) and low-

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resolution MS are not suitable for detection of low-level impurities and provide only limited structural resolution. To match the growing complexity of today's materials, analytical platforms must be more sophisticated.

Advanced techniques can be applied during early stage development and fit-for-purpose screening assays to establish material suitability. A few methods also are being validated and formalized to support formal release and comparability programs of later stages in product development. High-resolution LC-MS enables fingerprint-level impurity profiling for chemically modified excipients and nucleotides. Novel next-generation sequencing (NGS) and digital PCR (dPCR) provide unparalleled precision in confirming genetic integrity for plasmids, viral vectors, and engineered cell systems. Meanwhile, orthogonal techniques such as capillary electrophoresis and Fourier-transform infrared (FTIR) and NMR spectroscopies can be integrated to cross-verify and detect subtle compositional shifts that traditional assays otherwise would miss.

Equally important is the growing emphasis on data integrity and life-cycle management. Regulators expect analytical control strategies to evolve as scientific knowledge deepens, with methods refined and revalidated in alignment with process understanding. Automated data systems, digital laboratory management platforms, and analytics enabled by artificial intelligence (AI) have become key enablers for such an iterative approach to improve both reproducibility and regulatory defensibility.

Cross-functional collaboration is essential to success. Analytical scientists, process engineers, and quality assurance and control (QA/QC) teams must work closely to define critical material attributes and select assays that directly link those to process or product performance. For example, material-science teams must consider the amino-acid balance, trace-metal content, osmolality, and pH of cell-culture media. When those teams work closely with process engineers and quality specialists, data about such parameters can be correlated to bioreactor information about cell-growth, expression titers, and PQAs such as glycosylation and aggregation, thus tying material attributes directly to process performance and critical quality attributes (CQAs). Such integration supports QbD principles to ensure that each material assay contributes to a robust understanding of overall process capability and product safety.

Ultimately, the analytical toolkit for raw materials is expanding beyond a regulatory-compliance activity; it is becoming a competitive advantage. Organizations that adopt modern, phase-

Regulators expect analytical control strategies to **EVOLVE** as scientific knowledge deepens, with methods refined and revalidated in alignment with process understanding.

appropriate strategies can derisk development, shorten their IND timelines, and position themselves for smooth regulatory interactions across the product life cycle.

Ask the Experts

As analytical expectations increase, choosing the right CRO partner can be as critical for many sponsors as selecting the raw materials themselves. Not all testing laboratories are equipped to handle the diversity and complexity of those used in manufacturing biologics and advanced therapies. An ideal partner not only uses the latest analytical platforms, but also has the scientific understanding to interpret results in the context of bioprocess performance and regulatory compliance.

Expert CROs integrate specialized capabilities (e.g., for high-resolution MS, NGS, and dPCR) together with deep experience in phase-appropriate method development and validation. Facilities and infrastructure are just as important. Dedicated cleanroom environments, contamination-control systems, and validated reference standards ensure data integrity and reproducibility across projects.

Partnerships are most effective when built upon transparency and scientific dialogue. Engaging early with a CRO enables codevelopment of testing strategies that align with regulatory expectations and process realities. Such collaboration allows sponsors to focus their internal resources on development while leveraging their partners' analytical depth for qualification, release, and stability programs. Outsourcing analytical control also reduces the burden of instrument maintenance and specialized staffing so that internal teams can focus on development priorities while ensuring scientific continuity.

Ultimately, the best partner is more than a mere service provider, but rather a strategic extension of the sponsor's quality organization that can anticipate regulatory trends, troubleshoot process deviations, and support a program's transition from research and development (R&D) to commercial readiness. In an environment defined by innovation and complexity, finding the right experts ensures analytical precision, operational agility, and lasting confidence in every material entering a biomanufacturing process.

Trends and Expectations

The biopharmaceutical industry is entering a new phase of analytical maturity that will be defined by data-driven precision, digital integration, and proactive QC. As biologics and next-

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Organizations that adopt modern, **PHASE-APPROPRIATE** strategies can derisk development, shorten their IND timelines, and position themselves for smooth regulatory interactions across the product life cycle.

generation therapies diversify, raw-material assays no longer will be viewed as ancillary compliance activities — becoming instead strategic enablers of speed, safety, and regulatory confidence.

One key trend shaping that evolution is the adoption of multiattribute methods (MAMs) and high-resolution analysis for raw-material "fingerprinting." Such techniques enable drug developers to detect subtle compositional differences that can affect product consistency long before manufacturing scale-up. The shift toward real-time and predictive analytics powered by automation, digital twins, and machine learning can transform how laboratories monitor material quality. Instead of reacting to deviations, biomanufacturers increasingly will be able to predict and prevent them.

Meanwhile, regulatory expectations are tightening. Agencies around the world are signaling a move toward deeper source transparency and traceability for all raw materials, whether chemically synthesized, recombinant, or animal derived. Demand for data integrity and continuous monitoring will extend across the global supply chain, requiring integrated systems that connect supplier analytics, in-house testing, and CRO data in real-time.

As a result, outsourcing partnerships could play an even greater strategic role. Sponsors should look beyond transactional testing relationships to seek analytical collaborators that can translate complex data into actionable insight. The most valuable partners will combine advanced instrumentation with regulatory fluency, digital infrastructure, and scientific agility.

Ultimately, success in 2026 and beyond will come to those companies that treat raw-material analytics not as a mere checkbox, but rather as a cornerstone of innovation and control. Organizations that apply the best expertise at the right time are likely to be first in bringing the safest, most consistent, and most innovative therapies to market.

As the biopharmaceutical industry advances toward increasingly complex biologics and novel modalities, raw-material testing has become a defining pillar of QA/QC and regulatory compliance. What was once a supporting activity is now a strategic differentiator linking supplier reliability, analytical innovation, and regulatory trust into one continuous framework. The next generation of therapies will depend on developers' ability to understand their materials at the molecular level and to act on that knowledge with speed and confidence.

Building partnerships with expert CROs that can deliver sophisticated, phase-appropriate assays and data-driven insights will be important to navigating the new landscape. Those sponsors

The shift toward real-time and **PREDICTIVE ANALYTICS** powered by automation, digital twins, and machine learning can transform how laboratories monitor material quality. Instead of reacting to deviations, biomanufacturers increasingly will be able to predict and prevent them.

that invest early in robust analytical control will satisfy evolving regulatory expectations while accelerating development, strengthening process robustness, and delivering thorough quality for patient safety.

In the era of increasingly complex biologics ahead, analytical excellence for raw materials will not be optional; it will form a foundation for competitive success. Through the right analytical foundation and expert partnerships, the therapies of tomorrow can reach patients faster, safely, consistently, and with confidence.

Those sponsors that invest early in robust analytical control will satisfy evolving regulatory expectations while accelerating development, strengthening process robustness, and delivering thorough quality for **PATIENT SAFETY.**

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Validating Your NGS Assays? Here's Our Take

Ludwig Macko and Valentina Armiento

Cell and gene therapies (CGTs) are shaping modern medicine by targeting diseases at their source through cellular and genetic modifications. The true game-changer for such therapies will lie in rigorous quality control (QC), with next-generation sequencing (NGS) technology providing the fastest and most comprehensive way to ensure their safety and efficacy.

With the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) increasingly endorsing NGS for virus detection as an alternative to animal testing (**1**), more companies are adopting that approach, reflecting the industry's readiness for next-generation technologies. However, the critical step will be mastering validation of NGS assays within a good manufacturing practice (GMP) environment, which involves validating instruments, methods, and software.

Virus detection is one important use case for NGS, but the technology also is being validated for other critical applications in CGT. Those include confirming vector identity and integrity, analyzing integration sites, and detecting off-target effects. In genome-editing approaches such as those based on clustered, regularly interspaced palindromic repeats (CRISPR), off-target analysis is particularly important for assessing unintended modifications. Regulatory agencies including the FDA have issued guidance emphasizing the need for robust characterization of those effects (**2**). Such applications are gaining regulatory recognition and reinforce the role of NGS as a central tool for product characterization and safety assessment. With the scope of NGS applications continuing to expand, validating these assays to meet regulatory expectations becomes increasingly important.

The bottom line? NGS validation will become an essential step in ensuring CGT safety and efficacy while helping to streamline processes with a single, robust QC assay.

A Validation Journey: Insights and Best Practices

Organizations venturing into NGS assay validation need to understand the critical steps of the process. Here are key practices that can make or break a validation journey.



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NGS validation will become an essential step in ensuring CGT **SAFETY AND EFFICACY** while helping to streamline processes with a single, robust QC assay.

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Before diving into best practices for compliance, it's important to define the essential toolkit for a reliable NGS workflow. Although specific technologies can vary, high-performing laboratories share a common foundation. At the heart of every NGS setup is the sequencing system itself, which generates considerable genetic data with speed and precision. Whether optimized for short reads, which offer high accuracy and throughput, or long reads, which are better suited for resolving complex regions, the choice depends on the assay's goals. Surrounding the sequencer are tools for sample preparation, QC, and data management. Those include systems for DNA/RNA extraction, library preparation, and QC, as well as the computational infrastructure needed to process, interpret, and manage a substantial amount of sequencing data.

Together, those elements form a tightly integrated ecosystem. Each tool must not only perform reliably on its own, but also integrate seamlessly into the complete workflow.

Laboratory Equipment Compliance: Ensuring that laboratory equipment is up to par is foundational for reliable NGS assay validation. It is not just about having the right tools; every piece must meet stringent specifications and be managed meticulously. Setting up a validated lab environment requires robust methods and thoroughly trained personnel to keep everything running smoothly.

Detailed standard operating procedures (SOPs) should cover every aspect of the workflow, from equipment calibration to data management, ensuring consistency, accuracy, and compliance. The equipment used in GMP workflows must undergo rigorous qualification and validation to confirm that it meets all user requirements and specifications. That is not a one-time task; it involves ongoing monitoring and maintenance to ensure continued compliance.

What does qualification look like for NGS systems? It typically involves a combination of vendor and user documentation, internal verification studies, and cross-functional activities that confirm reliable system performance in its intended context. That includes reviewing factory acceptance tests for new facilities, conducting site acceptance checks, and running assay-specific performance studies to establish baseline functionality.

What sets NGS systems apart from other analytical instrumentation is their reliance on tightly integrated components. Sample-preparation instruments, sequencers, and data-capture tools all must work in concert, making qualification not just about individual instruments, but also about validating the continuity and consistency of the entire workflow and ensuring data integrity.

QUALIFICATION for NGS systems typically involves a combination of vendor and user documentation, internal verification studies, and cross-functional activities that confirm reliable system performance in its intended context.

Validation of Data-Analysis Platforms: Data-analysis platforms are pillars of NGS processes. Start by defining specific user requirements and functional specifications for your platform. What GMP functionalities are needed? How will it integrate with existing systems? Have you defined your strategy for long-term data management? A robust validation plan should outline validation activities, user requirement specifications, acceptance criteria, and documentation requirements. Moreover, during computerized system validation, always ensure data integrity, security, and traceability.

When choosing an NGS data analysis platform, consider both its operational and compliance capabilities. Our advice is to prioritize platforms that offer comprehensive functionalities, even if full compliance requirements will be addressed later. Implementing missing functionalities might not be possible at later stages. Platforms from established companies with proven track records help to ensure long-term stability for your validated NGS workflows.

Your chosen platform should include capabilities for audit trails, data-integrity checks, comprehensive reports, and documentation for installation (IQ), operational (OQ), and performance qualification (PQ). Access to data and software features should be restricted based on clearly defined roles and responsibilities for users and managers to ensure data integrity.

Don't underestimate the user experience. A software platform should be user-friendly, enabling both bioinformaticians and laboratory scientists to use it without needing the command line. By being able to track all data from sample registration to analysis and visualization on one platform, users can obviate errors from exporting and copy–pasting.

Users should consider future needs as well. You eventually might work with a number of NGS assays, from adventitious-virus detection to starting-material and product-release testing. For gene therapies and viral vaccines, that might include identity and integrity testing of plasmids and viral vectors. To support scalability and flexibility, consider validating the analysis platform separately from the data-analysis workflows so that the system can be extended across multiple assays, modalities, and locations. That strategy provides process control, customization opportunities, and scale-up possibilities, leading to a significant return on investment in the long run.

Finally, be cautious of marketing claims that seem too good to be true. Consulting a team of experts from the lab as well as quality assurance (QA), information technology (IT), and even legal

Consulting a team of experts from the laboratory as well as quality assurance (QA), information technology (IT), and even legal functions can help you to select the best software solution that is **FIT FOR PURPOSE**.

functions can help you to select the best software solution that is fit for purpose.

Method Validation and Optimization: Method validation is where everything comes together. Start by defining clear objectives and desired outcomes, including controls with relevant acceptance criteria. Developing detailed protocols for each step of the workflow — from sample preparation to data analysis — is essential. Assess accuracy and precision by comparing results to known standards to ensure data reliability. Here, accuracy refers to quality per sequencing read and how closely variant calls match a reference; precision measures how consistently those results are reproduced across replicates.

Experiments should yield reproducible outcomes across runs and operators, demonstrating that your method performs reliably under varying conditions. In practice, accuracy above 99% and precision above 95% are strong indicators of a robust assay. Sensitivity and specificity are equally important, especially when detecting rare variants or viral contamination in a product. Establishing and respecting limits of detection and thresholds will help to ensure that your assay reliably detects variants and contaminations at the lowest possible concentrations. Doing so also helps in maintaining consistent performance across conditions.

Your bioinformatics pipeline must be validated rigorously for accurate processing and interpretation of sequencing data. Unlike development approaches that focus on process optimization, validation workflows are locked and must be reproducible every time.

Monitor performance using defined QC metrics. QC should be embedded throughout a workflow and monitored routinely, typically per run or batch. Monitoring includes tracking key indicators such as sequencing depth, signal quality, alignment efficiency, and coverage consistency, along with assay-specific metrics such as variant frequency, read count, and breadth of coverage. Those metrics act as early warning signals, helping teams to catch deviations before they influence results.

Don't forget documentation. Every detail and finding should be meticulously documented and summarized in a validation-compliant report. Thorough record-keeping ensures compliance, saves time, and prevents issues down the line.

Project Management: NGS validation projects require orchestration. Assigning an experienced manager from the outset can facilitate the process by coordinating the activities and needs of different teams, including scientists/experts from analytical development, QA, IT, legal, procurement, and life-cycle

Every detail and finding should be meticulously **DOCUMENTED** and summarized in a validation-compliant report. Thorough record-keeping ensures compliance, saves time, and prevents issues down the line.

management. Validation-project leadership is essential because there are no ready-made solutions for NGS assay validation. It's like having all of the parts to build an airplane; coordination, expertise, and collaboration among multiple stakeholders are required to assemble it and make it operational.

Without a project manager, there is a high risk of significant delays — potentially up to ten times longer than the intended timeline — or even complete failure in validating workflows. A project manager plans every milestone, ensuring that a project stays on track and within its defined scope.

A Rewarding Journey

NGS validation is a journey with long-term, business-critical benefits. Success hinges on organizing your validation team from the start and carefully considering both current and future NGS validation needs. Engaging with regulatory bodies offers strategic benefits, providing invaluable feedback and streamlining the validation process. Our experience shows that the FDA supports applying a single validated platform across multiple assays, enhancing efficiency and consistency.

As biotherapeutics evolve, NGS will enable more precise and comprehensive analyses than less-sophisticated technologies can, helping to address the complexities of CGTs. Innovations in automation and data analysis will streamline workflows further, reducing the time and cost of NGS assays. Companies investing now into in-house NGS capabilities will be well positioned to develop safe and effective therapies in the future.

Success hinges on organizing your validation team from the start and carefully considering both current and future needs. Engaging with regulatory bodies offers strategic benefits, providing invaluable feedback and **STREAMLINING** the validation process.

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