



From Bench to Commercial Reality:

Development of
Complex Formulations



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Executive Summary

Decades of medicinal chemistry have produced an unprecedented pipeline of potent, precisely targeted drug candidates, yet an estimated 70 - 90% of them are almost insoluble, and many are unstable, impermeable, or toxic at effective doses. Even when a formulation works at the bench, it hasn't historically survived scale-up, sterilization, and steady GMP manufacturing.

New frontiers in drug delivery are emerging to enable development of candidates previously limited by formulation challenges. **Complex formulation technologies**, including nanocrystals, lipid nanoparticles, liposomes, polymeric micelles, and long-acting injectables are becoming increasingly important across drug development pipelines. Complex generics alone are projected to have a market potential of \$170 billion by 2035, with demand for high-potency API manufacturing climbing in parallel. The decisive advantage is shifting to those who can map the design space around a working formulation, and hold it through commercial production.

This paper explores why complex formulations matter now, surveys the technology platform landscape, and confronts the bench-to-commercial translation gap through two cases: an amikacin liposome formulation that demonstrated improved performance relative to the reference product across the evaluated attributes, and nanocrystals that lifted the achievable ocular concentration 250-fold while holding their polymorph intact through terminal sterilization. Across the platforms, four capabilities stand out: a flow-controlled system for nanomedicines, twin precipitation and milling routes for nanocrystals, a standardized workflow for oral peptides, and a long-acting injectables with single-injection and accelerated-release advantages. The paper closes with the regulatory, engineering, and GMP infrastructure at Asymchem that enables this transition.



Why Complex Formulations Matter

Industry estimates that 70 to 90% of compounds in today's development pipelines are almost insoluble, followed by poor permeability, instability, and dose-limiting toxicity.¹ A molecule might work in principle; **however, clinical performance depends on successfully bridging the gap between the drug product and its intended site of action.** Complex formulations address that gap by changing what the molecule can do. Their value shows up in three places.

Improved drug exposure and therapeutic performance. Nanotechnology can improve the solubility of poorly soluble drugs and improves bioavailability. Encapsulation shields the drug in vivo, while targeted, controlled delivery concentrates exposure where it is needed; reducing systemic toxicity and widening the therapeutic window.

Better adherence and convenience. Long-acting injectables and oral extended-release systems cut dosing frequency from daily to weekly or monthly, while holding plasma concentrations steady, avoiding the peaks and troughs.

Addressing unmet formulation needs. Complex formulations are needed to solve pharmacology that demands a specialized route, a more complex API design, or a workaround for poor solubility, permeability, toxicity, or stability. Highly potent APIs increasingly fall into this category: compounds so active that safe containment and precise delivery become formulation challenges in their own right.

Positive outlook for complex formulations' projected market value reflects its rise in demand. The complex generics segment is projected to grow from roughly 84 billion in 2024 to 170 billion by 2035.² Most important from a development perspective is the growing need for technologies that can translate complex formulations into robust, scalable manufacturing processes. As these technologies become table stakes, the edge is shifting from finding a formulation that works to mapping the design space around it: which factors move which critical attributes, how wide the safe operating window is, and whether that window survives a GMP manufacturing line. The sections that follow show what that means in practice: the platforms available, what closing the development-to-manufacturing gap looks like, and the infrastructure to do it routinely.



Technology Platforms Behind Complex Formulations

There is no single "complex formulation" technology: there is a toolkit. Each platform family below addresses a different facet of the delivery problem.

Nanotechnology-based delivery – including nanocrystals, nanoemulsions/nanosuspensions, and polymeric nanoparticles and micelles to overcome poor solubility and exposure.

Lipid-based and targeted delivery – including liposomes and lipid nanoparticles (LNPs), targeting strategies such as ligand decoration, charge optimization, and antibody conjugation for fragile or targeting-dependent payloads

Oral solubilization and modified release – including amorphous solid dispersions, novel excipients, and sustained/modified-release systems that enables development of poorly soluble small molecules and flatten the PK curve.

Long-acting injectables and in-situ forming systems – including microsphere and nanoparticle depots and in-situ forming gels that can reduce dosing frequency from daily administration to weekly or monthly injections.

Specialized dosage forms and enabling process technologies – including microemulsions, transdermal, and oral sustained-release formats, made possible by continuous manufacturing, terminal sterilization, high-viscosity aseptic processing, and particle coating.

Technology Platforms Behind Complex Formulations

Five platform families — each with its own design space to map



Each platform can be made to work at the bench — the harder question is whether its design space survives scale-up, sterilization, and steady GMP manufacturing.

The platforms above are the industry established toolkit. Later sections illustrate how Asymchem has developed differentiated capabilities across these platform areas.

The bench work only answers part of the question, the harder parts are **how wide the design space is around a chosen platform and whether that space survives scale-up, sterilization, and steady GMP manufacturing.**

From Bench to Commercial Scale: Closing the Translation Gap

From a promising bench process to a steady GMP manufacturing line, programs across the industry encounter similar challenges: process understanding and raw material control, changes in equipment performance at scale, and the aseptic and analytical demands of GMP production.

What does closing that gap look like in practice? Below, we examine two cases from Asymchem's own portfolio: one at the development stage where formulation and method decisions shape everything downstream, and one at the manufacturing stage where manufacturability is either a design input or a downstream cost.

The development stage: mapping the space, not finding a point

Complex formulation development is often described as a search for a single composition that works. In practice, the more valuable deliverable is a **map of the relevant design space** because success depends on knowing which levers move which attributes, and by how much.

An amikacin liposome program at Asymchem shows what that looks like. The objective was a drug product development program targeting the profile of the reference liposomal product:

Attribute	Reference product	Asymchem platform capability
Particle size	200–300 nm	Controllable across 80–300 nm
Lipid composition	DPPC	SPC, DPPC, HSPC with tunable ratios
Lipid-to-drug ratio (w/w)	0.6–0.79	0.25–0.8
Encapsulation efficiency (%)	20–25	20–30
Room-temperature stability	Up to 4 weeks	Up to 7 weeks

For a self-assembling lipid system, these attributes are interconnected and must be controlled simultaneously, hitting all of them at once, reproducibly, is a search problem as much as a chemistry problem.

Asymchem's liposome development platform combines a high-throughput sample preparation system with microfluidic mixing guided by large-scale data simulation, deep nanoformulation development experience, and a broad excipient library. Formulation space that a conventional one-batch-at-a-time program would explore in months could be mapped in days.

The result was not a point but a territory. Particle size proved controllable across 80–300 nm. The platform accommodated DPPC, SPC and HSPC, with tunable lipid ratios. The lipid-to-drug ratio spanned 0.25–0.8 against the reference 0.6–0.79. Encapsulation efficiency reached 20–30%, and room-temperature stability extended to seven weeks, nearly double the reference product's four-week stability. Critically, formulation attributes were reproducible on demand, allowing the team to recreate the reference profile exactly or to tailor it to the client's specification.

The manufacturing stage: designing for predictable scale-up

If the development stage is where manufacturing problems are born, they are either prevented or paid for by how early manufacturability is designed in.

Consider a nanocrystal program for a poorly soluble ophthalmic API. Reaching the back of the eye demanded 50 mg/mL or more, against a starting point of 1 mg/mL. Nanocrystals close that gap by grinding the drug into nanoscale particles, whose larger surface area lifts apparent solubility. **Size, however, is also the problem.** To survive sterile filtration, the particles had to be brought below 200 nm and held there; to remain a usable suspension, they had to resist the aggregation nanoscale particles are prone to; and the crystal form had to survive both milling energy and terminal sterilization. All of this had to be accomplished using as little as 3–5 g of API at the preclinical candidate stage. The bench process worked. Nothing about that guaranteed a sterile, filterable product at scale.

At Asymchem, the team explored two routes in parallel. Milling was studied as a system: stabilizers were screened to keep the particles from aggregating, while milling media and process conditions were tuned until the team held a range inside which particle size stayed below 200 nm and the suspension remained sterile-filterable, with a polymorph that held intact through autoclaving and no solvent to remove. In parallel, a precipitation route dissolved the API in 1M NaOH before controlled mixing and removal of the neutralizing salt, yielding amorphous nanoparticles stable for two weeks at room temperature. Sterilizability was treated as a design input rather than a downstream checkbox.

From just 3–5 g of API, milling delivered sterile-filterable nanocrystals below 200 nm in two weeks, lifting the achievable concentration from 1 mg/mL to 250 mg/mL; the precipitation route reached 90 mg/mL within a single week. Every critical attribute: particle size, filterability, and polymorph stability, held from the first screening panel to the finished suspension.

From programs to platform

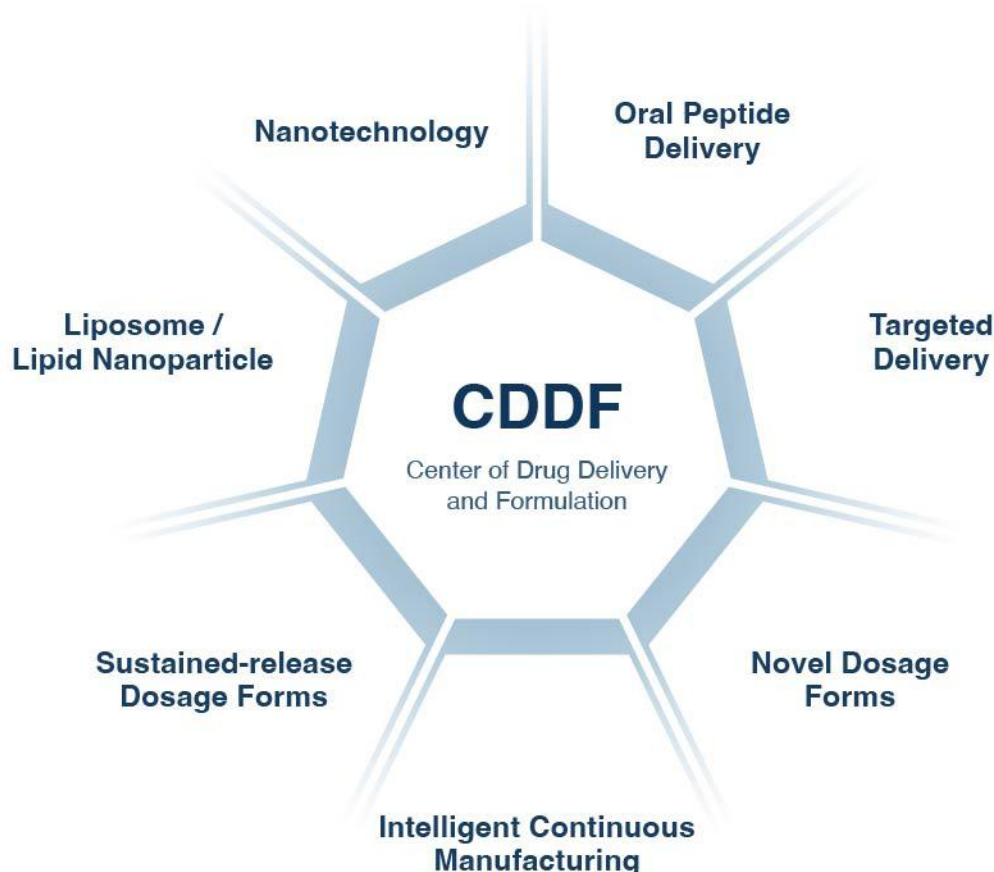
The two cases illustrate a common development approach: interrogate the science early, develop unit operations as a connected whole, and treat manufacturability and sterility assurance as design inputs. Whether the platform is a liposome or a nanocrystal, the key output is an understanding of the design space around it, not the single point that happens to work.

An approach, however, is only as credible as the infrastructure behind it. Which raises a fair question: what, exactly, sits behind it?



The Asymchem Platform: Built for Development and Manufacturing Alike

Behind the cases sits Asymchem's **Center of Drug Delivery and Formulation (CDDF)**, an infrastructure built deliberately around the translation gap:



Asymchem's Differentiated platforms

Nanomedicines on a flow-controlled platform. A purpose-built flow-controlled system accelerates formulation development and scales linearly. Above all, this platform is technology-agnostic; the same flow platform produces liposomes, lipid nanoparticles (LNPs), PLA nanoparticles, and precipitation-based nanocrystals, with IND-enabling scale-up already demonstrated in manufacturing.

Nanocrystals through two parallel systems. Nanocrystals increase surface area to lift the solubility of poorly soluble drugs, most often for oral delivery of insoluble small molecules and for long-acting injectables. Asymchem runs two development systems simultaneously: precipitation for micro- and nanocrystals, and milling. Together, the two systems carry a program from preclinical research through clinical manufacturing. Their advantage is the most apparent when API is scarce: minimum of 3-5 g of API required compared to conventional nanocrystal equipment that demands 30–50 g or more.

Oral peptides are a repeatable specialty. Asymchem has successfully delivered more than 20 oral peptide programs including several clinical-stage projects spanning from linear, cyclic to macrocyclic peptides. While the typical bioavailability for oral peptides are 1–2%, Asymchem has established a standardized in-house workflow for identifying viable formulations and screening peptide candidates through establishing a standardized in-house workflow that identifies viable formulations and screens peptide molecules.

Long-acting injectables with two advances. For extended-duration peptide delivery, conventional PLGA-based systems may present compatibility and formulation limitations, and some approaches require multiple injections. However, Asymchem has developed a patented peptide in-situ gel that delivers 4–12 week duration in a single injection. One bottle neck in long-acting injectable development is the duration of in-vitro release testing, which require four to eight weeks. Asymchem's team has optimized the analytical method through model analysis system that condenses 4 weeks of work to 7 days.

The capabilities behind them

CDDF fits into a broader Asymchem ecosystem designed to support formulation development from R&D through commercial manufacturing.

Regulatory experience. Asymchem's regulatory affairs platform engages route selection process, evaluating compliance, GMP requirements, and filing pathways to identify viable regulatory and development pathways while managing risk through dossier preparation, on-site inspection, and proactive communication with review agencies. This approach is validated by a documented inspection record: Asymchem's drug product operations have completed 34 regulatory audits, including 16 Pre-Approval Inspections (PAIs), with successful FDA and PMDA PAIs in 2025, and EMA PAI in 2026.

Process science. CMC strategy is embedded from the earliest development work, so that process development is guided end-to-end by its eventual filing and manufacturing requirements. Development is mechanism-based and systematic: from molecule to dosage form, the team builds full-chain process understanding and maps the links between critical process parameters and quality attributes — supporting development of a coherent control strategy rather than relying on iterative trial-and-error. This approach is supported by substantial development experience: Asymchem has delivered more than 800 drug product projects, including around 90 complex formulations under sterile preparation, alongside 135 Amorphous Solid Dispersion (ASD) and 160 oral dosage form projects.

Engineering integration. Scale-up at Asymchem is driven by engineering models that predict scale behavior before material is committed, converting laboratory processes into scalable, automated manufacturing solutions with equipment equivalency, process robustness, and

PAT-based process control considered during development. The company's **Center of Flow and Continuous Technology** (CFCT) extends this philosophy to continuous processing, spanning process simulation, scale-up, equipment development, and implementation of continuous manufacturing processes.

Quality systems and intelligent manufacturing. Manufacturing operates under established sterility assurance and process control systems, backed by a comprehensive validation framework covering process, cleaning, and analytical method validation. The **Center of Intelligent Manufacturing Technology** (CIMT) layers digital platform integration and automation on top, supporting a shift from reactive monitoring toward more predictive process control.

Specialized manufacturing processes. Asymchem also offers specialized formulation manufacturing routes beyond conventional approaches: continuous flow-controlled manufacturing, aseptic manufacturing, and terminal sterilization by irradiation — the last of which remains rare across the industry.



Expanding high-potency manufacturing capacity

As previously noted, highly potent APIs are increasingly among the molecules most likely to require complex formulations strategies. For such projects, containment and manufacturing capacity can become key constraints on development timelines. Asymchem operates approximately **8,800 m²** of GMP OEB5 high-potency manufacturing space across **two Tianjin campuses, TJ1 and TJ4**, 15 km apart. The **20 high-potency production lines** — the five most recent commissioned in June 2026, doubling capacity at TJ4 — support programs from hundred-gram development batches to multi-kilogram commercial supply, with reactors from **5 L to 2,000 L** and purification capability from **DAC150 to DAC600**. Containment is designed to ISPE guidance and verified by third-party assessment at an occupational exposure limit of $\leq 1 \text{ ng/m}^3$, a record reinforced by repeated customer and regulatory audits, including recent NMPA pre-approval inspections.

The expansion is part of a continuing investment in high-potency manufacturing, as Asymchem builds capacity ahead of a broader range of project needs.

From white paper to working conversation

The challenges described in this paper are best addressed when formulation, engineering, and manufacturing considerations are integrated early in development. Whether you are formulating a first-in-class complex product, matching a challenging reference, or preparing a high-potency program for scale-up, Asymchem's teams are ready to discuss your molecule.

References

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