

An Integrated State-of-the-Art Site for ADC DS and DP, from IND to Commercial Supply

Antibody-Drug Conjugates (ADCs) represent one of the most powerful and complex classes of cancer therapies ever developed – combining the precision of a monoclonal antibody with the potency of a cytotoxic payload.

Their multi-step, hazardous manufacturing process has made specialist ADC CDMO manufacturing one of the fastest-growing and most technically demanding segments in pharmaceutical outsourcing – and a critical strategic priority for both large pharma and emerging biotech sponsors.

The global ADC contract manufacturing market reached an estimated USD 11.08 billion in 2026 and is projected to expand to approximately USD 29.65 billion by 2035, at a CAGR of 11.56%, according to Towards Healthcare (2026).

The market is expanding steadily, fuelled by rising oncology therapies, expanding clinical pipeline, sustained commercial revenue from approved products, increasing R&D investment from both large pharma and emerging biotech, and the emergence of next-generation ADC technologies – including site-specific conjugation, bispecific ADCs, and novel payload classes – that demand more advanced CDMO platforms.

The availability of CDMOs that genuinely understand protein engineering, conjugation technologies, and next-generation ADC formats is far more limited than general-purpose biologics capacity – and that scarcity is what positions specialist CDMOs as strategic partners rather than commodity suppliers.

The complexity of ADCs creates several manufacturing challenges. Traditionally, producing an ADC required multiple CDMOs, multiple quality systems, multiple technology transfers, and multiple regulatory inspections – across different sites, different countries, different standards.

As the first CDMO in the world to offer a fully integrated supply chain for ADCs under a single roof and a single quality system, BSP

delivers Drug Substance and Drug Product manufacturing in seamless operational continuity.

At its Latina, Italy site, BSP Pharmaceuticals has addressed a significant industry bottleneck in ADC manufacturing: a fragmented supply chain. The site co-locates drug substance (DS) conjugation and drug product (DP) fill-finish within a single facility under one quality system. This eliminates multiple inter-site transfers, reduces cold chain risks, improves traceability, accelerates batch release and regulatory preparedness, enhances worker safety when handling highly potent compounds, and shortens time to market. The result is a more resilient and efficient supply chain that supports the production of life-saving oncology therapies.

Consolidating Conjugation and Fill-finish at One Site

Founded in 2006, BSP Pharmaceuticals is an Italian contract development and manufacturing organization (CDMO) specialising in the production of oncology, cytotoxic, and immunotherapy drugs for pharmaceutical and biotechnology partners. It operates from investigational new drug to commercial supply. The company currently manufactures 13 of the 19 ADCs approved for the commercial market and provides service support for more than one hundred bioconjugated clinical programmes.

Traditionally, the critical steps needed to manufacture an ADC are managed in separate, often geographically distant sites, resulting in a highly fragmented supply chain. Monoclonal antibodies are shipped from one facility, the linker-payload complex is shipped from another, and conjugation occurs at a third site. This DS is shipped again to a fill-finish facility to produce the DP. Each handover runs the risk of cold chain interruption, transportation problems, and delays that affect product integrity and delivery to patients.

The Latina facility consolidates conjugation and fill-finish operations within a single facility, which represents a fundamental shift in the structure of ADC supply chains. It is unusual to have a fully integrated supply chain for commercial-scale DPs as complex as ADCs, making the

Latina unique in the industry. Monoclonals, cytotoxin-linkers, and intermediates are protected from exposure risks, handling complexity, and extended storage. Cold chain logistics are streamlined, while on-site storage as low as -80°C eliminates the need to move temperature-sensitive materials between sites. All critical components are received at one site, which means fully packaged DP is produced and shipped through a unified supply chain.

“Inter-site transfers of highly potent, cytotoxic intermediates introduces exposure risk, cold chain challenges, and the potential for quality deviations during transit,” said Aldo Braca, Chief Executive Officer and President. *“By housing both steps at Latina, end-to-end integration compresses the overall manufacturing cycle, strengthens batch traceability, and gives us a unified point of accountability for the entire ADC production process.”*

A Single Quality System for DS and DP

A single quality management system (QMS) across the entire manufacturing process delivers full traceability, improved compliance, and faster batch release, while harmonised documentation reduces complexity and drives higher quality outcomes.

“Co-locating drug substance and drug product operations creates a continuous quality oversight loop that simply isn’t achievable when the two steps are separated,” said Aldo Braca. *“QC teams can monitor critical quality attributes – conjugation efficiency, drug-to-antibody ratio, aggregation levels – and immediately apply those insights to the downstream fill-finish process without the delays inherent in inter-site communication.”*

Any out-of-trend result detected at the DS stage can trigger a real-time review before the material advances, preventing quality risks from propagating. Shared analytical infrastructure also avoids the need to repeat or transfer testing between sites, reducing variability in results.

“Ultimately, the proximity of drug substance and drug product operations fosters a culture of integrated quality ownership, where every team member

understands how their work connects to the final product delivered to patients,” said Aldo Braca.

Accelerated Regulatory Pathway

When DS and DP operations are split across multiple sites, regulatory agencies must inspect and approve each location separately. Each site requires its own set of manufacturing authorisations, SOPs, and QMS. Coordinating across those different regulatory frameworks adds considerable overhead and risk. By integrating DS and DP manufacturing, the Latina facility streamlines regulatory pathways for fast-track approvals, reduces post-approval changes, and speeds commercial readiness.

“At Latina, inspectors can assess the full manufacturing journey in a single visit, from conjugation through final fill-finish,” said Aldo Braca. “There is one integrated quality system, one unified set of batch records, and one accountable manufacturing team. This transparency simplifies the inspection process for authorities, accelerates responses to queries, and reduces the likelihood of cross-site inconsistencies being flagged. It also streamlines CMC dossier preparation and post-approval change management, since changes affecting both drug substance and drug product can be addressed in a single regulatory submission.”

Safety by Design

The cytotoxic payloads used in conjugation are among the most hazardous substances handled in pharmaceutical manufacturing, and those handled at the Latina site have an occupational exposure limit (OEL) below 10 nanograms per cubic meter. Every transfer of these materials between facilities introduces occupational exposure risk, packaging complexity, transport hazards, and emergency response challenges across multiple jurisdictions.

“The design of the Latina plant confines the handling of HPAPI-conjugated intermediates to one containment-engineered environment with a highly trained workforce operating under a unified safety management system,” said Aldo Braca. “There is one containment strategy, one spill response protocol, one set of engineering controls – all optimised for ADC-specific hazards.”

This consolidation dramatically reduces the number of touchpoints where exposure incidents could occur and enables a more proactive, coherent approach to occupational health across the entire production chain.

Accelerated Time-to-Market

One of the most significant timelines in ADC drug development is the period between clinical batch release and first patient dosing, or between regulatory submission and commercial launch. Any inefficiency in manufacturing, such as delays at batch handover, inter-site shipping, redundant QC testing, and misaligned release schedules, directly compounds patient wait times. The resilience of the Latina supply chain reduces these delays and has meaningful impacts on time to market.

“Thanks to Latina’s integrated supply chain, we have eliminated many of these points of inefficiency,” said Aldo Braca. “Batch release decisions are made with full visibility across both drug product and drug substance, without waiting for material to arrive from a remote site. This allows a faster, more agile response to demand fluctuations or clinical trial schedule changes. For innovative oncology therapies where urgency is critical, the ability to reduce cycle time without compromising quality is not just a competitive advantage, it is a patient-centred imperative.”

BSP Pharmaceuticals has shown that the production of complex ADCs can be dependable and efficient while addressing one of the most critical challenges in oncology manufacturing.

“The expansion of the Latina site establishes a new standard for supply chain resilience and rapid product delivery,” said Aldo Braca. “For patients and partners alike, it means a more reliable, predictable supply of complex, life-saving therapies.”

What makes BSP truly unique is the design and operation of its fully integrated manufacturing site, which combines integration, flexibility, scalability, and technological depth in a way that is unparalleled in the industry.

The site offers an integrated system that ensures seamless coordination between development, drug substance manufacturing, conjugation, drug product manufacturing, fill finish, storage, cold chain management and quality control. This integration delivers multiple benefits: optimised material flows, enhanced product safety, and significant reductions in working capital, allowing clients to achieve faster, safer, and more cost-efficient pathways to market.

The co-location of development laboratories, quality control facilities, and GMP manufacturing at multiple scales allows for a smooth scale-up process. Scientists and technical experts work in close collaboration, ensuring that every step of the journey from formulation development to commercial supply is aligned and optimised. This integrated approach minimises handover gaps, quickens FDA approval, one inspection for DS and DP, reduces costs, accelerates timelines, and increases the probability of success for complex bioconjugates and next-generation modalities.

Flexibility of scale is another cornerstone of BSP’s offering, which provides a broad range of capacities that can adapt to the evolving needs of its partners. For conjugation, BSP has implemented scales from 40 grams up to 15 kilograms of mAb, enabling both small-scale clinical projects and large-scale



commercial production under one roof. This range of options demonstrates BSP's ability to serve projects at every stage from early clinical batches to global commercial launches without requiring technology transfers to multiple facilities, optimising both timelines and budgets for clients. Whether a customer requires toxicology batches, small-scale GMP-equivalent runs, or full commercial production, BSP provides a continuum of services that ensures consistency, quality, and speed.

A critical enabler of this success is BSP's internal technology transfer structure. Dedicated teams oversee projects from early development through PPQ, ensuring that knowledge, processes, and quality standards flow seamlessly across phases. This reduces the risk of scalability issues that often arise when products move from early to late stages, protecting both clients and patients from delays or failures.

The company's commitment to innovation is also evident in its approach to risk-sharing in product development. By lowering the barriers to entry for promising therapies, BSP ensures that more breakthrough products can advance to clinical testing and ultimately to patients: a tangible support from BSP to projects that carry high levels of scientific and financial uncertainty. BSP not only fosters innovation but also strengthens long-term partnerships built on trust, transparency, and shared objectives.

To back this vision, BSP's Board has approved a €700 million financed expansion plan, adding four new conjugation suites and 4 drug product filling lines. By 2030, DS



capacity will increase (to over 4,700 Kg mab/year), while DP capacity will reach over 155 million units annually. These investments will support ADCs, liposomes, RNA-based onco-vaccines, and advanced polypeptides, reinforcing BSP's role as a global leader in oncology, immunotherapy, CNS and type 2 diabetes therapeutics.

BSP Pharmaceuticals combines scientific excellence, operational flexibility, and a collaborative spirit. Its fully integrated and scalable site, extensive technical capabilities, innovative risk-sharing approach, and unwavering commitment to patient safety

clearly set BSP apart. By enabling faster, safer, and more efficient development and commercialisation of critical oncology and specialty medicines, BSP not only advances the biopharmaceutical industry, but also contributes to the global mission of improving patient outcomes.

REFERENCES

1. <https://pharmasource.global/content/antibody-drug-conjugates-adc-contract-manufacturing-market/>
2. <https://www.towardshealthcare.com/insights/antibody-drug-conjugates-adcs-cmo-and-cdm0-market-sizing>



Aldo Braca

Aldo is the President and founder of BSP Pharmaceuticals since 2006, year of the incorporation of the company. He is a member of the Advisory Board of "PM & Partners", a private equity firm specialised in investing in small and middle-sized companies. Aldo has been President of Patheon Europe, a subsidiary of Patheon Inc., since 2010 and developed the company in Europe starting from 1999. Aldo is trained as an Industrial Chemist. He is a graduate of Advanced Management Program at the Harvard Business School.



CDMO for INNOVATORS

BSP is the strategic partner for innovators, seeking a CDMO which provides an integrated full range of services in full containment from development of a proof of concept to commercial supply of cytotoxic and non cytotoxic candidates in oncology, immunoncology and immunotherapy

CAPABILITIES



BIOCONJUGATES

- Integrated supply for DS, DP and QC testing
- Single use, Stainless steel or Customized configuration
- Cold chain management from -80°C to Room Temperature
- Batch size from 10 mg to 15 Kg



LIPIDIC BULK SOLUTIONS

- Liposomes, LNP, Micelle, Nano emulsions
- Small molecules, mRNA, siRNA, Oligonucleotides, Synthetic Peptides
- Explosion Proof Equipment
- Extrusion, Microfluidics, Mixing Technologies



CYTO & NON CYTO

- Small and Large molecules
- Liquid and Lyo vials
- Isotechnology configurations (up to Oeb 6) in full containment for both categories
- Batch size from 1.000 to 250.000 vials



HEADQUARTER and MANUFACTURING PLANT BSP PHARMACEUTICALS S.p.A.

Via Appia km 65,561 04013 Latina Scalo (LT) – Italy
+39 0773 8221

bsp-pharmaceuticals.com
business.development@bsp-pharmaceuticals.com

Innovative Formulations and Processing Technologies for Oral Drug Delivery

Oral drug delivery remains one of the most important and widely adopted routes of administration in pharmaceutical development. Tablets and capsules continue to offer clear advantages in terms of patient acceptance, convenience, stability, scalability and cost-effective manufacture. Yet the science behind oral dose development has changed significantly. Today's oral medicines are increasingly expected to do more than deliver an active ingredient in a conventional immediate-release format. They must overcome solubility and bioavailability limitations, support challenging drug substance properties, enable modified or targeted release, align with paediatric and patient-centric needs and transition efficiently from early clinical supply to commercial-scale manufacture.

This evolution is being driven by the changing nature of pharmaceutical pipelines. Many contemporary small molecule candidates present formulation challenges, particularly poor aqueous solubility, limited permeability, complex solid-state behaviour or potency-related handling requirements. Poor solubility remains one of the most persistent barriers in drug development, making early understanding of API characteristics essential to maximising solubility, stability and therapeutic impact. At the same time, the industry is seeing increased interest in more complex oral dosage forms, including modified-release systems, paediatric-friendly presentations, liquid-filled capsules, amorphous solid dispersions and other enabling technologies designed to improve *in vivo* performance.

For drug developers, the key question is no longer simply whether a compound can be made into a tablet or capsule. It is whether the selected formulation and process are sufficiently robust, scalable and clinically appropriate to support the product across its lifecycle. That requires a development strategy that integrates formulation science, material understanding, process engineering, analytical capability and regulatory foresight from the outset.

Oral Delivery Remains Central – But Expectations Are Rising

The continued dominance of oral solid dosage forms reflects their practical value. They are generally easier for patients to take than injectable therapies, comparatively stable during storage and distribution and suitable for large-scale production. However, the simplicity perceived by patients often masks the complexity involved in development and manufacture. As pipelines have shifted towards more challenging molecules, the oral dosage form has had to become more sophisticated.

Recent industry analysis points to sustained growth in oral solid dose development, with innovation focused on improving drug efficacy, adherence and manufacturability through advanced delivery systems, modified-release technologies and formulation platforms that address bioavailability challenges. The sector is also seeing increased demand for CDMO support across formulation development, testing, analytical services, clinical supply and manufacturing as companies seek specialist expertise to manage greater technical complexity.

In practical terms, this means oral dose development must balance speed with scientific depth. Early clinical programmes often require rapid delivery of fit-for-purpose formulations for first-in-human studies, while later-phase programmes require deeper product and process understanding, control strategies and scale-up pathways. The most successful programmes are those in which these requirements are not treated as separate phases, but as part of a continuous development pathway.

The rise of targeted therapies and precision medicines is reshaping oral dose manufacturing. As products are increasingly developed for smaller patient populations, commercial volumes are often significantly lower than those associated with traditional blockbuster drugs. In response, manufacturers are adopting more flexible, small-scale production models, often utilising equipment and technologies traditionally associated with development-phase manufacturing.

CDMOs have been at the forefront of this transition, investing in flexible infrastructure,

advanced processing technologies and contained high-potency capabilities that enable the efficient manufacture of small-volume, high-value medicines while supporting seamless progression from development to commercial supply.

Bioavailability Enhancement: Addressing a Critical Development Challenge

One of the most prominent areas of innovation in oral drug delivery is bioavailability enhancement. A high proportion of new chemical entities present poor aqueous solubility, which can limit absorption and make it difficult to achieve therapeutic exposure through conventional formulations. In these cases, simple blending, granulation and compression may not be sufficient. Instead, more advanced formulation strategies may be required to improve dissolution rate, maintain supersaturation, stabilise amorphous forms or enhance absorption.

Amorphous solid dispersions, spray drying, hot melt extrusion, particle engineering, lipid-based systems and liquid-filled capsules are among the technologies increasingly used to address solubility and exposure challenges. Industry commentary has highlighted amorphous solid dispersions prepared through spray drying or hot melt extrusion as important tools for improving solubility and bioavailability in oral solid dosage development. These technologies are not interchangeable; each has advantages, constraints and development implications. Selection should be based on compound properties, target dose, stability profile, manufacturability, clinical objectives and commercial considerations.

For example, spray drying can be valuable where rapid solvent removal is needed to generate an amorphous dispersion with improved dissolution characteristics. Hot melt extrusion may be suitable where the API and polymer system can withstand thermal and mechanical processing.

Liquid-filled capsules, semi-solid-filled hard capsules and non-sterile oral liquids can provide efficient early-phase solutions for poorly soluble compounds, particularly where speed to clinic is a priority. Particle size reduction or other particle engineering

techniques may be appropriate where dissolution rate, content uniformity or downstream processability are limiting factors.

The scientific challenge lies not only in selecting a technology, but in understanding the formulation system. Polymer selection, drug loading, residual solvent control, physical stability, recrystallisation risk, dissolution behaviour and scale-up feasibility must all be considered. The formulation must be robust enough to support clinical supply, but also capable of evolving into a commercially viable product.

Processing Technologies: Where Formulation Meets Manufacturability

Innovative formulation design must be matched by appropriate processing technology. Oral drug delivery success depends on the ability to manufacture a product reproducibly, at the right quality, and at the required scale. This is particularly important for complex formulations, highly potent compounds or products requiring tight control of critical quality attributes such as dissolution, assay, content uniformity, impurity profile, stability or release performance.

Traditional oral solid dose processes, including blending, granulation, compression, encapsulation and coating, remain essential. However, the level of process understanding required has increased. Developers must understand how material attributes and process parameters influence product performance. This deeper understanding has also enabled the incorporation of novel and functional excipients that can enhance product performance while maintaining robust and reproducible manufacturing processes.

This includes properties such as particle size distribution, polymorphic form, flowability, glass transition temperature, compressibility, moisture sensitivity and excipient compatibility. It also includes process variables such as mixing time, granulation endpoint, drying conditions, compression force, coating parameters and environmental controls.

Advanced processing approaches can help address specific development challenges. Wet granulation may improve flow and content uniformity for low-dose products. Dry granulation can be advantageous for moisture- or heat-sensitive compounds. Coating technologies can support taste

masking, moisture protection, enteric release or modified-release performance.

Encapsulation may provide flexibility during early development, especially where dose range exploration is required. For potent compounds, contained processing and appropriate facility design are central to operator safety, product quality and cross-contamination control.

Quality by Design and the Move Towards Deeper Product Understanding

The regulatory and scientific direction of travel is clear: quality should be built into the product and process, not tested in at the end. ICH Q8(R2) provides a framework for pharmaceutical development and describes how greater understanding of formulation and manufacturing sciences can support flexible regulatory approaches. The FDA's Q8(R2) guidance further describes the principles of Quality by Design, including the value of development knowledge and process understanding.

For oral dosage forms, Quality by Design begins by defining the Quality Target Product Profile. What should the product do? What dose, release profile, stability, presentation and patient requirements must it meet? From there, developers identify critical quality attributes and assess which material attributes and process parameters may influence them. Design of experiments, risk assessment, predictive modelling and analytical characterisation can then be used to build a more complete understanding of the product and process.

This approach is particularly valuable when dealing with complex oral formulations. For a bioavailability-enhanced product, for example, the critical quality attributes may include amorphous content, dissolution profile, residual solvent, particle morphology, impurity formation and physical stability. For a modified-release tablet, they may include release rate, coating uniformity, tablet hardness, friability and robustness under different physiological conditions. For a highly potent product, containment, cleaning strategy and cross-contamination control become central to the development plan.

A QbD approach does not necessarily mean longer timelines. In many cases, it can reduce risk by identifying potential failure points earlier, avoiding repeated reformulation and supporting more efficient scale-up. The value is in making development decisions based on scientific evidence rather than trial and error.

Analytical Science as an Enabler of Oral Dose Innovation

Analytical capability is often the unsung enabler of successful oral drug delivery. Innovative formulations require robust methods to characterise both the API and finished dosage form. This may include solid-state characterisation, assay and impurity testing, dissolution method development, stability studies, content uniformity, residual solvent analysis, water content, particle size analysis and physical characterisation of intermediate materials.

For amorphous solid dispersions, analytical science is essential to confirm amorphous form, detect recrystallisation, monitor stability and understand dissolution behaviour. For modified-release formulations, discriminatory dissolution methods are critical to link in vitro performance with product quality and, where possible, *in vivo* behaviour. For paediatric formulations, analytical methods must often support dose flexibility, taste-masking assessment, stability and compatibility with administration routes. For potent compounds, analytical procedures must be aligned with containment and safe handling requirements.

Patient-Centric Formulation: Beyond Manufacturability

Innovation in oral drug delivery is not solely about overcoming technical development barriers. It is also about improving the patient experience. Patient-centric dosage form design considers how the medicine will be used in real life, including swallowability, dose burden, taste, dosing frequency, packaging, administration with food or liquids, and suitability for paediatric, geriatric or other specialist populations.

Modified-release technologies can reduce dosing frequency and support adherence. Mini-tablets, multiparticulates, oral liquids or sprinkle formulations may help paediatric or dysphagic patients. Taste masking can be decisive for adherence, particularly in children. Smaller tablet size, improved coating or alternative capsule formats may make a meaningful difference for patients managing chronic therapy.

The challenge is that patient-centric features must be scientifically and commercially feasible. A formulation that is ideal for the patient but unstable, difficult to manufacture or hard to scale will struggle to progress. Conversely, a formulation that is easy to manufacture but poorly suited to patient needs may not deliver the intended

therapeutic benefit in practice. The optimum development strategy therefore considers patient use, product performance and manufacturing reality together.

This is especially important for products intended to move from early phase to commercialisation. Early development formulations may be fit for initial clinical assessment, but developers should maintain a view of the likely commercial presentation. Decisions around excipients, capsule versus tablet, liquid versus solid, release profile and packaging should be informed by the long-term target product profile wherever possible.

Scalability: Designing with the End in Mind

A recurring challenge in oral drug delivery is the transition from small-scale development to larger-scale GMP manufacture. A process that works well at laboratory scale may behave differently when batch size, equipment geometry, mixing dynamics, drying efficiency or compression speed changes. Scale-up risk can be particularly significant for complex formulations, low-dose products, poorly flowing materials, moisture-sensitive APIs or modified-release systems.

Where precision medicines is driving towards lower commercial volume this is influencing how scalability is defined. Rather than simply increasing batch size, developers must ensure processes remain robust across smaller manufacturing scale and equipment. Flexible equipment platforms and process design are enabling efficient production for targeted therapies, orphan medicines and other lower-volume products, while maintaining the quality, control and supply reliability expected of commercial manufacture.

Designing with scalability in mind does not mean over-engineering early clinical formulations. It means making informed choices that preserve future options. For example, selecting excipients with a strong regulatory and supply track record, understanding whether a process is likely to be transferable, choosing analytical methods capable of supporting later-phase control strategies, and documenting development rationale clearly.

The Role of Partnership in Modern Oral Dose Development

As oral formulations become more complex, the role of the CDMO is also changing. Sponsors are not simply looking for capacity; they are looking for scientific input, problem-



solving, regulatory awareness and practical manufacturing experience. The most effective partnerships are built around transparent technical dialogue. This includes early discussion of molecule properties, clinical objectives, dose projections, formulation risks, timelines, regulatory expectations and commercial ambitions.

A capable CDMO should be able to challenge assumptions constructively. Is an immediate-release capsule sufficient for first-in-human studies, or is an enabling technology required? Is the selected bioavailability approach scalable? Are there stability risks that should be addressed before GMP manufacture? Is the analytical method sufficiently discriminatory? Can the process accommodate future dose strengths? Are there containment implications? What data will be needed to support regulatory submissions?

These questions are not barriers to progress; they are safeguards against avoidable development risk. In oral drug delivery, speed is important, but speed without scientific understanding can create costly delays later. A disciplined development strategy can support both efficiency and robustness.

Looking Ahead: A More Integrated Future for Oral Drug Delivery

The future of oral drug delivery will be shaped by continued innovation in formulation science, processing technologies, data-driven development and patient-centric design. Artificial intelligence, predictive modelling and digital tools are expected to play a greater role in formulation screening and process optimisation, although these tools will need to be grounded in high-quality experimental data and practical manufacturing knowledge.

However, the fundamentals will remain the same. A successful oral medicine must deliver the right dose, at the right rate, with

consistent quality, in a form that patients can use and manufacturers can reliably produce. Innovation is valuable when it solves a real development or patient problem. The goal is not complexity for its own sake, but purposeful formulation and process design.

For companies developing oral medicines, the opportunity lies in integrating enabling technologies earlier, applying QbD principles pragmatically and selecting experienced development partners with the scientific and operational capability to support the product across its lifecycle. As pipelines continue to challenge conventional formulation approaches, this integrated model will become increasingly important.

Advances in formulation science and processing technology are enabling developers to address increasingly complex molecules while delivering robust, scalable and patient-centric oral medicines.

Oral drug delivery has always been central to pharmaceutical development. What is changing is the level of science required to make oral delivery work for today's molecules and tomorrow's patients. Through advanced formulation technologies, robust processing strategies and lifecycle-focused development, the industry can continue to expand what is possible through the oral route – delivering medicines that are not only manufacturable, but meaningful for the patients who depend on them.



**Sander
van den Ban**

Director | Operations, Manufacturing,
Almac Pharma Services



Your **trusted** CDMO.



Almac Group is delighted to be exhibiting at CPHI Milan 2026.

Join our team at **Booth 6A28** to find out more about our extensive range of integrated services to the pharma and biotech sectors globally.

almacgroup.com

From OEL to Commercial Supply: Designing Robust High-Potency Oral Solid Manufacturing

Highly potent APIs are becoming more significant across the pharmaceutical development pipeline. Market estimates vary, but the direction is consistent: the global HPAPI market hit around USD 29.87 billion in 2025 and forecasts growth to USD 48.29 billion by 2033^[RG1.1], driven by demand for targeted medicines, oncology therapies and other potent molecules.¹

For oral drug products, however, the challenge is not simply to handle HPAPI safely. Whether the intended medicine is a tablet, capsule, or liquid formulation, success depends on integrating toxicology, formulation science, process engineering, containment and lifecycle planning from the outset.

An isolator, negative-pressure suite or stated occupational exposure band (OEB) may be an important part of the answer. None, in isolation, demonstrates that a product can be manufactured safely, reproducibly and at commercial scale. The more meaningful test is whether the proposed operating model protects people, prevents cross-contamination, preserves critical quality attributes and remains practical through development, technology transfer and routine supply.

Starting With Exposure

Containment discussions often begin with an OEB designation, such as OEB 4 or OEB 5. Although useful as an operational shorthand, OEBs are not universally harmonised across the industry and should not replace compound-specific assessment.

The starting point is the occupational exposure limit, or OEL: the average airborne concentration of an API considered acceptable over a defined period, commonly an eight-hour time-weighted average. The OEL defines the exposure outcome that a control strategy must achieve. It does not prescribe a particular piece of equipment, room classification or facility layout.

Other toxicological limits also inform manufacturing decisions. Permitted daily exposure (PDE), also known as acceptable

daily exposure (ADE), is relevant to the assessment of product carryover, cross-contamination and cleaning limits in multiproduct facilities. The no-observed-effect level may contribute to defining an acceptable daily exposure where appropriate toxicology data are available.

These distinctions have practical implications. Two products within the same broad OEB may require different containment strategies because they differ in batch size, particle characteristics, powder flow, dose, route of administration, process route and handling requirements. A fine, cohesive and electrostatically charged powder handled through multiple open transfers presents a different risk profile from a material processed through closed charging and transfer systems.

A robust new-product-introduction process should therefore assess the molecule before it reaches the manufacturing floor. The review should bring together toxicology, pharmacology, OEL and PDE data, proposed batch size, formulation route, equipment requirements and operational tasks. A risk assessment can then identify where material could be released, where product may be retained, and what controls are required before development or manufacture begins.

Containment as an Operating System

For potent products, containment is often described in terms of equipment or facility

features. This risks missing the broader point: containment is the demonstrated performance of the complete operating system.

Exposure and cross-contamination risks should be assessed across four principal pathways:

- Airborne transfer of dust or aerosol.
- Mechanical transfer through equipment, materials or movement between areas.
- Personnel transfer, including garments, gloves and movement patterns.
- Product retention on contact surfaces, seals, components or difficult-to-clean locations.

The highest risks frequently occur at interfaces between operations. Material receipt, dispensing, charging, transfer, sampling, discharge, cleaning, maintenance and waste handling can all create exposure opportunities, even when the principal unit operation is enclosed.

Primary containment should be positioned as close as possible to the material source. Suitable equipment operates under negative pressure and is designed to prevent release during normal processing. Secondary containment is then provided by the surrounding facility, including air-management systems, pressure cascades, airlocks, access controls, cleaning and decontamination areas, and appropriate filtration.





granule-size distribution, fines and final tabletability. Development must therefore establish conditions that produce not simply acceptable granules, but a consistent final dosage form with the required hardness, friability, disintegration, dissolution and content uniformity.

The risk profile for oral liquids is different. They can improve administration and dosing flexibility, but may be more vulnerable to degradation and microbial growth, increasing demands on formulation design, preservation, packaging compatibility and dose accuracy. With potent APIs, the greatest containment risk is often at charging and wetting: once the material is fully wetted, airborne exposure potential is substantially reduced.

Fine powders can disperse during transfer, and static charge may intensify dusting. Poorly controlled liquid addition can cause splashing or aerosolisation, while particle size, hydrophobicity and wettability can delay dispersion or cause clumping. Contained charging and closed processing must therefore be designed alongside order of addition, mixing energy, wetting rate and vehicle selection to achieve safe dispersion without compromising product quality or manufacturability.

Building Containment into QbD

Quality by Design provides a useful structure for integrating these decisions. It begins with the quality target product profile and identifies the critical quality attributes that the finished medicine must achieve. Development work then determines the critical process parameters that affect those attributes and establishes a proportionate control strategy.

This layered model is more robust than relying on a negative-pressure room alone. It also provides a framework for evaluating what happens if containment is breached. Air handling, dust collection, room segregation and safe material flow are important, but their purpose is to support the primary barrier, not to substitute for it.

The strategy must account for normal and abnormal operations. It is not enough to assess a process while equipment runs as intended. Teams should consider foreseeable interventions: material charging, sampling, container changes, clearing a blockage, responding to alarms, replacing components, cleaning and maintenance. A process that is technically enclosed but routinely requires manual intervention may introduce operational weakness.

PPE remains important for work within a controlled environment and for response to a system failure. It should not, however, be treated as the primary containment barrier during normal operations. Where potency demands a high level of control, engineering and process design must do the bulk of the protective work.

Oral Formulation Changes the Risk Profile

For oral products, formulation choice determines where and how containment must perform. The aim is not only to prevent material release, but to do so while maintaining the critical quality attributes of the finished medicine.

For solid oral dosage forms, key risk points include dispensing, blending, milling, granulation, compression or encapsulation, sampling and cleaning. Fine powders can become airborne during charging and discharge, while particle size, electrostatic

charge, cohesiveness and flowability influence dusting, segregation and material hold-up. For low-dose products, containment must also protect blend uniformity and avoid transfer steps that increase segregation risk.

Roller compaction illustrates the connection between formulation, process design and containment. In this dry-granulation route, a powder blend is compacted between counter-rotating rollers into a ribbon, then milled into granules for tableting, encapsulation or sachet filling. It can be valuable where direct compression is unsuitable and wet granulation creates stability concerns, particularly for moisture-sensitive, heat-sensitive or poorly flowing materials. Its integration with contained feeding, sealed transfer and milling can also reduce open powder handling.

However, enclosure alone does not make the process robust. Compaction force, roller gap and speed, feed rate and milling conditions affect ribbon density,



For a high-potency programme, containment must sit within this framework. Early formulation and process studies should identify not only whether a product is technically feasible, but also where dust may be generated, what material-handling steps are required, where manual intervention may occur, how samples can be obtained and how equipment can be cleaned.

This approach can reduce the risk of developing a process that performs well in a laboratory but cannot be transferred safely or efficiently into a contained manufacturing environment.

Process analytical technology can help where inline or real-time information reduces the need to open equipment. Automation and programmable adjustments can also reduce manual intervention, provided the process is well understood and teams can manage deviations. The technology alone is not the strategy. Its value lies in delivering relevant process information and enabling timely control of conditions that affect both product quality and containment performance.

For roller compaction, structured design-of-experiments work can define how compaction force, roller gap, roller speed and feed conditions affect ribbon properties, granule attributes and final-tablet performance. This creates a stronger basis for establishing a design space and identifying the parameters that must remain under control as a process moves towards larger-scale manufacture.

Designing for Transfer and Commercial Supply

A development batch conducted safely does not prove that a process is commercially sustainable. Scale-up may change material quantities, feed behaviour, dust load, transfer routes, cleaning burden and the practical nature of interventions.

Containment therefore needs to be addressed explicitly during technology transfer. The transfer package should cover more than formulation composition, manufacturing instructions and analytical methods. It should capture material flow, equipment interfaces, containment-critical steps, sampling requirements, cleaning rationale, waste handling and anticipated deviations.

A gap analysis is valuable before transfer begins. Differences in equipment geometry, feeder design, vessel size, transfer routes and cleaning access can alter powder behaviour



and exposure potential. Identifying these differences early makes it possible to determine whether process parameters, equipment arrangements or operating procedures need to change before batches are executed at the receiving site.

Cleaning is particularly important in multiproduct facilities. Potent materials may remain on product-contact surfaces, seals, transfer assemblies or inaccessible areas of equipment. A sound cleaning strategy begins during new-product assessment and is informed by toxicology, product characteristics, equipment design and the risk of carryover to the next product.

Appropriate swab and rinse sampling methods, cleaning verification and lifecycle validation provide the evidence that the strategy remains effective. The aim is not necessarily to require a dedicated facility for every potent product. It is to establish whether the facility, equipment train, cleaning programme and operating procedures can provide an appropriate, demonstrable level of control.

Questions That Matter

A stated OEB capability is only a starting point for sponsor due diligence. The questions that determine whether a manufacturing strategy is truly robust are more specific:

- Has the compound been assessed using appropriate toxicological and pharmacological information before site acceptance?
- How will the OEL be translated into controls across dispensing, transfer, processing, sampling, cleaning and waste?

- Does the process protect both operator safety and the product's critical quality attributes?
- How are routine and non-routine interventions managed?
- What evidence supports containment performance at the intended scale and for comparable operations?
- How will containment-critical knowledge transfer from development into clinical and commercial manufacturing?
- How are cleaning, carryover and multi-product risk managed over the product lifecycle?

High-potency oral manufacturing is not defined by an OEB label, a facility claim or one item of containment equipment. It is defined by the ability to translate toxicological requirements into a repeatable manufacturing system: one that protects operators, preserves product quality and remains viable from the first development batch through commercial supply.

REFERENCES

1. High Potency Active Pharmaceutical Ingredients Market (2026 – 2033) <https://www.grandviewresearch.com/industry-analysis/high-potency-active-pharmaceutical-ingredients-hpapi-market>



David O'Connell

Director, Scientific and Technical Affairs at PCI Pharma Services.

Today's CDMO.

Inspired by tomorrow.

Our CDMO services include:

- Development & Manufacturing
- Clinical Trial Services
- Advanced Drug Delivery & Drug-Device Combination Products
- Commercial Packaging Technology

Supported by *speedsolutions*™



AI in Lyophilised Product Development: Opportunities and Limitations

Artificial intelligence (AI) is beginning to influence many aspects of pharmaceutical development, including areas once thought too specialist or product-specific for generic digital tools. In lyophilisation (also known as freeze-drying), AI can already help teams frame protocols, suggest first-pass cycle parameters and organise early technical thinking more quickly. That makes it useful, particularly when a project is still taking shape and development teams are deciding what to test first.



Yet freeze-drying remains a process governed by formulation behaviour, critical temperature data, equipment characteristics and product quality requirements that cannot be inferred reliably from pattern recognition alone. For scientists working on biologics, vaccines, peptides and other sensitive products, the key question is not whether AI has a role, but what are its limitations. Used well, it can support the early stages of development. Used uncritically, it can create false confidence in outputs that still require experimental confirmation and expert interpretation.

Why AI is Entering Lyophilisation Process Development

Artificial intelligence has entered pharmaceutical workflows because it offers the speed research and development teams are keen to harness. AI can save valuable time by summarising information quickly, organising technical ideas into a useful framework, and generating draft protocols and project reports. As a niche part of this drug development workflow, freeze-drying is no exception. Lyophilisation projects involve recurring questions around cycle design, formulation options, analytical methods, equipment choice and scale-up strategy, so it is unsurprising that AI is now being tested as a practical support tool in this area. When asking current AI Large Language models, a scientist can receive a draft cycle, a list of analytical considerations or a summary of typical formulation factors within seconds.

However, these useful responses should not be confused with scientific understanding.

While AI can help structure analysis and identify patterns in the information available, it does not yet understand how a specific formulation behaves under freeze concentration or where a true process limit lies for lyophilisation.

“What matters in freeze-drying is not whether a lyophilisation cycle looks plausible, but whether it stands up to product-specific data, experimental testing and the realities of scalable manufacture,” confirms Dr Kevin Ward.

Where AI Can Genuinely Help

For that reason, the real value of AI is not to completely replace the role of scientists, but to act as a tool to increase efficiency in the R&D workflow. The strongest use case for AI in freeze-drying is at the front end of development, where it can help a team create a sensible starting framework before experimental work begins. That might include drafting protocols, creating Gantt charts for

project timelines, generating a list of common excipients for formulation development, or suggesting a rough first-pass cycle concept for discussion.

It can also help non-specialists understand the terminology and ask more informed questions before speaking with scientists, engineers or CDMO partners. That can be especially useful in cross-functional teams, where discussions often involve people from formulation, analytical, manufacturing and regulatory backgrounds. Even so, its role needs to stay in proportion. AI works best as a tool for early thinking, communication and preparation. It is far less reliable when its outputs are treated as evidence-based conclusions.

Why Freeze-Drying Remains Product-Specific

In early development, AI is most useful as a practical starting point: it can help teams move faster, but it cannot replace scientific



5

Reasons

to Choose
Biopharma Group
as your Trusted
Pharma & Diagnostics CDMO Partner
for Lyophilised Products
& Liquid Formulations



1 EXPERTISE

2 FLEXIBILITY

3 FAST TURNAROUND

4 COMPETITIVE PRICING

5 QUALITY CONTROL & COMPLIANCE



Biopharma Group's Pillars of Excellence

Discuss your requirements with a CDMO specialist

www.biopharmagroupcdmo.com

judgment. That matters in lyophilisation, where plausible outputs can be accepted too quickly if they are not rigorously tested, and where the knowledge base is niche and not readily available online. Freeze-drying remains highly product-specific, with the physicochemical behaviour of each formulation shaping what kind of cycle is safe, robust and commercially viable. Monoclonal antibodies, peptides and vaccines may all require lyophilisation for stability, but they cannot be developed using identical process. Even with a purpose-built formulation, confident cycle design still depends on understanding the thermal properties of the mix and its associated critical temperatures such as collapse temperature, eutectic melting and glass transition. Without that data, the process window is inferred rather than defined.

That is why analytical techniques such as Freeze-Drying Microscopy (FDM) – Lyostat analysis – and Modulated Differential Scanning Calorimetry (MDSC) remain central to development: they provide product-specific data rather than generalised assumptions. They help establish suitable product temperatures during the freeze-drying process; whether additional annealing steps are required for largely crystalline systems; and what margin may exist between a robust process and a risky one. Equally important is the empirical evaluation that follows lyophilisation. Cake appearance, residual moisture and reconstitution behaviour are core indicators of whether the chosen process has produced a usable and stable product. AI models can describe these considerations but cannot replace the experimental work required to define them for a novel formulation. This limitation goes to the heart of why lyophilization remains a hands-on scientific discipline rather than a text-generation exercise.

Formulation, Scale-Up and Regulatory Limits

The same principle applies to formulation development. Though AI can be a useful co-pilot in the earliest stages of cycle thinking, formulation work is where that role narrows considerably. A wide range of excipients are used to modify certain aspects of a liquid formulation to make it 'lyo-ready', with a goal of improving functionality, stability, mechanical strength and solubility in the dry state. Formulation design requires an understanding of molecular behaviour, excipient interactions, physical stability, chemical stability and how the product must perform after drying and reconstitution. How these excipients interact with the liquid



formulation is extremely product specific, and current AI systems lack the intricate knowledge to design these formulations from scratch. A proposed formulation may sound plausible in theory but prove unsuitable once tested because it protects one quality attribute while compromising another; supports acceptable cake structure while introducing problems in reconstitution; or appears stable under only specific conditions.

These problems cannot be resolved reliably through generic pattern matching but depend on data, interpretation and trade-offs. Formulation development therefore remains rooted in laboratory work and expert review, with AI-generated formulation suggestions treated with caution. Unlike a broad process outline, a formulation recommendation can imply a level of precision and suitability that simply has not been earned.

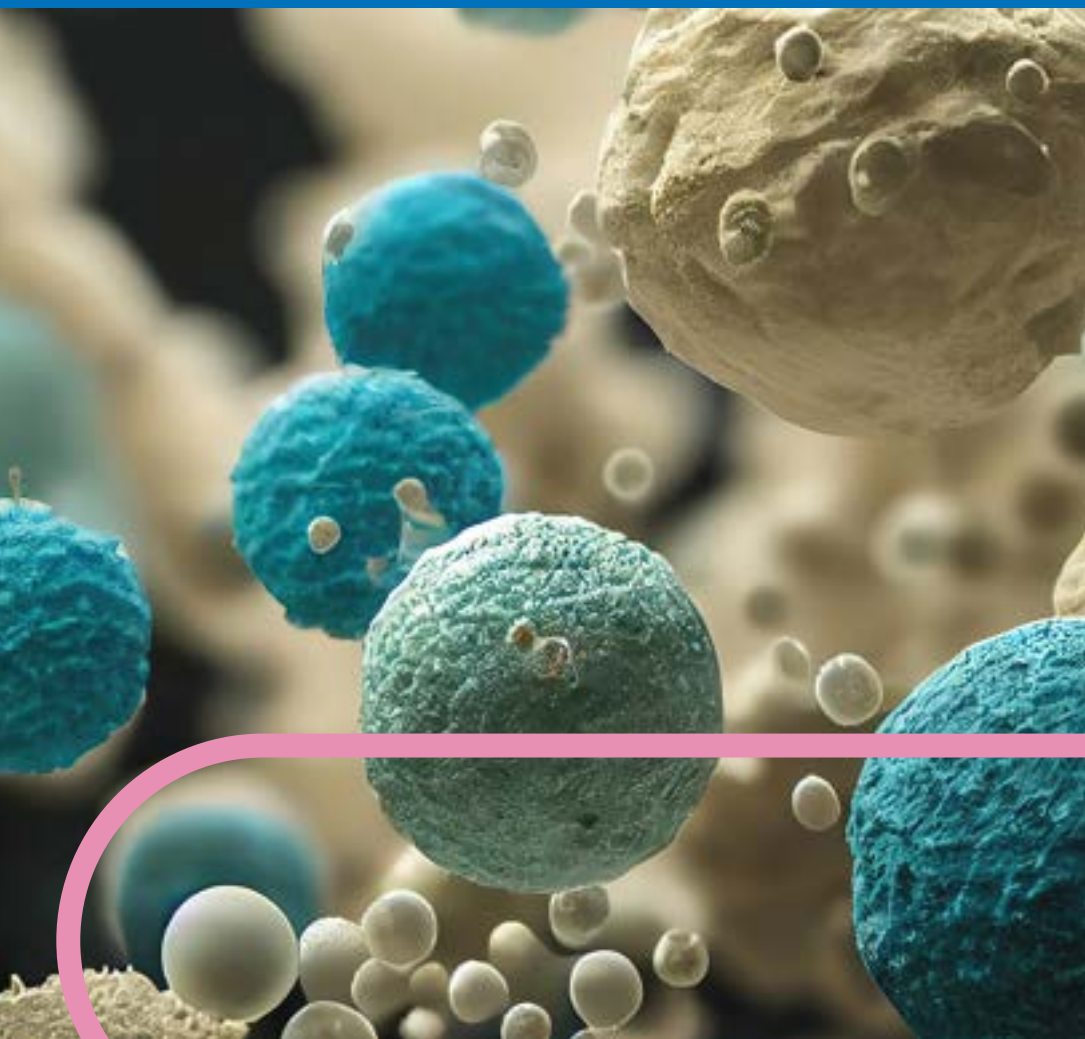
Another area where AI reaches its limits is equipment and scale-up. Freeze-drying happens on real systems with their own behaviour, constraints and performance characteristics. Not all freeze-dryers operate in the same way, and those differences become increasingly important when a process moves from laboratory feasibility to pilot, clinical or GMP manufacture. Shelf heat transfer, condenser capacity and chamber pressure all influence how a cycle performs in practice. A generic cycle may look technically possible but still fail to deliver the desired balance of product quality, reproducibility and efficiency when transferred to a specific machine or different laboratory environment.

This is one of the clearest examples of the gap between plausibility and robustness. An AI-generated cycle may include temperatures

and pressures that appear sensible at first glance and even avoid obvious technical errors. Yet if it cannot account for the behaviour of a given system, it cannot reliably predict how long drying will take, how evenly the load will behave, or whether product temperature will track safely through the critical parts of the cycle. All of these variables will change at different scales, with larger batch sizes having different thermal properties (greater thermal lag and longer drying times), meaning a cycle developed for 1000 vials may not be suitable for a batch of 10000 vials. Predictions can be made by machine learning models to determine additional drying times/temperature changes, but these conditions will always need to be validated in real-world environments.

Differences in equipment type and batch size affect throughput, cost, transferability and confidence in the process. A development team needs a cycle to perform consistently and do so within an acceptable commercial framework. That level of judgment still depends on experience, data and equipment-specific understanding.

Regulatory and quality considerations reinforce the same conclusion. One of AI's most convincing traits is that it can produce language that sounds polished, structured and professional. In technical and regulated environments, that can be helpful for drafting and organisation but can also be misleading. AI models do not always distinguish well between robust scientific information and weaker source material, especially as peer-reviewed literature in the field of lyophilisation is not as abundant as other sections of the pharmaceutical industry. The result can be inconsistency, overconfidence



The workhorse of antimicrobials

In need of safe and reliable control against bacteria, fungi, and viruses?

With its unmatched broad-spectrum efficacy at very low concentration, Benzalkonium Chloride is known as the **workhorse of antimicrobials**. As a surfactant, it mixes well in both aqueous and oil-based formulations, making it a versatile choice for multi-dose applications.

Our Benzalkonium Chloride is manufactured following the cGMP guide ICH Q7 for APIs. Get peace of mind with full traceability, high product purity, full pharmacopoeia compliance (PhEur, USP/NF, JP, ChP), audit access, and 30+ years of cGMP manufacturing experience.

Scan to obtain samples and discover how Benzalkonium Chloride can work for you.



novonordiskpharmatech.com

enabling better

**Novo Nordisk
Pharmatech A/S**



or recommendations that require substantial correction. In pharmaceutical development, regulators and quality teams are interested in whether the underlying process understanding is real, traceable and supported by data. Documentation is only as strong as the development logic behind it.

This is particularly relevant in areas such as CMC (Chemistry, Manufacturing, and Controls) strategy, analytical validation planning and technology transfer. AI may assist with drafting internal text or helping teams structure a submission narrative, but it does not remove the need for scientific ownership. Development decisions must still be justified through evidence and process choices understood in context. Transfer activities must still reflect what the product and equipment have actually shown in practice. In that sense, AI can speed up the packaging of information, but it cannot replace the responsibility carried by scientists, engineers and quality professionals. The more regulated the environment, the more important that distinction becomes.

A Practical Comparison: AI Machine Learning Model Versus Expert Design

A useful way to assess these boundaries is through direct comparison. In a case study ChatGPT 4 was prompted as follows: "Simulate a freeze-drying cycle trace for a 10% Dextran solution in a DIN10R Vial with a 2ml fill and present as a graph". The output was then directly compared to a recipe designed by experienced lyophilisation scientists for the same concentration, fill volume and container size.¹ The comparison is valuable because it moves the discussion away from abstract debate and into a real development scenario. Instead of asking whether AI can provide recommendations about the freeze-drying process, it asks whether AI can fully simulate a cycle that is genuinely efficient and robust in practice.

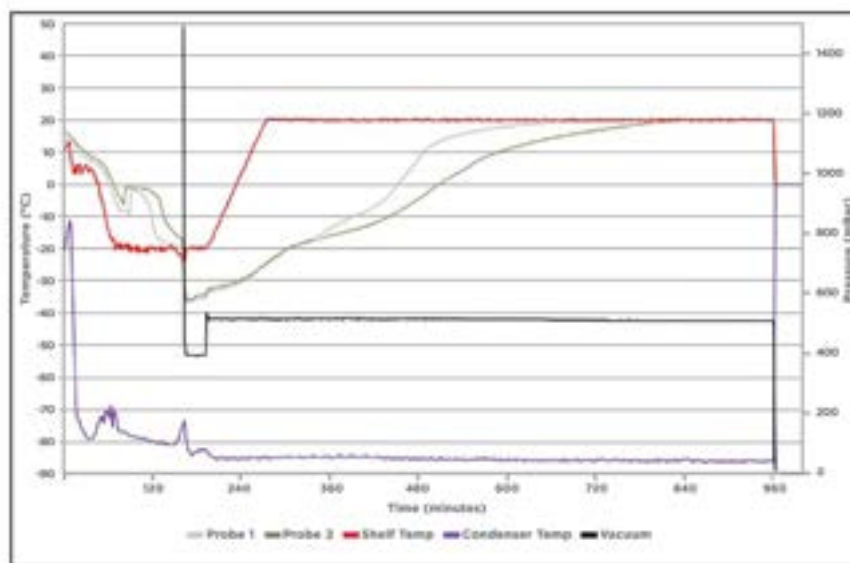


Figure 1: Graph showing cycle designed at Biopharma Group

Based on that comparison, the answer is nuanced. The AI-generated output was not worthless: on the contrary, it provided a reasonable starting point and included viable shelf temperatures and chamber pressures. This is significant, as it shows that AI can already contribute something useful at the beginning of a project. It can produce a shape for discussion, and in some cases that may save time. Where the limitations became more obvious was in the detail that separates a draft from a development-ready process. In the case study, the simulated recipe was less reliable in its representation of product temperature change over time, the length of the secondary drying step and the overall cycle duration. Those issues impact directly on cycle efficiency, process confidence and how practical the recipe would be in a real setting. This can also lead to product failure by providing process parameters that are not just inefficient, but unsuitable for the specific product being freeze-dried.

The reported outcome was that the expert-designed cycle produced visually excellent cakes using a process approximately half the length of the simulated AI cycle. That is the most telling part of the exercise. It suggests that AI can help establish a starting framework, but not yet the kind of optimised, experimentally informed process that experienced scientists can create when working from data and practical understanding. Put another way, the AI cycle was plausible, but the expert cycle was purposeful.

"Efficiency matters in lyophilisation," emphasises Dr. Ward. "A cycle that is unnecessarily long can affect capacity, cost and commercial viability. For a development team, the difference between a workable concept and an efficient, scalable process is often where the real value lies."

The case study also highlights a broader lesson. AI is most convincing when it produces outputs that are close enough to good practice to look dependable. That is precisely why disciplined use matters. When a result is broadly reasonable, the temptation is to move forward without sufficient challenge. In highly specialised development work, this is where risk begins. The real danger is that AI can generate answers that appear sufficiently credible to delay the moment when deeper scientific scrutiny is applied.

Where AI Fits Today

A more productive way forward is therefore neither uncritical enthusiasm nor blanket rejection. AI should be used in lyophilisation in proportion to what it can genuinely do

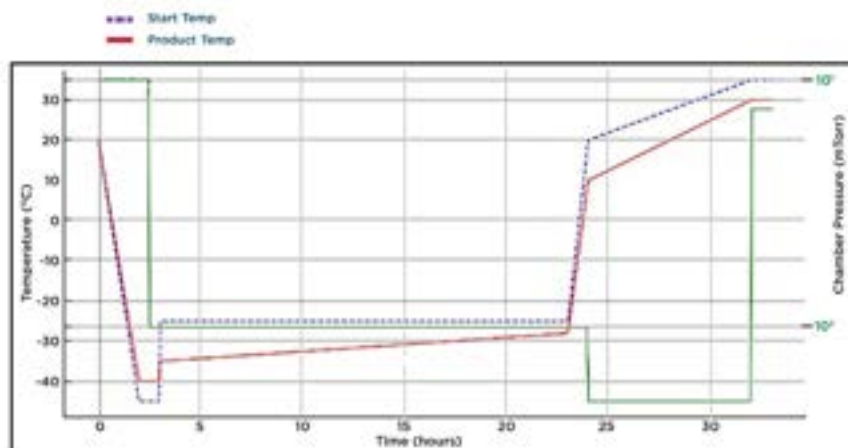


Figure 1: Graph showing simulate freeze-drying cycle conditions using ChatGPT 4

well. At present, that means helping teams begin faster, structure ideas more clearly and prepare for experimentation more efficiently. It does not mean bypassing formulation studies, critical temperature

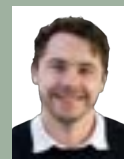
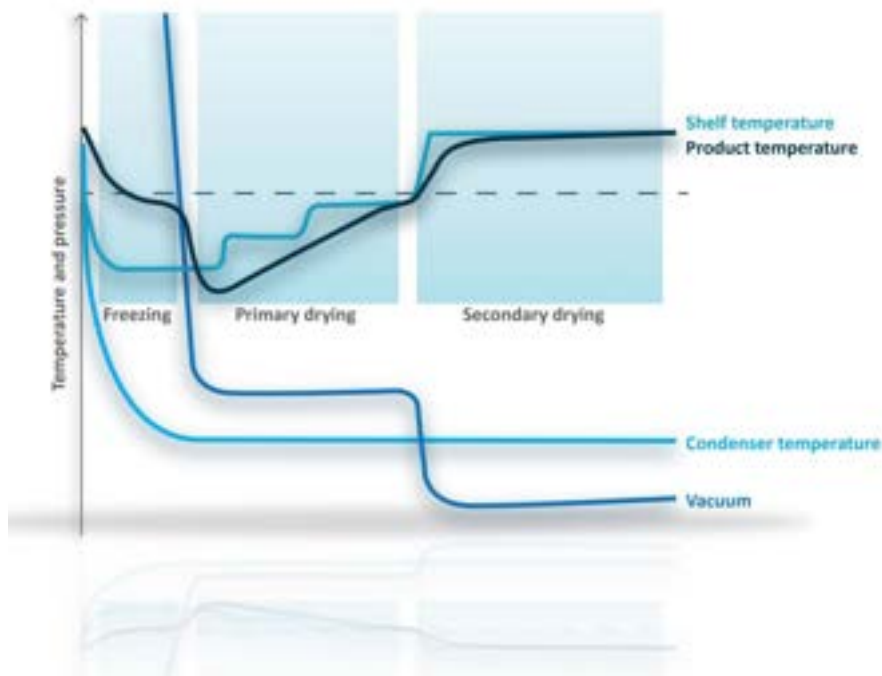
determination, empirical cycle development or equipment-specific review. A sensible workflow is AI-assisted rather than AI-directed. The tool can support preparation and communication, but scientific decisions

should remain firmly anchored in data-led human judgment.

Viewed in that light, current machine learning models already have a meaningful place in freeze-drying cycle development. It can reduce friction at the start of a project and make some technical tasks more accessible. At the same time, lyophilisation remains a product-specific, evidence-driven process in which performance, quality and transferability cannot be secured through generic outputs alone. For all the progress AI has made, there is still no substitute for the combination of analytical testing, practical development knowledge and critical scientific interpretation that robust freeze-drying requires.

REFERENCES

1. 'Leveraging AI as a tool for freeze-drying process development' at <https://biopharmagroupcdmo.com/articles-resources/leveraging-ai-as-a-tool-for-freeze-drying-process-development/>



**Sam
Woodyard**

Sam Woodyard is a Research Scientist at Biopharma Group, specialising in freeze-drying formulation, cycle development, project management and pre- and post-lyophilisation analysis.



**Erin
Kuhn**

Erin Kuhn is Head of Pharma R&D Sales at Biopharma Group, supporting pharmaceutical companies with the handling, processability and scalability of liquid and freeze-dried formulations.



**Dr. Kevin
Ward**

Dr. Kevin Ward is Director of R&D at Biopharma Group, with extensive experience in freeze-drying process development, formulation support and analytical characterisation across pharmaceutical applications.

