Why CMC and Manufacturability Matter in Early Drug Discovery

San Diego, California Sep 23, 2026 (Issuewire.com) - Key Takeaways

- **Early chemistry, manufacturing, and controls (CMC) assessment helps teams evaluate biological promise alongside developability and manufacturability.** Assessing synthesis, formulation, analytical control, and scale-up before candidate selection can identify liabilities and guide further investigation while development options remain open.
- **CRO/CDMO providers should be evaluated on how their scientific teams work together.** Teams should examine whether findings from discovery chemistry, process chemistry, formulation, and analytical work inform decisions before candidate selection and support continuity into development.
- **WuXi AppTec's published cases illustrate complementary lessons for candidate evaluation.** The cyclic-peptide case documents developability as a selection criterion and subsequent progression into process scale-up. The targeted protein degrader case highlights process and formulation challenges that teams can consider earlier in discovery.

Drug discovery has traditionally focused on a core scientific question: does a molecule engage the right target and produce the desired biological effect? Yet a promising candidate also needs a credible path

to reproducible synthesis, reliable characterization, appropriate formulation, and manufacturing at the scale and quality required for clinical development.

Early CMC considerations can help connect these requirements with discovery decisions. For teams evaluating contract research organizations (CROs) and contract development and manufacturing organizations (CDMOs), early CMC integration means bringing discovery chemistry, process chemistry, formulation, and analytical expertise together so that candidate selection and optimization can take into account the molecule's developability and manufacturability.

WuXi AppTec's published case studies offer two complementary lessons for evaluating CRO/CDMO providers. The cyclic-peptide case study documents the use of developability as a candidate-selection criterion and the candidate's subsequent progression into process development and scale-up. The targeted protein degrader program illustrates how process and formulation teams addressed development liabilities that discovery teams can consider when evaluating candidates.

What Should Early CMC Assessment Cover Before Drug Candidate Selection?

Early CMC assessment should evaluate whether a biologically promising candidate has a practical path to synthesis, formulation, analytical control, and scale-up. Its purpose is to identify potential development liabilities while teams still have flexibility to adjust the molecule or its development strategy.

Discovery teams typically optimize candidates for potency, selectivity, and other pharmacological properties. However, a molecular change that improves one attribute may introduce a development challenge elsewhere. A modification that enhances potency or tissue uptake, for example, may increase synthetic or analytical complexity. Similarly, a delivery approach that performs well in an early biological model may present subsequent challenges in scale-up, characterization, release testing, or interpretation of toxicology findings.

This is particularly evident in oligonucleotides, targeted protein degraders, and conjugated therapeutics, where chemistry and biology are increasingly inseparable. Sequence design, chemical modifications, linkers, ligands, and delivery architectures can influence both testing and manufacturing feasibility. For peptide-conjugated oligonucleotides, for example, chemically modified nucleotides and unnatural amino acids may become sourcing bottlenecks as a candidate advances toward the clinic.

Candidate selection therefore needs to consider biological performance alongside developability and manufacturability. A strong assay result becomes more meaningful when accompanied by a credible path to clinical supply.

When evaluating a CRO/CDMO, discovery teams should ask:

- Synthesis and scale-up: How will the provider assess synthetic complexity and identify steps that could constrain manufacturing?
- Formulation: How will solubility, stability, and delivery requirements inform the candidate's development strategy?
- Analytical control: How will the provider evaluate characterization and testing needs as the molecule advances?
- Decision-making across disciplines: How will findings from chemistry, formulation, and analytical assessments inform candidate optimization, selection, and subsequent development?

The value of early CMC assessment lies in translating these findings into actionable decisions. It should

provide enough insight to identify potential liabilities, guide further investigation, and preserve development options.

How WuXi AppTec Connected Cyclic-Peptide Candidate Selection with Process Scale-Up

WuXi AppTec's cyclic-peptide case provides a documented example of developability being considered alongside potency and stability during candidate selection. The subsequent process and analytical work illustrates how the selected candidate progressed from discovery chemistry into larger-scale production.

According to WuXi AppTec's published cyclic-peptide case study, more than 1,700 cyclic peptides were synthesized and screened, followed by hit validation and lead optimization. Within approximately one year, a preclinical candidate was selected based on potency, stability, and developability. The discovery chemistry team subsequently delivered eight consecutive batches of approximately 50 g each, with a lead time of 2–3 weeks per batch, to support the client's evolving testing needs.

The transition from the discovery chemistry team to the active pharmaceutical ingredient (API) development and analytical teams took one business day. The process was then scaled from approximately 50 g to a 1 kg demonstration batch and a 6 kg batch supporting good laboratory practice (GLP) studies within six months.

For teams selecting a CRO/CDMO, this case illustrates the inclusion of developability in candidate selection and continuity through process development and scale-up. Although the reported timelines are specific to this program, the case offers a useful evaluation question: how do discovery, process development, and analytical teams coordinate their findings and responsibilities as a candidate advances?

Early CMC Lessons from WuXi AppTec's Targeted Protein Degrader Case

WuXi AppTec's targeted protein degrader case describes process and formulation development for an existing candidate. It shows how coordinated work addressed synthetic complexity, poor solubility, and scale-up challenges. Although the report does not describe CMC assessments guiding candidate selection, these challenges highlight practical issues that discovery teams can investigate earlier.

In WuXi AppTec's published targeted protein degrader case study, The original synthetic route involved 24 steps and had an overall yield of 0.3%. The candidate's high molecular weight and poor solubility contributed to oral bioavailability of 0.9%, while several palladium-catalyzed steps added process and cost challenges.

WuXi STA's process chemistry, biocatalysis, and crystallization teams redesigned the route, reducing it from 24 steps to 16 and replacing palladium catalysts with biocatalysts in two steps. In parallel, formulation scientists selected spray-dried dispersion to address poor solubility, improving oral bioavailability by approximately 30-fold. Coordinated process and formulation development enabled delivery of materials for investigational new drug (IND)-enabling studies and clinical trial formulations within 12 months.

The case highlights questions that discovery teams can raise before candidate selection: how complex is the synthetic route, which steps may constrain scale-up, and what formulation strategy might be needed to address poor solubility?

Although the case demonstrates coordinated development work, it does not establish that early CMC

assessment prevented redesign. Its relevance to candidate selection lies in the liabilities identified and the complementary expertise required to address them.

Considering these questions earlier can help teams judge whether a promising molecule has a credible development path and determine where further investigation is needed.

Choosing a CRO/CDMO for Early CMC Assessment

Early CMC assessment can help discovery teams decide what to optimize, which uncertainties to resolve, and what evidence is needed before advancing a candidate. WuXi AppTec's cases provide practical reference points for these discussions. When selecting a CRO/CDMO, teams should examine how specialists translate development concerns into actionable plans, with clear priorities and responsibilities that connect candidate evaluation to the work required at the next stage.

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