PHARMA FOCUS EUROPE
Issue 07 | 2025
www.pharmafocuseurope.com

Uwe Hanenberg
Head of Product Development, Oral Solid Dose, Recipharm

Lyophilisation

Key to Overcoming Stability Hurdles for Complex Therapeutics

Pioneering the Future of Pharma

Innovation, Strategy, and Transformation

Step inside the latest edition of **Pharma Focus Europe,** Issue 07, where the pharmaceutical industry's most transformative conversations take center stage. This issue goes beyond headlines, providing an exclusive perspective on how the pharma sector is evolving through innovation, digital breakthroughs, and patient-centric strategies that are shaping the future of the pharmaceutical industry.

Covering key stories from strategy to innovation:

- **Lyophilisation - A Stability Game-Changer:** In this cover story, Uwe Hanenberg explores how lyophilisation is revolutionizing the stability of complex therapeutics, enabling longer shelf life, reduced cold-chain dependence, and improved global accessibility.

- **Digital Transformation in Pharmaceutical Quality** Dr. Sophie Fröhlich presents the integration of AI, automation, and real-time data in pharmaceutical quality systems, highlighting the challenges and opportunities of digitalisation in a highly regulated industry.

- **In-Vivo CAR-T Therapy: The Next Frontier** Peter Robinson discusses the transformative potential of in-vivo CAR-T therapies, which promise scalable, rapid intervention for oncology and autoimmune diseases.

- **B-Cells in Immunotherapy** Daniel-Paul Bednarík, Kristi Jones, and Mathias Oelke highlight the emerging role of B-cells in immunotherapy, transitioning from broad depletion to antigen-specific precision for cancer and autoimmune treatments.

- **Digital Infrastructure for Cell and Gene Therapies** Akshay Peer and Antonios Spanos emphasise the need for standardisation and scalability in the fragmented digital landscape of cell and gene therapy orchestration.

- **Nanomedicine Manufacturing: From Lab to Scale** Mark van Eldijk highlights how flow manufacturing is overcoming scalability and quality challenges in nanoparticle production, paving the way for consistent and reproducible results.

- **Agentic AI: The Next Leap in Drug Discovery** Raghuraman Sridharan explores the potential of Agentic AI to autonomously act on data insights, accelerating drug discovery, clinical trial setup, and regulatory submissions.

- **Dermal Drug Delivery Systems: A New Era of Patient-Centric Care** Andrew Riso discusses the promise and challenges of transdermal and microneedle-array patches, emphasizing the need for integrated formulation, device design, and manufacturing.

- **Nanotechnology in Therapeutics:** Professor Costas Demetzos offers a comprehensive framework for developing bio-inspired nanosystems, highlighting the role of AI and machine learning in advancing nanomedicine.

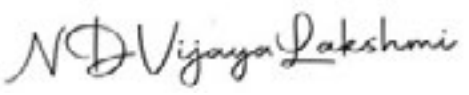
- **Nanoparticle-Based Drug Delivery Systems** Philipp and Martin discuss the scientific bottlenecks, regulatory challenges, and the role of CDMOs in scaling nanoparticle delivery systems.

- **Expert Insights:** Dr. Humberto Vega and Dr. Bassem Gayed provide expert insights into process validation as a continuous, data-driven commitment to quality, ensuring consistent product performance and patient safety. Oliver Overheu shares strategies to overcome systemic inefficiencies in oncology trials, emphasizing patient-centric designs, digital innovations, and collaborative models.

Turn the pages to explore a curated selection of articles, interviews, whitepapers, and analyses in this edition, revealing the key innovations and strategies steering the pharmaceutical industry forward.

We sincerely thank our contributors for sharing their expertise and insights, and we extend our gratitude to our readers for joining us in exploring the advances that are transforming the pharma sector and redefining patient-centric care.

Stay connected!



N D Vijaya Lakshmi

Editor

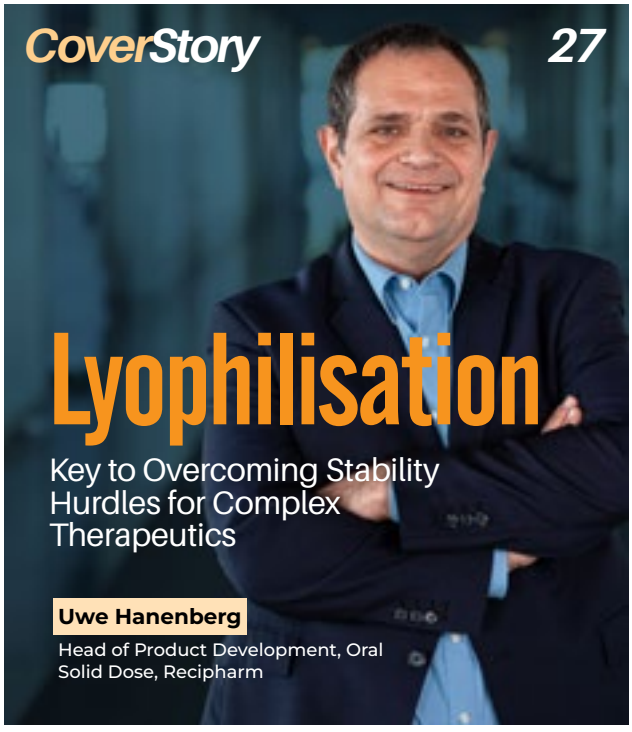
CONTENTS

STRATEGY

RESEARCH & DEVELOPMENT

BIOPHARMA

CLINICAL TRIALS



MANUFACTURING

INFORMATION TECHNOLOGY

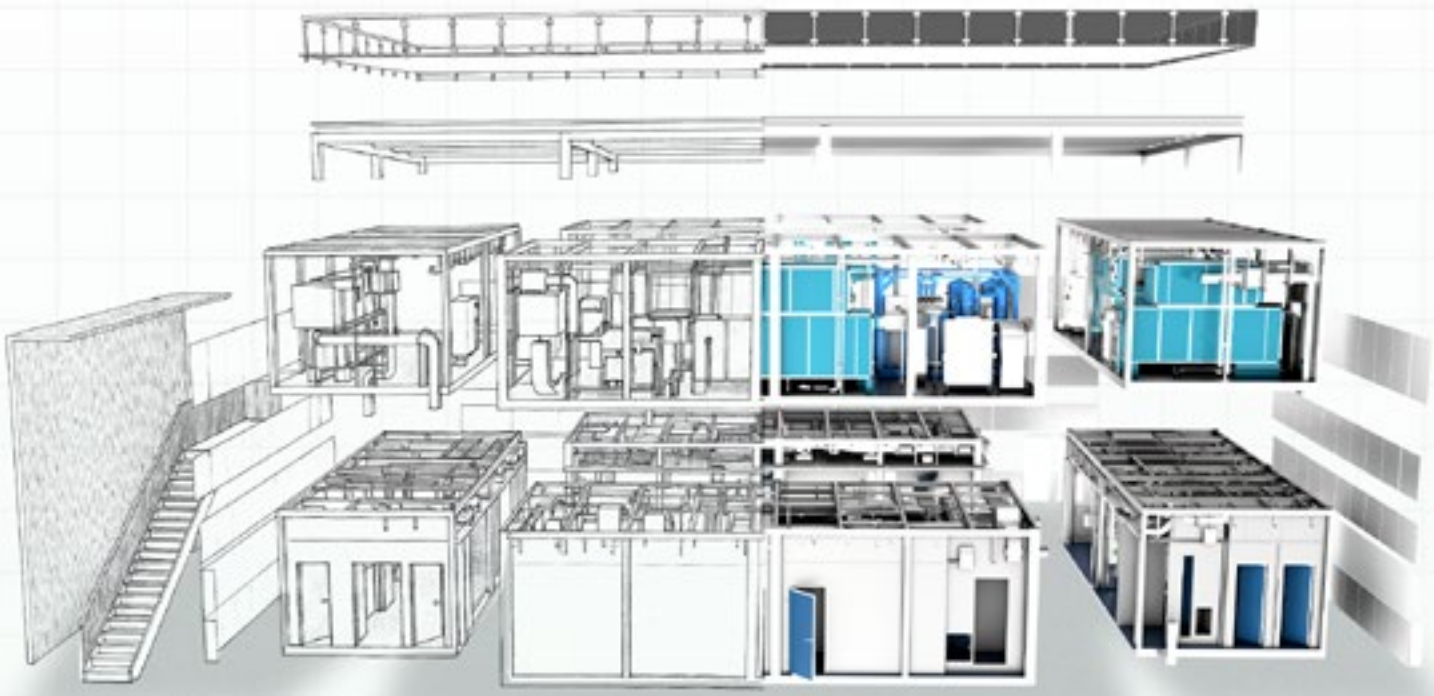
INDUSTRY SENSE

pharmaaccess
Engineering a Healthier Life

MODULAR MOBILE FACILITY
HEALTHCARE RE-ENGINEERED

Faster. Smarter. Modular.

Modular Mobile Facility offers turnkey solutions engineered for agile, scalable, and rapidly deployable pharma operations.



Key Differentiators

- Cost Reduction
- Effortless Site Installation
- Accelerated Construction and Seamless Integration
- Resource Efficient
- Rapid Launch Approach
- Sustainable-Reduced CO_2 Footprint

+91 98207 75650 | + 91 22 6819 3888
info@mmfacility.org
www.mmfacility.org
www.pharmaaccess.net

ExpertTalk

PHARMA FOCUS EUROPE

EDITOR
Vijaya Lakshmi N D

EDITORIAL TEAM
Sarah Richards
Debi Jones
Sravanthi Korra
Harry Callum
Supraja BR

ART DIRECTOR
M Abdul Hannan

PRODUCT MANAGER
Jeff Kenney

ASSISTANT MANAGER
David Nelson
Peter Thomas

SENIOR PRODUCT ASSOCIATES
Maheshwari
Mercy Vincent

BUSINESS EVENTS
Sussane Vincent

CIRCULATIONTEAM
Sam Smith

SUBSCRIPTIONS IN-CHARGE
Vijay Kumar Gaddam

HEAD-OPERATIONS
Sivala VNR

PHARMA FOCUS EUROPE

www.pharmafocuseurope.com

Ochremedia®

Ochre Digi Media
www.ochre-media.com

Magazine Subscribe

LinkedIn

Advisory Board

Alessio piccoli
Director & Head, Business Development Europe presso Aragen
Italy

Amine Bekkali
Director,
Medfields, UAE

Dmitrii Vitalievich Kriuchkov
Executive Director
Axon Clinical Trial Lab
Russia

Gustavo Samojeden
CEO, Eriochem S.A
Argentina

Hassan Mostafa Mohamed
Chairman & Chief Executive Officer
ReyadaPro
Saudi Arabia

Hoda Gamal
Director of Regulatory and Corporate Affairs Middle East and Africa,
Allied associate, Egypt

Joaquin D. Campbell
Global Director
Managed Access Services
Spain

Josipa Ljubicic
QA Director / Principal GCP and GVP auditor, Proqlea Ltd
Croatia

Juris Hmelnickis
CEO, Grindeks
Latvia

Nicoleta Grecu
Director, Pharmacovigilance Clinical Quality Assurance
Romania

Nigel Cryer FRSC
Global Corporate Quality Audit Head
Sanofi Pasteur
France

Paola Antonini
Chief Scientific Officer,
Meditrial Global CRO
Italy

Pinheiro Neto Joao
Chief Executive Officer
Meu Doutor
Angola

Shamal Jeewantha Fernando
Managing Director,
Slim Pharmaceuticals (Pvt) Ltd
Srilanka

Svetoslav Valentinov Tsenov
Senior Pharma Executive and Global Transformation Lead
Bulgaria

Tamara Miller
Senior Vice President, Product Development, Actinogen Medical Limited, Sydney

Teresa Derbiszewska
Clinical Quality Director
G42 Healthcare/IROS
UAE

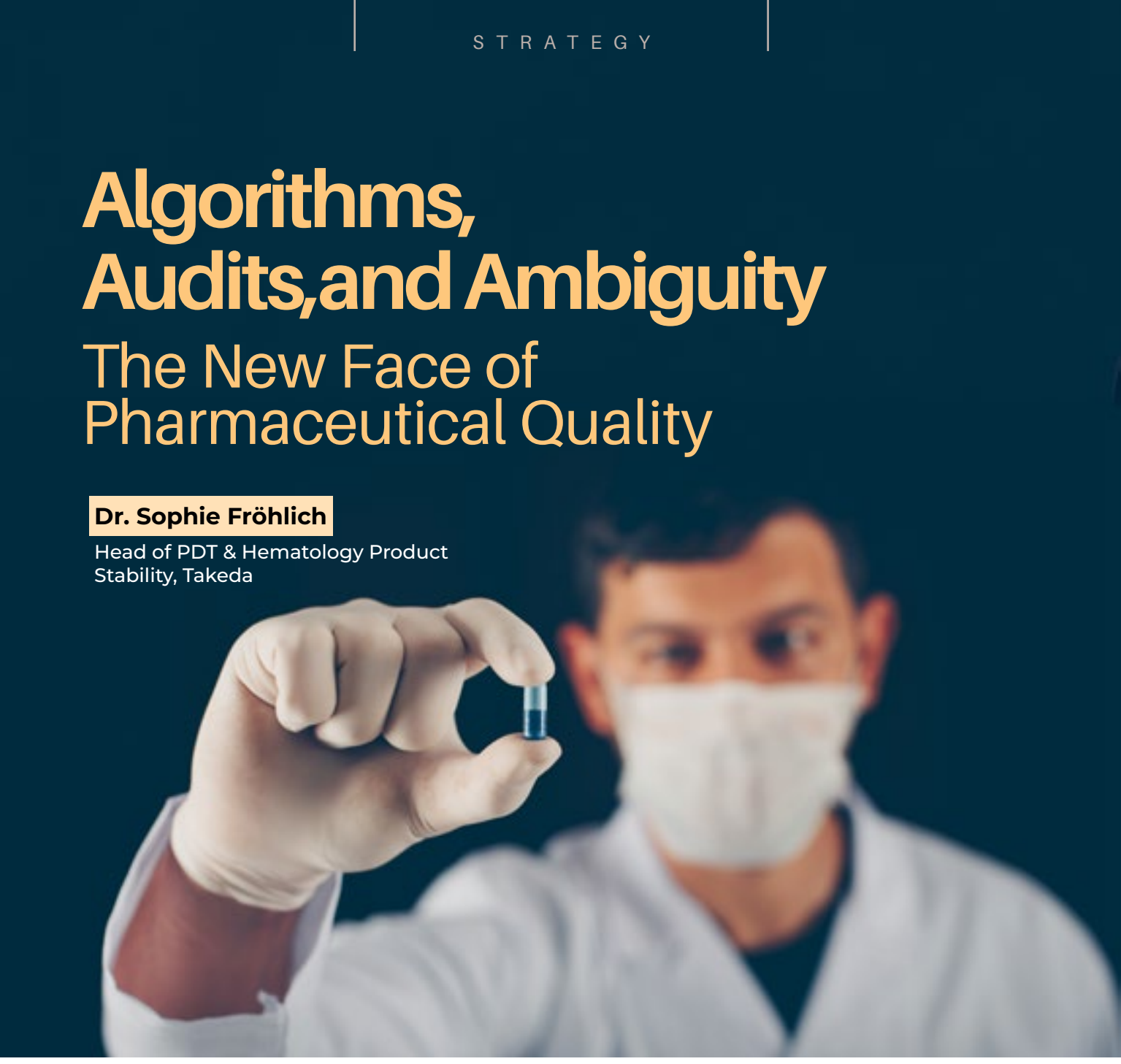
Thitisak Kitthaweesin
Chief of Phramongkutklao Center of Academic and International Relations Administration, Thailand

Vicknesh Krishnan
Associate Medical Director at Fresenius Medical Care Malaysia Sdn Bhd
Malaysia

Algorithms, Audits,and Ambiguity

The New Face of Pharmaceutical Quality

Dr. Sophie Fröhlich
Head of PDT & Hematology Product Stability, Takeda



Digital transformation is redefining quality and regulatory compliance, turning static processes into intelligent, agile systems. AI, automation, and real-time data unlock faster decisions, proactive risk management, and seamless global compliance. It is not just evolution, it's a revolution in how pharma ensures quality, accelerates approvals, and delivers safer products to patients, faster.

Digital transformation is reshaping pharmaceutical quality systems with the promise of speed, precision, and predictive power. It is a shift from manual oversight to algorithmic assurance, from static SOPs to intelligent and self-improving processes. However, while the destination is clear, the journey is anything but, the transformation phase is fraught with

ambiguity - from unclear roles and redefined responsibilities to uncertain regulatory expectations and shifting justifications for ROI. What appears to be a path toward clarity often introduces layers of complexity that challenge traditional thinking. This article explores the tension between promise and process: the ambiguity digitalisation introduces during its implementation phase, the regulatory and organisational challenges it brings, and the structural decisions shaping pharma's digital future.

Digitalisation in pharmaceutical quality refers to the integration and use of digital technologies (such as data analytics, automation, cloud platforms, and artificial intelligence) to enhance quality assurance, compliance, and efficiency across the pharmaceutical manufacturing and quality management lifecycle. It helps ensure regulatory adherence, data integrity, and continuous improvement in line with Good Manufacturing Practice (GMP).

Some examples include the following: Electronic Quality Management Systems (eQMS) are replacing paper-based deviation, CAPA (Corrective and Preventive Actions), and change control records with digital platforms that allow real-time tracking, faster approvals, and complete audit trails. Digital Batch Records often systematically referred to as electronic batch records (EBR) instead of manual paper documentation during production can reduce human error, ensure compliance and enable faster product release. Predictive Analytics in Quality Control applies machine learning to process data to predict potential deviations before they occur and thereby can improve product consistency and reduce the risk of non-conformances. Automated Data Integrity Monitoring uses software to continuously check laboratory and production data for anomalies, while ensuring compliance with regulatory requirements like the FDA's 21 CFR Part 11.

Ambiguity at the Intersection of Quality and Technology

The pharmaceutical sector operates in a highly regulated, risk-averse environment. Quality and compliance functions are built on the foundations of repeatability, documentation, and control. Digital tools, particularly those powered by AI and real-time data analytics—threaten this stability, not through failure but through transformation.

During implementation, ambiguity emerges in multiple dimensions. Process ownership and accountability are key as systems take on decision-making roles (e.g., anomaly detection in manufacturing data). Consequently, it's often unclear where human oversight ends and machine responsibility begins. On the other hand, while regulators are increasingly open to digital innovation, guidance is still evolving to enhance regulatory acceptance. There is limited precedent for how advanced algorithms should be validated or how autonomous systems should be audited. Traditional compliance frameworks are document-driven and digital systems are data-driven. Bridging this gap requires not only technical but also cultural transformation. ▶

> The real promise of digital transformation is not headcount reduction but repurposing human capability for higher-value work.

Implementation Challenges: From Vision to Reality

Implementing digital solutions in pharmaceutical quality is not a simple technology upgrade; it is a fundamental reengineering of operational logic. Even highly promising tools often struggle to cross the chasm from proof-of-concept to enterprise adoption.

However, some key barriers need to be considered. Many quality systems are deeply entrenched, with interconnected processes that resist modular replacement. The shift from documentation managers to data stewards and AI auditors demands reskilling that is often underestimated. Digital quality initiatives often sit at the crossroads of IT, quality, manufacturing, and regulatory affairs. Misaligned priorities and unclear governance frequently stall progress. Ironically, systems designed to reduce human error are often met with human skepticism. Building confidence in automated decision-making requires transparency, training, and time. In the digital age, regulatory compliance is no longer a fixed set of checkboxes but a dynamic interplay between evolving guidance and rapidly changing technology. This has given rise to the concept of "regulatory intelligence"—the continuous scanning, interpretation, and application of global regulatory changes.

However, the pursuit of regulatory intelligence introduces ambiguity of its own. Different markets interpret data integrity and AI validation requirements differently. Harmonisation is a goal, not a reality. Technologies like machine learning, blockchain, and digital twins often outpace existing regulatory frameworks. Companies must make risk-based decisions in regulatory grey zones. Maintaining regulatory awareness across global markets can become a significant overhead, particularly as regulatory updates accelerate. The organisations that succeed are those that embed regulatory intelligence into digital transformation itself, not as an afterthought, but as a design principle. Digitalisation has become a central theme in global pharmaceutical quality regulations, with guidelines across agencies emphasising its role as both a compliance requirement and a driver of efficiency.

The International Council for Harmonisation (ICH) Q10 framework outlines the pharmaceutical quality system (PQS), focusing on elements such as process performance monitoring, CAPA, change management, and management review. While Q10 does not

explicitly prescribe digitalisation, its effective application is increasingly dependent on digital tools like electronic Quality Management Systems (eQMS) and electronic batch records, which help ensure data integrity, streamline workflows, and enable risk-based decisions.

In the United States, the FDA's 21 CFR Part 11 defines requirements for electronic records and signatures, mandating validation, audit trails, and secure controls equivalent to paper-based processes. Similarly, the European Union's GMP Annex 11 focuses on computerised systems within GMP environments, requiring robust validation, incident management, data security, and user training. Together, these frameworks form the foundation for compliance in a digital context. Complementing them, the GAMP 5 (Good Automated Manufacturing Practice) guidance provides practical principles for validating automated and digital systems, emphasising risk-based approaches.

Beyond compliance, regulators are advancing digital transformation through standardised data models. The FDA and EMA have aligned on digital data exchange frameworks using HL7 FHIR and ISO IDMP-based SPOR systems, enabling structured, real-time regulatory submissions. The eCTD (Electronic Common Technical Document) has already replaced paper dossiers as the global standard for submissions, while the eTMF ▶

(Electronic Trial Master File) is now widely accepted for clinical documentation, provided systems meet validation, access control, and audit trail requirements. Recent initiatives extend digitalisation to innovation.

The EMA has launched a Quality Innovation Group and issued reflection papers on the use of artificial intelligence (AI/ML) in pharmaceutical development and manufacturing. Similarly, the FDA released draft guidance on AI applications across drug lifecycle activities, from manufacturing controls to real-world data analysis. Meanwhile, EMA's data quality framework is shaping standards for ensuring the reliability of digital and real-world data used in regulatory decision-making.

Headcount Reduction and the Human Question

One of the most sensitive consequences of digitalisation is the impact on workforce structures. Automation often leads to headcount rationalisation, especially in routine roles such as document review, data entry, and batch release support.

While cost reduction is often touted in business cases, this transition introduces deeper organisational questions.

Much of pharma quality relies on tacit knowledge, experience, intuition, and judgment. Can systems replace this, or should they be designed to enhance it? As machines take over repeatable tasks, quality professionals must evolve into analysts, interpreters, and digital stewards. This requires not only training but also a cultural shift in how quality work is valued. When roles are threatened, morale suffers. Transparent communication and meaningful upskilling are essential to managing this disruption. The true promise of digital transformation lies not in reducing headcount, but in repurposing human capability toward higher-value, more strategic contributions.

> Quality in pharma has long relied on tacit human expertise. The challenge is not to replace it, but to enhance it.

Business Cases That Shape the Future

Digital transformation initiatives live or die by their business cases. These documents determine funding, prioritisation, and ultimately, success or failure. However, traditional ROI models often fail to capture the nuanced value digitalisation

Ambiguity in business case development is evident and ranges from quantifyable intangibles to strategy and tactics in framing as well as cost horizons. How do you measure the value of improved decision speed, predictive insights, or reduced regulatory

risk? Digital projects often require significant upfront investment with payback periods beyond typical budgeting cycles. Is the transformation viewed as a one-time efficiency project or a foundational shift in how quality operates? Organisations that succeed in digital transformation often develop hybrid business cases that blend financial metrics with strategic positioning, regulatory agility, and innovation capacity.

Ambiguity as a Design Challenge

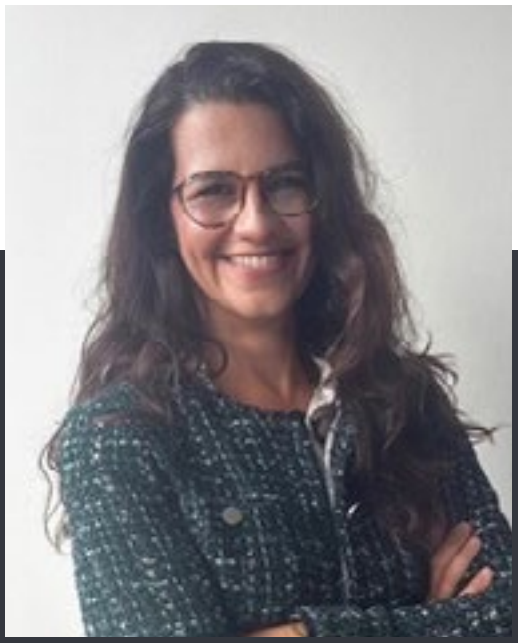
Rather than viewing ambiguity as a threat, forward-thinking organisations treat it as a design challenge. Ambiguity is not a failure of planning, but a feature of complex change. Systems should be designed to explain their logic, not just deliver outcomes. This supports trust and auditability. Implementation should not be a single event but a continuous adaptation. Agile governance and modular architecture enable this. Instead of replacing human oversight, digital systems can elevate human insight. Designing for co-intelligence—where humans and machines complement each other, is key. Implementation should not be led by IT or quality alone. Cross-functional teams with shared ownership reduce silos and clarify purpose.

Conclusion - Navigating the In-Between

Digital transformation in pharmaceutical quality is not a clean break from the past, but a negotiated transition. It moves through a space of ambiguity—technological, regulatory, organisational—before arriving at a new equilibrium.

The most successful organisations are not those that avoid ambiguity those engage with it deliberately. They invest in clarity where it counts, tolerate uncertainty where needed, and build systems—both digital human—that are resilient, explainable, and ready for change.

In the end, compliance begins to think for itself, the question is no longer whether we can trust the system, but whether we have prepared ourselves to understand what it's telling us.



AUTHOR BIO

Dr. Sophie Fröhlich is the Head of PDT & Hematology Product Stability at Takeda. She is a pharmaceutical executive specialising in CMC, innovation, and quality strategy. With extensive experience in biologics, rare diseases, and digital transformation, she leads global teams to deliver regulatory-compliant and cost-effective solutions. Her work integrates science, technology, and leadership to drive impactful, patient-centred pharmaceutical development.

From Reactive to Proactive

The Strategic Imperative for Eliminating Risk in Pharmaceutical Stability Studies

The pharmaceutical industry must adopt a proactive stability strategy using Quality by Design (QbD) to eliminate risk. By leveraging scientific understanding of degradation Pathways early, manufacturers can proactively manage risks. This approach enhances product quality, reduces costs, and accelerates development timelines.

Sneha Chauhan
Senior Product Development Specialist,
Multisorb Filtration Group

The pharmaceutical industry's core mission, to deliver safe, effective, and quality medicines, hinges on the integrity of its products throughout their shelf life or expiry dating. This assurance is provided by rigorous pharmaceutical stability studies, which are scientific investigations designed to determine a drug substance or product's shelf life and expiration date. A traditional, reactive approach to this critical function, a ‘test and assess mentality,’ is fundamentally flawed and financially ruinous. It exposes manufacturers to the significant

Cost of Poor Quality (CoPQ), a figure estimated to range between 25% and 40% of total sales revenue in the pharmaceutical sector. The financial and reputational damage from a non-proactive stability program is staggering. Internal failures, such as lost batches, can cost a company up to $500,000 each. External failures, product recalls, carry a heavier burden, with the average pharmaceutical recall costing between $10 million and $100 million, excluding lawsuits and long-term reputational damage.

Regulatory scrutiny remains intense, with analysis of FDA enforcement actions showing that deficiencies in stability testing programs are cited in approximately one-quarter of all warning letters issued to pharmaceutical manufacturers. To navigate this high-risk environment, a paradigm shift is necessary: a move from reactive compliance to a strategic, proactive framework driven by science and the principles of Quality by Design (QbD). This approach is not merely the best practice; it is a direct defense against costly failures and market disruption.

The Scientific Foundation: Anticipating Degradation

A proactive strategy begins with a deep scientific understanding of drug degradation. A drug's instability is a function of both intrinsic factors, like the physicochemical properties of the active pharmaceutical ingredient (API), and extrinsic factors, such as temperature, humidity, and light. By identifying a drug's specific vulnerabilities early, a robust formulation and packaging system can be proactively designed to counteract them. The majority of chemical degradation occurs via three primary pathways:

Hydrolysis: Moisture content is known to be the leading cause of the degradation of nearly 50% of medicinal products, especially solid dose formulations. The chemical stability of solid APIs and drug products is significantly affected by the relative humidity (RH) the sample experiences. It is particularly common in drugs containing ester or amide functional groups, such as aspirin and lidocaine, respectively.

Pathway	Example/Affected Functional Groups	External Stressors	Key Control Metrics (QbD)
Hydrolysis	Esters (Aspirin), Amides (Lidocaine)	Water, High relative humidity, pH	Water Activity (Aw), Loss on Drying (LOD)
Oxidation	Amines, Phenols (Epinephrine, Estradiol	Oxygen, Metal ions, Impurities	Headspace Oxygen Control, Metal Ion Specifications, Antioxidant Use
Photolysis	Nifedipine, Riboflavin	UV light, Fluorescent light exposure	Container Opacity, Light Exposure Time

Table 01

A key metric in a proactive strategy is the control of Water Activity (Aw) and Loss on Drying (LOD), which measures the "free" or unbound water available to drive hydrolytic reactions, providing a more accurate predictor of stability than Karl Fisher, which measures 'total' moisture content.

Oxidation: Oxidation is the second most common degradation pathway. Drugs that are highly oxygen-sensitive generate oxidative degradants when exposed to oxygen, characterised by the loss of electrons from a molecule. This complex process can be initiated by impurities, metal ions, or reactive oxygen species. For oxygen-sensitive drugs, such as epinephrine or the injectable chemotherapy agent Pemetrexed, control of headspace and dissolved oxygen becomes a critical quality attribute (CQA) to prevent the formation of oxidative degradants.

Photolysis: Degradation caused by exposure to light, especially UV light, can lead to both oxidative and non-oxidative reactions. Photostability testing is a standard component of stability studies, and a common mitigation strategy is the use of amber or opaque containers that block harmful light wavelengths.

The cornerstone of a proactive scientific strategy is the use of forced degradation studies, also known as stress testing . These studies intentionally subject a drug to extreme conditions of heat, humidity, light, Oxygen and pH to generate degradation products in an accelerated manner. The knowledge gained serves two critical purposes: it elucidates the drug's potential degradation pathways, and it is used to develop and validate a robust "stability indicating analytical method". Such a method is essential, as it must be able to accurately separate and quantify the active drug from its degradation products, a fundamental requirement frequently cited in regulatory failures.

Aspect	Traditional Approach	QbD-Based Strategy
Primary Objective	Meet regulatory requirements and pass audits.	Ensure a robust and Product from the outset.
Product Understanding	Confirmatory testing for expiration dating.	Integrated tool to gain knowledge, inform decisions, and confirm a robust design
Key C0A Control	Measure total moisture (KF) as a final specification.	Control and monitor Aw and LOD during manufacturing to ensure the product remains within the established design space
Risk Management	Reactive; addressing problems as they occur (e.g., CAPA).	Proactive; anticipating and mitigating risks through a scientific framework.

Table 02

Building on this understanding, if a drug product is sensitive to moisture or oxygen over its shelf life within the primary packaging, active packaging solutions, such as desiccants or oxygen scavengers, may be required to ensure stability. These technologies directly counter the primary degradation pathways. Desiccants, such as silica gel and molecular sieve, adsorb excess moisture from the package headspace, thereby lowering the water activity and inhibiting hydrolysis . Oxygen scavengers, often iron-based, irreversibly bind to and remove residual oxygen within the sealed package, protecting sensitive molecules from oxidation. An effective packaging strategy can be designed through close collaboration between the pharmaceutical company and specialised active packaging vendors to ensure the final product remains safe and efficacious.

"Quality by Design (QbD): Building Quality In

The ultimate framework for mitigating stability risk is Quality by Design (QbD), a systematic approach based on science and risk management. As regulatory bodies like the FDA and ICH have long recognised quality cannot be "tested into" a product at the end; it must be "built in by design". A QbD-driven stability strategy is built upon five core elements:

1."Quality Target Product Profile (QTPP)" This is the starting point, defining what the final drug product is supposed to do from a patient-centric perspective. For stability, the QTPP defines the desired shelf life, storage conditions, and key performance criteria over time.

2."Critical Quality Attributes (CQAs)" These are the physical, chemical, or microbiological properties that must be kept within an appropriate limit to ensure the desired product quality. Key CQAs for stability include assay (drug content), purity (degradation products), dissolution, and Water Activity (aw).

3. Critical Material Attributes (CMAs) & Critical Process Parameters (CPPs): This involves gaining a deep knowledge of the input

> Pharmaceutical stability studies are central to ensuring patient safety and product integrity, but a reactive, 'a test and assess' approach exposes manufacturers to enormous risks and costs.

materials (CMAs) and manufacturing steps (CPPs) that can influence the CQAs.

4. Design Space (DS): This is the multivariate combination of material attributes and process parameters that have been demonstrated through scientific study to assure quality. Operating within this scientifically justified space is not considered a change by regulators and provides significant manufacturing flexibility.

5.Control Strategy: Based on all the knowledge gained, a comprehensive control strategy is developed to ensure the process remains within the design space. This includes a robust, ongoing stability program, real-time process monitoring, and the use of a validated stability-indicating analytical method.

This proactive approach fundamentally transforms the role of stability testing. In a traditional model, it is a required, confirmatory step at the end of development. In a QbD model, it becomes an integrated tool used throughout the lifecycle to gain knowledge, inform decisions, and confirm a robust design.

From Strategy to Action: Practical Benefits of a Proactive Approach

Implementing a proactive, QbD-based stability program translates into tangible business and operational benefits that extend far beyond compliance.

Accelerated Timelines and Regulatory Flexibility: A deep understanding of a product's vulnerabilities creates substantial "prior knowledge". For post-approval changes (PACs), such as onboarding a new excipient supplier, this knowledge can be used to perform a risk assessment and justify a reduced stability data commitment, saving significant time and resources. Furthermore, predictive models to assess accelerated stability can be used to forecast stability profiles and shorten initial development timelines.

Rational Cost and Process Trade-Offs: The scientific understanding gained through QbD allows for intelligent, data-driven decisions that balance cost and quality. the strike-through text with this one "For example, an oxygen sensitive drug product may require expensive nitrogen purge during packaging and a thicker wall bottle to ensure protection throughout the two year shelf life. However, by utilizing the appropriate amount of oxygen scavenger, the same two year shelf

life can be achieved without the expensive nitrogen purge process and while using a standard, less costly bottle."This ability to make rational trade-offs between process controls and packaging costs is a direct result of a proactive QbD approach.

Mitigation of Physical and Operational Risk: Stability risk is not just chemical. The loss of valuable samples stored for years due to equipment failure, power outages, or other disasters can derail a product launch. A proactive strategy includes a robust business continuity plan. A leading multinational pharmaceutical company successfully reduced this risk by deploying ICH-compliant stability chambers with continuous monitoring, integrated alarm systems, and backup power, shifting from reactive risk exposure to proactive process control.

Conclusion

The modern pharmaceutical landscape demands a definitive shift away from the traditional, reactive model of stability testing. That approach, focused on minimal compliance and end-product testing, is fraught with risks to patient safety, regulatory standing, and financial performance. A strategic, proactive approach, driven by the principles of Quality by Design, transforms stability from a mere regulatory obligation into a powerful source of competitive advantage.

By building quality, safety, and efficacy into a product from its inception, manufacturers can enhance patient safety, dramatically reduce the Cost of Quality, accelerate time to market, and gain significant regulatory flexibility. The objective is not to eliminate risk entirely, an impossibility in a complex environment, but to proactively manage and robustly mitigate it by making science- and knowledge-based decisions at every stage of the product lifecycle. This strategic imperative is crucial for ensuring product quality, protecting patients, and achieving sustained commercial success.

References are available at www.pharmafocuseurope.com

AUTHOR BIO

Sneha Chauhan is a Senior Product Development Specialist at Multisorb Filtration Group, with over 12 years of experience in product development, formulation sciences, and process optimisation. In her current role, she leads cross-functional initiatives and develops stability solutions using active packaging technology. She specialises in stability prediction modeling, helping clients maintain drug product stability throughout its shelf life. To date, she has delivered stability solutions for more than 500 drug products, accelerating their path to market.

ASPIRE PHARMA

Continuing Our Expansion into Europe

Dave Lampard
Global Alliance Director, Aspire Pharma Ltd

Aspire Pharma is a rapidly growing European specialty pharma business, headquartered in the UK, devoted to delivering true value to patients, healthcare professionals and the NHS. The company manufactures and supplies quality branded and generic medicines not only in the UK, but also to an expanding international market.

Starting with a single drug licence in 2009, the company now has more than 400 products in 16 therapeutic fields, over 250 employees and 7 offices around the globe. Our vision is to create a business which is agile to opportunity, unconstrained by market segment, and whose products make a valuable difference to patients and payors.

Innovation is a core focus of our growth strategy, which we demonstrate by bringing innovative products to existing and new markets, with fresh ideas, ways of working and creating value and sustainability for our product portfolio.

Mergers and Acquisitions

Since being acquired in 2021 by an affiliate of H.I.G. Capital, a leading global alternative investment firm, Aspire continues to supplement strong organic growth with acquisitions and strategic partnerships. These acquisitions further validate the long-term growth plan to create one of the largest and fastest-growing UK-based pharma companies that will see accelerated growth potential in its current and future product portfolio.

International Expansion

The internationalisation of the company has been a constant since its inception 16 years ago. Aspire has understood that the access to knowledge around the world is fundamental to establish both scientific and commercial collaborations that would lead to a solid and sustainable growth.

Through our partnership principles that are key to address complex healthcare challenges, Aspire establishes transparent, honest relationships and maintains and grows these partnerships through shared knowledge and resources that accelerate progress. The alliances allow us to unlock potential and maximise the performance of every alliance business and every brand in the markets we serve to ensure patients receive their essential medicines when they need them.

> Aspire establishes and maintains transparent, honest partnerships, leveraging shared knowledge and resources to accelerate organisational progress

With strong backing from H.I.G. Capital, and a clear long-term vision from the management team, Aspire has recently successfully established a presence in Germany and the Nordic countries, some of Europe's most sophisticated healthcare markets. Entering both the hospital and pharmacy tender sectors, the first products will be commercialised directly to customers in 2026. Furthermore, Aspire is in the final stages of setting up its commercial operations in the Netherlands and Spain.

We chose these markets due to their strategic importance and growth potential in the healthcare sector. Each of these markets is quite sophisticated, with high demand for innovative healthcare solutions, but with a different approach to delivering value to patients.

We have completed over 45 licensing agreements in the last 12 months alone. We will continue to expand our presence in continental Europe and are actively seeking bolt-on acquisitions as well as partnerships with other pharma companies.

The continued expansion demonstrates our commitment to our vision to make a difference in the lives of patients through the development and supply of innovative products and medicines throughout the world through our strategic pillars of a strong UK base, with international expansion and IP growth.

This European expansion is the result of a well-structured growth plan that combines strategic acquisitions, the creation of local subsidiaries, and the development of highly experienced regional teams.

Future Focus

Aspire will continue to explore challenging areas and seek new investments, including mergers and acquisitions. We have a strong track record of both company and product acquisitions, which bring innovative healthcare solutions to market, while ensuring our long-term success and a competitive edge.

The future for Aspire is of continued development of differentiated products that meet the market need in niche generic and specialty medicine; upweighting clinical development; new investment opportunities to bring products and companies into the portfolio with a synergistic fit to the Aspire values and areas of therapeutic focus; growth of our own portfolio of intellectual property and a corporate focus on internationalisation of the Aspire brand.

AUTHOR BIO

Dave Lampard is a commercial leader with over 20 year's experience in both the innovator and generics parts of the pharmaceutical industry. He joined Aspire Pharma with the Morningside acquisition in 2022 and leads on Commercial Alliance Management, partnering for global expansion and ensuring Aspire's partnerships operate smoothly and deliver mutual value.

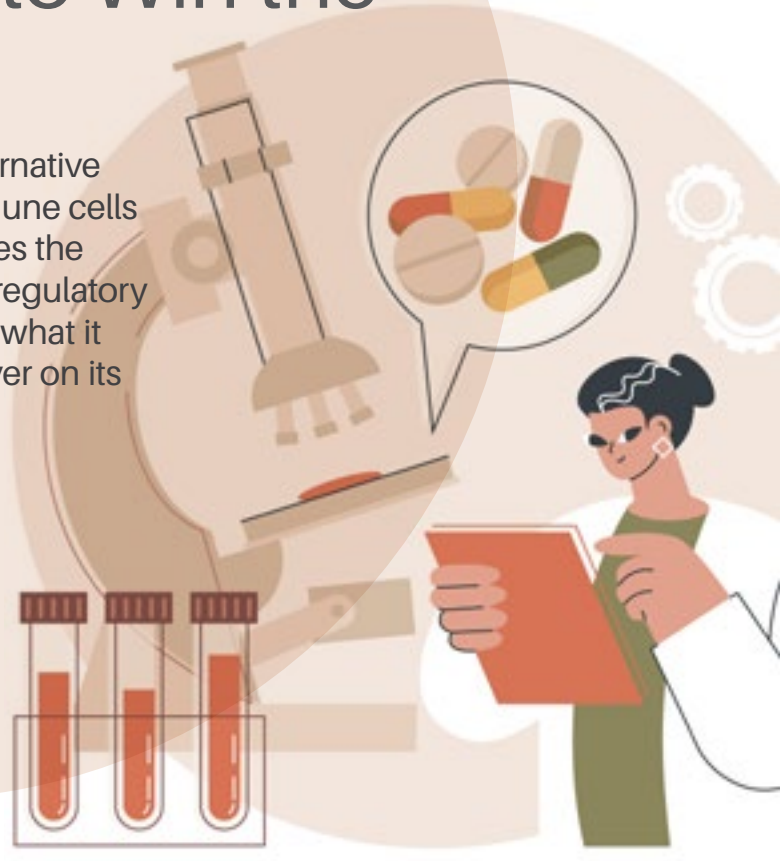
Advertorial

In-Vivo CAR-T

From Concept to Clinic – What It Will Take to Win the "Age of In-Vivo"

In-vivo CAR-T therapy offers a scalable alternative to ex-vivo approaches by engineering immune cells directly inside the body. This article explores the scientific advances, clinical progress, and regulatory strategies driving the "Age of In-Vivo," and what it will take for this emerging modality to deliver on its transformative potential for patients.

Peter Robinson
MBA, Director Therapeutic Strategy, Novotech



For the past decade, ex-vivo CAR-T therapies have set a new bar for clinical impact in hematologic malignancies. Yet their own success story exposes the limits of the model: intensive apheresis, bespoke manufacturing, narrow site networks, high costs, and long vein-to-vein times that too often disqualify or delay patients. In-vivo CAR-T, the ability to engineer therapeutic cells directly inside the body, aims to rewrite those constraints. If it delivers on its promise, in-vivo CAR platforms could merge the potency of autologous cell therapy with the scalability of traditional biologics, expanding access, bending cost curves, and accelerating time to treatment.

Momentum is real. Capital is flowing into viral and non-viral delivery platforms; big-pharma partnerships have validated multiple approaches; and a first wave of clinical trials is underway across oncology and autoimmune indications. But the path from elegant mechanism to reliable medicine will turn on a familiar triad: precise targeting and dosing, predictable safety, and scalable, regulator-ready execution. ▶

This byline synthesises where the field stands and what it will take to reach durable clinical and commercial adoption.

Why In-Vivo, and Why Now?

The core limitation of ex-vivo CAR-T therapy is not biological; it is logistical. Autologous are effective but require individualised cell collection, ex-vivo manipulation, and fit-for-release testing for every patient. Allogeneic products promise off-the-shelf convenience, yet potentially introduce higher risks of graft-versus-host reactions, immune rejection, and scale-up challenges.

In-vivo CAR approaches invert the model: deliver genetic instructions to the right cell population within the patient and allow biology to handle manufacturing. Whether using targeted lentiviral particles, adenoviral or AAV vectors, mRNA-lipid nanoparticles, or hybrid nanocarriers, the goal is consistent: program, expand, and sustain therapeutic effector cells in situ.

If successful, this model could resemble a single-dose or redosable biologic rather than a bespoke product, unlocking broader access and faster treatment initiation.

Recent regulatory approvals of TIL, TCR, and next-generation CAR-T therapies especially in relapsed or refractory settings, rapid in-vivo generation in solid tumors and autoimmune conditions have normalised advanced cellular modalities across agencies and payers, creating a favorable environment for in-vivo CAR innovation.

The Platform Race: Targeting, Kinetics, and Control

Vectors and nanocarriers are the fulcrum of in-vivo CAR development. Across platforms, three engineering questions dominate:

Cellular specificity. Most early programs focus on T-cell targeting (CD3, CD4/CD8, or CD19-directed), but the field is expanding into myeloid, NK, macrophage, and Treg populations. The challenge remains balancing efficient tropism with minimising off-target effects.

Expression durability. Integrating vectors (lentiviral, transposon-based) support long-term CAR expression but require close insertional safety monitoring. Non-integrating systems (AAV, mRNA-LNPs) favor modularity and redose potential but need repeated dosing for durable activity. Hybrid strategies are emerging, using transient expression to establish safety before durable integration.

On-demand control. Future differentiation will hinge on controllability, including drug-gated CARs, safety switches, titratable promoters, and dosing strategies that give clinicians finer control of activity and safety.

What the First Clinical Wave Is Teaching Us

Early-stage clinical programs are distributed across diverse technologies: lentiviral systems for durable T-cell reprogramming, mRNA-LNP approaches prioritizing redosability, and AAV variants optimized for T-cell selectivity.

Key lessons so far include:

- **Speed to pharmacology matters**. In oncology, especially in relapsed or refractory settings, rapid in-vivo generation of functional effector cells can be critical. Non-human primate data showing rapid B-cell aplasia with CD19 constructs are encouraging, pending confirmation in humans.
- **Safety profiles may differ by indication**. Autoimmune indications may tolerate in-vivo CARs with fewer severe cytokine-related events than oncology, though vector-related immune responses and reactogenicity remain important considerations. Emerging phenomena such as Local Immune Cell-Associated Toxicity Syndrome (LICATS) highlight the need for specialised centres and predefined management algorithms.

Regulatory Strategy: Global, Harmonised, and Data-Rich

In-vivo CAR therapies occupy a regulatory landscape adjacent to gene therapy, allowing developers to leverage established precedents while addressing novel vector-specific issues.

> In-vivo CAR-T therapies are not replacements for autologous or allogeneic ex-vivo modelsbut valuable complements

Key focus areas include:

Translationally relevant preclinical models. Immunocompetent, humanised, and non-human primate studies should be used to clarify biodistribution, immune memory, and vector persistence.

Early agency interaction. Pre-IND and scientific advice meetings help align expectations on vector tropism, insertional mutagenesis, and long-term follow-up.

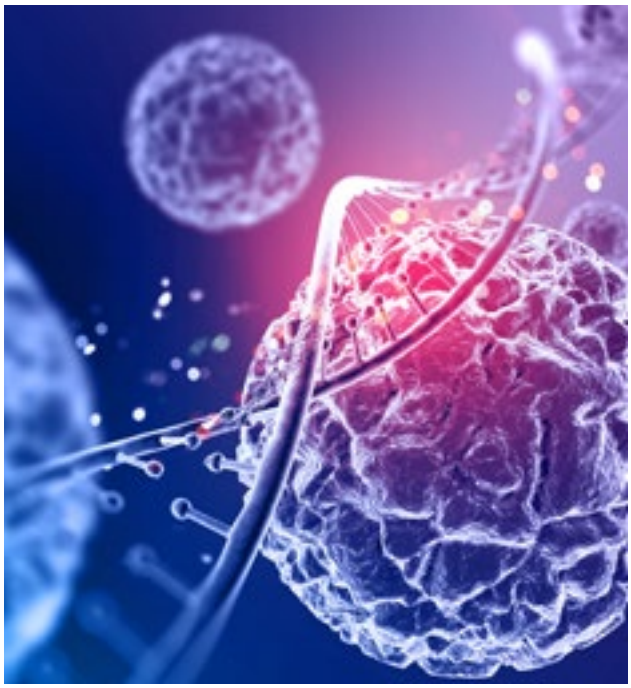
Long-term safety frameworks. Whether using integrating or and fibrotic applications. Goals include deep depletion systems, robust monitoring for persistence, replication-competent virus, and clonal evolution is essential.

Solid Tumors and Beyond: Designing for the Hard Mode

Hematologic cancers remain the fastest path to validation, but solid tumors and autoimmune diseases represent the true test of the in-vivo model. Success will require combining vector engineering with tumor- or tissue-specific strategies:

Trafficking and infiltration. Approaches such as chemokine receptor engineering, stromal modulation, and oncolytic virus combinations can improve tumor access.

Antigen heterogeneity. Multi-specific and logic-gated CARs, or “one cell, multiple CAR” designs, may mitigate antigen escape. ▶



Autoimmune and fibrotic applications. Goals include deep depletion of pathogenic cells, durable immune reset, and functional recovery without chronic immunosuppression.

Five Design Principles for Next-Generation Programs

Start with the clinic, not the vector. Let indication biology drive platform selection.

Design trials for real-world relevance. Capture time-to-treat, infusion logistics, and patient resource use.

Treat CMC as a clinical variable. Analytical precision directly impacts safety and comparability.

Plan globally. Harmonise early with major regulatory regions to streamline later development. Use regions like Australia to accelerate first-in-human trials while preparing harmonised data packages for the FDA and EMA, and other key markets such as China.

The Outlook: Coexistence, Not Replacement

In-vivo CAR-T therapies are not replacements for autologous or allogeneic ex-vivo models but valuable complements. Each approach will serve distinct clinical and logistical niches: autologous constructs for personalised therapy, allogeneic for off-the-shelf use, and in-vivo systems for scalable, rapid intervention.

The promise is clear: engineer immune cells directly where they reside, eliminate the slowest steps, and give clinicians tools to modulate therapy dynamically. The scientific foundation is strong; the next phase will test whether precision, safety, and durability can converge to make in-vivo CAR-T a reliable therapeutic reality. ■

AUTHOR BIO

Peter Robinson, MBA, Director Therapeutic Strategy, Novotech. He is a Clinical Operations and Development Leader with more than 20 years of experience in CRO and biotech settings. His focus is on advancing cell and gene therapy programs from concept to clinic, with a passion for improving patient access to transformative treatments.

CoverStory

Lyophilisation

Key to Overcoming Stability Hurdles for Complex Therapeutics

As next-generation therapeutics become more widespread, ensuring their stability presents significant challenges. Lyophilisation offers a reliable solution by enhancing shelf life, reducing cold-chain dependence, and preserving product integrity. This article explores how lyophilisation supports the development of diverse complex therapeutics, including lipid nanoparticle (LNP)-based formulations, viral vectors, and nucleic acid-based medicines, while addressing formulation, scale-up, and regulatory hurdles.

Uwe Hanenberg
Head of Product Development, Oral Solid Dose, Recipharm

The pharmaceutical landscape is rapidly evolving, driven by an influx of advanced treatments such as biologics, nucleic acid-based medicines, gene therapies, and nanoparticle-based delivery systems. These innovative therapies are transforming how diseases are treated, offering new options for conditions once considered untreatable. However, they present significant formulation and stability challenges.

These sensitive molecules are prone to degradation when exposed to environmental stressors like moisture, temperature fluctuations, and mechanical agitation. This fragility complicates ▶

manufacturing, storage, and distribution, particularly when considering the logistical strain on global supply chains. Cold-chain infrastructure has traditionally addressed this problem, but it is expensive, energy-intensive, and often impractical for remote or resource-limited regions. Beyond cost and accessibility, the environmental impact of maintaining extensive cold chains, with their significant energy consumption, is also a growing concern for the industry's sustainability goals.

To bridge this gap, lyophilisation presents a robust stabilising strategy. While lyophilisation has long been used for proteins and antibodies, it is now proving indispensable for a broader range of next-generation modalities. Whether applied to lipid nanoparticles (LNPs), viral vectors, enzymes, messenger RNA (mRNA), or other nucleic acid-based therapeutics, lyophilisation improves shelf life, protects molecular integrity, and enables more flexible global distribution without heavy reliance on ultra-cold storage. This shift allows for greater flexibility in storage and transportation, ultimately improving patient access globally.

Addressing the stability challenge with lyophilisation

Water is one of the biggest contributors to the degradation of pharmaceutical compounds. Lyophilisation mitigates these risks by removing water through a sublimation process that transitions ice directly into vapour under vacuum conditions. The fundamental principle relies on the phase diagram of water, where a combination of low temperature (below freezing) and low pressure (vacuum) allows ice to bypass the liquid phase and directly sublimate. This gentle drying process minimises thermal and chemical degradation, which are common issues with conventional drying techniques.

Unlike heat-based drying methods, sublimation occurs at low temperatures, making it especially suitable for fragile biologics and nanoparticles. This process halts hydrolytic degradation and other chemical reactions that destabilise sensitive pharmaceutical compounds, thereby preserving structural integrity and efficacy.

The key benefits of lyophilisation offers complex therapeutics are:

- **Improved long-term stability:** By removing water, lyophilisation significantly reduces

degradation reactions, the product's shelf life at various temperatures, including ambient conditions.

- **Reduced need for cold chain storage:** Lyophilised products often eliminate the requirement for ultra-cold storage and transportation, leading to savings and improved accessibility, with added sustainability benefits.
- **Enhanced shelf life**: The removal of water inhibits microbial growth and enzymatic activity, contributing to a longer shelf life compared to liquid formulations.
- **Increased convenience**: Lyophilised products are easier to handle, store and transport. They can be reconstituted quickly and easily before administration.
- An example use case for lyophilisation is with mRNA products. Lyophilisation reduces the need for ultra-cold storage by stabilising both the fragile mRNA molecules and the LNP delivery systems that protect and transport them. Without lyophilisation, mRNA therapies typically require storage at temperatures as low as -70 degrees Celsius to prevent degradation.

Formulation and process optimisation

Selecting the right excipients is a critical first step in successful lyophilisation. These supporting ingredients protect sensitive molecules from stresses encountered during freezing and drying. Cryoprotectants guard

against damage during the freezing phase, while lyoprotectants stabilise active ingredients during the drying stage.

The interaction between the active and the chosen excipients must be thoroughly understood, as incompatibilities can lead to unforeseen degradation or reduced stability. This often requires extensive screening of various excipient combinations and concentrations. Selecting incorrect excipients or improper concentrations can lead to cake collapse, poor reconstitution, or loss of biological activity. Thus, excipient screening and optimisation are fundamental steps in ensuring a successful freeze-dried formulation.

Common excipients include sugars such as sucrose and trehalose, which act as stabilisers by forming a glassy matrix around molecules. Polyols like mannitol are often used to add structural integrity to the dried cake. Amino acids help prevent protein aggregation during both the freezing and drying phases, while surfactants are critical for stabilising nanoparticle-based formulations by preventing particle fusion or aggregation. The primary function of these excipients is to replace water's hydrogen bonding network, thereby preserving the native structure of proteins, nucleic acids, and complex nanoparticles throughout the lyophilisation process.

Cycle development and product characterisation

Developing an effective lyophilisation cycle involves managing three key phases:

1. Freezing: Controlled nucleation techniques help ensure uniform ice crystal formation, which promotes consistent drying and minimises variability.
2. Primary drying: Ice sublimation occurs under vacuum, requiring careful control of shelf temperature and chamber pressure to avoid collapse or melt-back of the product matrix.
3. Secondary drying: This phase removes tightly bound residual moisture, critical for achieving long-term stability without compromising the molecular structure.

Achieving the right balance between drying efficiency and product stability is crucial. Optimising the cycle reduces processing time and energy consumption while protecting the integrity of the therapeutic product.

Equally important is comprehensive quality control to ensure the lyophilised product maintains safety, efficacy, and stability. Residual moisture measurement, i.e., Karl Fischer titration, is critical to gauge shelf life. For nanoparticle-based systems, like LNPs, it is especially important to test particle size distribution. Molecular integrity assessment using high-performance liquid chromatography (HPLC) and electrophoresis can check for degradation. Evaluation of reconstitution time is also key to ensuring rapid and clear dissolution upon mixing with diluent.

For LNPs, dynamic light scattering (DLS) is commonly used to measure particle size and polydispersity, ensuring the particles remain within the desired range for optimal delivery. Electron microscopy (e.g., cryo-

TEM) can provide visual confirmation of LNP integrity and morphology post-lyophilisation. Additionally, functional assays are essential to confirm that the biological activity of the therapeutic is retained after the lyophilisation and reconstitution process.

Scaling up from bench to commercial manufacturing

Successfully scaling lyophilisation from laboratory to commercial manufacturing requires not only technical adjustments but also strict adherence to global regulatory standards. Regulatory agencies, including the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), require comprehensive validation data to demonstrate that the lyophilisation process consistently produces a stable, high-quality product.

Meeting these expectations involves rigorous stability testing under various storage conditions to establish product shelf life and to verify that the freeze-dried formulation maintains its intended quality attributes over time. This includes confirming consistent moisture content, potency, purity, and reconstitution performance across different batches.

Process validation must confirm that every stage of the lyophilisation cycle, from freezing to primary and secondary drying, is repeatable and tightly controlled. Manufacturers must also implement a robust product control strategy, including detailed documentation, risk management plans, and quality assurance systems.

> As pharmaceutical companies push toward net-zero goals, the ability of lyophilisation to contribute to carbon reduction will make it even more essential in future drug development

Transitioning lyophilisation processes from small-scale development to commercial production introduces complex challenges. Uniformity remains a significant hurdle; large-scale lyophilisation involves maintaining consistent temperature and pressure across thousands of vials. Variations can lead to inconsistent moisture content and compromise stability.

Solutions for scale-up include implementing Process Analytical Technology (PAT) tools such as further product temperature measurement, comparative pressure measurement, and Manometric Temperature Measurement (MTM) to monitor water vapour concentration and product temperature in real time. ▶

Extensive development protocols ensure that processes developed at the lab scale can be replicated reliably at the commercial scale. Advanced control systems are also being integrated into commercial freeze-dryers to enhance process robustness and efficiency.

Supply chain factors also play a critical role. Ensuring a reliable source of GMP-grade excipients, validating commercial-scale equipment, and maintaining redundancy in manufacturing to prevent production delays and maintain quality consistency. Robust supply chain management, including supplier qualification and contingency planning, is paramount for uninterrupted commercial supply.

Looking ahead

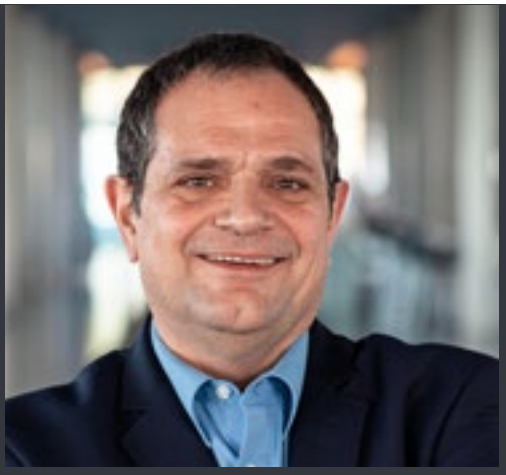
The demand for stable, accessible, and patient-friendly pharmaceutical products will continue to accelerate as more complex therapeutics enter the market.Several key technological advances are shaping the future of lyophilisation.

One of the most promising trends is the development of continuous lyophilisation technologies, which offer increased throughput, improved energy efficiency, and enhanced process control. Spray freeze-drying is gaining traction for applications reconstitution are critical. Microfluidic-based drying approaches are being explored to enable highly controlled processing for nanoformulations and delicate biologics.

Sustainability is also an increasing focus. Lyophilisation reduces reliance on ultra-cold storage, lowering energy consumption and the environmental footprint associated with cold-chain logistics. As pharmaceutical companies push toward net-zero goals, the ability of lyophilisation to contribute to carbon reduction will make it even more essential in future drug development.

For developers working on cutting-edge medicines, integrating lyophilisation strategies early in the development process is becoming a critical success factor. The future of medicine will depend not only on innovation in therapeutic molecules but also on innovation in how those molecules are stabilised, stored, and delivered to patients worldwide.

AUTHOR BIO



Uwe Hanenberg is the Head of Product Development for Oral Solid Dose (OSD). He is responsible for implementing and executing the OSD Product Development strategy, ensuring the science-driven and timely development of new products and services. With 25 years of experience in the pharmaceutical industry, Uwe's areas of expertise include oral formulation development, oral manufacturing technologies, stick pack technologies, and pharmaceutical contract services and project management.

The Emerging Role of B-cells in Immunotherapy

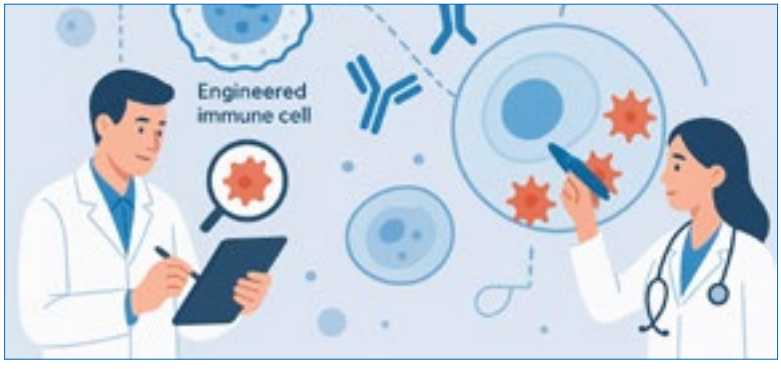
From Broad Depletion to Antigen-Specific Precision

B cells are emerging as central players in immunotherapy and immune regulation, poised to lead the next wave of immunotherapies spanning cancer, infectious diseases, and autoimmunity, to offer safer and more durable, antigen-specific immune modulation. Here, we examine the transition from B cell depletion to precise antigen-specific modulation of B cells for in vivo applications

Daniel-Paul Bednarík
PhD, Chief Technology Officer, Black Canyon Bio, Inc.

Kristi Jones
Executive Consultant, Kytara Bio

Mathias Oelke
PhD, Kytara Bio



Immunotherapy has entered a new era, and B-cells, long considered secondary to T cells, are now recognised as central to both disease and therapy. Beyond the well-established antibody production function, B-cells have direct effector function, are potent antigen-presenting cells, shape T cell responses, and exert profound regulatory functions. The broader role of B-cells in cancer, infectious disease, and autoimmunity is becoming well understood, and the potential to harness B-cell multi-functional therapeutic benefits is rapidly coming into focus; the future path for translational development is paramount and unlocks an opportunity for a new arm of therapy.

The challenge lies in the transition from blunt interventions, such as broad B-cell depletion, to precision approaches that leverage specific B-cell subsets. Both adoptive transfer of engineered B-cells and in vivo manipulation are advancing, with antigen-specific strategies emerging as the ▶

B-cells function and potential areas for harnessing their power to develop new therapy approaches

Integrates humoral and cellular immunity

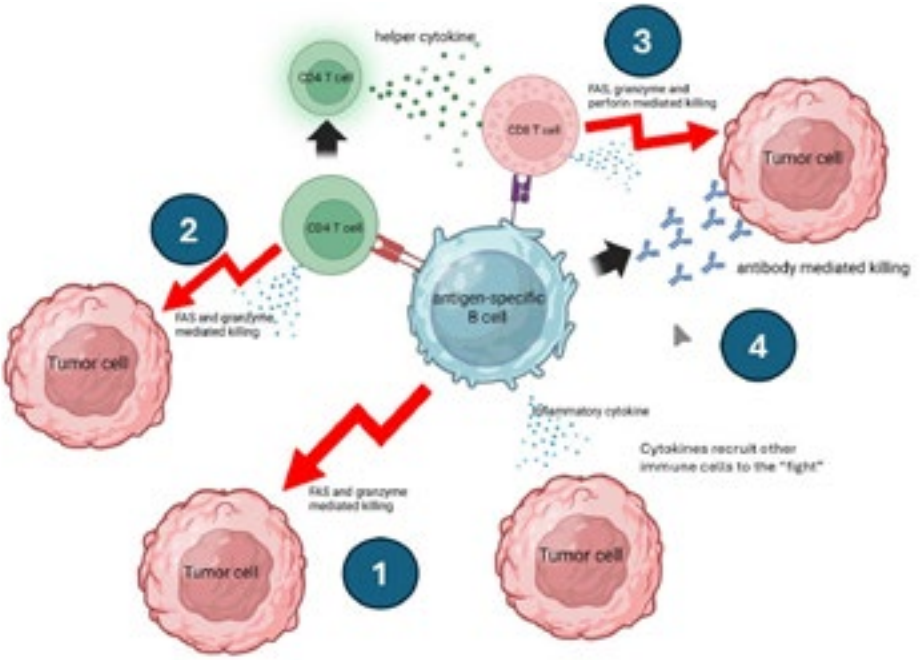


Figure 1. Current therapeutic strategies primarily exploit B cells for antigen presentation, antibody production, and in vivo delivery (points 3 and 4), or employ broad B-cell depletion in autoimmune diseases. However, numerous additional functions remain to be harnessed for the development of next-generation treatment approaches.

Created with BioRender. Jones, K. (2025)

most promising way to balance efficacy with safety (Figure 1).

A Historical Timeline: The evolution of B-cell targeting

1990s–2000s: Anti-CD20 antibodies (rituximab, ocrelizumab) revolutionised the treatment of B-cell lymphomas and multiple B-cell-related autoimmune diseases. These early successes validated B-cell surface proteins as effective therapeutic targets to deplete all B-cell modalities, revealing unintended consequences of indiscriminate B-cell depletion, including hypogammaglobulinemia, recurrent infections, and loss of protective immunity. For example, repeated rituximab courses required for maintenance of response, combined with higher glucocorticoid doses in ANCA-associated vasculitis, increased the risk of hypogammaglobulinemia (very low IgG) at 6 months in ~43% of treated patients; lower IgG levels were associated with serious infections.

In children with autoimmune diseases, hypogammaglobulinemia after rituximab was frequent, particularly in CNS disease or vasculitis, and correlated with serious infections.

2010s: B-cells gained recognition in cancer biology, with tumor-infiltrating B-cells (TIL-Bs) and tertiary lymphoid structures (TLS) linked to improved survival in melanoma, lung cancer, and breast cancer. In melanoma, baseline high T cell/low B-cell gene signatures

were associated with better overall survival in a trial of dabrafenib + trametinib. Meanwhile, recognition of memory B-cells has refined our understanding of durable vaccine responses, which may impact new vaccine development.

2020s: Emerging preclinical studies of engineered B-cells demonstrate the feasibility of adoptive transfer for antibody delivery and antigen presentation. For example, in mice, engineered B-cells expressing broadly neutralizing antibodies (bNAbs) against HIV showed durable secretion, homing to germinal centers, and neutralization activity. Simultaneously, experimental models of autoimmunity suggest that regulatory B-cells (Bregs) could be expanded or transferred to promote tolerance. For instance, ex vivo expanded B10 cells (an IL-10-producing Breg subset) markedly inhibited disease symptoms in experimental autoimmune encephalomyelitis (EAE).

In cancer, Tertiary lymphoid structures (TLS) correlate with response to checkpoint inhibitors, suggesting that reprogramming intratumoral B-cells could enhance current therapies.

2030 and beyond: There is a lot of potential for the development of antigen-specific B-cell therapies in clinical trials spanning oncology, chronic viral infection, and autoimmunity.

Cancer: Toward Precision Activation of Specific B-cells

In cancer, the most important accomplishment has been the recognition that B-cells within tumors are not passive bystanders but active participants in anti-tumor immunity. Their presence often predicts better outcomes, and adoptive transfer of engineered B-cells is showing early therapeutic promise and supports the move from tumor tolerance to immune coordination.

> We're entering a future where antigen-specific B-cell therapies become not only possible, but personal—modular, precise, and ready to transform oncology, chronic infection, and autoimmunity.

Current accomplishments:

Engineered B-cells in mice secreting tumor-specific antibodies have shown sustained antibody production, coupled with antigen presentation that bolsters T cell responses. For instance, a recent preclinical study engineered B-cells to express an anti-HPV antibody targeting an intracellular tumor-antigen; those B-cells not only secreted antibody but also induced CD4+ and CD8+ T cell activation.

Adoptive B-cell transfer using antigenic engineering has been shown to reduce tumor growth in several mouse models. For example, in the review "Exploiting B-cell Transfer for

Cancer Therapy," engineered B-cells were modified ex vivo (e.g., forced expression of costimulatory ligands, antigen loading) and transferred, resulting in improved immune responses and tumor control.

Current accomplishments: Pre-clinical evidence of antigen-specific B cell potential.

Tumor-associated regulatory B-cells (Bregs) remain a barrier. These subsets secrete immunosuppressive cytokines such as IL-10 and TGF-β, dampening anti-tumor immunity.

Systemic depletion strategies risk eliminating both beneficial and detrimental subsets, including those that contribute to tumor surveillance or protective immunologic memory.

Tumor antigen heterogeneity and immune evasion must be addressed: precise targeting and modulation of antigen-specific B-cells and targeted delivery are key for tipping the balance toward immunity.

This strengthens the rationale for antigen-specific manipulation: programming or expansion of B-cells to respond to tumor antigens, sparing protective compartments such as memory B-cells and non-pathogenic B-cell subsets.

Infectious Disease: Beyond Broad Vaccination

B-cells are the backbone of vaccines based on immunologic antibody responses. Annual vaccination cycles are a symptom of B-cell dysfunction combined with inefficient target decisions, yielding transient responses. The next wave of B-cell development is to direct their therapeutic use. Adoptive transfer of engineered B-cells could provide long-term, renewable antibody production against conserved epitopes in mutable viruses like HIV, influenza, and other viruses—avoiding the need for repeated monoclonal antibody infusions and reducing or eliminating annual development of new or annually updated vaccines.

Current accomplishments:

In vivo engineering of B-cells via adeno-associated virus or "AAV" plus CRISPR/Cas9 has allowed for endogenous B-cell integration of broadly neutralising antibody (bNAb) genes. Engineered B-cells homed to germinal centers and bone marrow, secreted multiple isotypes, and neutralised heterologous viruses.

Transfer of engineered "emAb" B-cells against RSV in mice demonstrated durable protection with phenotypes consistent with both long-lived plasma cells in the bone marrow and switched memory in the spleen.

Precise targeting and modulation of antigen-specific B-cells and targeted delivery are key for tipping the balance toward cancer immunity and must overcome:

Tumor-associated regulatory B-cells (Bregs) in the immunosuppressive tumor microenvironment (TME). These subsets secrete cytokines such as IL-10 and TGF-β, which dampen anti-tumor immunity and T cell function.

Tumor-antigen heterogeneity and immune evasion (precise targeting and modulation of antigen-specific B-cells and targeted delivery

Strategy	Advantages	Challenges & Risks
Adoptive Transfer	Provides control over cellular phenotype and function; antigen specificity can be selected or engineered; ex vivo expansion can ensure purity; early proof-of-principle in animal models for cancer, infectious disease, and autoimmunity.	Logistics, cost; autologous treatment or need for matching to avoid rejection; avoiding transformation; safety of gene modification; possible off-target immune modulation.
In Vivo Manipulation	Scalable; no ex vivo cell handling; potentially more acceptable for repeated dosing; may be able to mobilise regulatory subsets or antigen-specific clones within the patient.	Targeting efficiency (how to deliver stimuli to the right B-cell subset in the correct tissue); risk of activating non-desired B-cells; controlling amplitude and duration; monitoring for off-target effects.

Table1: Together, these approaches point toward a future where B-cell therapies are not only possible but personalised and precise.

are key for tipping the balance toward immunity; moved)

Risk of non-disease-specific B-cell depletion that eliminates both helpful and harmful subsets, including those contributing to tumor surveillance or protective immunologic memory.

Current issues:

Conventional vaccination strategies can fail in the elderly or immunocompromised populations as well as in chronic infection settings, where B-cell exhaustion or antigenic variation reduces antibody quality.

Polyclonal activation of non-disease-specific B-cells can generate off-target or autoreactive responses.

Ensuring the safety of gene editing (off-target effects, vector immunogenicity) and long-term persistence is non-trivial.

These limitations support the shift toward antigen-specific B-cell manipulation, whether through the adoptive transfer of engineered cells or in vivo expansion of targeted clones.

Autoimmunity: From Depletion to Regulation

The autoimmune field has been transformed first by anti-CD20 therapy and more recently with CD19 CAR-T. cells mediated B cell depletion that also eliminates plasma cells, continues to validate B-cells as drivers of disease in multiple sclerosis, lupus, and rheumatoid arthritis. The current accomplishment is undeniable: B-cell depletion has provided durable remission for many in a set of disease areas.

However, these therapies are not without cost: Non-disease-specific B cell depletion results in systemic immunosuppression. Long-term depletion can cause serious infections, impair vaccine responses, and eliminate protective or regulatory subsets.

In pediatric autoimmune conditions, rituximab-associated hypogammaglobulinemia is frequent and often persistent, especially in patients with central nervous system disease, and correlates with infections that are more serious.

Secondary hypogammaglobulinemia has also been documented in nephrotic syndrome patients treated with rituximab; persistent hypogammaglobulinemia in ~22% of patients.

These clinical realities highlight the need for the development of antigen-specific approaches. Expanding or engineering regulatory B-cells offers the first truly antigen-specific tolerance strategy.

Adoptive transfer of regulatory B-cells (Bregs) to suppress autoimmune responses while preserving protective compartments. Ex vivo expanded B10 cells have been shown to suppress EAE in mice

In vivo manipulation of Bregs, using cytokines, small molecules, or engineered ligands to selectively expand regulatory subsets at sites of inflammation. Studies have identified IL-21 plus CD40 stimulation as a potent driver of B10 cells in mice, yielding 10^6-fold expansion and disease suppression.

Expanding or engineering regulatory B-cells offers the first truly antigen-specific tolerance strategy—potentially the immune equivalent of gene therapy.

Mixed antigen-peptide chimeric B-cells: In the non-obese diabetic (NOD) mouse model, B lymphocytes treated ex vivo with LPS, electroporated with MHC-peptide constructs (class I or II) linked to autoantigenic peptides, could specifically suppress autoreactive CD8+ or CD4+ T cells and prevent autoimmune diabetes.

Adoptive Transfer vs. In Vivo Manipulation: Converging Paths

The two dominant strategies in B-cell immunotherapy are adoptive transfer and in vivo manipulation, and are likely to progress in parallel, as each approach has its own advantages and drawbacks. Table1

Outlook

Lessons learned from the T cell field are clear: blunt strategies yield early success, but antigen-specific precision is needed for durable impact. For B-cells, the time has come to move beyond depletion

AUTHOR BIO

Daniel Bednarik is the Chief Technology Officer at Black Canyon Bio, Inc. previously, he served as SVP of the Molecular Engineering Unit at NexImmune, Inc., where he led a molecular design team focused on creating novel immunotherapeutic multispecific proteins and antibodies. He is currently developing cancer vaccines using an innovative neoantigen discovery process.

and toward targeted, antigen-specific immunotherapy. Together with tof the past decades—anti-CD20 depletion in cancer and autoimmunity, recognition of the role of B-cells in cancer, and proof-of-concept engineering in infectious disease—have laid the groundwork. The side effects of non-specific therapies now highlight the urgent need for antigen-specific B-cell approaches that can preserve protective functions while targeting pathogenic ones.

Looking forward, it is reasonable to expect over the next decade:

First-in-human studies using engineered B-cells in adoptive for infectious disease and cancer.

Initial l trials of in vivo to target and expand or suppress specific B-cell subsets in autoimmunity.

Thus, the next decade may not just broaden the scope of immunotherapy—it may redefine it, centered on what could become the ‘B-cell Decade.

Thus, the next decade may not just broaden the scope of immunotherapy—it may redefine it, with center as the “B-cell Decade”. ■

References are available at www.pharmafocuseurope.com

AUTHOR BIO

Kristi Jones is a visionary biotech executive and public company CEO with a proven track record in strategic transformation, advanced therapy innovation, translational science, and company growth. As CEO of NexImmune, she led the company through a pivotal shift toward multiplexed T cell-based therapies for cancer and autoimmune diseases, achieving clinical proof-of-concept and establishing key partnerships to advance the company’s pipeline.

AUTHOR BIO

Dr. Mathias Oelke, a chemist by training, earned his PhD in Biology. Following his postdoctoral work at Johns Hopkins University, where he developed an artificial Antigen-Presenting Cell—he joined the faculty and later co-founded NexImmune. He has over 25 years of experience in immunotherapy, with a long-standing focus on developing antigen-specific cell therapy modalities.

Digital Infrastructure for Cell and Gene Therapies

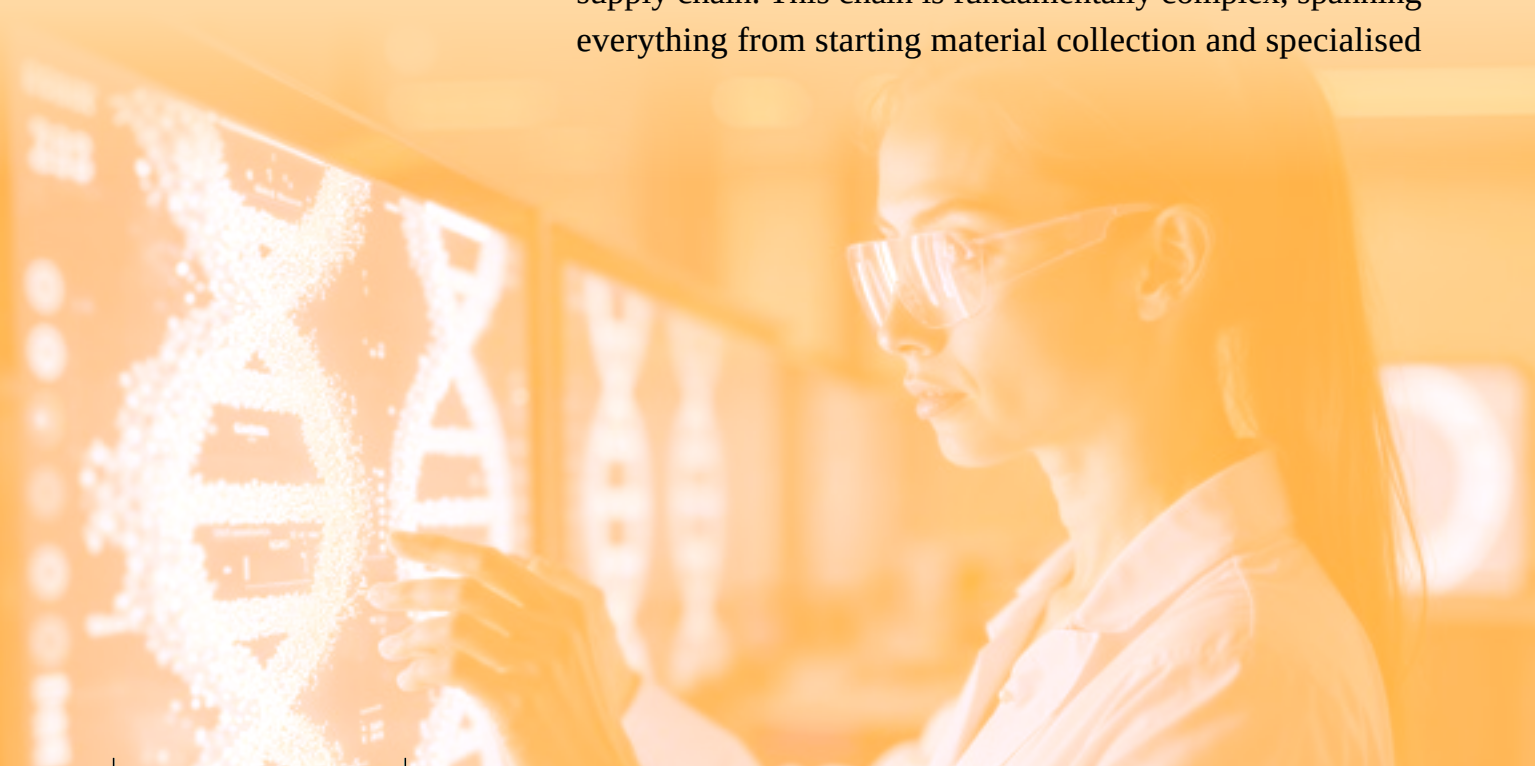
The Shift to Standardisation and Scale

CGTs can offer curative potential for previously untreatable diseases due to their personalised, patient-specific nature. However, these advantages also demand strict management of their supply chain. This article explores the growing challenges created by the current fragmented digital landscape for CGTs and makes the case for a transition toward standardisation and scale.

Akshay Peer
Chief Product Officer, TrakCel

Antonios Spanos
Industry Advisor, TrakCel

Cell and gene therapies (CGTs) can offer curative potential for previously untreatable diseases due to their personalised, patient-specific nature. However, these advantages also demand strict management of their supply chain. This chain is fundamentally complex, spanning everything from starting material collection and specialised



manufacturing to stringent temperature-controlled logistics and ultimately, timely delivery of the therapy back to the patient.

In this article, Dr Akshay Peer (Chief Product Officer) and Antonios Spanos (Industry Lead) at TrakCel explore the growing challenges created by the current fragmented digital landscape for CGTs and make the case for transitioning toward standardisation and scale. This shift is crucial to help unlock the full potential of these therapies, reduce the burden on clinical teams, and ensuring scalable access for patients globally.

The challenge of standardising orchestration in CGTs

The complexity of orchestrating the CGT supply chain is significantly increased compared with traditional pharmaceutical logistics. Due to the personalised nature of these therapies, the intricate orchestration process involves multiple stakeholders and stringent, often non-negotiable, temperature and timing requirements. To ensure timely and successful delivery of CGT products, all stages must be diligently coordinated with careful management of the Chain of Custody (COC) and Chain of Identity (COI).

For early CGT pioneers, coordinating these steps often relied on inadequate, manual processes and disparate systems, which immediately introduced systemic risks. Reliance on disparate systems can lead to transcription errors, a lack of standardisation, fragmented data, communication gaps, and no real-time visibility, all inevitably hindering efficiency. In addition, already busy Authorised Treatment Centre (ATC) staff are forced to navigate fragmented processes, contributing to inefficiency and a cumbersome customer experience.

Faced with these challenges, the developers of currently approved CGTs, like CAR-T products, have attempted to overcome them by leveraging bespoke software solutions to support their specific products and pipelines. While an understandable effort to gain control, this customised approach established a precedent that would ultimately lead to a larger, industry-wide issue, which has proven to be expensive, time-consuming, and most critically, a significant impediment to standardisation across the industry.

The resulting proliferation of disparate portals is now creating systemic inefficiencies, particularly at the treatment center level and across community care settings, manifesting as a pervasive issue known as “portal fatigue.”

How bespoke portals create inefficiencies at the treatment center level and community care settings

The core problem with portal fatigue lies in the structural differences across platforms, such as variations in nomenclature, process steps, definitions, and data formats. The issues with bespoke, proprietary solutions

are multifaceted and include:

1. Financial and time burden of bespoke development

Developing custom digital solutions often takes longer and costs more than expected, straining budgets and delaying key milestones. Updating bespoke systems to meet new regulations or clinical standards demands costly redevelopment and IT support, diverting funds from innovation and patient care. As technology evolves, these tailored platforms risk obsolescence, requiring continual investment to stay functional and compliant.

2. User experience failures and impact on patient safety

Custom-built platforms often overlook the daily needs of healthcare staff, resulting in inconsistent interfaces and inefficient workflows that cause confusion and frustration. Without or feedback integration, these systems can increase the risk of miscommunication and clinical errors, ultimately compromising patient safety and quality of care.

3. Fragmentation and systemic integration challenges

When systems lack standardisation, sharing data across platforms becomes difficult, hindering collaboration and slowing decision-making. Healthcare providers waste time navigating multiple systems instead of focusing on patients, while organisations struggle to adapt to new technologies or regulations, limiting innovation and progress across the CGT sector.

> FDA anticipates an influx of novel CGT products, which will exacerbate the challenges posed by custom-built solutions, making it increasingly difficult for healthcare providers to cope and threatening to bottleneck patient access.

4. Costly integration of bespoke solutions with the broader CGT network

CGT products require a network of stakeholders to work together to deliver for each patient, including:

- Hospitals
- Community clinics
- Payers
- Distributors
- Courier providers
- Manufacturing facilities
- Operations
- Supply chain functions
- CDMOs
- QA/QC labs

Maintaining and updating these ever-growing network integrations presents a substantial, ongoing challenge.

5.Lack of specialised features

Custom-built platforms often lack the agility and specialised capabilities needed to keep pace with the fast-evolving CGT sector. Even when built on commercial systems, their slow adaptation to new technologies and processes limits innovation and responsiveness. This lack of flexibility ultimately constrains manufacturers' ability to evolve, hindering progress across the entire industry.

The FDA anticipates an influx of novel CGT products, which will exacerbate the challenges posed by custom-built solutions, making it increasingly difficult for healthcare providers to cope and threatening to bottleneck patient access. To address this looming crisis, the industry must transition towards standardised practices across CGT orchestration platforms.

Standardisation is the key to unlocking multi-site delivery and scale

The complexity of the CGT supply chain can be addressed with a decisive shift toward standardised, widely adopted practices. This is particularly crucial in settings where therapies are delivered across multiple, geographically disparate sites such as hospital sites, specialised collection centers and decentralised clinics.

Standardised orchestration platforms serve as the central hub necessary for coordinating every stakeholder, securely tracking the COC and COI, managing complex logistics, and ensuring global regulatory compliance. By moving to standardised platforms:

- **Interoperability is guaranteed:** Standardisation enables seamless, secure data exchange between manufacturers, treatment centers, labs, logistics partners and Electronic Health Records (EHRs). This eliminates the reliance on costly, custom point-to-point integrations and creates true, real-time visibility across the end-to-end supply chain.
- **Workflow risk is reduced:** A consistent digital experience across multiple therapies and sites minimises the cognitive burden on ATC staff, drastically reducing the training time and the potential for clinical error rooted in navigating unfamiliar systems.
- **Scalability is achieved:** A standardised foundation allows manufacturers to onboard new clinical sites, distributors, depots and CDMOs rapidly and efficiently, turning a previous integration hurdle into a repeatable deployment process.
- **Global and community expansion is supported:**

As CGT manufacturing expands into new regions beyond traditional U.S. hubs, standardised orchestration platforms become essential for maintaining interoperability across diverse geographies. Standardisation ensures that regional facilities, suppliers and treatment centers can seamlessly integrate with global networks, enabling consistent processes, reliable data exchange and unified compliance standards regardless of location.

> CGT manufacturing expands into new regions beyond traditional U.S. hubs, standardised orchestration platforms become essential for maintaining interoperability across diverse geographies.

Technology providers play a vital and active role in driving this industry-wide shift. Their mandate is to develop standardised platforms that not only adhere to established industry standards but also actively promote interoperability by design. These commercial platforms must be designed as agnostic tools, serving as the central, intelligent hub for secure and efficient communication across all stakeholders.

This requires deep commitment to industry collaboration. Open communication and knowledge sharing among different stakeholders, including manufacturers, technology vendors, and healthcare professionals, are essential to fostering the development and rapid adoption of unified practices. Technology providers can champion standardisation by actively participating in industry initiatives, adhering to established guidelines, and building platforms with open Application Programming Interfaces, the foundational tools for enabling seamless, "plug-and-play" data sharing with existing enterprise systems. By working together, stakeholders can create a unified digital ecosystem that facilitates seamless data exchange, reducing ambiguity and ultimately accelerating the delivery of life-saving therapies.

Key considerations for selecting the right orchestration platforms

Given the inherent complexity of CGT orchestration, selecting a technology platform is a crucial, strategic decision. Various factors must be considered to ensure the platform aligns with the vendor's needs, while maintaining standardised good practice and fostering collaboration:

- **User-centric design and ease of use for ATCs:** Look for platforms with intuitive interfaces and workflows that are streamlined but robust enough for CGT specifics. This approach directly combats portal fatigue by minimising the training required for ATC staff and ensuring consistent processes across different therapies. Ultimately, a focus on user experience is a focus on patient throughput and clinical time preservation. For end users, this means less time navigating multiple systems and more time focusing on what matters most: delivering safe, efficient care to patients.

- **Adaptability and future-proofing**: The CGT landscape is constantly evolving, with new therapies, technologies, and regulations emerging regularly. Choosing an adaptable platform that can readily accommodate these changes is vital for long-term success. Configurability, modular design, and a commitment to ongoing development from the technology provider are key factors to consider. For clinicians and coordinators, this adaptability ensures the systems they rely on remain relevant and responsive, reducing disruption and keeping workflows familiar even as therapies advance.
- **Robust integration capabilities:** Digital fragmentation introduces risk, whereas seamless data flow reduces it. A high-quality orchestration platform should offer robust, open integration capabilities. This means the system must readily connect with existing core infrastructure. Open Application Programming Interfaces and established partnerships are non-negotiable, as they ensure secure data exchange and eliminate the costly, bespoke, point-to-point integration projects that previously caused issues. Prioritising solutions that already champion industry standards secures interoperability by design. For users, this translates to a smoother, more consistent experience across systems, removing redundant data entry and reducing errors that slow down care delivery.
- **Commercial viability and value:** The platform should be built for the future scale of the CGT market. Decision-makers should prioritise solutions that address cost-effectiveness and scalability. Look for vendors who offer a clear and transparent pricing model with options that cater to different needs and budgets. Decision-makers must also consider the platform's potential for maximising value, assessing factors like robust data security and a clear

AUTHOR BIO

Dr Akshay Peer is Chief Product Officer at TrakCel. He has many years of experience in creating technology-based solutions for the cell and gene therapy industry. His long-standing tenure in this field reflects a dedicated commitment to advancing innovation and contributing to the industry's growth.

product roadmap that outlines future innovation and development. For end users, this means a stable, well-supported system that's continuously improved without adding new complexity or unexpected costs.

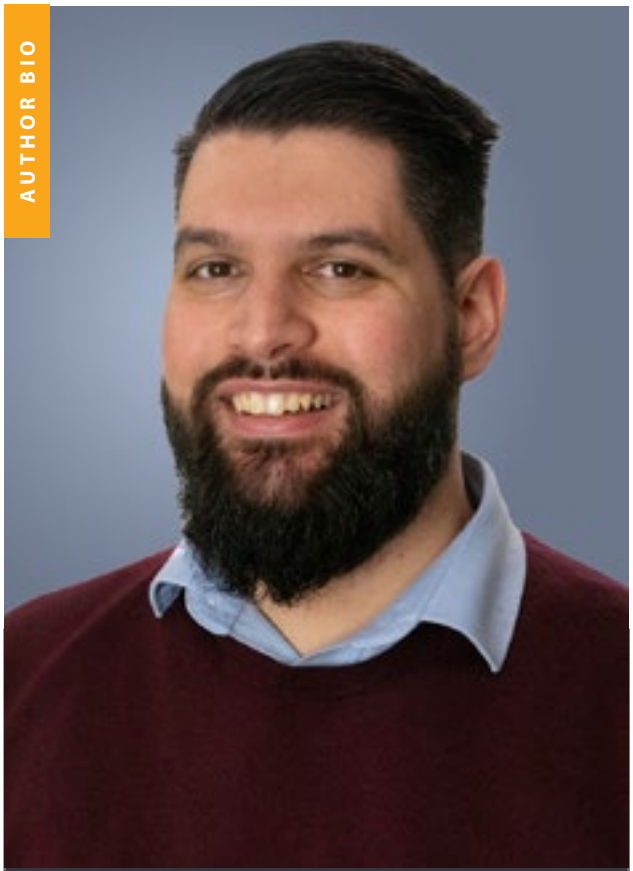
- **Choosing the right vendor as a strategic partner:** Beyond the technology itself, the commitment of the vendor is a vital factor. Deep industry experience, regulatory knowledge, strong vendor support, ongoing maintenance, timely updates, and responsive support are essential for smooth operation. Furthermore, a vendor who actively participates in industry initiatives and promotes standardisation demonstrates a fundamental commitment to the long-term success of the CGT ecosystem. For those on the front lines, this partnership ensures reliable tools, fewer workflow disruptions and confidence that their platform will evolve alongside industry needs.

Securing the future of CGTs at scale

The digital foundation of CGTs is reaching a critical inflection point. The early-stage necessity of bespoke, proprietary portals has become the primary bottleneck to scaling these potentially life-saving treatments. The inherent inefficiencies they create, from clinical burden and financial overruns to heightened patient safety risks, are becoming more unsustainable as the industry moves toward mass commercialisation.

The transition to standardised, collaborative and purpose-built orchestration platforms is an essential shift required to help achieve genuine scale. By prioritising solutions that champion interoperability, alleviate the on clinical teams and offer a truly future-proof design, manufacturers can secure the efficiency, safety and broad patient access necessary to realise the full curative potential of CGTs globally.

AUTHOR BIO



Antonios Spanos is the Industry Advisor at TrakCel , As a geneticist with over a decade of experience, including six years in pathology laboratories and clinical trial operations, Antonios has a wealth of knowledge in Cell and Gene Therapy supply chains and a proven track record of delivering transformative digital solutions in healthcare and cell & gene therapy.

Beyond Blood Cancers

CAR-T's Expanding Frontier

CAR-T cell therapy is entering a new era. After transforming outcomes in blood cancers, researchers are now tackling the tougher frontier of solid tumors. This article outlines the scientific and logistical challenges that have historically limited CAR-T's reach, tumor heterogeneity, antigen selectivity, and complex manufacturing, and the innovations reshaping the field. It discusses advances such as universal "off-the-shelf" cells, faster on-site manufacturing, dual-target and logic-gated constructs, and cytokine-releasing "fourth generation" CAR-Ts. These advancements aim to overcome previous biological and logistical challenges, making cellular therapies a practical reality for patients with solid tumors.

Victor Moreno

MD, PhD, Director of Clinical Research, START-Madrid-FJD

CAR-T cell therapy has transformed treatment paradigms in hematologic oncology, reshaping clinical practice in B-cell malignancies by achieving durable remissions in patients with limited therapeutic options. Translation to solid tumors, however, has proven substantially more difficult.

Solid tumors present biological and logistical barriers that are fundamentally different from those in leukemia or lymphoma. Unlike B-cell malignancies—where a single, well-defined antigen such as CD19 can be targeted with limited off-tumor toxicity, solid tumors are more complex, genetically diverse, and physically ▶

shielded by their microenvironment. These differences have challenged scientists to rethink how CAR-Ts are designed, manufactured, and delivered.

Progress continues despite these challenges. In 2025, the FDA approved afamitresgene autoleucel, a MAGE-A4-directed T-cell receptor therapy for synovial sarcoma—the first engineered T-cell product approved for a solid tumor. While mechanistically distinct from CAR-T, the approval demonstrates that targeted cellular immunotherapies can meet regulatory endpoints in solid tumors. As researchers continue to refine cell engineering, antigen targeting, and production technologies, the next era of CAR-T therapy is beginning to take shape.

Understanding the Barriers in Solid Tumors

Translation of CAR-T therapy to solid tumors has required confronting fundamental biological differences. Unlike circulating malignancies, solid tumors contain heterogeneous cell populations with variable antigen expression, mutational profiles, and microenvironmental features. Identifying targets that are highly tumor-specific while sparing normal tissue remains challenging. Even partial antigen expression in healthy organs can trigger severe inflammatory toxicity.

A second obstacle is the tumor microenvironment itself. Solid tumors develop dense stromal barriers and secrete immunosuppressive cytokines that impede T-cell trafficking and function. The physical structure of the tumor limits immune-cell penetration, while inhibitory pathways—such as PD-1/PD-L1 and TGF-β signaling—further dampen T-cell activity. An extreme example of these challenges is pancreatic cancer: its fibrotic stroma and highly immunosuppressive milieu make it one of the most resistant targets for any immune-based approach.

These biological barriers have historically stalled CAR-T development in solid tumors, but they have also catalyzed new strategies in cell engineering. Current strategies include multi-antigen targeting constructs, integrated safety switches, and armored CARs that secrete immune-modulating cytokines locally. The 2025 approval of afamitresgene autoleucel for synovial sarcoma demonstrates that with appropriate target selection and engineering approaches, T-cell therapies can achieve clinical efficacy in solid tumors.

Engineering the Next Generation of CAR-T Cells

Overcoming the inherent barriers of solid tumors has required a wave of innovation in CAR-T design. Investigators are advancing beyond single-target constructs toward architectures that account for tumor heterogeneity and immune evasion. Dual-target CARs recognize two antigens simultaneously to reduce escape variants. Logic-gated circuits activate only in the presence of specific antigen combinations, improving selectivity and minimizing off-tumor toxicity.

Fourth-generation CAR-Ts, often referred to as TRUCKs (T cells Redirected for Universal Cytokine Killing), incorporate genes enabling local cytokine secretion within the tumor microenvironment that can recruit endogenous immune cells and counteract immunosuppression. Early-phase data from studies targeting Claudin 18.2 in gastric and gastroesophageal cancers, mesothelin in mesothelioma and ovarian tumors, and MAGE-A4 in several epithelial malignancies are beginning to show encouraging safety and activity profiles.

Combination approaches are also under investigation. Pairing CAR-T or TCR therapies with checkpoint inhibitors such as anti-PD-1 aims to mitigate T-cell exhaustion. Initial data suggest manageable safety profiles, though efficacy remains to be established. Bispecific antibodies represent a complementary strategy—redirecting endogenous T cells without ex vivo modification. While logistically simpler, these agents require continuous infusion over extended periods, unlike the single-administration model of CAR-T. Together, these advances signal a decisive shift toward more intelligent, adaptable, and durable cellular therapies for solid tumors.

The Manufacturing Challenge — From Lab to Patient

While engineering advances have addressed biological barriers, manufacturing remains a critical constraint for CAR-T deployment in solid tumors. The autologous workflow, encompassing leukapheresis, viral transduction, expansion, and quality control—typically requires two to three months from collection to reinfusion. This timeline often necessitates bridging therapy to maintain disease control during manufacturing.

> Some platforms have the potential to deliver a complete CAR-T product within 7 days, which could dramatically improve clinical practicality for rapidly progressing cancers.

To shorten these timelines, several technologies are converging. Automated, closed-loop manufacturing systems capable of on-site production are reducing process times from weeks to days. Using fresh rather than cryopreserved cells preserves viability and reduces expansion requirements. Some platforms have demonstrated the potential to deliver a complete CAR-T product within seven days, a step that could dramatically improve clinical practicality for rapidly progressing cancers.

Parallel progress is being made in allogeneic or “off the shelf” CAR-T products derived from healthy donors. These cells are genetically edited to prevent graft versus host disease and immune

rejection, removing the need for patient-specific manufacturing. However, risks of immunogenicity and limited persistence remain open challenges. As these approaches advance, decentralised manufacturing capabilities and on-site automation may allow cellular therapies to be produced closer to the point of care, an essential advance for expanding access and accelerating treatment initiation.

Managing Toxicity

Safety remains the defining challenge for wider CAR-T. adoption. Toxicities such as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) are well recognized in hematologic malignancies and remain areas of active management in solid tumor trials. These events arise from powerful immune activation, which—if unchecked—can lead to systemic inflammation and neurological symptoms.

Efforts to mitigate toxicity are evolving rapidly. Lower intensity lymphodepleting chemotherapy regimens are being tested to preserve T cell expansion while reducing collateral toxicity. Early or prophylactic use of IL 6 and IL 1 blockade has shown promise in minimizing CRS severity. Genetic control mechanisms, including engineered “safety switches” that can be triggered by small molecules such as antibiotics, offer clinicians the ability to deactivate infused cells if severe adverse events occur.

Clinical experience is also reshaping outcomes. As more centers gain hands on familiarity with CAR-T. protocols, toxicity recognition and management have improved markedly. Multidisciplinary teams of oncologists, neurologists, and critical care specialists now anticipate complications earlier, allowing most adverse effects to be reversed without long term impact. Ongoing research aims not only to enhance the safety profile of CAR-T.therapy but also to balance intensity and tolerability so that potential cures do not come at the expense of quality of life.

Making CAR-T Accessible

Access and cost will determine whether CAR-T. becomes a realistic treatment option beyond academic centers. Manufacturing complexity, prolonged inpatient stays, and stringent regulatory oversight contribute to high costs. Even in high income regions, the overall price of treatment can limit patient eligibility and strain healthcare budgets.

Academic and publicly funded centers have begun to explore lower cost production models that rely on shared infrastructure and streamlined workflows.In Spain, for instance, academic institutions have demonstrated the feasibility of manufacturing CAR-T products at much lower costs, illustrating the role of publicly supported initiatives in improving accessibility.. As automation advances and more treatment facilities gain the expertise to handle cellular therapies, the geographic reach of CAR-T is expected to expand beyond metropolitan hospitals.

Decentralised, on site production and broader clinician training will be key enablers of this transition. In the long term, competition among commercial, academic, and hybrid models should drive efficiency and cost reduction, mirroring the evolution seen with other complex biologics. Expanding accessibility will require not only technological advances but also coordinated policy and reimbursement frameworks to ensure that the promise of CAR-T extends equitably to patients worldwide.

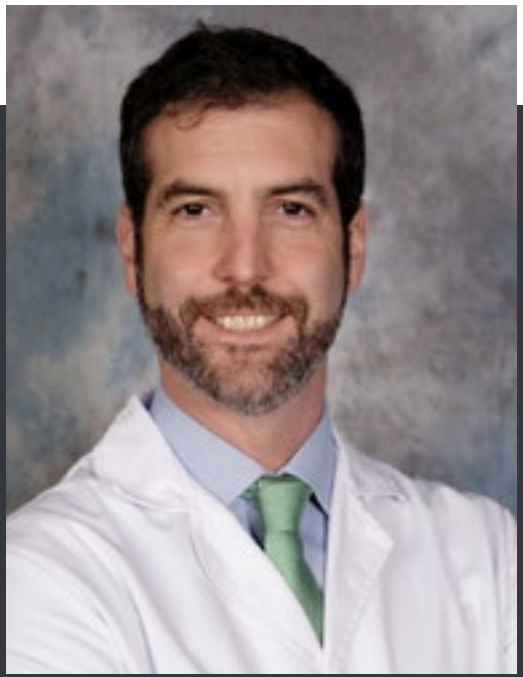
The Road Ahead—Progress & Promise

The future of CAR-T therapy will depend on the convergence of biology, bioengineering, and systems innovation. Advances in antigen discovery, including surface proteomics or "surfaceome" profiling, are accelerating the identification of tumor specific targets that are both selective and widely expressed. These data driven methods may uncover new antigens that enable more precise targeting in solid tumors.

Clinically, combination regimens are being actively explored. Integrating CAR-T with checkpoint inhibitors, cytokine modulators, or bispecific antibodies could enhance persistence and overcome resistance mechanisms, with efficacy signals still maturing. Lessons from hematologic oncology—particularly dual-target and logic-gated CAR designs—will continue to inform strategies for heterogeneous solid tumors.

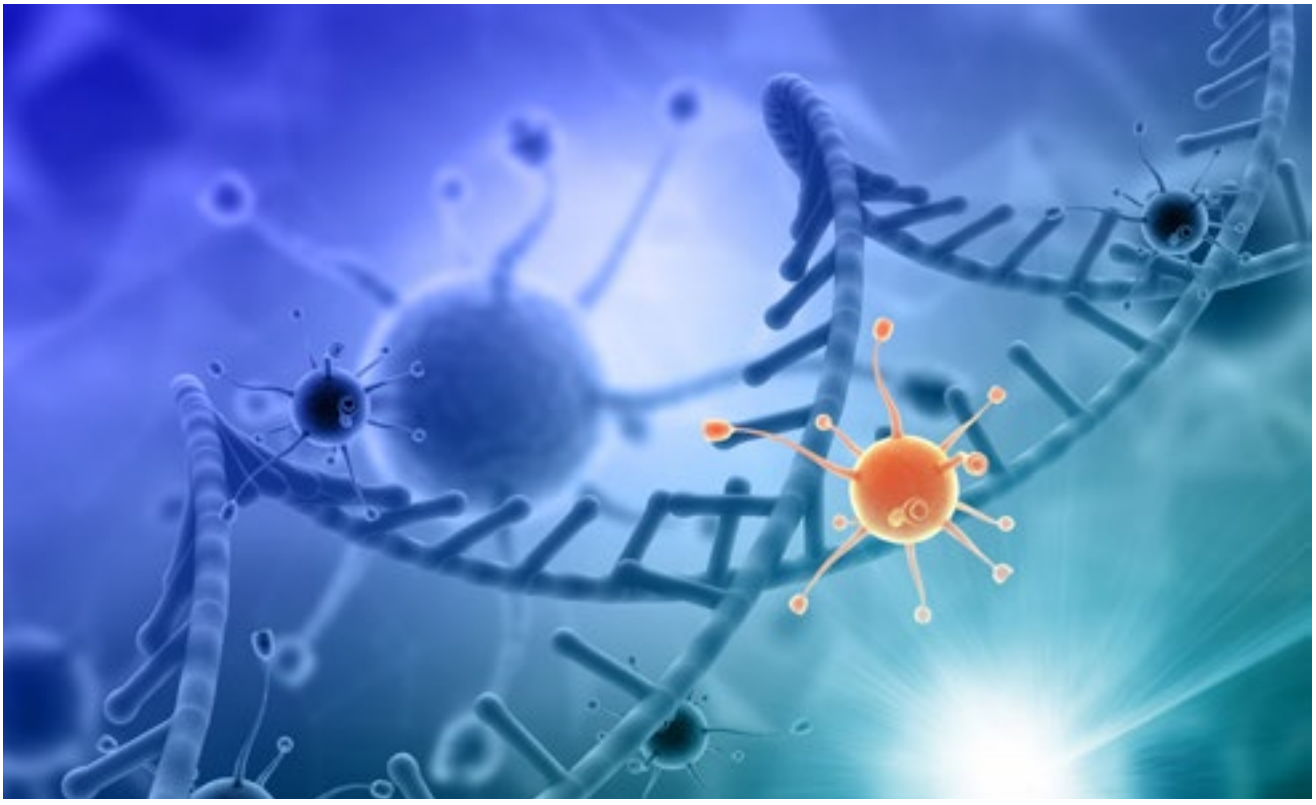
Equally important will be refining delivery and accessibility. As technology and expertise spread, CAR-T therapy could move gradually from a highly specialised procedure toward a more scalable clinical service if efficacy and safety continue to improve. Progress will also depend on practical advances in manufacturing speed, cost, and clinical experience. The path forward is one of integration: combining scientific ingenuity with practical frameworks that make cellular therapy a sustainable and more broadly accessible option for patients with solid tumors. ■

AUTHOR BIO



Victor Moreno, MD, PhD, is the Director of Clinical Research at START-Madrid-FJD and a medical professor at Universidad Autónoma de Madrid and CEU San Pablo. Part of The START Center for Cancer Research global network, START-Madrid-FJD is the largest Phase 1 clinical trials unit in Europe dedicated to oncology and hematology.

Meeting the Promise of Allogeneic Cell Therapies



Allogeneic cell therapies are poised to redefine immunotherapy by overcoming the limitations of donor-based models. In this article, Stefan Braam, Chief Technology Officer at Cellistic, explores how induced pluripotent stem cell (iPSC) derived NK cell therapies are providing a scalable, off-the-shelf alternative to donor-derived models, reducing manufacturing variability and accelerating clinical access. Leveraging unique insight, Braam explores the role of automation, gene editing, and process innovation in enabling future growth in this expanding therapeutic area.

Stefan Braam
Chief Technology Officer, Cellistic

A turning point for cell therapy

The global cell and gene therapy (C&GT) market is undergoing a significant transformation. Driven by the urgent need for scalability, consistency and affordability, the field is moving away from highly personalised, patient-specific approaches toward standardised, industrialised models. This evolution echoes the earlier shift seen in monoclonal antibody produc-

tion, where bespoke processes gave way to scalable platforms capable of serving global patient populations. Now valued at more than $20 billion and projected to grow further by 2030, the C&GT landscape is increasingly focused on allogeneic solutions that promise wider accessibility and reduced manufacturing complexity.

Autologous therapies, while groundbreaking in their personalised approach, are increasingly recognised as commercially unsustainable on a large scale. Each patient's therapy requires individualised manufacturing, beginning with cell collection from the patient, followed by a multi-week production cycle that includes genetic modification, expansion, and rigorous quality testing before the therapy is returned to the clinic. This process often exceeds four to six weeks, during which patients with aggressive diseases may experience disease progression. Furthermore, manufacturing at this scale is hindered by labor constraints and logistical challenges, including cold-chain management, as well as challenges arising from variable patient health statuses, which can significantly impact cell yield and quality. These factors contribute to the exceptionally high costs of autologous therapies, often reaching hundreds of thousands of dollars per patient, alongside limited accessibility.

In contrast, allogeneic therapies offer the potential for an "off-the-shelf" solution produced from master cell banks, breaking the dependency on patient-specific manufacturing and enabling treatments to be made at an industrial scale. This shift is a response to the urgent need for accessible, scalable and economically viable cell therapies worldwide.

The rise of iPSC-NK therapies

Allogeneic iPSC-derived cell therapy platforms are specifically designed to enable highly complex gene edits and accurately select cells carrying the intended modifications, minimising off-target effects. Key design criteria for a platform include:

- Precise multiplex gene editing: The ability to introduce multiple, targeted genetic modifications without off-target effects.
- Efficient selection of edited cells: Rapid and accurate identification of cells that carry the intended modifications.
- Sterility and traceability: Maintaining a contamination-free environment and ensuring full digital traceability throughout the development process.
- Monoclonality assurance: Confirming that therapeutic clones originate from a single, genetically stable cell to meet regulatory expectations.

Within this shift, NK cells derived from iPSCs have emerged as a promising modality. These cells combine innate cytotoxicity with the benefits of a renewable, genetically stable cell source. Emerging clinical data continue to validate their potential, with iPSC-derived CAR-NK therapies, such as FT596, showing encouraging results in hematologic cancers, demonstrating favorable response rates and lower toxicity compared to autologous CAR-T

treatments. As the industry seeks more scalable solutions, iPSC-NK therapies are increasingly viewed as an essential component of the future immunotherapy landscape [2,3].

However, moving iPSC-NK therapies from laboratory research into clinical and commercial practice presents a distinct set of challenges. Developers must navigate science, technology, and regulatory complexities to ensure these therapies can be reliably and effectively delivered to patients at scale.

> Now valued at more than $20 billion and projected to grow further by 2030, the C&GT landscape is increasingly focused on allogeneic solutions that promise wide accessibility and reduced manufacturing complexity

Navigating the challenges of scale and complexity

From lab bench to GMP

The leap from early-stage research to clinical-grade manufacturing of iPSC-NK therapies introduces significant hurdles. Processes that are robust at a laboratory scale often do not seamlessly translate to the larger volumes, regulatory standards, and operational complexity required in GMP manufacturing. One of the primary challenges is maintaining consistency in cell quality and function as production scales. Variability in culture conditions, even subtle fluctuations in oxygen levels, shear stress, or nutrient gradients, can significantly impact cell viability and therapeutic potency.

Traditional two-dimensional culture systems, a staple of laboratory research, are particularly problematic for scaling. These systems require large amounts of physical space, intensive manual labor, and frequent interventions, all of which increase the risk of contamination, batch failure, and process variability. For example, scaling from ten 2D plates to hundreds or thousands introduces physical and operational bottlenecks that are unsustainable in a clinical or commercial environment.

Adopting suspension-based, closed bioreactor systems is now viewed as essential for scale-up. These systems provide a controlled environment that supports larger batch sizes with significantly reduced manual input. Bioreactors allow precise control over parameters like dissolved oxygen, agitation rates, and pH, ensuring more reproducible results. However, the transition from adherent to suspension culture requires re-optimising differentiation protocols, validating shear tolerance thresholds for cells, and ensuring the media composition remains supportive of both cell expansion and differentiation at scale.

In addition to mastering suspension-based bioreactor operations, developers must also consider how to introduce flexibility into the manufacturing process. One effective

strategy is process modularity. Introducing cryopreservation steps at defined points in the workflow, such as after creating a master cell bank or lineage-specific intermediates, adds crucial flexibility. This modular approach enables developers to separate early-stage production from final cell expansion, improving scheduling and inventory management while reducing waste.

Driving toward economic feasibility

Innovation, while crucial for scalability and product quality, comes at a considerable cost. Manufacturing remains resource-intensive, with complex workflows involving multiple stages of cell isolation, gene editing, expansion, differentiation and formulation. Each stage requires specialised materials and highly trained personnel, driving up costs. Manual handling introduces not only variability but also higher labor expenses, increased facility downtime and greater risk of contamination.

Drug developers and manufacturers of iPSC-NK therapies must carefully consider how different technologies and approaches could impact economic feasibility and provide potential benefits:

- **Single-use systems**

The field is increasingly adopting closed, single-use bioreactor systems, driven by their consistency as well as their cost benefits. These systems minimise contamination risks, reduce labor input, and streamline cleaning requirements. By eliminating the need for stainless steel infrastructure, they lower facility construction costs and shorten turnaround times between production runs.

- **Modular manufacturing**

The shift toward modular manufacturing, where discrete units handle specific steps like expansion, harvest or formulation, enhances flexibility. Facilities designed for parallel, rather than sequential, workflows can process multiple batches simultaneously. This greatly improves throughput and provides redundancy, reducing the impact of potential batch failures.

- **Real-time monitoring**

Real-time monitoring tools are becoming indispensable. Sensors capable of screening pH, dissolved oxygen, glucose, and lactate concentrations enable early detection of deviations that could compromise cell quality. Integrated data platforms collect and process parameters from multiple batches, feeding into predictive models that help optimise process conditions over time.

- **Economic modeling**

Economic modeling has become a critical tool in process development, helping manufacturers navigate the financial realities that accompany these advanced, resource-intensive workflows. Companies use sensitivity analyses to identify the most significant cost drivers, whether they stem from raw material usage, labor or equipment downtime. These insights inform decisions about where to invest in automation or process optimisation, ensuring that capital investments deliver the highest return while supporting reliable, scalable production. ▶

Building in quality from the start

Ensuring regulatory compliance becomes increasingly complex as cell therapies, such as iPSC-NK therapies, scale from laboratory production to widespread clinical use. Unlike small-molecule drugs, cell therapies are living products. As a result, quality depends heavily on the integrity of the manufacturing process itself. This makes rigorous quality management essential from the earliest stages of development.

Regulatory agencies, including the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), require detailed documentation demonstrating that manufacturing processes consistently produce a product that meets predefined quality standards. These standards include identity (confirming the presence of key surface markers such as CD56, CD16 and NKG2D) as well as viability, purity, and safety.

Potency assays present a particularly challenging area, as they must reliably demonstrate the functional ability of NK cells to target and destroy tumor cells. These assays often use standardised target cell lines and are validated to ensure consistent performance across batches. Similarly, tests to confirm the absence of undifferentiated iPSCs are critical for safety, as any residual pluripotent cells could pose a tumorigenic risk.

Beyond product-specific testing, regulators also focus on the manufacturing environment. Emerging regulatory frameworks are beginning to accommodate real-time release testing (RTRT) for advanced therapies [6]. By integrating in-line sensors and predictive analytics, manufacturers can potentially release batches based on process data rather than waiting for extensive post-production testing. This shift not only accelerates delivery but also aligns with regulators' increasing comfort with data-driven quality assurance in the C&GT space. Requirements for environmental monitoring, raw material traceability, equipment validation and change control processes remain critical. As production scales, electronic batch records and centralised quality management systems become essential for maintaining compliance. These digital systems provide real-time oversight, reduce the risk of human error and facilitate audits by delivering transparent, traceable data across multiple manufacturing sites.

Gene editing at scale: Complexity meets precision

Gene editing is foundational to allogeneic iPSC-based therapies, enabling enhancements such as improved tumor targeting, immune evasion and extended persistence. Unlike other cell types, iPSCs present unique challenges for gene editing. Their lower transfection efficiency and sensitivity to culture conditions make multiplex editing particularly complex.

Introducing multiple gene edits simultaneously, often a combination of knock-ins for enhanced functionality and knockouts for immune cloaking or checkpoint inhibition, requires extremely precise tools. CRISPR-based

> As demand for off-the-shelf, standardised treatments continues to grow, the industry must prioritise continued innovation in bioprocessing, quality control, and regulatory alignment

systems are the most commonly used, but even high-fidelity nucleases can introduce off-target effects if not carefully managed.

The challenge extends beyond executing the gene edits; it also involves the complex task of identifying and isolating the correctly edited clones from a large pool of candidates. After editing, hundreds or thousands of candidate colonies are screened using PCR, next-generation sequencing and functional assays to verify both on-target success and absence of unwanted changes. This is a labor- and data-intensive process.

Clonal stability is critical. A clone selected for manufacturing must not only contain the desired edits but also retain genomic integrity over multiple passages. Any chromosomal abnormalities, translocations or unexpected mutations could compromise safety or efficacy, and as a result, extensive genomic screening is essential.

Automation can help overcome these challenges. Robotic systems now handle tasks such as single-cell seeding, media exchanges and clone picking. These systems not only reduce contamination risks but also improve the reproducibility of complex gene editing workflows. Furthermore, automated imaging tools allow real-time monitoring of clone growth and morphology, flagging any anomalies early in the development process.

How automation supports modern cell line development

Manual methods are no longer sufficient to edited iPSC manufacturing. The complexity of these workflows, especially when dealing with multiple gene edits, clonal selection and stability assessment, makes automation not just beneficial but essential. Automation can be leveraged throughout iPSC cell line development in different ways:

Clonal assurance

Automated platforms enable clonal assurance by precisely executing single-cell deposition, often with imaging-based double confirmation of monoclonality. This ensures that each clone can be tracked from initial isolation through expansion and final selection, which is a critical requirement for regulatory submissions.

Sterility control

Enclosed robotic systems operating under Grade A air supplies eliminate the need for manual interventions during sensitive steps such as media changes, transfection and clone expansion. This can significantly reduce contamination risks while improving batch reliability. ▶

Digital traceability

Full digital traceability can be built into modern automation platforms, allowing seamless audit trails and data capture. Every action, from liquid handling to imaging and colony screening, is recorded and associated with each clone. This data integrity becomes vital for regulatory filings and ongoing quality management.

Parallel processing and artificial intelligence (AI) integration

Parallel processing capabilities mean that hundreds of clones can be developed, monitored and characterised simultaneously, dramatically compressing development timelines. The rich datasets generated from these automated systems can be fed into machine learning algorithms that refine clone selection, predict growth characteristics and identify potential process improvements, ultimately driving greater efficiency and precision in manufacturing.

The future requires continued adaptability

As the iPSC allogeneic cell therapy field advances, regulatory landscapes are evolving alongside technological innovations like AI-driven process optimisation and decentralised manufacturing models. Developers must continue investing in infrastructure, sustainability and data-driven strategies to ensure long-term success.

The lessons learned in scaling iPSC-NK platforms will set the foundation for a broader range of cell therapies in the years ahead. As demand for off-the-shelf, standardised treatments continues to grow, the industry must prioritise continued innovation in bioprocessing, quality control, and regulatory alignment. At the same time, developers must be prepared to adopt new technologies, such as AI-driven process optimisation and decentralised manufacturing models. These forward-looking strategies will be crucial in ensuring that cell therapies not only achieve clinical success but are delivered reliably, efficiently, and at scale to meet the global needs of patients.

References are available at www.pharmafocuseurope.com

AUTHOR BIO

Stefan Braam is the co-founder and Chief Technical Officer of Cellistic, with over a decade of experience in stem cell technology, product development, and general management. He won the NGI Venture Challenge (2009) and the Niaba Biobusiness Masterclass (2010), has published in several leading scientific journals, is an inventor on multiple patent families, and has secured numerous grants and commercial research collaborations.

Blockchain in Securing Clinical Trial Data

Blockchain technology enhances the security and integrity of clinical trial data by providing a decentralised, immutable ledger. This ensures transparent, tamper-proof records, improving data accuracy and trust among stakeholders. Its cryptographic features safeguard sensitive information, fostering compliance with regulatory standards and enhancing the overall reliability of clinical research.

Debasish Kar
Senior Clinical Project Coordinator,
Thermo Fisher Scientific

Blockchain for Securing Clinical Trial Data: Safeguarding Integrity in Medical Research

Clinical trials are the foundation of medical progress. They determine the safety and effectiveness of new treatments, from life-saving vaccines to advanced cancer therapies. However, the integrity of trial data has long faced challenges, including unauthorised access, selective reporting, and even deliberate manipulation.

Blockchain technology, once associated primarily with cryptocurrency, is now being explored as a secure and transparent way to record and manage clinical trial data. Its unique combination of immutability, decentralisation, and cryptographic protection

Threat	Impact on Trials
Data tampering	Misleading results and possible patient harm
Selective reporting	Skewed scientific evidence
Hacking or data theft	Breach of patient confidentiality
Loss of records	Regulatory non-compliance and trial delays

Table 01

offers a framework that could transform the way research data is stored, shared, and verified.

This article examines how blockchain can enhance data security in a feasibility and site identification process that considers not only historical site/investigator-which they are committed. The path to rapid clinical trials, the practical advantages it offers, the challenges it faces, and what the future may hold for its use in medical research.

The Need for Stronger Clinical Trial Data Security

Clinical trial data is both highly sensitive and extremely valuable. Breaches or inaccuracies can harm patients, lead to regulatory penalties.

Key reasons data protection is critical:

- **Patient confidentiality:** People who take part in trials give out private, genetic information that needs to be kept safe by laws like the General Data Protection Regulation (GDPR) in the EU and the Health Insurance and Accountability Act (HIPAA) in the US.
- **Scientific credibility:** Altered or incomplete data undermines research outcomes and public confidence.
- **Regulatory compliance:** Drug approvals depend on verifiable, complete evidence submitted to authorities such as the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA).
- **Commercial stakes:** Pharmaceutical companies invest heavily in research, and the value of their products can hinge on trial outcomes.

SIDEBAR: Common Data Integrity Threats (Table1)

How Blockchain Works in Clinical Trials

Blockchain is a distributed ledger, a database duplicated across multiple computers (“nodes”) in a network. Data is stored in blocks, each containing a time-stamped record linked to the previous block via cryptographic methods.

SIDEBAR: Blockchain vs. Traditional Trial Databases

Feature	Traditional Databases	Blockchain
Alteration resistance	Vulnerable	Tamper-evident
Data access control	Centralized	Distributed permissione d
Audit process	Manual and delayed	Automatic and real-time

Table 02

Key attributes relevant to clinical trials:

- **Immutability:** Once recorded, data cannot be altered without leaving a trace.
- **Transparency:** People who are allowed to can see a record of all the comments.
- **Decentralisation:** No single party can control the system unilaterally.
- **Security:** Cryptographic techniques protect against unauthorised access.

Clinical trial blockchains are often permissioned, meaning only approved parties—such as researchers, sponsors, and regulators, can access or add data.

Ways Blockchain Improves Trial Data Security

Immutable Audit Trails

Once trial data is added to a blockchain, any changes are evident, all of this directly on blockchain can be slow and deterring manipulation. This creates a permanent, verifiable record that can be audited at any stage.

Accurate Time-Stamping

Every entry, such as patient enrolment, consent, or reporting of side effects, is ▶

precisely time-stamped. This prevents backdating and ensures events are recorded in the correct sequence.

Secure Consent Management

Informed consent is fundamental in research ethics. Blockchain can store encrypted, time-stamped consent records linked to anonymised patient identifiers, ensuring a verifiable consent history.

Safe, Decentralised Data Sharing

Multi-site and multinational trials require secure data exchange. Blockchain allows encrypted sharing without a single central repository that could be vulnerable to attacks.

Mitigation of Selective Reporting

Trial protocols, results, and amendments can be recorded from the outset, making it evident if unfavourable outcomes are omitted.

SIDEBAR: Blockchain vs. Traditional Trial Databases (Table2)

Examples of Blockchain Use in Clinical Research

- **TrialChain (University of British Columbia):** Uses Hyperledger Fabric to record trial events and data submissions for verifiable audit trails.
- **IBM–FDA Pilot Project:** Tested blockchain for secure exchange of clinical and real-world evidence data, improving efficiency and trustworthiness. This creates consent is fundamental in

> When clinical trial data meets blockchain, manipulation becomes impossible and trust becomes inevitable

- **Ethereum Protocol Storage:** Some researchers use public blockchains to store cryptographic "hashes" of trial data, proving authenticity without exposing raw data.

Current Challenges

Scalability

Clinical trials generate large datasets, including imaging and genetic information. Storing all of this directly on can be slow and costly. Hybrid approaches, storing large files off-chain but on-chain, are often preferred.

Privacy Regulations

Blockchain's immutability conflicts with GDPR's "right to erasure", requiring innovative solutions security legal obligations.

Technical Complexity

Integrating blockchain with existing trial secure data exchange. making it eviden allows data systems requires specialist expertise and may increase operational costs.

Regulatory Uncertainty

Guidance on blockchain use in clinical trials is still evolving, and global trials face differing jurisdictional requirements.

BOX: Hybrid Storage Model

On-chain: Hashes, time-stamps, consent records, and protocol metadata reliable, transparent, and patient-focused

Off-chain: Raw clinical data stored securely in cloud or institutional servers, linked to blockchain entries

The Road Ahead

Emerging trends suggest blockchain's role in clinical trials will expand:

- **Integration with Wearables**: Continuous patient monitoring devices could feed secure, authenticated data into trial blockchains.
- **Smart Contracts:** Self-executing code could automatically enforce trial rules, trigger alerts for deviations, and release milestone-based payments.
- **Global Registries:** A universal blockchain registry of all trials could improve transparency and reduce duplication.
- **Patient-Controlled Data Access:** Patients could grant and revoke access to their data via blockchain systems, empowering them in the research process.

Conclusion

Blockchain offers an innovative approach to securing clinical trial data, addressing long-standing concerns around integrity, . While challenges in scalability, privacy compliance, and regulation remain, early initiatives demonstrate significant potential.

As the life sciences sector seeks more reliable, transparent, and patient-focused research systems, blockchain is poised to of future clinical trial infrastructure—helping to ensure that medical advances are built on a foundation of trust.

AUTHOR BIO

Debasish Kar is a Senior Clinical Project Coordinator at Thermo Fisher Scientific. A PMP-certified professional and Master of Pharmacy graduate, he has over 11 years of experience in the pharmaceutical domain, clinical research, and clinical data management. He is skilled in eTMF and clinical document management systems and is dedicated to enhancing data quality, regulatory compliance, and operational efficiency in global clinical trial environments.

Melissa Hutchens
VP Research & Benchmarking, WCG

Gar Crowell
Sr. Manager, Benchmarking & Analytics, WCG KMR Group

Optimising Clinical Trial Start-Up

Site Activation as a Key Performance Lever

Optimising study startup and site activation plays a critical role in the efficiency of clinical trials. Several factors, including regulatory submissions, country startup, site identification, contracting, and site initiation, can significantly impact overall trial timelines. Comparative studies have illustrated how variations in these processes can affect overall clinical trial duration.

A well-orchestrated start-up process can significantly accelerate the time to patient enrollment, reduce operational costs, and increase the likelihood of meeting study milestones.

Among the multitude of measurable metrics for a clinical trial, the cadence of site initiation (the rate at which sites progress from selection to being fully operational) proves to be a key variable that drives the pace of clinical trials. As companies set strategic objectives for trial activation, this metric should be at the forefront of conversations and goal-setting targets.

An ML-based stochastic gradient boosting model that leveraged 287 Phase III Oncology studies found that reducing the site initiation cadence by as little as 3 days could reduce overall trial timelines by about 20% or as much as 7-8 months.

Common Countries Used – Phase III Oncology Trials

Source: WCG KMR Clinical Benchmarking Program

Figure 01

Achieving such a reduction can be enabled by a feasibility and site identification process that considers not only historical site/investigator- which they are committed. The path to rapid initiation requires meticulous planning, with precise focus on site identification and feasibility that begins as soon as, or perhaps even before, a protocol is conceptualised.

This article will examine systematic methods for measuring site activation efficiency, such as the number of sites initiated each month, as well as the intervals between these activations (site initiation rate). Monitoring the number of sites activated during a study provides information about the performance of parallel start-up processes and how quickly new sites become operational. Tracking the interval between activations enables companies to assess the impact of their start-up initiatives on activation timelines. Such metrics not only offer a window into operational performance but also highlight avenues for accelerating trial timelines and optimising resource allocation across clinical programs.

Model Methodology & Results

Predictive Analytics Illuminate Key Drivers

To analyse trends in site activation rates, a dataset of 287 Phase III Oncology studies that completed enrollment over the past five years was examined. On average, these studies involved approximately 15 countries worldwide. The chart below indicates the frequency with which each country participated in these trials. (Figure 01)

A machine-learning model was developed to predict enrollment cycle times based on site initiation metrics, trial characteristics,

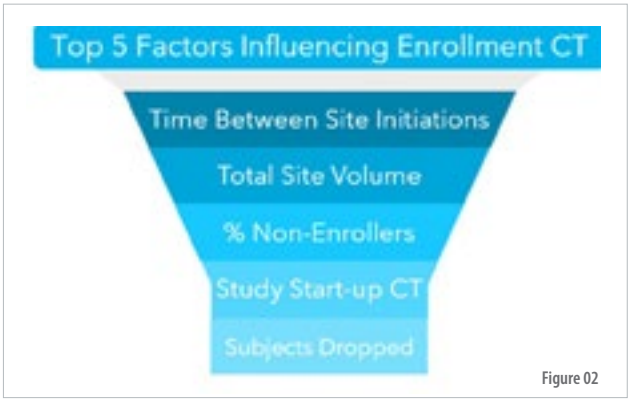


Figure 02

geography, and operational characteristics. The model employed was a stochastic gradient boosting model with a Cox proportional hazard loss function. The model included disease, line of treatment, disease rarity, number of endpoints, number of subject visits, start-up time, CRO involvement, number of patients, volume and geographic spread of the sites, average time between sites initiated over the course of the study. The resulting predictions were evaluated to identify the factors most associated with influencing enrollment cycle times. The following graphic presents the five factors associated with having an on enrollment cycle times in the dataset. (Figure 02)

Site Activation as a Primary Driver

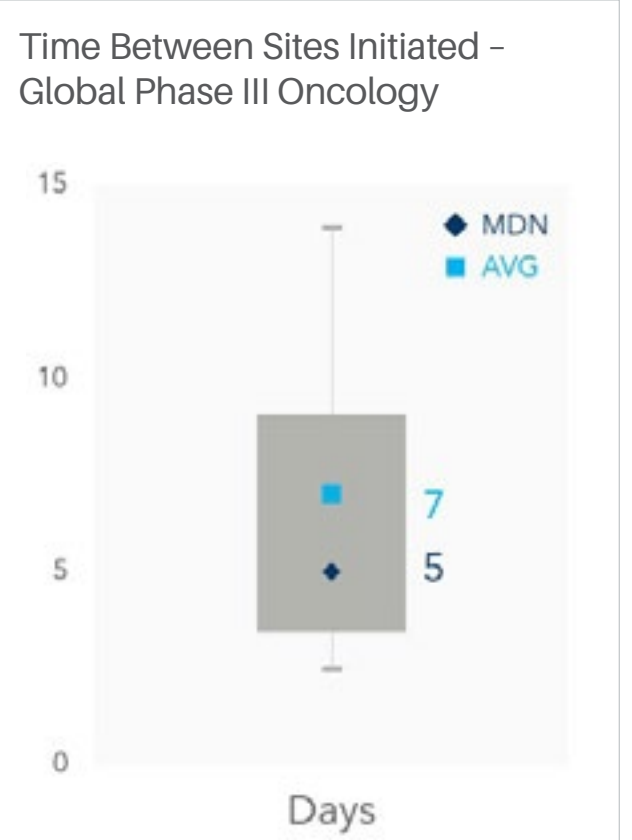
The Cadence of Initiation Determines Success

From the model results, the average interval between sites initiated stands out as a crucial determinant of enrollment duration. This cadence of site initiation proves to be a key of clinical trials.

Across all studies in the dataset, the median time between each site initiation was The top quartile of trial performance is about three days apart. (Figure 03)

This pace changes as the trial progresses. Time between sites starts out at six days, is fastest around months seven through nine (three days), and then slows for the remainder of the study(Figure 04)

To assess the direct effect of this metric on enrollment times, model inputs were subjected to random permutation before being evaluated by the model. Ridge regression models were subsequently employed to quantify the contribution of each feature within the model's predictions. A forward selection approach identified up to 10 variables per trial that exerted the greatest influence on predicted outcomes, with each quantitative variable partitioned into eight quantile bins. The aggregated feature



Source: WCG KMR Clinical Benchmarking Program
Figure 03

Time Between Sites Initiated – Global Phase III Oncology

Source: WCG KMR Clinical Benchmarking Program

Figure 04

weights were then analyzed to determine which variables had the most significant, cumulative impact on enrollment duration.(Figure 05)

The graphic above presents the average predicted effect on enrollment time at eight quantiles of feature impact, based on the complete dataset of trials in the model. This analysis isolates the impact of the average gap in site initiation dates, with other variables held constant. In doing so, we aim to quantify the magnitude of reducing site initiation intervals.

The chart illustrates the average effect on predicted cycle time corresponding to various mean intervals between sites initiated throughout the trial period. The x-axis represents evenly distributed quantiles for the average duration between site initiations, while the bars depict the anticipated impact on enrollment constant for each specific site initiation rate. For example, an average initiation of 2.2 days is associated with a reduction of 7.6 months in enrollment cycle time, compared to an average initiation rate of around five days. Overall, an average site initiation interval below five days between sites is associated with a decrease in enrollment cycle time for Phase III Oncology trials.

Setting Site Initiation Goals

Benchmarking Performance and Driving Accountability

To improve initiation timelines, organisations should establish ambitious site activation objectives and ensure team accountability for meeting these targets. A practical approach is to set monthly benchmarks for the number of sites launched throughout the duration of the trial. By leveraging benchmarking data and predictive analytics, companies can evaluate prevailing industry trends and assess the top quartile performance.

The chart below illustrates the pattern of a clinical trial. Given that these studies span

> The average interval between sites initiated stands out as a crucial determinant of enrollment duration.

an average of fifteen countries, the initiation numbers naturally increase as more regions commence their startup processes. This global scope underscores the importance of coordinated site activation strategies, revealing how synchronised efforts across diverse locations can expedite trial progress and enhance overall efficiency. The median number of sites initiated in the first month of a study is three, though the top quartile is a minimum of six sites, with some studies able to achieve more. (Figure 06)

By analysing these site initiation gaps within countries, as well as identifying the "best performer" initiation rate, we can identify significant opportunities to compress trial timelines. The space between site initiations represents an opportunity for efficiency gains. By reducing these gaps, sponsors and CROs can enhance the overall momentum of the study.

Considerations for Streamlining Site Activation

Overcoming Hurdles from Site Selection to Contracting

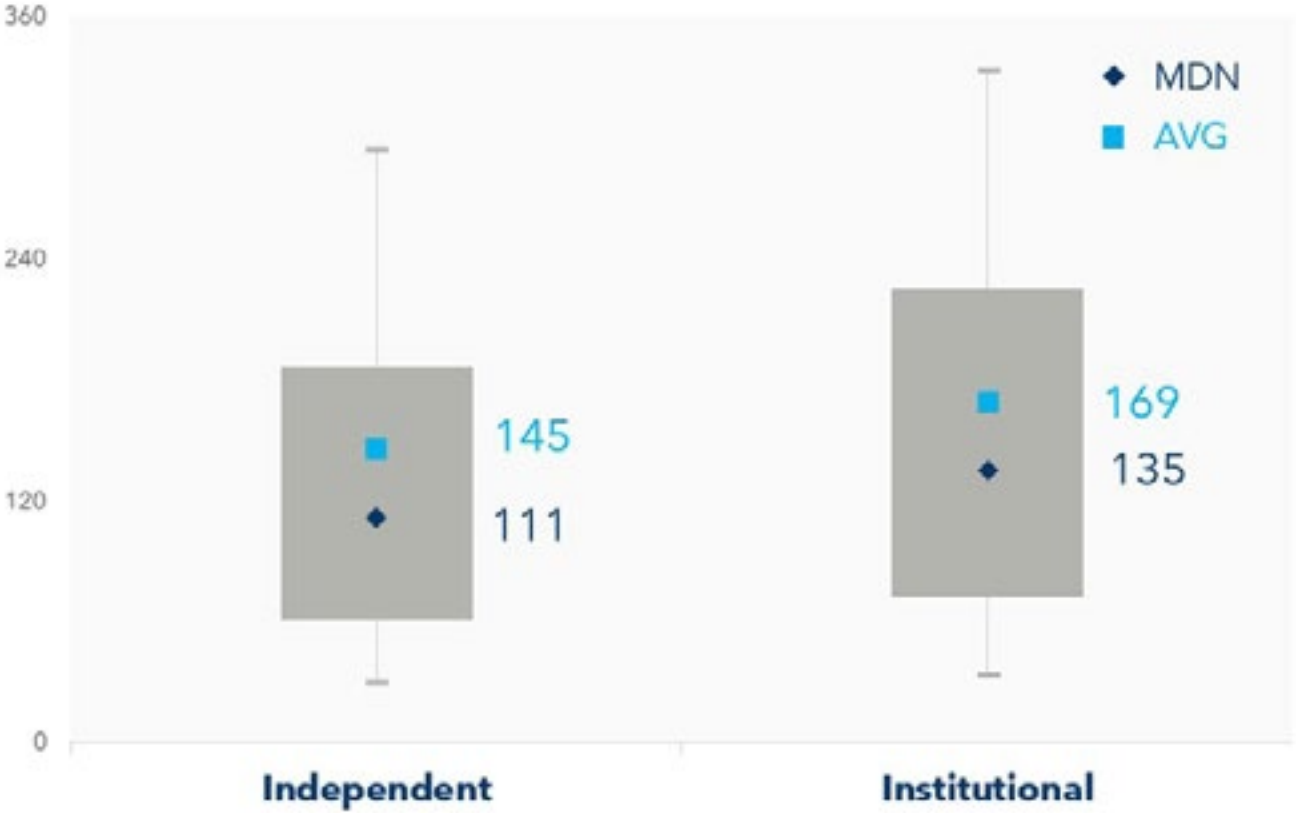
Several critical processes can contribute to delays in site activation. Prior to selecting sites, it is necessary to identify those suitable for potential participation in the clinical trial. Optimising site identification based on well-defined study criteria is crucial for an effective

Average Impact on Enrollment Cycle Time (Months)
By Time between Initiations

Figure 05

Source: Model Results

Distribution of Sites Initiated by Month Within the First 12 Months of Global Initiation



(Figure 06) Source: WCG KMR Site Contracts Benchmarking Program

selection process. Relying solely on established site relationships, traditionally common, has proven to be inefficient and may incur significant resource and time costs. In today's environment, where advanced analytics and technology are readily available, organisations should leverage both historical site experience and comprehensive performance data. Incorporating supplementary data sources, such as claims and electronic health record (EHR) data, can further enhance the development of optimised site lists.

During the site selection process, it is essential to evaluate sites for their compatibility and willingness to participate in the clinical study. The feasibility assessment can present challenges for all parties involved; however, leveraging a platform with established site capabilities and capacities can streamline this process and facilitate the efficient achievement of site selection objectives. Working with site networks or preferred partners can be effective, given that key site attributes are well known to the sponsor, and alignment to a study can study faces a competitive market, sponsors may need to approach research-naïve sites, which can pose further challenges in training and the setup of site resources. ▶

Following site selection, several key activities occur before site initiation, including IRB review, IBC approval, coverage analysis, budgeting, and contract negotiation. Among these steps, budget development and contract execution constitute the most time-intensive components of the process. The graph below illustrates current contract timelines in the United States by site type for Oncology in Phase III. Institutional sites require approximately 135 days to finalise contracts, whereas independent sites average around 111 days.

Site Contracting Time (Days) By Site Type – Global Phase III Oncology

An integrated process of site activation activities can prove to be beneficial in reducing activation timelines. Given the unique needs of each site, companies should strive to align their processes and identify a tailored solution.

Conclusion

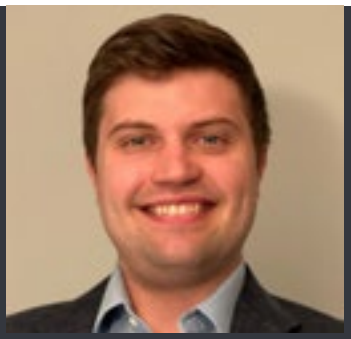
Accelerating Clinical Trials Through Strategic Site Activation

The efficiency of site activation stands as a pivotal determinant of clinical trial success, influencing the overall timeline, resource allocation, and ultimate outcomes in drug development. By focusing on streamlining adopting data-driven approaches to activation cadence, organisations can reduce white space, significantly decrease enrollment cycle times, and bring breakthrough therapies to patients more swiftly. As the clinical research landscape grows increasingly complex, those who prioritise and innovate in the site start-up phase will be best positioned to achieve operational excellence and competitive advantage. ■

AUTHOR BIO

Melissa Hutchens is the Vice President of Research & Benchmarking at WCG KMR Group. She joined KMR Group in 2001 and brings over 24 years of experience in R&D benchmarking and analytics for the biopharmaceutical industry. Melissa has developed extensive benchmarking frameworks, analytical applications, and AI-driven models across the Research & Development lifecycle.

AUTHOR BIO



Gar Crowell is the sr. Manager of Benchmarking & Analytics at WCG KMR Group, where he leads efforts to provide data-driven insights and performance measurement for leading pharmaceutical and biotech organizations. With 10 years of experience at WCG KMR Group, Gar has contributed across the R&D spectrum, from site engagement to organizational R&D productivity.

Translating Nanomedicine Potential into a Scalable Reality with Flow Manufacturing

Nanomedicines are revolutionising drug development by enhancing precision, control and therapeutic performance. This article explores how flow manufacturing overcomes the scalability and quality challenges of nanoparticle production, enabling consistent, reproducible results from lab to commercial scale. With expert insight from Ardena, it highlights strategies to ensure reliable, scalable nanomedicine manufacturing.

Mark van Eldijk
Business Unit Director, Nanomedicines, Ardena

Nanomedicines are transforming modern drug development by enabling therapies to act with greater precision and control. As formulations become more sophisticated and the market continues to expand, developers face growing pressure to ensure nanoparticle quality and scalability. Achieving this balance between innovation and manufacturability demands production approaches that ▶

deliver consistent performance and deep process understanding.

In this article, Mark van Eldijk, Business Unit Director Nanomedicines, at Ardena, explores how flow manufacturing is reshaping nanomedicine production, offering a more controlled, scalable and reproducible path from laboratory design to commercial supply, and helping to bring advanced therapies to patients with greater reliability.

The growing role of nanomedicines in modern drug development

At the intersection of materials science and medicine, nanomedicines are reshaping how therapies are designed, delivered and controlled. By applying the tools of nanotechnology to drug development, researchers are creating medicines that can act with exceptional precision.

At its core, a nanomedicine is a therapeutic that contains nanoscale components, typically between 1 and 100 nanometres in size. With different material classes, lipids, polymers or metals, with precise control over particle size, composition and surface characteristics, developers can tailor nanoparticles to achieve specific functions. The diversity of nanomedicine platforms reflects the wide range of therapeutic goals they can address:

Lipid-based nanoparticles

Including liposomes and lipid nanoparticles (LNPs), these systems are widely used in gene delivery and vaccine formulations. They can efficiently encapsulate and protect nucleic acids or small molecules until they reach their target site.

> The growing diversity of nanomedicines is mirrored in the expansion of the global market, valued at approximately USD 265.9 billion in 2025 and projected to reach USD 632.1 billion by 2034

Polymeric nanoparticles

Formed from tailored polymers, polymeric nanoparticles and dendrimers enable controlled or targeted drug release, supporting therapies that benefit from sustained delivery, such as those used to treat cancers or chronic diseases.

Metal and metal oxide nanoparticles

Comprising materials such as gold and iron oxide, these nanoparticles are primarily used in imaging and targeted cancer therapies, where their optical and magnetic properties enable precise localisation and treatment.

Each of these nanoparticle systems leverages nanoscale engineering to optimise

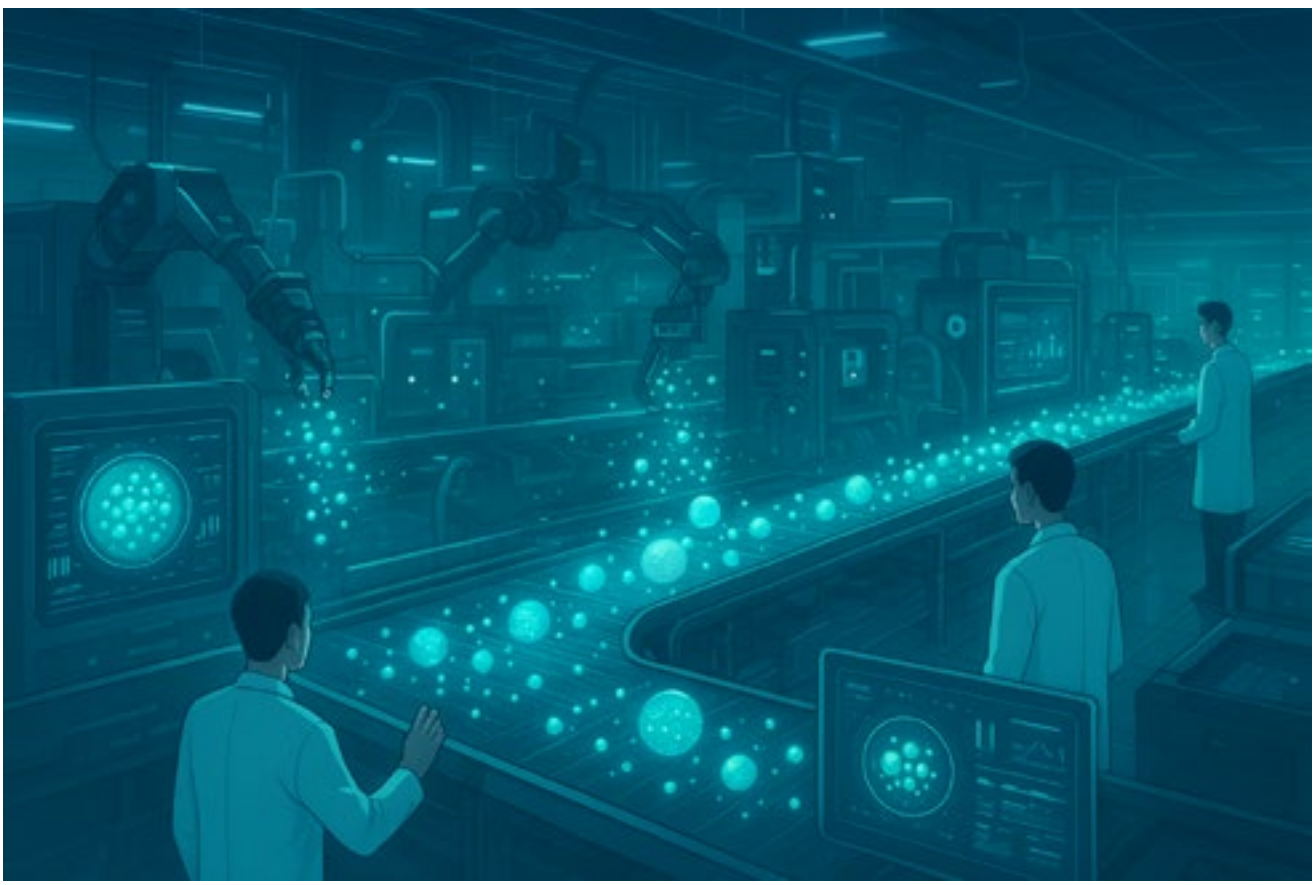
how a formulation interacts with biological systems, influencing circulation time, cellular uptake and biodistribution to deliver a defined therapeutic response.

Meeting the demands of the expanding nanomedicine market

Nanomedicines have already demonstrated meaningful clinical success across multiple therapeutic areas. Applications now span oncology, chronic disease management, regenerative medicine and gene therapy.

More than 100 nanomedicines are already approved, and over 550 candidates are in clinical development, marking the sector's steady evolution from early innovation to established industrial maturity. The growing diversity of nanomedicines is mirrored in the expansion of the global market, valued at approximately USD 265.9 billion in 2025 and projected to reach USD 632.1 billion by 2034, representing a compound annual growth rate of 10.1%.

As demand for nanomedicines expands, manufacturing has become a defining factor in realising their full potential. Meeting market and clinical expectations requires production processes that deliver consistency, scalability and precise control over complex nanoparticle systems. However, achieving precision can be challenging, and developers and manufacturers must carefully consider the optimal approach for their nanomedicine production. ▶



Flow manufacturing of nanomedicines

Conventional batch production often struggles to deliver the level of precision and reproducibility needed to maintain consistent nanoparticle quality at scale. Even small variations in process parameters, such as temperature or mixing dynamics, can alter key particle attributes, which in turn influence clinical performance.

Flow manufacturing offers an effective alternative. Rather than processing materials in separate steps, this method maintains a continuous flow of reactants through controlled environments, allowing nanoparticle formation to occur under steady-state conditions. The benefits of flow manufacturing are most evident in two key areas:

Scalability

Scalability remains one of the most significant hurdles in nanomedicine manufacturing. In traditional batch systems, scaling from laboratory synthesis to production quantities often requires complete process reoptimization because reaction kinetics, mixing efficiency and heat transfer behaviour change with reactor volume. This scale dependence increases development timelines and introduces variability across stages of production. Flow manufacturing minimises scalability issues, as once process parameters are optimised at a small scale, they can typically be translated directly to higher-throughput systems with only minor adjustments.

Output with flow manufacturing can also be increased by extending run time or operating multiple flow channels in parallel. This linear scalability enables developers to transition from gram-scale to kilogram-scale production without redefining critical process conditions.

Continuous flow systems also enable faster, more flexible scale transitions between early development and clinical manufacturing. As the same process parameters can be retained, formulation consistency is maintained across the product lifecycle. For nanomedicines, such predictable scalability provides a major advantage, ensuring adequate material supply for clinical phases without compromising quality or timelines.

Quality

Quality in nanomedicine manufacturing depends on achieving uniformity at the molecular and particulate level. Flow manufacturing strengthens quality assurance through continuous, tightly controlled operating conditions. Once steady-state operation is reached, process parameters such as flow rate, temperature and concentration remain constant, reducing variability and improving reproducibility across production runs.

The small internal dimensions of flow reactors create high surface-area-to-volume ratios, typically improving heat and mass transfer compared with batch reactors. This prevents local fluctuations in temperature or

> The impingement jet mixers operate by colliding liquid streams at high velocity to create intense turbulence, achieving efficient mixing at higher flow rates, a configuration well-suited to largerscale nanoparticle production.

concentration that can lead to uneven particle formation. As a result, nanoparticles exhibit narrower size distributions and consistent encapsulation efficiency, as well as stable physicochemical properties, all of which contribute directly to clinical performance and regulatory reliability.

Additionally, flow systems lend themselves to real-time process monitoring and control. Inline analytical tools can track parameters such as particle size or composition during production, allowing operators to adjust conditions immediately if deviations occur. This capability supports a quality-by-design (QbD) approach to nanomedicine manufacturing, one that ensures quality is built into the process rather than tested into the final product.

Selecting flow technologies for nanoparticle production

Realising the full potential of flow manufacturing in nanomedicine production depends on selecting the right system configuration for the specific nanomedicine being produced. While the principles of continuous processing remain consistent, the performance of a flow setup can vary greatly depending on the choice of pumps, mixing geometry and reactor design. Understanding how each component influences particle formation is, therefore, critical to achieving the desired product characteristics and maintaining flexibility as formulations evolve.

Flow systems, whether commercially available or custom-built, typically share three key functional elements:

Pumps

Precision pumps ensure a continuous, controlled flow of reactants. In nanomedicine production, this is typically achieved using either syringe pumps or high-pressure dosing pumps. Syringe pumps are favoured in early formulation work, where smaller volumes and high dosing precision are critical for screening process parameters. High-pressure dosing pumps, by contrast, enable higher throughput and stable operation over longer production runs, making them suitable for scale-up and GMP environments. Selecting between the two depends on the desired throughput and process stability.

- **Mixing configurations**

The mixing configuration determines how materials combine to form nanoparticles and directly affects particle size and ▶

uniformity. Commonly used designs in flow manufacturing include: microfluidic chips, T-junction mixers, impingement jet mixers and multi-inlet vortex mixer (MIVM). Microfluidic systems employ microscale channels that enable rapid, controlled mixing, making them ideal for fine-tuning formulations during early development. T-junction mixers are the simplest mixer units and provide scalable manufacturing. Impingement jet mixers and multi-inlet vortex mixers also provide scalability but offer improved mixing. The impingement jet mixers operate by colliding liquid streams at high velocity to create intense turbulence, achieving efficient mixing at higher flow rates, a configuration well-suited to larger-scale nanoparticle production.

A modular design

The overall flow architecture determines the system's flexibility and cost-efficiency. Commercial platforms often feature modular designs, allowing pumps and mixers to be interchanged as process needs evolve. encapsulation efficiency, as well as stable physicochemical properties nanomedicine that contains nanoscale components, typically between 1 and 100 nanometres in size. This adaptability supports iterative optimisation without major capital investment. As development progresses, custom-built flow systems can be tailored to specific formulation and throughput requirements, providing improved control, process robustness and long-term efficiency.

A clear understanding of how each component interacts is fundamental to process design. Early assessment of system architecture helps developers balance performance, flexibility and cost-effectiveness, ensuring that processes established during formulation can be efficiently scaled to clinical and commercial manufacturing. Partnering with experienced contract development and manufacturing organisations that understand flow technologies and system components can give developers a valuable edge, helping translate strong design principles into reliable, scalable nanomedicine production.

A case study: Evaluating a multi-inlet vortex mixer (MIVM) for nanoparticle production

Understanding the influence of flow system design on nanoparticle formation was central to a study carried out by Ardena using a multi-inlet vortex mixer (MIVM). This mixer combines multiple inlet streams within a confined chamber, generating rapid vortex mixing that promotes uniform contact between solvent and antisolvent phases. Ardena applied the system to produce a liposomal formulation comparable to a liposomal formulation of doxorubicin, assessing how total flow rate, solvent ratio and lipid concentration influenced particle characteristics.

Results showed clear relationships between process conditions and product quality. Increasing flow rate reduced particle size

until turbulent flow was reached, while higher antisolvent ratios and lower lipid concentrations produced smaller, more homogeneous liposomes. All test conditions yielded polydispersity index (PdI) values below 0.2, confirming consistent particle uniformity.

The study demonstrated how detailed knowledge of mixer geometry and flow behaviour supports informed component selection and process optimisation, key factors in achieving scalable, reproducible nanomedicine manufacturing.

Preparing for the future of nanomedicines

Looking to the future, the nanomedicine space can be expected to continue advancing rapidly, with increasingly complex formulations and expanding therapeutic applications. As innovation provide digital assistance, such as searching, analysing and accelerates, the challenge will be to translate these scientific advances into consistent, scalable products that meet both clinical and commercial expectations. Achieving this will rely on manufacturing approaches that combine precision, reproducibility and control.

Flow manufacturing provides a strong foundation for this next stage of development. By maintaining continuous control over critical parameters, flow systems deliver the consistency and flexibility needed to support the production of complex nanoparticle formulations while meeting evolving regulatory standards for quality and process understanding.

However, realising these advantages relies as much on expertise as on technology. Working with partners who combine practical experience in flow manufacturing with a deep understanding of system components enables processes to be designed and scaled with confidence and precision. As demand for nanomedicines grows, such collaboration will be key to delivering advanced therapies efficiently, reliably and at the scale needed to reach patients worldwide ■

References are available at www.pharmafocuseurope.com

AUTHOR BIO

Mark van Eldijk is the Business Unit Director of Nanomedicines at Ardena. He earned his PhD for his work on biopolymer-based nanoparticles and completed a postdoctoral fellowship at the California Institute of Technology. Mark joined Ardena in 2016 as a scientist and project leader before transitioning into business development for the company's nanomedicine services. Since January 2023, he has served as the Business Unit Director of Nanomedicines.

Agentic Ai

The Next Leap in Drug Discovery and Development

In a competitive landscape, many companies are responding by embracing advanced technologies that optimise efficiency and improve outcomes. Agentic AI is one such solution. This promising emerging technology harnesses the analytic capabilities of generative AI, but is also capable of acting autonomously on its recommendations. In this article, Raghuraman Sridharan, Practice Leader Life Sciences R&D EMEA at Cognizant, explores the potential of Agentic AI and how it can help overcome several challenges in pharmaceutical drug discovery and development.

Raghuraman Sridharan
Practice Leader for Life Sciences R&D, EMEA & APAC, Cognizant

Drug discovery, research and development is becoming more complex, with life sciences companies encountering a range of challenges. Traditional processes are already slow and inefficient, with 90% of drug development projects failing before reaching patients. Companies must also contend with a challenging regulatory landscape, supply chain and manufacturing delays, and rising research and development costs.

To respond to issues and developments proactively, companies need to be able

to make informed decisions to improve efficiency through effective use of data, not just from discovery, but from elsewhere in the development and manufacturing process. Used well, this information - production records and supply chain information - can inform research and development approaches and support efforts to streamline the path from discovery to clinical trial. However, many pharma companies are still unable to mine their data effectively, due to issues with poorly connected legacy systems and siloed data. This is making an already-challenging drug discovery and development process even more taxing.

In a competitive landscape, many companies are responding by embracing advanced technologies that optimise efficiency and improve outcomes. Agentic AI is one such solution. This promising emerging technology

harnesses the analytic capabilities of generative AI, but is also capable of acting autonomously on its recommendations.

The challenge of acting on data effectively

At every stage, the pharmaceutical R&D process generates valuable data. Companies must be able to capture all of this data - from all stages - on-demand, and use it to create meaningful insights and strategies.

If a company is unable to do this, it can disrupt its ability to make decisions that improve efficiency and can limit valuable insights in the discovery process.

Many companies are limiting their potential because they are working with disparate legacy systems, creating data siloes that are more difficult to access and analyse - particularly in conjunction with data from other parts of the product life cycle.

Furthermore, there is an industry-wide recognition that traditional workflows can no longer keep pace with today's challenges.

In many cases, operations still require human action to authorise a variety of routine tasks, which can create bottlenecks that can slow down or delay discovery and development projects.

Standard AI systems are adept at mining data for insights much more rapidly and effectively than human agents. However, these insights still require human approval and action, which can lead to delays.

Agentic AI is an intriguing development in AI technology addressing this problem. Unlike traditional AI, which examines data for human consideration, Agentic AI can both interpret and act autonomously on its recommendations. It leverages multiple agents to investigate complex situations, weigh potential outcomes, and make independent decisions based on its learned knowledge and programmed objectives. While having a human in the loop is still crucial, Agentic AI can provide a far greater level of assistance and unlock a range of possibilities.

> Agentic AI can identify promising drug candidates and optimise the structure of lead compounds to improve their pharmacological properties and reduce side effects

This promises a number of key benefits for life sciences companies, such as:

- **Accelerated drug discovery:** Agents can autonomously analyse vast datasets of biological information and explore how targets interact within complex biological pathways, even before in vivo or in vitro testing has occurred.
- **Optimised analytical development:** Agentic

AI can autonomously design and execute in silico experiments to test target viability, reducing the time required to identify and validate drug targets.

- **More effective formulation development:** Agentic AI can identify promising drug candidates and optimise the structure of lead compounds to improve their pharmacological properties and reduce side effects.
- **More efficient clinical research:** Agents can analyse preclinical data, identify safety concerns and optimise designs for in vivo studies, and assist in patient recruitment, data monitoring and event reporting.
- **Hyper-accelerate clinical trial setup and conduct**: Agentic AI can add a valuable experience layer on top of traditional processes and SaaS solutions. Agents can empower protocol authors by auto-generating protocol content, and significantly increase productivity for data managers by automating several tasks in trial setup, conduct and closure.
- **Empower R&D stakeholders with intelligence:** Agents can support strategic asset-level decision-making based on regulatory intelligence and provide insights that inform operational and commercial decision-making
- **Enable right-first-time submissions**: Agents can compare draft submissions content with previous submissions, health authority correspondence, and external regulatory intelligence, to select content that will best increase the probability of submission success
- **Increase speed to productivity for R&D stakeholders:** Agents can be personified to provide digital assistance, such as searching, analysing and providing contextual answers (like human SMEs) from multiple sources of information
- **Smoother transfer into clinical manufacturing**: Agents can review and analyse data in the discovery and research process to identify efficiencies that can accelerate the transfer of projects into clinical manufacturing.

Agentic AI can also assist with strategic decision-making, optimise regulatory submissions, and provide impact assessments when regulations or standards are updated.

Responsibly integrating Agentic AI

The benefits of this approach are compelling. However, life sciences companies need to consider a range of factors before implementing.

For example, it is vital to address issues with siloed data and disparate legacy systems, so that Agentic AI can access the data it needs. This includes harmonising information through actions such as the standardisation of datasets and using application programming interfaces (APIs) to connect different systems.

Companies must also clean, curate and validate data to maximise model accuracy and reliability, and conduct rigorous validation across diverse datasets to ensure that agents are robust.

Standardised metrics for tracking the performance of AI agents remain essential. Companies must ensure that there are ▶

effective security safeguards for sensitive data, and that strong regulatory frameworks establish clear lines of accountability when an error occurs. A degree of human oversight is also important for monitoring quality and spotting issues, such as algorithmic bias.

While surmountable, technical challenges such as these often fall beyond the internal expertise of life sciences organisations. This is where informed digital transformation partners can and should step in as partners to establish the right safeguards - and make sure that crucial questions are addressed and considered at the outset.

Agentic AI and the future of drug discovery and development

The integration of industrial AI agents into processes promises a wide range of benefits, particularly in the life sciences space.

Agentic AI can offer more proactive and predictive capabilities, which can help to deliver faster and more effective drug development. Companies will be able to develop more personalised treatments and explore new avenues for tackling previously intractable diseases. More efficient discovery and development will have significant cost implications, and agents will be able to optimise processes to better adhere to regulatory requirements.

When combined with other emerging technologies such as advanced robotics and quantum computing, the pace of discovery looks set to accelerate still further.

This technology will also be able to complement automated systems in fields such as smart manufacturing, with expert human workforces increasingly working seamlessly alongside AI agents.

For this future to be realised, forward-thinking life sciences companies must ensure that they consider the potential of innovations such as Agentic AI today. Perhaps more importantly, they need to work with the right people.

By collaborating with digital transformation experts with experience in Agentic AI, companies can ensure their systems are soundly designed, have the ability to scale, and can help them harness the full potential of this exciting shift. ■

AUTHOR BIO

Raghuraman Sridharan is a seasoned professional with over 20 years of experience in IT and life sciences. As the Practice Leader for Life Sciences R&D across EMEA and APAC at Cognizant, he leads large-scale transformations in the clinical, regulatory, quality, and safety domains. Raghuraman drives innovation through process optimisation and the adoption of next-generation technologies, including Agentic AI.

Driving Pharma Innovation with Augmented and Virtual Reality

Dr Humberto Vega

Chemical Engineer and former Global Head of Technology Transfers & Validation at JnJ and Executive Director of Global MS&T, Bristol Myers

Mr Brian Kesselmeyer

Digital transformation leader and former Associate Technical Director, Bristol Myers Squibb Squibb

As pharma manufacturing grows more complex, so does the need for effective communication, training, and troubleshooting. This article shares lessons learned and key requirements for implementing Augmented and Virtual Reality as validated, scalable solutions in regulated biopharma environments.

Augmented reality (AR) and Virtual Reality (VR) are two evolving digital tools with significant impact on the way communications, technology transfers, troubleshooting, and training activities are conducted. A third emerging tool involving AR and VR is Mixed Reality (MR), where we blend AR, VR, and the physical world to unlock the next generation of experiential learning, simulation, and collaboration.

The use of these tools requires proper alignment between the business needs and the intended use of the ▶

Device	Manufacturer
Navigator	Realware
Blade, Z100, M400, M4000	Vuzix
Magic Leap 2	Magic Leap
ThinkReality 3	Levono

Table 01

technology. AR and VR are not the same, each one has its unique benefits. Each tool has specific requirements and constraints that must be considered. We will discuss each tool and provide our guidance. Names of suppliers, available hardware, and applications will be provided as reference, but their mention does not represent an endorsement from the authors.

Augmented Reality (AR)

AR is focused on providing real-time access to information (e.g., documents, procedures, forms, videos) required to execute tasks using headsets containing both a monitor for the user to see the information and a camera for the system to capture the environment where the user is working. In addition, most applications include two-way communication involving either another headset or device (e.g., tablets, laptops, desktops, cell phones), allowing remote support by subject matter experts not available at the site/place where the user is located.

The following are examples of AR hardware available in the market. Names of suppliers, available hardware, and applications will be provided as reference but their mention does not represent an endorsement from the authors.

Virtual Reality (VR)

VR is mainly focused on providing a safe immersive digital environment where the user has a full interactive simulation of the work environment (e.g., GxP facility), training on real procedures, using virtualised versions of actual equipment and materials without consuming any resources or disrupting operations. This virtual space, presented to the users via headsets, provides the opportunity to master the required actions expected during the actual execution of procedures in real life. VR is also used to simulate and practice potential scenarios by the users without potential safety risks or wasting materials.

The following are examples of VR hardware available in the market. Names of suppliers, available hardware, and applications will be provided as reference, but their mention does not represent an endorsement from the authors.

Software and Applications for AR and VR

On the software front, we have evaluated both lightweight communication tools and fully

Device	Manufacturer
Meta Quest	Meta
Apple Vision Pro	Apple
Lenovo ThinkReality VRX	Lenovo
Pico Neo	Pico

Table 02

validated, GMP-ready platforms like Apprentice.io for AR applications. Meanwhile, for VR, where the headset is only a portal, the real value lies in what happens inside it. We have worked with multiple development partners, including Gronstedt Group, Tipping Point Media, and Resolve, each bringing specialised expertise in regulated training environments. You will find additional development partners across the industry.

Critical considerations for software and applications include:

- Licensing and delivery models (per user/device or pre-loaded)
- Regulatory readiness (CSV, audit trail, documentation)
- Internal vs. full-service development (do you have SMEs available)
- Change management support for adoption

With the right ecosystem, hardware, software, and content, AR and VR can become a cornerstone of your digital training strategy.

GxP Environments – Expectations and Requirements

Procedures: The implementation of AR in GxP-regulated applications provides the option of augmenting procedures with videos and overlaying graphics to guide the user while executing a task. The videos will allow reviewing the proper execution of an activity prior to its actual execution, besides the written instructions. The use of overlaying graphics provides sequential instructions and highlights of specific details to ensure satisfactory

completion of the tasks. Also, the AR application may facilitate the documentation of activities by means of pictures and voice commands.

This type of application requires approval and qualification of the augmented procedure versus the approved process description or method. Controlled access to the augmented procedure is a basic requirement to avoid unauthorised changes. Any change must follow the change control systems/procedures of the organisation.

The use of VR provides users with the experience of executing a task or procedure in a simulated environment. This allows either to develop experience or refresh the skills on such procedure ahead of the actual real-life execution of the tasks.

Training: AR makes possible the training of personnel via remote real-time presentations. The subject matter expert (SME) can do a show & tell of a procedure while the trainees observe at their work stations located at ▶

different rooms, facilities, and sites. The two-way communication capability of AR hardware allows the trainees to ask questions and receive feedback from the SME as the training is progressing. Also, a trainee will have real time feedback while using augmented procedures when the overlayed images detect a potential issue or error while executing a training task.

VR-designed training modules are intended to reinforce muscle memory, as the learner/ trainee will practice the tasks as many times as needed until mastering the execution. It is critical to design VR modules considering instructional design factors to take full advantage of VR: (a) Clear training goal and skill development (e.g., why and how tasks are executed); (b) Understanding of consequences of failing to execute the tasks as designed (e.g., impact of product quality); (c) Recognition of successful execution of the tasks (e.g., Pass/Fail). The use of VR results in a reduced variability between trainers and offers consistent, audit-ready experiences across global teams.

VR adapts to each learner. A senior technician could fast-forward through basics, while a new graduate could safely explore concepts in depth. That's the power of immersive, patient, and repeatable learning in biopharma.

Deviations and Problem Solving: AR and VR tools can be used for the resolution of deviations and facilitate problem-solving activities. AR headsets (e.g., used as two-way communication devices) are used to "bring" SMEs to witness activities on the shopfloor. The presence of remote SME reduces the need for travelling and expedites troubleshooting activities. Meanwhile, VR applications can be used to simulate errors and assess the potential result of such mistakes.

In any case, AR or VR, the outcome of the activities must be properly documented once the witnessing or simulation is completed.

AR and VR Implementation in GxP Environments

Data integrity and privacy: The use of digital tools requires data collection (e.g., process parameters, pictures, video, time, date, etc.) AR and VR are no exceptions to this fact. The implementation of AR and VR must satisfy the regulatory expectations of data integrity (e.g., ALCOA+) as well as privacy laws (e.g., personal data).

Information Technology Requirements and Challenges: AR and VR implementation in pharma must prioritise fit-for-purpose design. During the selection process, you should evaluate the headsets under consideration for the following factors:

- **Durability** in caustic GMP environments (AR) or training lab handling and use (VR)
- **Form factor,** does it obscure vision or integrate seamlessly with the work environment in the case of AR
- **Connectivity** (WiFi, USB, Bluetooth) – Both AR and VR
- **OS compatibility** (Android, Windows, iOS)

> With the right ecosystem, hardware, software, and content, AR and VR can become a cornerstone of your digital training strategy

- **Total cost of ownership** (inclusive of price of software, hardware, and potential ongoing subscription fees)
- **Device managemen**t to ensure version control, remote troubleshooting, and application governance, all essential for compliance. Scaling beyond a USB cord means investing in enterprise-grade platforms (e.g., Meta Horizon, Microsoft Intune, and ArborXR.) These allow for secure remote updates, usage monitoring, and compliance across sites and geographies.
- **Hardware Evaluation** to assess equipment strengths, from image clarity and passthrough to durability and battery life. The right choice depends on your use case: manufacturing floor vs. training lab, clarity vs. cleanability.

Implementation Strategies: Augmented Reality and Virtual Reality in a GMP environment must be backed by the organisation. An example of the strategy to implement AR and VR using a **three-tiered model** focused on impact and adoption follows:

- **Tier 1: Communication**

Clear communication of the benefits of the technology. In the case of AR headsets, they are used for real-time collaboration, enabling GEMBA walks, audits, tech transfers, training sessions, and virtual tours. These low-risks, high-reward use cases help ease teams into the technology with immediate benefits.

- **Tier 2: Immersive Training**

The design of interactive training modules is directly linked to SOPs, replacing paper screenshots with contextual, audiovisual guidance and augmented documentation. The results are faster learning, better retention, and greater confidence on the floor. In the case of VR, the advantage of developing muscle memory ahead of final qualification of the trainees in critical activities (e.g., Aseptic manipulations, use of welders and sealers, aseptic gowning) is a training accelerator.

- **Tier 3: Smart Integration**

The potential use of AR in MES platforms (e.g., SAP, ORACLE), enabling just in time, and hands-free support during live batch execution. This approach transformed SOPs from static documents to dynamic, real-time performance tools.

Lesson Learned

Implementing new technology is a journey, it requires both a clear starting point and a well-defined problem statement. Waiting for a “perfect” solution will leave you stuck in ▶

a potential paralysis by analysis while your competitors move forward. Instead, define the challenge you are trying to solve and use that to establish your baseline requirements for hardware and software. Know what "good enough" looks like to get started.

In large organisations, visibility and alignment are critical. You will need to secure endorsement, raise capital, and momentum. That means early and proactive engagement with key stakeholders — IT, Compliance, and beyond. Leaving these teams out until implementation is a guaranteed roadblock.

Equally important: validation. Especially in regulated environments like biopharma, AR/VR tools need to be treated like any other system, tested, documented, and risk-assessed. Build trust by starting small, demonstrating value, and scaling based on real outcomes.

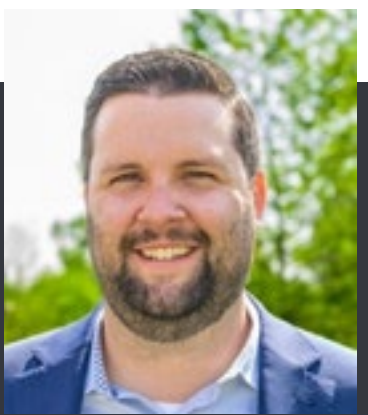
Finally, do not underestimate change management. The tech is only as good as the people using it. Train thoughtfully, gather feedback, and design for adoption, not just deployment.

Final Remarks

AR and VR are no longer future-facing luxuries, they are current-state tools proactive engagement that improve compliance, consistency, and efficiency in biopharmaceutical operations.

These technologies help use of welders and accelerate onboarding, improve right-first-time execution, and ultimately, get therapies to patients faster and more reliably. ■

AUTHOR BIO



Brian Kesselmeyer is a digital transformation leader and former Associate Technical Director at Bristol Myers Squibb, with extensive experience in cell therapy platforms including Abecma® and Breyanzi®. He is a certified LSS Black Belt, serves on advisory boards in the emerging technology space, and currently leads strategy development at an AI and visualization startup.

AUTHOR BIO

Dr. Humberto Vega is a retired Chemical Engineer and former Global Head of Technology Transfers & Validation at Johnson & Johnson, as well as Executive Director of Global MS&T at Bristol Myers Squibb. He has more than 37 years of experience in the pharmaceutical and food industries. Dr. Vega holds professional memberships in PDA, IFT, and ISPE.

Embedding Intelligence

How AI and Vector Databases Are Transforming Pharmaceutical Marketing

Artificial intelligence is reshaping pharmaceutical marketing by embedding company knowledge into vector databases, enabling content generation and real-time customer engagement. These systems store both semantic representations and original text, allowing AI to extract meaning and respond contextually. This article explores how secure, structured data enables scalable, intelligent marketing in life sciences.

Jon Reed
Head of Strategic Business Planning, Recipharm

Pharmaceutical marketing is undergoing a significant shift. Rather than relying solely on static brochures, presentations or agency-driven campaigns, companies are increasingly embracing artificial intelligence (AI) to deliver tailored content and enhance responsiveness. Central to this change is a modern data architecture built on vector databases, which capture not only company knowledge but also how it can be interpreted by AI systems.

By embedding organisational capabilities into a secure, searchable knowledge base, life sciences companies can leverage large ▶

language models (LLMs) to draft white papers, technical documents, presentations and thought leadership content. These systems can also respond to customer questions on topics such as sustainability or manufacturing capacity. This article examines how AI, vector databases and structured embeddings work together to support scalable, intelligent pharmaceutical marketing, while maintaining essential human oversight.

Why Structured Data Matters in AI-Driven Marketing

Much of the knowledge that underpins pharmaceutical marketing is unstructured: PowerPoint decks, PDF brochures, regulatory documents, and internal emails. While these may serve human readers, they are not easily digestible by machines. In order for AI to be genuinely useful in marketing, this information must be transformed into a format that both captures its meaning and allows for intelligent retrieval.

This is where semantic embedding comes into play. Embeddings are numerical representations of text that capture its meaning and context. For instance, the sentence "Our Masate site specialises in sterile manufacturing using lyophilisation technology" can be transformed into a vector—a long string of numbers—that reflects its semantic content. Sentences with similar meanings will have vectors that are mathematically close to each other, even if the wording differs.

By embedding company materials in this way, an AI tool can later be prompted with a question like:

"Which European site has lyophilisation capability for sterile products?"

Rather than scanning every document word for word, the system uses vector similarity to instantly retrieve the most relevant information.

The Role of Vector Databases

A vector database is a specialised type of data store designed to support this AI functionality. Unlike traditional databases that store information in rows and columns, vector databases are optimised to store:

1. Embeddings – the numerical vectors representing the semantic meaning of each piece of text
2. Original content – the actual text (e.g. paragraph, slide, section) from which the embedding was derived

Each record in the database, therefore, contains both the machine-readable form of knowledge and its original, human-readable version. When a question is asked, the AI searches the vector space for embeddings that are closest to the query. Once these are found, the corresponding original text is retrieved and used to construct a response.

This dual structure is what enables natural language interfaces, such as a chatbot or content generator, to "understand" the underlying business and generate answers that are specific, accurate, and contextually aware.

From Embedded Knowledge to AI-Generated Content

Once a pharmaceutical organisation has embedded its materials and stored them securely in a vector database, a wide range of applications becomes possible. These include:

- **Drafting white papers and blogs**

A marketing manager can prompt the AI:

"Write a 750-word blog about our sustainability initiatives, with a focus on our Sweden and Italy sites."

The AI searches the vector database for relevant content, retrieves it, and drafts a coherent, brand-aligned article.

- **Answering customer queries**

A business development executive can ask:

"Do we have capacity for sterile biologics production in Q4?"

The AI retrieves recent site updates, capacity data (if integrated), and provides a fast, informed response.

- **Creating marketing collateral**

The system can be used to quickly generate capability overviews, FAQs, or slides tailored to specific customer types or therapeutic areas.

Importantly, all of this is done without starting from a blank page. The AI is not guessing or hallucinating, it is drawing from embedded, pre-approved knowledge stored securely in the database.

Ensuring Security and Data Governance

Embedding content into a vector database creates new opportunities, but also new responsibilities. Two types of data are being handled:

> AI is not just a future consideration for pharmaceutical marketing, it is already transforming the way companies communicate, respond, and grow.

1.**Original content**, which may include confidential or commercially sensitive material

2.**Embeddings,** which are abstract representations but can still reveal insights about company priorities or operations

Therefore, companies must treat both forms of data with equal care. Secure data storage, encryption, and strict access controls are essential. Furthermore, a robust data governance framework should be in place to ensure:

- **Regular content updates**

Embedded databases must be refreshed as capabilities evolve, sites are upgraded, or new regulatory approvals are gained.

- **Content approval protocols**

Only verified and approved materials should be embedded. Drafts or speculative content should not be included unless clearly marked.

- **Internal review workflows**

All AI-generated content should go through ▶

human review before publication to ensure scientific accuracy and compliance.

AI is not a replacement for quality control, it is a tool to enhance efficiency, reduce repetitive work, and ensure consistent messaging.

Sustainability Messaging: A Practical Example

Many pharmaceutical companies have committed to ambitious environmental, social, and governance (ESG) targets. However, communicating these to customers can be difficult, especially when sales teams are not fully up to date on each site's sustainability status.

By embedding ESG reports, carbon footprint audits, and presentation summaries into the vector database, the AI system can be prompted to:

- **Summarise emissions reduction initiatives**
- **Answer questions about packaging recyclability**
- **Draft RFP responses related to Scope 1, 2, or 3 emissions**

Because the AI is drawing from real, company-specific data, the messaging is consistent across teams and geographies. This ensures that sustainability claims are backed by evidence and remain aligned with the company's wider commitments.

Capacity and Capability Insights

Another high-impact use case is customer engagement around manufacturing capacity and technical capabilities. Procurement teams often ask:

- What are your batch size ranges?
- Can you handle OEB4 classified compounds?
- Which sites support pre-filled syringes?

Rather than relying on manually curated PDFs or Excel trackers, the AI system can instantly extract this information from the embedded content and provide a structured, accurate response. If integrated with live systems or regularly updated summaries, it can also reflect changes in spare capacity or operational availability.

This significantly accelerates the pre-sales process and ensures that prospects receive timely, credible information.

Empowering Internal Teams

One of the lesser-discussed advantages of AI in marketing is its ability to support internal teams. Technical staff, salespeople, and even new hires often struggle to locate the most up-to-date, accurate information about their own organisation.

A conversational AI tool, powered by a vector database, allows internal users to ask:

- "What is our high-potency handling capability in France?"
- "What types of formulation do we support in India?"
- "What ESG targets have we set for 2030?"

This removes bottlenecks caused by reliance on a small number of internal experts and encourages knowledge sharing across departments.

AI Plus Human: A Hybrid Model

While AI can automate many aspects of content creation and customer engagement, it must not operate in isolation. In pharmaceutical marketing, where regulatory constraints, scientific precision, and brand reputation are critical, human oversight is essential.

The most effective approach is a hybrid model:

1. **AI drafts the content** using embedded data
2. **Experts review and finesse** for accuracy, tone, and compliance
3. **Final outputs are approved** for publication or sharing with customers

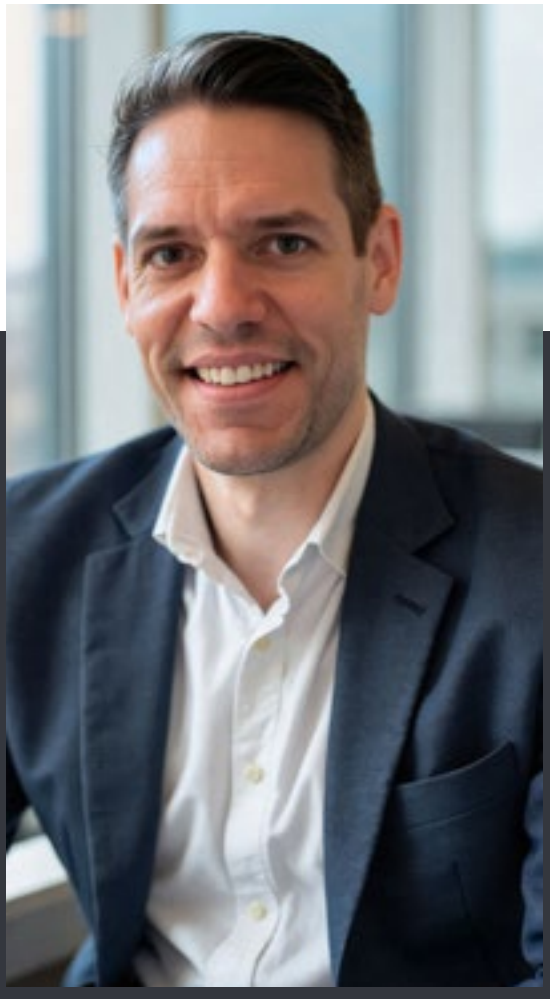
This workflow not only ensures quality but also frees up human talent to focus on high-impact strategic work, rather than repetitive drafting or data retrieval.

Conclusion

AI is not just a future consideration for pharmaceutical marketing, it is already transforming the way companies communicate, respond, and grow. By embedding company knowledge into a secure vector database and using AI tools to retrieve and generate content, marketing becomes faster, smarter, and more consistent.

Crucially, success depends on more than just the AI model itself. It requires a structured, governed data foundation that stores both semantic embeddings and original content. With this in place, companies can use AI not as a novelty, but as a dependable extension of their marketing and business development teams.

When done responsibly, AI becomes a force multiplier: streamlining workflows, enriching engagement, and strengthening the voice of the organisation in an increasingly competitive pharmaceutical landscape.



AUTHOR BIO

Jon Reed is a strategic leader at Recipharm, driving innovation in pharmaceutical manufacturing and analytics. With an MBA and extensive experience in commercial excellence, he leverages emerging technologies to streamline processes and enhance performance. Passionate about the role of AI in marketing, Jon champions data-driven decision-making and scalable growth.

IndustrySense

Nanoparticle-Based Drug Delivery Systems in CDMO R&D Programs

I'm Maryam Daneshpour, PhD, MBA, a Biotech and Pharma Market Researcher, and I'm pleased to be the moderator for today's discussion on the Topic Nanoparticle-Based Drug Delivery Systems in CDMO R&D.

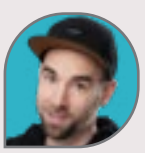
Nanoparticle-based drug delivery systems are redefining how therapeutics are formulated, protected, and delivered, from nucleic acid medicines to complex biologics. As drug modalities diversify, demand for precise, scalable, and reproducible delivery technologies has surged, placing Contract Development and Manufacturing Organisations (CDMOs) at the center of innovation and translation between discovery and commercial manufacturing.

To explore this rapidly evolving landscape, we're joined by two experts work spans formulation science, manufacturing strategy, and technology innovation.

Moderator:

Maryam Daneshpour, PhD, MBA
Biotech & Pharma Market Researcher

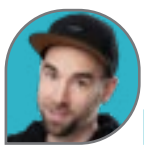
Panelists:



Philipp Beck, PhD
Formulation Development Manager at Ascend Advanced Therapies

Martin Rabel, PhD
Global Sales Specialist - Biopharma Services

1. Nanoparticle-based drug delivery has become central to biopharma innovation. In your view, what makes nanoparticles uniquely valuable for therapeutic delivery compared to other platforms?



Philipp:

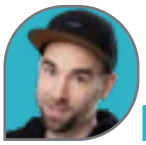
Nanoparticles bridge chemistry and biology. They encapsulate fragile or poorly soluble molecules, enable controlled release, and fine-tune biodistribution

through their composition and size. They also form a foundation for entirely new modalities such as mRNA–LNP vaccines while improving established therapies, as seen with liposomal doxorubicin compared to conventional formulations.

Martin:

Nanoparticles stand out for their ability to protect and precisely deliver fragile or insoluble therapeutics like RNA or hydrophobic molecules. They enhance potency by enabling targeted delivery to specific tissues, minimising side effects. Being fully synthetic, they're reproducible and scalable, offering biological precision with chemical control, making them invaluable for modern therapeutics.

2. What are the biggest scientific bottlenecks today in non-viral nanoparticle systems like LNPs and liposomes, and how do they compare to the challenges faced in viral delivery systems such as AAVs or lentiviruses?



Philipp:

The main bottleneck is our limited understanding of where systemic delivery truly leads us. Ethical library screening in NHPs that are euthanised for unrelated reasons, as done by James Dahlman's group, and Jude Samulski's detailed mapping after intravenous AAV dosing, both help reveal biodistribution, but true human predictability remains elusive.

Martin:

Great question! The main hurdles for non-viral systems are biological targeting and technological/manufacturing challenges. LNPs excel in RNA delivery but struggle beyond the liver. We're exploring ligand-based targeting and computational tools for smarter design. Manufacturing still needs tailored equipment and flexible workflows, especially for personalised therapies. Both viral and non-viral systems share challenges; precision and scalability remain key.

3. Philipp, you've done mRNA-LNP and AAV. What are the most non-obvious formulation differences teams only discover at scale?

Philipp:

LNPs scale more predictably, while AAV production depends on the variability of cell lines. For both, freezing large bulk volumes can become a major challenge that's hard to address early. In-use studies often reveal that formulation adjustments are needed only shortly before critical milestones such as toxicology studies.

4. Stability and shelf-life remain recurring challenges for nanoparticle formulations. Which strategies show the most promise in overcoming them? ▶

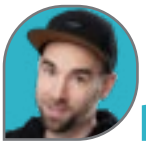
Philipp:

Many stability challenges can be mitigated by storing at –20 °C after an intentional –60 °C freezing step to ensure complete solidification. The common practice of long-term –60 °C storage often persists more from dogma than data. Combining smart freezing protocols with tailored buffers and surfactants remains the most effective approach.

Martin:

Stability is indeed a critical factor for the success of LNP formulations, especially when delivering RNA-based therapeutics. Interestingly, the core stability of the LNPs themselves is quite robust, the real challenge lies in the stability of the RNA payload. RNA-LNP stability largely depends on the RNA, not the particles. Lyophilisation helps extend shelf-life, though rehydration must preserve integrity. Advances in lipid design reduce degradation, while circular and chemically modified RNAs improve durability. Together, formulation science, nanoparticle engineering, and RNA chemistry are making RNA-LNPs more stable and accessible for global therapeutic use.

5. How do you see the role of CDMOs in advancing the adoption and scaling of nanoparticle delivery systems across the industry?



Philipp:

CDMOs sit at the intersection of creativity and reproducibility. They translate exploratory formulations into robust, manufacturable processes and preserve know-how across programs. Their value lies less in capacity than in continuity, where knowledge and data are converted into wisdom, the real asset if turnover rates remain low.

Martin:

CDMOs enable the scalability and accessibility of LNP manufacturing, especially for smaller biotech firms lacking infrastructure. They provide flexible capacity, regulatory guidance, and technical expertise from early development to commercial production. As nanoparticle manufacturing remains unstandardized, CDMOs are evolving from service providers into innovation partners, advancing new processes, materials, and quality frameworks for emerging modalities.

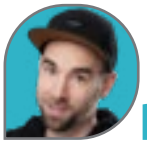
6. Martin, what is the most underestimated challenge biotech companies face when approaching CDMOs for RNA-LNP projects?

Martin:

A major challenge is translating lab-scale LNP formulations into GMP manufacturing. Some designs that perform well preclinically can't scale efficiently. Early de-risking with scalable

formulations saves time and cost. Another pitfall is underestimating material needs for testing and stability studies, especially in RNA-LNP projects. Open dialogue with the CDMO helps align technical, regulatory, and production strategies early.

7. How well are regulatory frameworks (FDA, EMA) keeping pace with the complexity of these advanced drug delivery systems? Where are the biggest gaps?



Philipp:

Regulation still trails complexity. Fyodor Urnov highlighted this when discussing the CRISPR–LNP therapy for baby KJ. Each guide RNA is still treated as a new product, which slows innovation. His proposal for platform-based regulation, focusing on shared delivery behaviour instead of sequence-level changes, captures what the field urgently needs.

Martin:

Regulators have made strong progress adapting to RNA-LNP technologies, accelerated by the pandemic. Yet definitions for key components like ionizable lipids remain unclear, and current testing frameworks often don't fit personalised therapies. Collaboration is improving, but clearer classifications and scalable release models are needed. Early engagement with agencies helps developers navigate this evolving landscape.

8. Comparability between preclinical formulations and clinical-grade material is always a challenge. How do CDMOs build confidence in these transitions?

Philipp:

Confidence comes from analytical continuity and transparent data flow across development stages. CDMOs should share their experience more actively through white papers, conference posters, and short videos. The topic may be dry, but creative communication is essential to anchor comparability thinking early in every developer's process.

Martin:

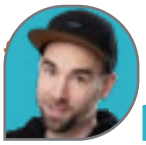
Transitioning from preclinical to GMP manufacturing often disrupts comparability. Early-stage mixing methods like microfluidics don't always scale well. Starting with scalable processes, including representative TFF systems, reduces surprises later. CDMOs build confidence by engaging early, aligning on technology choices, and leveraging experience across programs, turning scale-up from a risk into a collaborative advantage.

9. Martin, do you see the CDMO landscape moving toward specialisation (niche nanoparticle expertise) or consolidation (large players covering everything end-to-end)? ▶

Martin:

I believe we're seeing both dynamics play out, but at different stages of the innovative lifecycle. Early development needs specialised partners with deep nanoparticle expertise, while late-stage programs benefit from large-scale infrastructure and global reach. The most effective model combines both, a hybrid partnership where focused CDMOs innovate early and collaborate with larger organisations to ensure seamless progression from concept to market.

10. How do you see AI and machine learning influencing nanoparticle formulation and process optimisation in the near future?



Philipp:

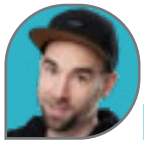
AI currently helps us work more efficiently, but true effectiveness still depends on human communication and interpretation. For formulation and process optimisation, it remains mostly smoke for now. The real challenge lies in understanding biodistribution and biological variability, which no model can yet capture or meaningfully predict.

Martin:

That's a fascinating and timely question, and also a complex one, because the AI space is evolving even faster than the nanoparticle field itself. AI's real value lies in decoding complex, data-heavy systems. It helps identify patterns in LNP screening and predicts structure–activity lipid components. Beyond science, it streamlines operations by automating analysis and reporting. The future isn't AI replacing scientists but enhancing their decisions, merging data-driven insight with human faster progress.

> The hype around systemic nanoparticle delivery has faded as unpredictable biodistribution persists, making local delivery the most reliable path where control consistently beats theory.

11. Philipp, you've been in the field since 2015. How has the "hype vs. reality" balance shifted in nanoparticle drug delivery?

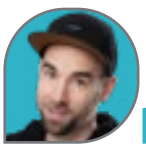


Philipp:

The hype has faded, and our understanding of biodistribution remains limited. After years

of chasing systemic delivery, one clear winner has emerged across nanoparticle platforms: local delivery. It offers control, predictability, and efficacy where systemic approaches still rely too much on luck and incomplete biological insight.

12. Finally, what's the next translational breakthrough most likely to change trial success rates for advanced drug delivery systems, whether nanoparticle-based or viral?



Philipp:

Real progress will come from technologies that reveal in vivo biodistribution with single-cell precision. Understanding where particles actually go, rather than assuming, will reshape formulation design and dosing. Better analytical access to living systems, not new chemistries, will likely drive the next major jump in clinical success.

Martin:

There are many exciting developments on the horizon, but if I had to choose one, I'd say the next breakthrough will come from precise, personalised delivery. Reaching the right cells with minimal toxicity could transform success rates and patient outcomes. Combining targeted nanoparticles or hybrid vectors with individualised therapies, RNA, DNA, or cells, brings true precision medicine closer. Achieving this will hinge on better targeting ligands, computational tools, and adaptable manufacturing.

Thank you, Philipp and Martin, for sharing your expert insights on the evolving landscape of nanoparticle and drug delivery. Your perspectives on formulation challenges, scale-up, regulation, and the role of CDMOs provided valuable insight into where the industry stands today and where it's headed.

AUTHOR BIO

Philipp has 10 years of experience in nanoparticle delivery. Trained in medicinal chemistry, moved from small molecules & protein crystals to nanoparticles: started in 2015 with mRNA/LNP, moved to AAV in 2020. From crystals to capsids, always the nanoparticle nerd at heart.

Martin leads Cytiva's BioPharma Services in EMEA, specialising in RNA-LNP technologies and CDMO solutions. With a background in Pharmacy and Nanomedicine, he supports nucleic acid therapy development and drives innovation in nanoparticle manufacturing, delivering scientific and commercial excellence across the biopharma landscape.

CoverStory

Process Validation in Bioprocessing

Process Validation spans Process Design, Qualification, and Continued Verification to ensure consistent product quality throughout the lifecycle. This paper reviews regulatory expectations, control strategies, and monitoring tools, emphasising that validation is a continuous, data-driven process, not a one-time event, essential for maintaining compliance, detecting variability, and ensuring patient safety.

Dr Humberto Vega

Chemical Engineer and former Global Head of Technology Transfers & Validation at JnJ and Executive Director of Global MS&T, Bristol Myers Squibb

Bassem Gayed

Former Senior Director Cell Therapy Technical Operation, Bristol Myers Squibb

Our Experience on Process Validation

Dr. Gayed and I had the experience of successfully transferring and validating drug products to commercial manufacturing facilities throughout our professional careers in biopharma. We have had the opportunity to shape the strategies leading to successful approval of the drug products. In this Expert Talk we provide the readers with a response to a few key questions commonly asked involving Process Validation as a continuous, data-driven process —not a one-time event—essential for maintaining compliance, detecting variability, and ensuring patient safety.

1.What is Process Validation?

Humberto: Process validation (PV) is a combination of activities resulting in a comprehensive consolidation of data supporting the design of the product and its manufacturing process, qualification of the manufacturing process, and continued monitoring of the manufacturing activities during the life of the product. In the past, PV was mainly used to highlight the execution of a validation protocol around the process. Later, the definition and scope of the term PV were expanded to capture three key stages that are now adopted across regulatory organisations and the industry:

Stage 1: Process Design, where process requirements, analytical methods, quality attributes, and process parameters are defined, leading to a comprehensive control strategy;

Stage 2: Process Qualification, where documented evidence that the process delivers product consistently meeting specifications via the process performance qualification (PPQ);

Stage 3: Continued Process Verification, where the validated process is closely monitored (e.g., CPV, APRs, lifecycle documents) to ensure no drifts or shifts affecting the quality of the product.

2.What are the key requirements to initiate PPQ activities?

Bassem: The initiation of PPQ requires the following: (1) Comprehensive validation master plan (e.g., contamination controls, cleaning, sterilization, filters, equipment qualifications, aseptic process simulations); (2) Complete knowledge transfer including process description and control strategy; (3) Approved procedures and batch records; (4) Approved and validated analytical methods; (5) Functional and qualified facility and equipment; (6) Fully trained and qualified personnel across all the functional groups (e.g., OPS, QA, Facilities, Technology); (7) Fully qualified suppliers and materials; (8) Functional quality management systems (e.g., deviations, change controls, LIMS); (9) Comprehensive risk assessments and validation protocols (e.g., defining number of lots, sampling plan, data analysis, management of deviations, acceptance criteria).

3.Are there differences between definitions of PV across Health Authorities (e.g., FDA and EU)?

Humberto: The basic concept of PV is similar across health authorities. Nevertheless, some specific terms may vary but the scope of the definitions are similar. For example, FDA defines PV as "the collection and evaluation of data, from the process design stage through commercial production, which establishes scientific evidence that a process is capable of consistently delivering quality products" while the EU GMP Annex 15 defines PV as "documented evidence that the process, operated within established parameters, can perform effectively and reproducibly to produce a medical product meeting its predetermined specifications and quality attributes". Additional terms that are used per PV stage include:

Stage 1: Process Design: Process Design vs. Pharmaceutical Development

Stage 2: Performance Qualification: Process Performance Qualification vs. Process Validation

Stage 3: Lifecycle: Continued Process Verification vs. On-going Process Verification

4.Can you use retrospective process validation?

Humberto: No. Retrospective validation is not an acceptable validation approach. The preferred approach is prospective validation (e.g., approved protocol defining validation expectations and acceptance criteria) followed by a full execution of validation studies or runs. A second option is concurrent validation, where a prospective validation protocol is in place, but validation runs are released ▶

to market as they are completed. The risk associated with concurrent validation must be evaluated and properly mitigated. A third option is a hybrid validation where the two approaches mentioned above can be used. A fourth validation element is the continuous process validation, where close monitoring of process and product performance is conducted to ensure the process remains under control after the regular PV runs.

5.How is the control strategy used during PV?

Humberto: The control strategy is the consolidation of the process and product knowledge defined during Stage 1 – Process Development. The CS defines the link between critical materials, process parameters, quality attributes, processing times, and hold times. This document is used to design the procedures and batch records as well as acceptance criteria for critical process parameters and critical quality attributes.

6.Who is required for review, approval and execution of PV activities?

Bassem: The responsibility of Process Validation is not department-specific. It is a cross-functional activity where different groups contribute to the successful execution of the validation runs: (1) Manufacturing Science & Technology: Owns the technical knowledge of process and product, and guides how the process shall be executed according to the control strategy. The group also develop and implements the PV protocol; (2) Manufacturing Operations: Owns the procedures and batch records that define the production steps required for the process. Also, ensure the personnel are properly trained and qualified to execute the manufacturing operations; (3) Engineering & Facilities: Own the physical facility and equipment. Ensure the equipment and utilities are properly installed and qualified according to the process requirements; (4) Quality Assurance: Own the quality management systems utilised to demonstrate compliance with regulatory expectations; (5) Quality Control: Own the analytical methods and QC testing activities required to confirm satisfactory execution of the manufacturing process. All these groups are responsible for reviewing, approving and executing specific activities, as described above, linked to PV.

> Process Validation is no longer a one-time compliance task it is a continuous, data-driven commitment to quality.

7.How are product and process variabilities incorporated into the PV studies?

Bassem: Incorporating variability into Process Validation is essential to building a robust understanding of how a process performs under real-world conditions. Product and process variability can originate from multiple sources—such as raw material attributes, operator technique, equipment performance, and environmental conditions. Rather than attempting to eliminate all variability, the goal of PV is to understand, quantify, and control it.

This begins in Stage 1 with risk assessments using tools like Failure Modes and Effects Analysis (FMEA), cause-and-effect (Ishikawa) diagrams, and multivariate data analysis to identify critical material attributes (CMAs), critical process parameters (CPPs), and critical quality attributes (CQAs). These assessments inform control strategies and determine which factors need enhanced monitoring.

During Process Performance Qualification (Stage 2), variability is addressed through appropriately designed sampling plans and the execution of multiple validation runs under normal operating conditions. Statistical tools such as Design of Experiments (DoE) and capability analysis may be applied to explore the range of acceptable variability, assess robustness, and establish process control limits.

Stage 3, Continued Process Verification (CPV), ensures that variability continues to be monitored across the product lifecycle using tools like control charts, process capability indices (Cp/Cpk), and trending dashboards. These tools help detect subtle process shifts early, enabling preventive actions to be taken before deviations occur.

By systematically incorporating and managing variability, manufacturers can ensure their processes are both capable and reliable—ultimately protecting product quality and patient safety.

8.How do you define the number of lots required for PV and the number of samples for the studies?

Bassem: Defining the number of lots and sampling plans for Process Validation is a risk-based decision guided by scientific rationale, regulatory expectations, and product complexity. Regulatory bodies such as the FDA typically expect a minimum of three consecutive commercial-scale PPQ batches produced under normal operating conditions to demonstrate process consistency and control.

However, the "three-lot rule" is not a regulatory requirement, and exceptions may be justified. For example, in cases where robust platform knowledge exists, a smaller number of lots may suffice if accompanied by strong supporting data. Conversely, for complex biologics—especially autologous or personalized therapies—additional lots may be needed due to inherent process variability and small batch sizes.

Sample size and sampling points are determined by factors such as:

- Process risk assessments, identifying critical steps
- Batch size and unit operation complexity
- Variability of the process and analytical methods
- Acceptance criteria for CPPs and CQAs
- Regulatory guidance and industry best practices

Ultimately, the number of PPQ runs and the extent of sampling must be scientifically ▶

justified, documented in the validation protocol, and agreed upon by all cross-functional stakeholders, including QA, MS&T, and regulatory affairs.

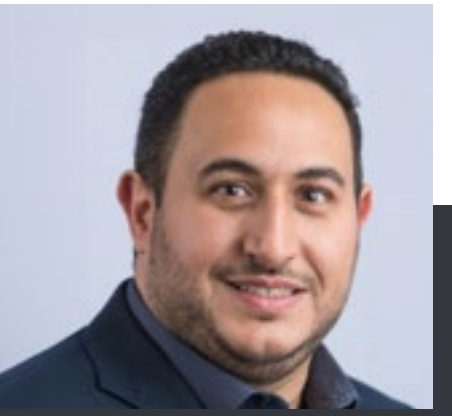
Final Remarks

Humberto & Bassem: Process Validation is no longer a one-time compliance task, it is a continuous, data-driven commitment to quality. As the pharmaceutical and biopharmaceutical industries evolve, driven by novel modalities and patient-centric therapies, PV must also evolve to keep pace.

Validation should be viewed not just as a regulatory requirement, but as a strategic tool to enhance operational excellence, build institutional knowledge, and reduce time to market. A well-executed PV program reduces the likelihood of batch failures, recalls, and costly remediation efforts. It also enables manufacturers to respond with agility to changes in scale, site, or supply chain, critical factors in today's globalised and dynamic environment.

The future of PV lies in its integration with digital technologies, real-time monitoring, and advanced analytics. This evolution enables a shift from reactive compliance to proactive assurance of quality, where variability is not feared but understood and managed.

By embracing PV as a lifecycle discipline, founded on science, rooted in cross-functional collaboration, and powered by data, we build the foundation for delivering safe, effective, and high-quality therapies to patients around the world. ■



AUTHOR BIO

Dr. Bassem Gayed is a senior leader in the biopharma industry with deep expertise in cell therapy, advanced manufacturing, and regulatory engagement. Dr. Gayed bridges science and execution across the product lifecycle to make therapies more accessible and efficient. He holds a B.S. and PhD in Biomedical Engineering from UMDNJ/NJIT.

AUTHOR BIO

Dr. Humberto Vega is a retired Chemical Engineer and former Global Head of Technology Transfers & Validation at Johnson & Johnson (JnJ), as well as Executive Director of Global MS&T at Bristol Myers Squibb (BMS). He has over 37 years of experience in the pharmaceutical and food industries and holds professional memberships in PDA, IFT, and ISPE.

CoverStory

Accelerating Oncology Trials

Oncology clinical trials remain the bottleneck in oncology drug development. They are often slowed by complex design, recruitment challenges, and regulatory requirements. By integrating patient-centric strategies, digital innovations, and collaborative trial models while navigating evolving FDA frameworks, oncology trials can deliver innovative therapies to patients faster, safer, and more efficiently.

Oliver Overheu
Senior Associate, Duke Capital Partners

1.Oncology trials are widely acknowledged as the bottleneck in cancer drug development. From your perspective, what are the root systemic inefficiencies that make oncology trials uniquely challenging compared to other therapeutic areas?

No two cancers are alike, each entity is basically a separate disease, and oncology has moved far beyond the era of one-size-fits-all medicine. Each clinical trial must navigate complex eligibility criteria, biomarker-driven subgroups, and stringent regulatory oversight. Protocols are lengthy, and long follow-up periods demand intensive safety monitoring. Together, these factors create structural inefficiencies – slowing innovation, inflating development costs, and delaying patient access to life-saving therapies.

2.Patient recruitment remains a persistent hurdle. How can patient-centric trial designs and engagement strategies not only improve recruitment rates but also enhance long-term retention in oncology studies?

Recruitment in oncology often falters because eligibility criteria fragment patient populations and trial participation imposes heavy logistical and emotional burdens. Patient-centric trial designs that integrate local care networks, telehealth visits, and digital engagement tools transform participation from a burden into a partnership and are important tools to increase trial access. By aligning trial design with patient needs, oncology studies enhance recruitment rates and foster long-term retention, leading to more reliable outcomes and faster development timelines. ▶

3.Digital innovations such as remote monitoring, AI-driven site selection, and adaptive trial platforms are becoming central to clinical research. Which of these technologies holds the greatest promise for accelerating oncology trials, and why?

Remote monitoring technologies hold transformative potential for oncology trials by expanding access beyond major academic centers. Patients in rural or underserved regions can participate without repeated long-distance travel, improving important recruitment diversity and retention. Integrated digital monitoring ensures continuous safety oversight, while adaptive trial platforms allow real-time data to guide protocol adjustments, combining inclusivity with accelerated development timelines.

4.Decentralised and hybrid trial models are gaining traction. In the oncology space - where treatments are complex and safety monitoring is critical - what adaptations are required to ensure these models remain both feasible and safe?

Decentralised and hybrid models can meaningfully accelerate oncology trials when adapted to the clinical complexity of cancer care. Hybrid frameworks that pair community-based treatment sites with tele-oncology monitoring reduce travel and broaden patient reach. Continuous digital safety tracking and real-time adverse-event alerts preserve oversight, while standardised workflows and regulatory-grade data capture ensure feasibility and patient safety across distributed networks.

5.With oncology trials often involving highly targeted patient subgroups, how do you see real-world evidence (RWE) and big data analytics shaping recruitment, protocol design, and regulatory acceptance?

The molecular fragmentation of modern oncology has dramatically reduced eligible trial populations, making patient recruitment slower and more resource-intensive. Real-world evidence can mitigate this constraint by serving as external or hybrid control arms, reducing the number of patients required for randomisation and expediting enrollment. Robust data curation and big-data analytics enable precise patient matching and bias adjustment, ensuring statistical validity. When appropriate frameworks are developed together with regulators, development timelines shorten without compromising evidentiary rigor.

6.Collaboration between academic institutions, industry sponsors, and regulatory bodies is increasingly emphasised. What are the most effective models of collaboration you've observed, and how do they directly impact trial acceleration?

The most effective collaboration models in oncology pair academic innovation with industry execution and regulatory insight

from the earliest stages. Tight, trust-based networks between academia and industry enable the translation of promising discoveries from concept to clinical testing. Transparent collaboration and aligned incentives ensure that translational findings rapidly evolve into viable therapeutic programs. Early regulatory engagement streamlines approval pathways, while data-sharing frameworks between institutions and sponsors shorten feedback cycles, improve resource utilisation, and translate discovery into patient benefit faster.

7.The FDA's evolving frameworks - such as accelerated approvals and real-time oncology review - are reshaping trial design. How should sponsors adapt to these evolving regulatory landscapes without compromising data integrity?

Accelerated approval pathways have helped bring innovative oncology therapeutics to patients faster. Yet these mechanisms demand tight, ongoing interaction with regulators, especially as the FDA has increased scrutiny on surrogate endpoints and confirmatory evidence. Sponsors that embed regulatory strategy early – validating endpoints, planning adaptive designs, and maintaining continuous data readiness – can meet this higher bar. Proactive engagement and transparent communication with agencies preserve data integrity while ensuring speed translates into safe, durable patient benefit.

8.Oncology trials frequently involve complex endpoints

> Accelerated oncology trials compress time-to-market and lower development costs, reshaping the economics of drug developmen

beyond survival, such as quality of life and biomarker-driven outcomes. How can innovative trial designs balance scientific rigor with patient relevance?

Traditional survival endpoints remain vital in oncology, but they sometimes fail to capture what patients value most. Modern trial designs should integrate patient-reported outcomes, quality-of-life measures, and biomarker-based efficacy signals into composite endpoint frameworks. Adaptive methodologies allow these measures to evolve as data mature, maintaining statistical integrity while reflecting what truly matters to patients. This alignment of scientific rigor and patient relevance yields evidence that regulators trust and patients value, accelerating both approval and adoption.

9.Given the rapid evolution of personalised medicine and ▶

biomarker-based therapies, what shifts are required in trial infrastructure to accommodate smaller, more precise patient cohorts?

Personalised oncology has fragmented trial populations into smaller, molecularly defined cohorts that come with unique logistical hurdles. Integrated testing and biobanks help identify eligible patients quickly and consistently across sites. Flexible trial platforms – such as basket and umbrella studies – reduce redundancy by utilising shared infrastructures. Trial systems must also be built for regulatory readiness, supporting adaptive designs and rolling submissions. Finally, strong industry–academic partnerships expand access to rare patient populations and accelerate translation into clinical impact.

10. Digital platforms promise efficiency, but they also introduce challenges around data privacy, interoperability, and standardisation. How should stakeholders navigate these competing priorities in oncology trials?

Digital platforms are now central to oncology research, yet their success depends on balancing efficiency with data responsibility. Robust privacy safeguards, harmonized standards, and interoperable systems protect patients while enabling collaboration across sponsors, regulators, and research sites. Clear governance frameworks that define ownership, consent, and access create trusted ecosystems where digital innovation aligns with ethical and regulatory compliance.

11. From a business and strategic perspective, how do accelerated oncology trials influence the broader economics of drug development and the sustainability of innovation pipelines?

Accelerated oncology trials compress time-to-market and lower development costs, reshaping the economics of drug development. Yet recent regulatory scrutiny of accelerated approvals has introduced uncertainty that can deter early-stage investment. Predictable, transparent frameworks are critical to sustaining high-risk innovation. When regulatory clarity and robust post-approval commitments align, accelerated pathways enhance capital efficiency and reinvestment – creating a sustainable model where financial performance and continuous innovation reinforce one another, ultimately improving patient access to breakthrough therapies.

12.Globalisation of oncology trials introduces both opportunities and challenges. How do regional regulatory differences, cultural patient factors, and infrastructure gaps affect the feasibility of scaling accelerated trial models worldwide?

Global oncology trials offer access to diverse patient populations but face significant disparities in regulation, infrastructure, and

patient engagement. Differing approval standards and ethics frameworks extend timelines, while uneven access to diagnostics and trial infrastructure limits participation in emerging regions. Overcoming these barriers requires harmonised regulatory frameworks and alignment on quality standards. When global trial networks coordinate around these principles, acceleration becomes both feasible and equitable, broadening worldwide access for patients to oncology innovation.

13.As oncology drugs increasingly integrate with companion diagnostics, how should trial designs evolve to test therapies and diagnostics in tandem while keeping timelines efficient?

Companion diagnostics have become integral to targeted oncology therapy, requiring trial designs that evaluate drugs and assays together from the outset. Early alignment between therapeutic and diagnostic development avoids sequential validation that slows progress. Adaptive platform trials and standardised biomarker assays enable concurrent testing of multiple targets under a single protocol, maintaining efficiency and scientific rigor. Close collaboration between sponsors, regulators, and diagnostic partners ensures synchronised approvals and delivers precision therapies to patients faster.

14.Looking ahead, what is your vision of an "ideal" oncology trial ecosystem in the next decade - one that is both patient-centric and innovation-driven? What milestones need to be achieved to make that vision a reality?

The ideal oncology trial ecosystem will be decentralised, data-driven, and genuinely patient-centric. Participation will no longer depend on geography, as digital platforms, interoperable data systems, and remote monitoring enable global inclusion. Regulatory frameworks must evolve to recognise real-world and digital evidence as complementary to traditional endpoints, creating pathways for faster, evidence-based approvals. True acceleration will come from a culture of collaboration—where academia, industry, regulators, and patients co-create solutions that turn scientific innovation into timely, equitable access to care.

AUTHOR BIO

Oliver Overheu, MD, is a Senior Associate at Duke Capital Partners, He is also a board-certified oncologist, an MBA candidate at Duke University's Fuqua School of Business, and an Associate at Duke Capital Partners. His background, beyond clinical practice, spans oncology research, clinical development, and biopharmaceutical strategy. By combining medical, business, and investment expertise, he helps bring new therapies to market through trial design, regulatory navigation, and patient-focused strategies.

Transforming Patient Care with Dermal Drug Delivery Systems

As interest grows in drug delivery methods that can improve adherence, enhance patient experience and support new therapeutic formats, dermal delivery devices are receiving renewed attention. By enabling minimally invasive and user-friendly administration, these systems can support better adherence, particularly for patients with chronic conditions, needle aversion or limited access to clinical care. Both transdermal and microneedle array patches offer the possibility to deliver drugs through the skin, but each brings distinct formulation, device and manufacturing challenges. Their development and scale-up require a coordinated approach that considers more than just bioavailability or skin permeability.

Andrew Riso,
Vice President, Dermal Delivery and Licensing, Kindeva Drug Delivery

We're only just scratching the surface of skin-based drug delivery

A closer look at how integrated formulation, device design and manufacturing can support the rise of dermal platforms.

We are entering an exciting era for dermal drug delivery. Recent innovations in transdermal and intradermal technology promise a future where patients can administer drugs in a more effective and less invasive way, even at home.

These advances look set to herald the next step-change in the delivery of vaccines, as well as a range of other therapeutic treatments. However, several challenges must be overcome before this technology can be widely commercialized.

Patients and crucially, regulators must be confident that the platforms can administer the appropriate doses consistently, and that they can be manufactured at the scale required realizing their full potential across the world.

This requires an understanding of what is required for effective manufacturing, even at the earliest stages of formulation and development. Companies will need to consider the regulatory requirements of the final product, as well as how to adhere to good manufacturing practice (GMP) and de-risk the leap from lab to market.

The potential of these new dermal technologies is enticing. However, their development will require close cooperation and collaboration between experts at all stages of the process, from innovative biotech companies to experienced manufacturers.

The promise of dermal drug delivery

In recent years, we have seen increasing interest in dermal drug delivery platforms across the industry.

Patients are calling for treatments that can be used to treat a range of conditions, including existing and emerging chronic diseases. They also want treatments that can be administered at home rather than at a hospital, and without the discomfort of needles where possible.

In 2024 the market for transdermal drug delivery systems was already valued at 7.32 billion USD, with projections suggesting a rise to 9.87 billion USD by 2030

The promise of at-home, personalized medicine has also attracted the attention of governments and funding organizations, who see an opportunity to reduce the strain on healthcare systems, improve patient take-up of medication, increase resilience against pandemics, and broaden access to drugs worldwide.

As a result, companies have launched several early-stage and pre-clinical studies aiming to advance transdermal and intradermal drug delivery technologies. In 2024 the market for transdermal drug delivery systems was already valued at 7.32 billion USD, with projections suggesting a rise to 9.87 billion USD by 2030 Innovative companies are considering the potential of

this approach to treat conditions including diabetes, migraines and hypertension.

There is also considerable excitement about the possibilities of intradermal microneedle-array patches (MAPs), which feature an array of microscopic needles designed to deliver medication through the outermost layer of human skin. This technology is less invasive than traditional injections, making it more suitable for patients with needle-phobia. Applying a patch is also considerably simpler than the traditional intradermal injection process, which requires the precision of a trained healthcare professional.

Delivering directly into the dermis means a vaccine is in contact with more antigen-presenting cells, and could therefore generate the desired immune response, even with a smaller dose. This is an approach used in "dose sparing", in which vaccine supplies are extended further by giving smaller amounts to each patient just under the top layer of skin.

MAPs can also potentially offer room temperature stability, which could allow them to be transported and stored worldwide without the need for rigorous cold-chain storage requirements. This could be vital in opening up products to markets without well-established healthcare infrastructure.

However, as of yet, no microneedle technology has been approved by the FDA for use in drugs or vaccine delivery.

Meeting the challenges

So, how do companies bring the potential of innovative dermal drug delivery platforms to market? The answer lies in collaboration. Biotech companies, academic institutions, and experienced contract development and manufacturing organizations (CDMOs) need to work together to develop a more holistic understanding of what is required at every step of the development process.

Companies and partnerships which consider the impact of formulation and design decisions on scaling and manufacturing from a very early stage have a far greater chance of bringing their products to market before the competition.

For example, choosing whether to deliver your drug using a transdermal or intradermal platform can come down to several factors. One of the main determinants is the desired pharmacokinetic profile for the drug – or how it is absorbed, distributed, metabolised and excreted in the body. Transdermal delivery is more suited to relatively low molecular weight drugs in which a slow, sustained release is beneficial to achieving the desired therapeutic outcome. Furthermore, the rate of diffusion of molecules through the skin will determine the size of the patch used, and the design will have to ensure that the drug is delivered over the required period, which is typically 1-7 days.

In the case of MAPs, the drug or vaccine will be delivered into the skin far more quickly, which is well suited for therapeutics and vaccines in which an immediate release profile is desired.

There are different types of MAPs currently in development, including solid needles coated with formulation, formulation moulded into dissolvable microneedles, and hollow microneedles through which liquid formulation is infused.

This means there are a number of complex considerations that developers and CDMO partners must consider, including:

- The microneedle material and how it releases the drug
- How the drug formulation is released, and its compatibility with the microneedle material
- How the drug is loaded
- How the patch is assembled
- How packaging maintains product stability
- The size and position of droplets on the microneedle

Ensuring that the required dosage of the drug is delivered in a sustained and consistent manner is integral to the process. There are a number of parameters that influence delivery from solid-coated MAPs:

- **Needle height:** Taller needles can carry more medication, but if taken to an extreme, can affect patient comfort
- **Needle sharpness:** A sharper needle can penetrate more easily, but may be more difficult to manufacture consistently.
- **Microneedle density:** Higher density can result in higher dose delivery, but can also reduce the effectiveness of penetration and result in greater local site reactions.
- **Patch size:** Larger patches can deliver more of the drug, but may cause inconvenience for the patient

Considering manufacturing from the outset

Developing any drug or combination product holds a certain degree of risk. However, considering manufacturing needs and challenges from the very start can help forward-thinking companies to anticipate and even avoid future challenges.

For example, it is vital that companies are able to produce dermal drug delivery products to scale and to a consistently high standard. These are drug-device products, which means that both the formulation and the device itself should be developed and optimized in sync to ensure that the final product is safe and performs to its potential.

An experienced CDMO can also work with a developer to ensure that the product can be scaled to the required level without sacrificing uniformity and quality. This comes with its own considerations, including the choice of materials for microneedles and how they are produced. By thinking ahead to manufacturing at the earliest possible stage, the right materials and approaches can be selected.

Companies must also consider issues such as quality control and adherence to regulatory standards. In the latter case, being able to maintain early and consistent contact with these bodies can be a strong advantage when it comes to maximising the chances of approval.

CDMOs with drug delivery expertise have the unique ability to address this demand. These partners have extensive knowledge of working with early-stage companies and calibrating manufacturing processes to specific patient needs, formulations, and market strategies. They ideally also have extensive knowledge of how to develop dermal products from concept to manufacturing, and how to work together to achieve optimal results.

A new era of collaboration

By working together effectively, drug developers and manufacturers will be able to achieve significant benefits.

They will potentially be able to deliver more effective treatments for a wider range of conditions and administer therapies in a less invasive and more personalized way. Governments and non-governmental organizations will be able to distribute essential care more widely, especially to places where transport and storage are an impediment.

However, to achieve this, we must make sure that these transformative products are given the best chance to succeed.

Complex combination products such as MAPs require a joined-up, holistic presenting cells, and could therefore generate the desired immune response, even with a smaller dose. This is an approach used in approach to development, where future challenges are anticipated and addressed. This means addressing manufacturing considerations from the very start, and working with experts who can smooth the path to regulatory approval and mass-market adoption.

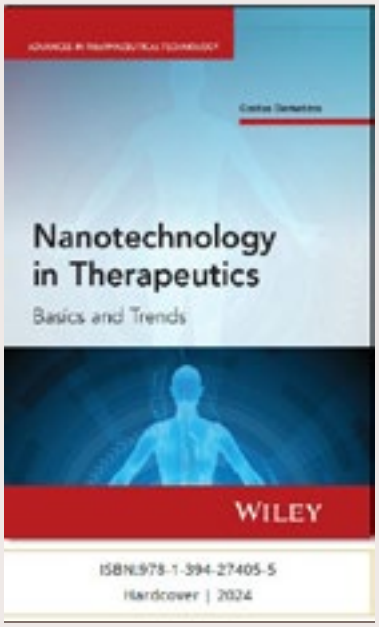
We are already seeing collaborations and knowledge sharing across the industry, with developers integrating manufacturing insight into their processes from the outset. It is important that this trend continues.

By prioritizing manufacturing optimization, partners can ensure that these products provide optimal patient comfort and convenience and deliver much-needed treatments reliably and consistently. ■

AUTHOR BIO

Andrew Riso is a seasoned business development and licensing executive with over 15 years of experience across the pharmaceutical and financial services sectors. He currently serves as Vice President of Dermal Delivery and Licensing at Kindeva Drug Delivery, where he leads strategic initiatives in transdermal product innovation and partnership development. Prior to his current role, Andy held multiple leadership positions within Kindeva and its predecessor, Meridian Medical Technologies, including Director of Business Development. He also provided strategic consulting services in business development and planning.

Nanotechnology in Therapeutics Basics and Trends



ISBN:978-1-394-27405-5
Hardcover | 2024

The book Nanotechnology in Therapeutics. Basics and Trends presents a framework for developing bio-inspired nanosystems for the delivery of drugs, genes, and vaccines. It analyses nanotechnology role in modern therapies, focusing on lipid nanoparticles, regulatory challenges, and safety concerns. Emerging tools like nanoinformatics, artificial intelligence, and machine learning are discussed as key to designing and approving nanomedicines. Divided into three parts, the book covers historical background, nanostructures in medicine, and regulatory perspectives. It offers an integrated, forward-looking approach and is a valuable resource for scientists, healthcare professionals, and students in the pharmaceutical and biomedical fields.

Costas Demetzos Professor

Department of Pharmacy, National & Kapodistrian University of Athens (NKUA), Greece

1.What inspired you to create Nanotechnology in Therapeutics: Basics and Trends, and how does it address the evolving landscape of nanomedicine today?

Nanotechnology has evolved from a research topic into a cornerstone of drug delivery, diagnostics, and personalised medicine. Its rapid development and transformative impact in these fields have inspired me to explore it further. Moreover, the need to design nanodrug ▶

delivery systems that mimic biological functions motivates me to work experimentally and in writing to develop nanomedicines that assist clinicians, researchers, and students in applying the principles of nanotechnology in therapeutic applications and in their education.

2.The book traces the journey of nanotechnology from concept to clinical reality. How has this evolution influenced modern therapeutic design and delivery?

The evolution of nanotechnology from bench to clinic has transformed modern therapeutics. The rational design of drug delivery nanosystems that mimic biological functions through biophysical algorithms enhances efficacy and minimises toxicity. 'Theranostic' platforms further bridge diagnostics and therapy, enabling real-time monitoring and advancing truly personalised medicine. Moreover, nanoplatforms composed of biocompatible and biodegradable materials are safe for use in the final nanoformulation, improving therapeutic outcomes.

3.Among the various nanostructures discussed - such as lipid nanoparticles, polymeric micelles, and dendrimers - which do you believe hold the greatest promise for future drug and gene delivery?

In my view, lipid nanoparticles are the most promising nanoplatforms. Compared with polymeric or dendrimeric nanoparticles, they are composed of naturally metabolisable lipids, minimising toxicity and enhancing biocompatibility and biodegradability, thus facilitating regulatory approval. Moreover, lipid nanoparticles have already demonstrated real-world clinical success and are regarded as promising nanocarriers for delivering drugs, macromolecules, and genetic materials against serious diseases.

4.Lipid nanoparticles revolutionised mRNA vaccine delivery during the COVID-19 pandemic. How do you foresee their role expanding beyond vaccines into broader therapeutic applications?

Lipid nanoparticles (LNPs) are promising nanoplatforms that could expand therapies across multiple therapeutic areas, including gene editing. They also hold great potential in cancer therapy, as LNPs can deliver RNA to silence or reprogramme oncogenes. Moreover, LNPs can encapsulate macromolecules such as proteins or peptides to selectively target tumour cells, as well as transport bioactive molecules for the treatment of metabolic or rare diseases. In personalised medicine, they can be tailored to a patient's genetic profile, optimising therapeutic response.

5.You emphasise "bio-inspired nanosystems." Could you elaborate on how mimicking biological systems enhances the functionality and safety of nanotherapeutics?

Bio-inspired nanosytems are composed of

biomaterials that are essential components of the human body and are designed as stimuli-responsive nanoplatforms that respond to bio-environmental stimuli (e.g. pH, enzymes, etc.). By mimicking lipidic rafts and cell surface properties, they can recognise specific cellular targets, enhancing the efficacy and safety of the encapsulated biomolecules. Through self-assembly, bio-inspired nanosystems mimic human cell membrane morphology while remaining functional. Furthermore, nanosystems such as lipid nanoparticles follow the fundamental principles of biological membranes.

6.The book highlights the convergence of nanoinformatics, artificial intelligence, and machine learning. How are these technologies reshaping the discovery and optimisation of nanoscale therapeutics?

Nanoinformatics, Artificial Intelligence (AI), and Machine Learning are enabling technologies essential for the intelligent development of nanomaterials and the rational design of nanoplatforms. Data mining combined with AI maximises the functional properties of nanodevices by analysing large datasets, uncovering biological patterns, and optimising key design parameters. For the pharmaceutical industry, the benefits include discovering new molecules and biological targets, precise data mining, optimising bioactive formulations, identifying effective biomaterials for nanocarriers, and accelerating development and regulatory processes.

7.How can computational modeling and predictive analytics improve translational success rates for nanomedicines from laboratory research to clinical use?

Computational modelling, predictive analytics, and in silico simulations enable the rational and precise design of nanocarriers by optimising their composition, physicochemical, and surface properties and predicting physical and biological stability of the final formulation. These approaches create a translational framework from bench to clinic of nanomedicines that improve efficacy, reduce toxicity and adverse therapeutic effects, accelerate manufacturing, and support safe-by-design development of nanocarriers encapsulating bioactive molecules. Furthermore, they enhance regulatory compliance, ultimately increasing the clinical success rates of nanomedicine.

8.Regulatory evaluation of nanotherapeutics remains a major challenge. What reforms or frameworks do you believe are most urgent for ensuring both innovation and safety?

The regulatory approval of nanotherapeutics is challenging due to the complexity, chaotic behaviour, and non-linear dynamics of self-assembled nanocarriers, making batch-to-batch reproducibility and the production of identical prototypes difficult. Regulatory agencies should take these issues into consideration and require clarification of the morphological characteristics of nanocarriers, ▶

whether alone or encapsulating a drug. Inspired by AI-based protein structure prediction, intelligent algorithms could precisely characterise nanocarriers' lyotropic phases, improving their efficacy, safety, and reproducibility, and supporting more reliable regulatory evaluation.

9.In what ways do current toxicity and biocompatibility assessments fall short when applied to nanoscale systems, and how can these gaps be addressed?

Nanoparticles exhibit properties different from the biomaterials from which they are composed, due to their self-assembly process. Factors such as size, surface area, surface properties, shape, and u-potential can alter biological interactions, biodistribution, immune responses, and ADME profiles. Consequently, their toxicity and biocompatibility differ from the original biomaterials. Standard assays often fail to identify such effects. To address this, essential testing protocols, advanced in vitro models, computational tools, and AI-driven simulations should be employed, ensuring safer nanomedicine development.

10.Collaboration between academia, industry, and regulatory bodies is crucial. What models or partnerships could accelerate the path of nanomedicine from bench to bedside?

Collaboration between academia, industry and regulatory agencies should be strengthened to accelerate the translation of nanomedicines from bench to clinic by shortening the development timeline. Promising models include science hub platforms, where regulators and researchers work together to guide compliance and clinical requirements. AI-driven models and shared databases for preclinical and clinical nanomedicine data can improve predictive accuracy, optimise design, and accelerate decision-making for safer and efficient nanomedicines.

11.What ethical or societal implications arise as nanotherapeutics begin interacting with sensitive biological barriers such as the brain or placenta?

Sensitive biological barriers raise ethical and societal concerns regarding safety, long-term effects, and informed consent. Transparency is essential to ensure patients are fully informed about potential risks. Scientists should actively engage with the public, explaining complex issues related to nanotechnology to reduce fear and build trust. Societal education is crucial for the acceptance of nanomedicine applications, promoting confidence in these innovations and addressing public concerns responsibly.

12.How do you envision nanotechnology contributing to precision medicine and personalised therapeutics in the next decade?

Nanotechnological platforms should be

designed based on biological targets and biophysical surface abnormalities well known as 'lipid rafts', reflecting the cell's 'cryptic codes' linked to infections or neuro-immune disorders. Nanocarriers must selectively target diseased tissues, minimising adverse drug reactions. Theranostics enable real-time monitoring and dynamic therapy, while nanomedicines tailored to a patient's genetic profile optimise dosing and pharmacokinetics. Enhanced drug penetration across sensitive barriers and AI-driven design further accelerate the development of personalised therapeutics.

13.The book also serves as a learning framework. How can educators and young researchers best use it to understand both fundamentals and emerging trends?

Educators and young researchers should have a thorough understanding of both the fundamentals and emerging trends in nanotechnology. Key aspects, such as stability, surface phenomena and particle-biological interactions, are vital for therapeutic applications. The development of nanotechnology-based vaccines and advanced characterisation techniques highlights current progress and should be studied. Moreover, Artificial Intelligence, Machine Learning, chaos theory, nonlinear dynamics, quantum phenomena and insights from biology and biotechnology guide innovative nanocarrier design. Finally, ethical, safety and regulatory considerations are essential for understanding nanotechnology advancements.

14.Finally, if you could leave readers with one defining message about the future of nanotechnology in therapeutics, what would it be?

Nanotechnology in clinical practice and in therapeutics is no longer an innovative field but a catalyst for biomedical sciences and their applications. Based on emerging technologies such as Artificial Intelligence, Machine Learning, computational modeling, bioinformatics and the evolving field of biotechnology, it is creating new approaches for targeted, personalised and efficient interventions against disease. The future of therapeutics, diagnostics and prophylactic approaches, including vaccination, is an emerging field and profoundly interdisciplinary, with nanotechnology at the core of this transformation.

AUTHOR BIO

Costas Demetzos is a Professor of Pharmaceutical Nanotechnology at the National and Kapodistrian University of Athens (NKUA). He has been recognised for his scientific contributions with multiple honors, including an award from the Academy of Athens in 2018 and designation as a Distinguished Professor by NKUA in 2025. In 2021, he was elected as a member of the European Academy of Sciences and Arts. Since 2023, he has served as an Associate Editor of the Journal of Lipid Research (JLR). His work focuses on pharmaceutical nanotechnology, nanomedicine, and advanced drug delivery systems.

Smoothing the Path to Drug Development with Accurate Clinical Data

Drug development is a long, costly, and complex process. At its core lies a critical question: **How does a drug affect the body—and how does the body respond?** The answers are derived from well-structured **pharmacokinetic (PK), pharmacodynamic (PD), and toxicokinetic (TK)** investigations conducted in both preclinical and clinical studies.

This whitepaper highlights the importance of accurate, standardized clinical data in reducing delays, overcoming bottlenecks, and ensuring that promising therapies progress smoothly toward regulatory approval.

Why PK, PD, and TK Data Matter

- **Pharmacokinetics (PK):** Describes how the body absorbs, distributes, metabolizes, and excretes (ADME) a drug—essentially, what the body does to the drug.
- **Toxicokinetics (TK):** Focuses on systemic exposure at different dose levels, linking toxicity findings to drug concentrations.
- **Pharmacodynamics (PD):** Explains what

the drug does to the body—its mechanism of action, magnitude of response, and duration.

Together, PK, PD, and TK provide a complete view of safety and efficacy. Regulatory agencies rely on these datasets to establish safe starting doses and assess the benefit-risk balance.

Challenges in Translating Data

While methodologies have advanced, one major hurdle remains: **translating data from animals to humans, and from in vitro to in vivo models.** These translations often cause delays in the development process.

In addition, toxicology data is frequently fragmented—scattered across reports, tables, and figures. Without standardization, these inconsistencies make it difficult to draw reliable conclusions and may slow regulatory approval.

NOAEL and Data Reliability

The **No-Observed-Adverse-Effect-Level (NOAEL)** defines the highest tested dose without adverse effects and is central to first-in-human (FIH) dosing. However, deriving NOAEL requires curated, consistent data. Errors or variability in datasets can delay decision-making and introduce risk.

The Value of Data Standardization

PK/PD/TK datasets are only as valuable as their quality and consistency. **Standardizing and digitizing toxicology data** transforms unstructured reports into reliable, analysis-ready outputs. This enables faster study reviews, supports regulatory compliance, and ensures insights are not lost across diverse datasets.

Real-World Impact

A leading pharmaceutical company partnered with Excelra to digitize and structure **65 investigator brochures (IBs)** across multiple therapeutic areas. Our team extracted unstructured PK/PD/TK data, standardized hundreds of variables, and delivered a consolidated dataset spanning key domains such as clinical, TK, safety, and NOAEL.

The result: a **comprehensive dataset** that accelerated preclinical review, improved dose selection, and supported regulatory submissions.

Why Read This Whitepaper?

This whitepaper provides:

- A clear overview of PK, PD, and TK studies.
- Insights into bottlenecks that delay drug development.
- Practical approaches for standardizing toxicology data.
- A case study demonstrating real-world impact.

If your teams handle complex preclinical and clinical datasets, this resource will help you improve reliability, reduce inefficiencies, and move faster toward regulatory milestones.

Download the Whitepaper to learn how accurate, standardized PK/PD/TK data smooths the path to safer, faster drug development.

Intelligent Insights

Navigating the New Era of B2B Event Marketing

This interview highlights the emerging trends, technologies, and strategies set to redefine pharma events. It's a forward-looking guide for organisers aiming to deliver measurable impact and lasting engagement.

Sussane Vincent
Media Relations Head,
Pharma Focus Europe

1. As an event partner exposed to diverse global audiences, what emerging themes should organisers prioritise before they become mainstream?

The most forward-looking organisers will double down on topics where scientific and operational transformation is accelerating. AI-driven clinical operations, next-generation digital quality, precision and continuous manufacturing, advanced real-world evidence strategies, and sustainable supply-chain models are rapidly gaining momentum. Prioritizing these themes early positions event organizers as thought leaders rather than followers.

2. If you could redesign the pharma event ecosystem from the ground up, what value would you build?

I would integrate a predictive intelligence layer at the core of the ecosystem. This would analyse audience behaviour, forecast emerging demand, and recommend the right topics, formats, and promotional strategies long before planning begins. Such an approach would replace intuition with evidence and ensure every event is built on data-led decision-making from day one.

3. How will AI change how pharma events are discovered, personalized, and attended in the next five years?

AI will completely reshape the event journey. Discovery will become algorithmic, matching professionals to events with the same precision as streaming platforms match users to content. Personalisation will evolve from static agenda builders to dynamic, AI-generated pathways tailored to each attendee. Networking will become smarter as AI analyses profiles and recommends high-value connections. The entire experience will feel intelligently curated.

4. What innovations or technologies will reshape pharma events in the coming years?

We are entering an era of adaptive, tech-enabled events. Expect AI-assisted networking tools, real-time personalisation engines, interactive digital show floors, and hybrid experiences enhanced by AR and VR. Predictive analytics will optimize session design and audience engagement. These innovations will shift events from passive attendance to immersive, insight-driven participation.

5. What early digital behaviours help you predict whether an event will succeed before it launches?

Three indicators consistently stand out: rising engagement with niche or emerging-topic content, increasing search intent around relevant therapeutic or technology areas, and repeated audience clustering across related channels. When these signals converge, they reliably forecast high market interest, strong attendee turnout, and robust sponsor demand.

6. What should the ideal attendee experience look like by 2030?

By 2030, attendees should experience a seamlessly personalized journey. Every touchpoint—from session recommendations to exhibitor interactions—will be tailored to their needs. Real-time content summaries, intelligent scheduling assistants, and integrated digital platforms will ensure that every moment feels purposeful. The event environment will adapt dynamically to audience behaviour, creating an experience that is both efficient and inspiring.

7. How can events evolve into 365-day knowledge networks rather than one-off gatherings? ▶

Organisers must extend their presence beyond the event dates by offering continuous value: micro-interviews, expert commentaries, on-demand sessions, community discussions, and exclusive industry updates. This transforms the event brand into a year-round hub for learning and thought leadership. Attendees stay engaged, sponsors stay visible, and organisers maintain momentum long after the event concludes.

8. What would a truly smart partnership ecosystem look like with real-time data sharing?

A smart ecosystem would unite organisers, media partners, and exhibitors around shared behavioural insights. It would provide a comprehensive view of audience demographics, engagement patterns, and rising topics across channels. This transparency enables more strategic content planning, targeted promotion, and evidence-based decision-making. The result is a collaborative environment where every partner contributes to—and benefits from—greater collective intelligence.

9. What is the most underrated opportunity organisers overlook that could significantly boost their global reach?

The power of co-created editorial content is still vastly underestimated. Thought-leadership articles, expert interviews, and insight-rich videos travel far beyond event promotion; they position the event as an authority in the global pharma landscape. While many organisers still focus heavily on logos and banners, it is high-quality content that truly enhances visibility, credibility, and international reach.

10. How can digital tools and data enhance audience engagement before, during, and after the event?

Before the event, data helps identify audience needs and refine programming. During the event, real-time analytics track engagement, optimise networking, and surface trending discussions. After the event, behavioural insights enable personalized follow-ups, targeted content, and smarter planning for future editions. Digital tools turn engagement into a measurable, actionable asset that continually elevates the event experience.

Concluding Remarks

This interview with Sussane Vincent provides a forward-looking roadmap for pharma event organisers, highlighting how AI, data, and innovative strategies are shaping the future of engagement. By embracing these insights, organisers can deliver impactful, personalised, and year-round experiences that set new industry benchmarks.

Key Takeaways

- Smart Partnerships and Content Strategy
- Data-Driven Event Design
- AI-Powered Personalisation
- Extending Events Beyond Single Occasions
- Real-Time Analytics During Events
- Evidence-Based Sponsorship Planning
- Collaborative Partner Ecosystems
- Hybrid and Tech-Enabled Experiences

Dennis Hom

Appointed as CFO and CMO at ProQR

Dr. Santiago Arroyo

Appointed as Non-Executive Director at Maxion Therapeutics

Bob Rodebaug

Appointed as Vice President of Technology at Gannet BioChem

Jeffrey Shane

Appointed as Chief Commercial Officer at Experic

Larry Lockwood

Appointed as Chief Commercial Officer at ElevateBio

Rhonda Pacheco

Appointed as President at Takeda

Emma Bush

Appointed as Vice President, Commercial at CNX Therapeutics

Gabriella Gentile

Appointed as Chief Operating Officer at Symeres

Drew Burch

Appointed as Chief Executive Officer at Primrose Bio

Patrick Lucy

Appointed as Chief Executive Officer at Wheeler Bio

Wheeler Bio

Dr. Zivjena Vucetic

Appointed as Chief Medical Officer at Mission Bio

mission bio

Dr. Yasmine Wasfi

Appointed as Chief Medical Officer at Savara

SAVARA

James Rawls

Appointed as Senior Vice President of Regulatory Affairs at LB Pharmaceuticals

David H. Deming

Appointed as Lead Independent Director at Phio Pharmaceuticals

Phio

Chris Guiffre

Appointed as Chief Financial Officer at NodThera

nodthera

Paul Edick

Appointed as Board of Directors at Vistagen

Vistagen

Philippe Alen

Appointed as Chief Business Officer at AbolerIS

ABOLERIS PHARMA

Dr. Thomas Broudy

Appointed as Chief Executive Officer at BioCina

BioCina

International Conference on Clinical Microbiology and Advanced Medicines

Dec 01-03, 2025

Rome, Italy

https://cognitionconferences.com/clinicalmicrobiology/

About Event: Advancing Clinical Microbiology and Therapeutics for Better Global Health, promises dynamic discussions on infectious disease outbreaks, transmission dynamics, and risk factor identification. Researchers, professors, and students will gather to exchange insights, discuss innovations, and explore practical implications for practitioners.

Listed Under: RESEARCH & DEVELOPMENT

Pharmaceutical Launch Excellence Summit 2025

Dec 02-03, 2025

London, UK

https://www.iqpc.com/events-pharma-launch-excellence

About Event: The Annual Pharmaceutical Launch Excellence Summit for a unique and unmissable opportunity to gain actionable strategies for every stage of the drug launch process. Through exclusive insights from leading industry experts, community collaboration, and invaluable networking, you'll refine your approach, overcome challenges, and drive success in today's dynamic pharmaceutical landscape.

Listed Under: BioPharma

2nd GPCRs-Targeted Drug Discovery Europe 2025

Dec 09-11, 2025

London, UK

https://gpcrs-europe.com/about-event/?utm_source=external&utm_medium=event-listing&utm_campaign=event-listing&utm_content=media-partner%2Fother-advancing-rna%2Funpaid%2Fev-62557

About Event: As GPCR-targeted drug discovery

continues to surge across Europe, driven by the commercial success of GLP-1 therapies and a wave of industry investment, biopharma companies are reinvesting in innovative GPCR strategies to expand the druggable landscape. The 2nd Annual GPCR-Targeted Drug Discovery Summit Europe is your chance to explore the latest clinical case studies, de-orphanisation strategies, and the application of AI and ML in structure-based drug design, unlocking previously inaccessible GPCR targets.

Listed Under: Information Technology

PFS & Injectable Drug Devices Europe

Jan 13-15, 2026

London, UK

https://smgconferences.com/pharmaceuticals/uk/conference/pre-filled-syringes

About Event: These events bring together senior government and industry executives/program managers to share knowledge and collaborate on key technology topics including military space, unmanned and autonomous systems, microbiology, biosensors, and much more.

Listed Under: RESEARCH & DEVELOPMENT

Global Pharmacovigilance and Risk Management Strategies Conference

Jan 26-28, 2026

North Bethesda, USA

https://www.diaglobal.org/en/conference-listing/meetings/2026/01/global-pharmacovigilance-and-risk-management-strategies-conference

About Event: Developed in collaboration with regulators and industry experts, this neutral forum provides unparalleled insights into global regulatory harmonization, AI-driven signal detection, and advanced safety analysis tools. At this conference, you'll hear about updates, opportunities, and challenges shaping the future of drug safety and learn innovative problem-solving strategies that matter most to safety professionals.

Listed Under: Manufacturing

Non-Opioid Pain Therapeutics Summit

Jan 27-29, 2026

Boston, USA

https://non-opioid-pain-therapeutics.com/about/hanson-wade/?utm_source=external&utm_medium=event-listing&utm_campaign=event-listing&utm_content=media-partner/other-pharma-focus-america/unpaid/ev-70764

About Event: The Inaugural Non-Opioid Pain Therapeutics Summit is the only meeting dedicated to overcoming the unique scientific and clinical barriers in pain drug development. Discussions will focus on optimizing trial design in chronic pain, advancing mechanism-specific biomarkers, addressing placebo response and patient stratification, and aligning with regulators on validated endpoints.

Listed Under: BioPharma

5th mRNA-Based Therapeutics Summit Europe

Jan 27-29, 2026

Berlin, Germany

https://mrnabased-therapeutics-europe.com/

About Event: This interactive meeting unites global leaders in mRNA R&D, CMC, Regulatory Affairs, Clinical Development, and Business Strategy to address the field's toughest challenges: broadening mRNA's scope beyond vaccines, unlocking targeted and tissue-specific delivery, overcoming CMC and stability hurdles in saRNA and circRNA, and restoring investor confidence in RNA's therapeutic promise.

Listed Under: BioPharma

The Digital Pharma Advances Conference 2026

Jan 28-28, 2026

London, UK

https://digitalpharmaconference.com/

About Event: Global Insight Conferences' founding directors boast an impressive track record of running hundreds of conferences globally with over 40 years' combined experience, ranging from sectors as diverse as marcomms to engineering, finance to human resources, regeneration to child services, energy to information technology and many more.

Listed Under: Strategy

EUCROF26

Feb 01-03, 2026

Amsterdam, Netherlands

https://conference.eucrof.eu/

About Event: The programme features keynote addresses, plenary discussions, breakout sessions, and networking opportunities designed to reflect the latest challenges and innovations shaping our field. From regulatory insight to emerging technologies and patient engagement, EUCROF26 offers a unique space to connect with expertise across the clinical research landscape.

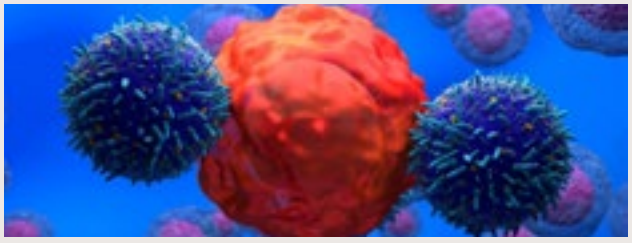
Listed Under: Clinical trials

Cue Biopharma and ImmunoScape Partner on Cell Therapy for Solid Tumours

Cue Biopharma, Inc., a clinical-stage biopharmaceutical company developing targeted T-cell therapies for autoimmune diseases and cancer, has entered a strategic collaboration and licence agreement with ImmunoScape Pte. Ltd., a biotechnology firm specializing in T-cell receptor (TCR)-based cancer therapies.

The partnership aims to advance an innovative in vivo cell therapy, leveraging Cue Biopharma's Immuno-STAT platform (CUE-100 series) and ImmunoScape's proprietary TCR technology to improve treatment outcomes for solid tumours.

The collaboration will focus on a novel "Seed-and-Boost" immunotherapy strategy. This involves administering a small dose of ImmunoScape's tumour-specific TCR-T cells ("Seed"), followed by Cue Biopharma's TCR-matched IL-2 Immuno-STAT molecules ("Boost"). The method enables precise in vivo activation and expansion of tumour-specific T cells, enhancing their persistence



and potency while reducing systemic immune activation and manufacturing complexities.

Cue Biopharma's CUE-100 series biologics are designed to selectively activate disease-specific T cells by combining a TCR-binding framework with engineered interleukin-2 (IL-2) variants. Early clinical data have demonstrated anti-tumour activity with fewer toxicities compared to conventional IL-2 therapies.

Under the agreement, Cue Biopharma will receive US$15 million in milestone payments - US$10 million in Q4 2025 and US$5 million in November 2026 - along with a 40% equity stake in ImmunoScape and potential royalties on future sales.

By integrating Cue Biopharma's precision T-cell engagement technology with ImmunoScape's TCR expertise, the partnership seeks to establish a transformative immunotherapy platform with the potential to redefine solid tumour treatment.

READ THE COMPLETE POST

Jupiter Neurosciences Gets FDA Nod for Phase 2a Parkinson's Trial of JOTROL™

Jupiter Neurosciences, Inc., a clinical-stage pharmaceutical company advancing therapies for neurodegenerative disorders, has received clearance from the U.S. Food and Drug Administration (FDA) to initiate a Phase 2a clinical trial of JOTROL™ in patients with Parkinson's disease.

JOTROL™ is a patented resveratrol-based therapeutic platform designed to target neuroinflammation and mitochondrial dysfunction - two key mechanisms implicated in Parkinson's pathology.

The FDA's approval of Jupiter's Investigational New Drug (IND) application enables the company to begin patient enrolment for the exploratory Phase 2a study. The trial will primarily evaluate the safety and tolerability of JOTROL™, with secondary and exploratory endpoints assessing pharmacokinetics and pharmacodynamics (PK/PD).

Jupiter will continue its collaboration with Zina Biopharmaceuticals, LLC, which has contributed to study design, biomarker strategy, and site selection. Patient enrolment is expected to commence in early 2026.

Preclinical studies using the MPTP model of Parkinson's disease demonstrated that JOTROL™ significantly improved motor functions such as grip strength and rotarod performance, suggesting strong neuroprotective potential.

The drug employs a proprietary micellar delivery system that provides over ninefold higher bioavailability compared to standard resveratrol while reducing gastrointestinal side effects.

With Parkinson's disease affecting more than 10 million people worldwide and no existing disease-modifying treatments, Jupiter's Phase 2a trial marks an important step toward addressing this critical unmet need. The global Parkinson's therapeutics market is projected to exceed USD 14 billion by 2030, highlighting the substantial opportunity for JOTROL™ to transform patient outcomes.

READ THE COMPLETE POST

Boehringer Ingelheim and CDR-Life Partner on New Autoimmune Antibody

Boehringer Ingelheim and CDR-Life Inc. have signed a global licensing agreement to develop CDR111, a trispecific antibody-based molecule designed to treat autoimmune diseases.

Known as an M-gager®, CDR111 is a novel T-cell engager that selectively targets and depletes disease-causing B cells, with the goal of rebalancing immune system function and addressing underlying autoimmune mechanisms.

B cells are key drivers of several autoimmune and inflammatory diseases, including lupus, multiple sclerosis, and certain forms of arthritis. By precisely depleting these pathogenic cells, CDR111 has the potential to deliver meaningful clinical benefits across a range of immune-mediated conditions.

This new agreement expands upon the companies' existing collaboration, which previously focused on an investigational antibody fragment aimed at preserving vision in patients with geographic atrophy (GA). That molecule, developed using CDR-Life's proprietary antibody fragment technology, is currently being evaluated in Boehringer's VERDANT™ Phase 2 clinical trial (NCT06722157).

Through this partnership, Boehringer Ingelheim will lead the clinical development and potential commercialization of CDR111, further strengthening its immunology pipeline. CDR-Life's advanced trispecific M-gager® platform will be leveraged to address autoimmune and inflammatory diseases with high unmet need.

Under the terms of the agreement, CDR-Life will receive up to CHF 456 million (approximately US$570 million) in total milestone payments, including CHF 38 million (about US$48 million) in upfront and near-term payments, as well as tiered royalties on future product sales.

READ THE COMPLETE POST

Eli Lilly to Build $3billion Manufacturing Facility in the Netherlands

Eli Lilly and Company has announced plans to invest US$3 billion in constructing a state-of-the-art manufacturing facility in Katwijk, located within the Leiden Bio Science Park in the Netherlands.

This landmark project underscores Lilly's strategic commitment to expanding its European production network and strengthening the regional pharmaceutical supply chain.

The new facility will significantly enhance Lilly's capacity to produce oral medicines across its core therapeutic areas, including cardiometabolic diseases, oncology, neuroscience, and immunology. Incorporating next-generation pharmaceutical manufacturing technologies, the site will feature dock-to-dock automation, fully paperless operations, and process analytical technologies for real-time quality control. Advanced methods such as spray-dried dispersion will also be employed to improve drug absorption and efficacy while increasing production efficiency.

According to David A. Ricks, Lilly's Chair and CEO, the Leiden Bio Science Park offers the ideal ecosystem with its strong talent pool and infrastructure to support innovation and sustainable growth. The facility is expected to create 500 skilled jobs in manufacturing, engineering, and life sciences, alongside 1,500 construction-phase positions, boosting South Holland's economy.

Aligned with Lilly's sustainability goals, the site will be designed for carbon neutrality and zero landfill waste, reinforcing the company's dual focus on innovation and environmental responsibility. This expansion adds to Lilly's growing European footprint, complementing its operations in France, Ireland, Italy, Spain, and Germany, and further solidifies Europe's role as a global hub for life sciences manufacturing.

Construction is scheduled to begin next year following permit approvals, marking a major milestone for both Lilly and the European pharmaceutical landscape.

READ THE COMPLETE POST


FLY BETTER
Emirates
SkyCargo
THE WORLD WORKS BETTER
WITH EMIRATES SKYCARGO
Transporting critical pharma and
medical devices across 6 continents.
SKYCARGO.COM