

Selecting a Drug Substance CDMO

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Selecting a CDMO to develop and manufacture your drug substance is one of the most important decisions a product developer can make.

The right partner can strengthen quality, control strategy, scalability and supply-chain resilience; the wrong fit can put milestones, budget and future regulatory readiness at risk. You need confidence in delivery, quality and partnership from the outset.

As with most decisions, the detail matters.

For drug substance, that detail may sit in route selection, impurity control, process safety, analytical capability, cell line or strain history, upstream and downstream robustness, raw material control, containment, sterility, viral safety, comparability, scale-up and regulatory readiness. A quick search and a few AI-generated emails will not be enough. However, with the right preparation, you can reach the necessary level of detail quickly and with greater confidence. Here's how.

This guide is designed to help you prepare for CDMO selection, decide whether an RFI or RFP is appropriate, compare responses consistently and complete focused due diligence before committing to a drug substance partner.

PREPARATION:

1. What is to be achieved?

Before beginning your search are you clear on what your project needs to achieve? This may seem obvious, but have you asked yourself the following questions?

What are the 'Target project milestones'?

- For example: completion of preclinical studies, proof of concept, first-in-human (FIH) supply, end of Phase 2 studies or process validation readiness.

What exactly am I trying to outsource during this exercise?

- Route/process development, analytical development, non-GMP toxicology batch, GMP clinical API manufacture, scale-up, process validation, technology transfer or commercial readiness.

What support do I need?

- Expertise to enable our ideas
- End to end support/one stop shop
- A platform technology to protect the asset

What activities will be managed internally or by other vendors?

- What don't we know?
 - Do we need additional expertise to manage this outsourcing activity?

What are our critical drivers in order of preference?

- Cost
- Duration to milestone delivery?
- Expertise
- Resource
- Quality

These questions help to form your outsourcing strategy.

2. What is our outsourcing strategy?

Before contacting service providers, be clear on the type of support you need. Are you looking for:

A provider to complete a defined activity?

- e.g. route scouting, process development, cell line/strain development, fermentation/cell culture optimisation, purification, analytical development, GMP clinical API manufacture or process characterisation

A development partner to help shape the technical approach?

- e.g. synthetic route strategy, impurity purge rationale, crystallisation control, bioprocess platform selection, cell line productivity, purification strategy, process robustness and manufacturability

A long-term manufacturing partner?

- e.g. late-stage clinical API supply, process validation, PPQ preparation, commercial API supply, lifecycle management, second-source strategy and regulatory inspection readiness

This decision will influence which CDMOs you approach and how you compare them.

A common mistake is to send the same request to very different types of provider and then try to compare the responses directly. A specialist development provider, clinical manufacturer and large end-to-end CDMO may all be useful, but they may not be solving the same problem.

Before reaching out, ask:

- Do we need specialist expertise or broad end-to-end support?
- Do we want one accountable provider or several specialist vendors?
- What will remain internal?
- What must the CDMO own?
- Are we selecting for the next milestone or the full product lifecycle?
- What risks are we asking the CDMO to manage?

If you are not clear on your outsourcing strategy, the market may define it for you.

RFI AND RFP

3. What to provide to the service provider?

A service provider is unlikely to have any background on your project unless you are continuing to the next milestone with an existing vendor. To get the best information back from your request for information (RFI) or request for proposal (RFP) and to save time in discussions and negotiation, you must be able to convey simply and exactly what you need.

If you do not know exactly what you need in specific areas, tell the service provider. How they respond to uncertainty is a good indication of how they engage with clients, solve problems and understand needs from the outset. If they cannot help or provide the services you need, they should be able to point you towards someone who can.

Preparing a comprehensive proposal for drug substance development and manufacture is also an investment for the service provider. They need to understand quickly whether the project fits their service offering, experience, platform, facilities, containment, GMP licences, capacity and commercial expectations.

Note: Some companies have minimum project revenue targets, below which they won't quote against.

In general, the information a service provider needs falls into two main categories:

1. Project expectations
2. Technical expectations

Project expectations include:

- Timelines, phase, project history
- Modality, molecule specifics, intended route to clinic or market, CMC assumptions and target control strategy
- Quality and licence requirements
- H&S, safety and handling requirements

Technical details include:

- Analytical approach, method status, reference standards, impurity/variant strategy and release testing expectations

- Small molecule: route, starting materials, intermediates, impurity profile, solid-state form, process safety and scale-up considerations
- Biological API: cell line or strain, vector/construct, upstream process, downstream purification, potency, glycosylation/heterogeneity, viral safety, adventitious agent control and comparability considerations
 - Required techniques, scale, equipment, containment, bioreactor/fermenter capacity, purification train, lyophilisation or isolation/drying capability as applicable
- Primary, secondary packaging and labelling requirements.
- Stability, storage, shipping, retest period, reference standard, release, CoA and regulatory documentation requirements.

4. Decide whether to send an RFI or an RFP

Before asking service providers for a full proposal, decide whether you need an **RFI** or an **RFP**.

An **RFI** — request for information — is useful when you are still learning the market. It helps you understand who has the right capability, experience, capacity and interest before asking for detailed proposals. This is most appropriate when screening companies.

An **RFP** — request for proposal — is used when you are ready to ask selected providers to propose a specific approach, timeline and cost for your project.

Both have value, but they are not the same.

Use an **RFI** when:

- You have a broad requirement but are not sure which providers are suitable
- You need to understand capability, technology fit, experience or capacity
- You want to screen a longlist before investing time in detailed discussions
- You do not yet have enough information to support a detailed proposal

Use an **RFP** when:

- Your scope is clear enough for providers to price and plan
- You have enough technical and project information to share
- You want comparable proposals from a smaller number of providers
- You are ready to assess approach, timeline, assumptions, risks and cost

A common mistake is to issue an RFP too early. If the scope is unclear, the responses will be difficult to compare and the real work will move into clarification calls.

Another mistake is to send an RFI to too many providers without clear screening questions. You may get a lot of information back, but not necessarily the information needed to make a decision.

Before deciding, ask:

- Do we know exactly what we want quoted?
- Do we have enough technical information to support a proposal?
- Are we trying to learn the market or select a partner?
- Do we need broad screening or detailed pricing?
- How many providers can we realistically manage through the process?

Use an RFI to screen quickly. This allows you to focus on service providers that engage well, understand your needs and may identify considerations that make your RFP more robust.

Once you have finalised your scope, assumptions, deliverables and decision criteria, move to an RFP. This should make the process more efficient, reduce the need for multiple rounds of discussion and focus activity on the service providers that can provide what you need. You can now focus on the detail.

SMALL MOLECULE VERSUS BIOLOGICAL API SELECTION CONSIDERATIONS

Selection area	Small molecule API	Biological API
Technical focus	Route selection, yield, impurity purge, crystallisation, solid-state form and process safety.	Cell substrate, expression system, upstream performance, downstream clearance, potency and heterogeneity.
Facility fit	Reactor capacity, isolation, drying, milling, containment, hazardous chemistry and solvent/catalyst handling.	Bioreactor/fermenter scale, purification train, aseptic or low-bioburden operations, biosafety and cold-chain capability.
Control strategy	Impurities, residual solvents, catalysts, genotoxic impurities, particle attributes and polymorph control.	Potency, purity, aggregates, glycosylation or other variants, host-cell proteins/DNA, viral safety and comparability.

SMALL MOLECULE VS BIOLOGICS DECISION CHECKLIST

Decision area	If selecting for a small molecule API, check...	If selecting for a biological API, check...	Decision note
Molecule and modality fit	Relevant chemistry, route complexity, starting material strategy, chiral control, solid-state risks and scale-up experience.	Relevant biologic class, expression system, cell line or strain experience, platform fit and prior work with similar CQAs.	Does the CDMO understand the specific API risk profile?
Process development depth	Route optimisation, impurity purge, crystallisation, process safety, solvent selection, robustness and manufacturability.	Upstream productivity, downstream recovery, clearance strategy, viral safety, process characterisation and comparability readiness.	Is the provider a true development partner or mainly a manufacturer?
Analytical capability	Impurity methods, residual solvents, catalysts/metals, genotoxic impurity assessment, polymorph/particle testing and reference standards.	Potency, purity, aggregates, charge variants, glycosylation or other variants, host-cell protein/DNA, bioburden and endotoxin testing.	Can the analytical package support release, stability and future regulatory questions?
Facility and equipment fit	Reactor train, isolation, drying, milling, containment, hazardous chemistry, hydrogenation or specialist unit operations as needed.	Bioreactor/fermenter scale, purification train, chromatography capacity, single-use strategy, low-bioburden controls and cold-chain capability.	Does the facility fit the next milestone and likely scale path?
Materials and supply chain	Starting materials, intermediates, solvents, catalysts, controlled materials, vendor qualification and long-lead items.	Cell banks, critical reagents, media, feeds, resins, filters, single-use assemblies, biological starting materials and cold-chain logistics.	Are material risks understood early enough to protect the timeline?
Quality and regulatory readiness	API GMP status, starting material justification, impurity control strategy, validation readiness and regulatory documentation support.	Biological starting material control, cell bank history, adventitious agent control, viral clearance, comparability and lifecycle documentation.	Can the provider support the quality story expected at the next submission?

5. Structuring an RFI/RFP

Keep the document simple. The aim is not to show how much you know, but to get the information needed to decide whether the CDMO can develop, characterise, manufacture and release your drug substance safely, compliantly and at the required scale.

For an **RFI**, focus on screening questions: drug substance capability, relevant modality experience, process development depth, analytical strength, GMP status, facility fit, containment or biosafety, capacity, raw material strategy, regulatory track record and whether the provider is genuinely interested in the project.

For an **RFP**, provide enough detail for a realistic proposal: scope, assumptions, deliverables, timelines, molecule or modality information, process and analytical history, quality expectations, regulatory requirements, material responsibilities, commercial requirements and decision criteria.

Ask providers to respond in a consistent format. If every response is structured differently, comparison becomes harder than it needs to be.

Be clear where you want a firm answer and where you are asking for advice. This helps separate capability from sales messaging.

A common mistake is to make the RFP too long, too vague or too restrictive. The best responses usually come from a clear scope, sensible assumptions and room for the CDMO to explain how they would approach the work.

COMPARING

6. Comparing service providers

Once proposals are received, avoid comparing providers on cost alone. Your preparation should drive your selection weighting. For drug substance, the cheapest route may not be the lowest risk, and the most technically detailed response may still fail if the facility, quality system, materials strategy or scale path does not fit the programme.

- Compare each provider against the same criteria.

- Separate must-have requirements from nice-to-have features.
- Score what matters to the project.
- Challenge assumptions, exclusions and dependencies in the proposal.
- Make sure the provider's proposed approach matches your milestone, budget and internal capability.
- A common mistake is to score the proposal rather than the provider. A good proposal is useful, but you are selecting the organisation that will deliver the work.
- Typical scorecard areas include technical fit, relevant modality experience, process development capability, analytical capability, quality and GMP status, regulatory track record, facility and containment fit, capacity, timeline realism, raw material and supply chain resilience, project management, communication style, commercial transparency and cultural fit.
- It is also important to consider some of the less tangible aspects of your interactions.
 - Did they listen to what we needed?
 - Do they really understand what we are trying to achieve, and by when?
 - Is the delivery team engaged during these discussions?
 - Who will deliver, oversee and be accountable for the work on the provider's side?
 - During early discussions, the "A-team" is often brought in to win new clients and showcase expertise. How close will that team be to your project once it starts?
 - If multiple sites will be involved, how does the provider manage those interactions? One brand does not always mean one fully aligned delivery team.

DUE DILIGENCE

7. What to check during due diligence

Once you are down to your favoured providers, due diligence is where you test whether the proposal can actually be delivered. The aim is not to catch the provider out, but to understand the real risks before committing. Drug substance CDMO due diligence should go deeper than reputation and brochure capability. You need

to test the people, process, equipment, quality system, materials, data integrity, regulatory history and the provider's ability to handle the specific risks of your API.

- Check the provider's relevant experience with similar drug substances, modalities, development stages, scales, impurity or variant profiles and technical challenges.
- Confirm GMP status, licences, inspection history, audit readiness and quality system maturity.
- Review how deviations, CAPAs, change controls and investigations are managed.
- Check whether the proposed equipment, scale, facility, containment, biosafety level, cleanroom classification and material flow fit the project need.
- Understand capacity, lead times, resource availability and competing priorities.
- Review analytical capability, method transfer expectations, stability support and release testing arrangements.
- Check supply chain assumptions, starting material or cell bank control, critical raw materials, resins, single-use components, solvents, catalysts, controlled materials, import/export constraints and business continuity.
- Assess project management, communication style, escalation routes and how issues will be handled.
- A common mistake is to treat due diligence as a quality audit only. Quality is critical, but technical fit, capacity, people, communication and commercial assumptions matter too.

Summary

Selecting the right drug substance CDMO is not about finding the best-known provider; it is about finding the right technical, quality, regulatory and operational fit for your molecule, modality, milestone and risk profile.

For small molecules, route, impurity control, process safety, solid-state control and scalable chemistry may dominate. For biological APIs, the emphasis may sit in cell substrate history, upstream and downstream robustness, potency, heterogeneity, viral safety, comparability and biological starting material control.

Clear preparation, structured information sharing, consistent comparison and focused due diligence will save time, reduce uncertainty and improve the chances of a successful partnership.

If you are preparing for outreach now, use the template downloads that support this guide to define your scope, prioritise your criteria and identify where provider input is needed before the first conversation.

Use Pharma Services Hub to turn that preparation into action; search for providers now at: www.pharmaserviceshub.com