*The content on this webpage was developed by NIH SEED based on its collective experience working with the NIH innovator community. This information has been developed, for informational purposes, to address questions frequently asked by NIH awardees, and represents the experiences of the subject matter experts who contributed to its development.*

# Innovator Checklist for Finding Contract Manufacturing Organization (CMO)

For many innovators choosing a CMO for their lead product candidate is critical for product manufacturing under current Good Manufacturing Practice (cGMP) compliant processes. Prior to starting outsourced activities and signing a contract, innovators should conduct due diligence to identify and chose the right manufacturing partner based on products needs and whether the CMO is a good fit for their product development life cycle. As part of this process, the innovator should first seek information about potential CMOs. This research usually involves the following steps.

- Circulate your Request for Proposal (RFP) to multiple CMO bidders
    - Itemize the services to be included in the quote. Depending on data in hand and maturity of the development process/platform, project scale, number of batches, process development, engineering batches, quality assurance, and regulatory support may be required. In addition, identify project management expectations, the number of meetings expected, and if on-site visits are included. This can be very helpful not only to the CMO, but also for comparing multiple quotes.
- Define the scope, including working assumptions and expectations, in writing.
    - List everything you expect or deem critical for the product, (even if not demonstrated) including the process, product, yield, release assays, product stability, regulatory filings and outcomes, as well as identify how future specifications or requests will be handled. Also, define, how material, processes, and product analytics will be transferred under a protocol to the CMO.
- In their response to your RFP, review the CMO responses to the various line-items, deliverables, milestones, and budget. Do the vendor proposals clearly address the requirements you identified for the phase-appropriate product development.
- Contractually ensure that the scope of services for proposal and quotation will address the required and supporting activities as defined in the RFP.

Selecting and contracting with a CMO is one of the most critical and complex business decisions for innovators. You will be sharing intellectual property with them, and they, in turn, will be creating significant intellectual property as they scale up the product and continue its development. Consider hiring an experienced expert who can assist with vendor selection and contracting (knows what to look for and how to avoid typical pitfalls).

The following tables, with an assorted checklist of questions and information matrix, provide general guidance for making a thoughtful, meaningful, and objective choice.

## Part 1: Technical Expertise[1]

| Screening/Evaluation Criteria | Good Fit, Capacity, and In-house Expertise | Rating[2] (Pass/Fail) |
|---|---|---|
| Process and current good manufacturing practices (cGMP); technical competence/expertise; experience with intended technologies[3]<br><br>(*Also seek external industry feedback*) | ☐ Biologics<br>☐ Monoclonal antibodies<br>☐ Cell therapies<br>☐ Small Molecules<br>☐ Research and master cell banks<br>☐ Vector engineering<br>☐ Synthetic chemistry<br>☐ API manufacturing<br>☐ Technology transfer process (receiving/outgoing) | |
| Assay development capabilities and instrumentation | ☐ Screening and selection<br>☐ Physicochemical and biophysical characterization<br>☐ Chromatography assays<br>☐ Mass Spectrometry<br>☐ Chirality assays<br>☐ Test for particulate contamination<br>☐ Binding assays<br>☐ Cell-based assays<br>☐ Quality Control<br>☐ Qualification, SOPs<br>☐ Validation<br>☐ Bioburden<br>☐ Endotoxin<br>☐ Sterility<br>☐ Assay optimization, troubleshooting<br>☐ Result interpretation<br>☐ Use of controls<br>☐ Materials dedicated for project (columns, buffers) | |

[1] Assessment of evaluation criteria should be done on a case-by-case basis, product requirements, suitability, and expertise of the CMO to meet the product development goals. The current list of criteria is to provide general guidance and framework regarding the areas for diligence and consideration prior to CMO identification and selection and can be further extended by the Innovator/Sponsor as per the requirements of the product/project and activities.

[2] Every innovator/start up should evaluate the comfort level when identifying, selecting, and rating a CMO based on the due diligence they conduct. Consulting with key opinion leaders or outsourcing and manufacturing experts can provide valuable insight while making these judgement calls. The rating system is an arbitrary number system based on how each innovator weighs select elements based on what factors are important to them to advance the product. One can assign, for example 20 points to each of the question (total = 160) and grade each element question (1-8) based on the overall assessment. Different CMOs will be graded differently for different questions based on multiple factors including good fit, expertise, capacity, institutional know how, cGMP readiness and quality etc. The comparison of total scores out of 160 between different CMOs would potentially inform about the lead CMO candidate(s) for developing the product.

[3] The innovator should include additional requirements specific to the product, platform which will be gating for defining the in-process testing and product critical quality attributes.

| | | |
|---|---|---|
| Formulation Development | ☐ Pre-formulation studies<br>☐ Analytics<br>☐ Essential experimental result<br>☐ Drug release studies<br>☐ Biologics<br>☐ Small Molecules<br>☐ Solubility screenings (dissolution rate, mechanical properties, hygroscopicity, physical/chemical stability)<br>☐ Compounding<br>☐ Granulation<br>☐ Troubleshooting | |
| Expertise in developing different dosage forms for delivery, route of administration | ☐ Solid<br>☐ Liquid<br>☐ Semi-solid<br>☐ Lyophilization<br>☐ Parenterals<br>☐ Inhaled/intranasal<br>☐ Topicals<br>☐ Understanding of FDA inactive and generally recognized safe agents | |
| Assess product development, manufacturing, and product release approach | ☐ Certificate of analysis<br>☐ Certificate of compliance<br>☐ Stability testing plan<br>☐ Reference standards<br>☐ Submission of quality section to FDA<br>☐ Production and batch records review process<br>☐ Turnaround time for quality assurance document review | |

## Part 2: CMO Process Development Scale Capacity/Capabilities

| Screening/Evaluation Criteria | Good Fit, Capacity, and In-house Expertise | Rating[ii] (Pass/Fail) |
|---|---|---|
| Scale of processing platforms for drug products, active pharmaceutical ingredients, or biologics (small, intermediate, large scale)[4] | ☐ Small scale (mL-1L scale)<br>☐ Different pilot scales<br>☐ 5-10L ☐ 25L ☐ 50L ☐ 100L ☐ 250L ☐ 1000L<br>☐ High-throughput screening platforms<br>☐ Prototyping<br>☐ Wave-bags<br>☐ Bioreactors<br>☐ Steel/glass tanks<br>☐ Disposable bags, single use<br>☐ Multi-use vessels<br>☐ Crystallization<br>☐ Tableting capacity<br>☐ Granulation process<br>☐ Bulk harvest material<br>☐ Use of patented platforms for product development | |

[4] The innovator should assess the scale requirements (cGMP and non cGMP) based on the quantity of product required for planned clinical trial, stability testing samples, overages required (at least ~25-30%) and use of the potential material for other IND-enabling nonclinical animal studies, analytical development, and other supporting studies.

| Screening/Evaluation Criteria | Good Fit, Capacity, and In-house Expertise | Rating[ii] (Pass/Fail) |
|---|---|---|
| Downstream/purification processes and scales | ☐ 5-10L ☐ 25L ☐ 50L ☐ 100L ☐ 250L ☐ 1000L<br>☐ Depth filtration<br>☐ Tangential flow filtration<br>☐ Capture/affinity<br>☐ Polishing | |
| cGMP manufacturing scale and clinical trial material | ☐ Engineering run<br>☐ cGMP compliant production<br>☐ Phase I<br>☐ Phase II<br>☐ Phase III<br>☐ Phase appropriate production<br>☐ Batch records | |
| Fill finish capacity | ☐ Onsite<br>☐ Outsourced<br>☐ Vial filing capacity<br>☐ Labeling, packaging, and quality Inspection | |
| Media fill and aseptic processes | ☐ Annual qualification<br>☐ Number of media fill simulations done in the last year | |

## Part 3. Quality Management

| Screening/Evaluation Criteria | Good Fit, Capacity, and In-house Expertise | Rating [ii] (Pass/Fail) |
|---|---|---|
| Quality management systems (QMS) and processes<br><br>Strength of quality department<br><br>(*Also seek external industry feedback regarding FDA standing, compliance*) | ☐ QMS plan<br>☐ Change control with manufacturing activities<br>☐ Insourcing of raw materials process<br>☐ Vendor selection/approval process<br>☐ Documentation and recording controls<br>☐ Compliance history and record<br>☐ Philosophy of deviation management<br>☐ Safety and environmental compliance<br>☐ FDA audit of site | |

## Part 4. Regulatory

| Screening/Evaluation Criteria | Good Fit, Capacity, and In-house Expertise | Rating [ii] (Pass/Fail) |
|---|---|---|
| Regulatory expertise and counsel<br><br>Reputation with regulatory agencies<br><br>(*Also seek external industry feedback*) | ☐ Regulatory familiarization<br>☐ Demonstrated manufacturing, regulatory expertise with same or similar products<br>☐ Writing different Investigational new drug modules<br>☐ Submission of chemistry, manufacturing, and controls file to FDA<br>☐ Drug master files | |

## Part 5. Facility and Equipment

| Screening/Evaluation Criteria | Good Fit, Capacity, and In-house Expertise | Rating [ii] (Pass/Fail) |
|---|---|---|
| Site Assessments | ☐ On-site storage policies<br>☐ Qualified packaging and shipping process<br>☐ Dry ice/-80°C ☐ 2-8 °C ☐ Frozen/-20°C<br>☐ Secondary packaging process | |
| Expertise, logistics, and governance to ensure project remains on track | ☐ Dedicated project manager<br>☐ Dedicated technical lead<br>☐ Dedicated quality lead<br>☐ Tools to control timeline and budget<br>☐ History of managing projects (timelines, budget)<br>☐ History of managing cost overruns<br>☐ Request resumes of potential project lead and staff | |

## Part 6. Program Management and Logistics

| Screening/Evaluation Criteria | Good Fit, Capacity, and In-house Expertise | Rating [ii] (Pass/Fail) |
|---|---|---|
| CMO oversight, responsiveness to issues and communication<br><br>(*Also seek external industry and feedback*) | ☐ Philosophy of risk mitigation, contingency planning<br>☐ Approach to communication, escalation process<br>☐ Communication in the event of deviations, out of specification results, production failures, etc.<br>☐ CMO responsiveness in the event of deviations, out of specification results, production failures, etc. | |
| GMP suites for production | ☐ Availability of GMP suites for production as per timeline<br>☐ Scheduling flexibility and adaptability<br>☐ Right of first refusal when GMP, formulation, fill suites become available<br>☐ Fee structure | |

## Part 7. Contract

| Screening/Evaluation Criteria | Good Fit, Capacity, and In-house Expertise | Rating [ii] (Pass/Fail) |
|---|---|---|
| Contract considerations<br><br>(*Also seek external industry and NIH Program Officer feedback on contract related matters*) | ☐ Written quality agreement<br>☐ Flexibility to accommodate on differences in requirements<br>☐ Contract stipulates paying advanced capacity fee to block the GMP suite<br>☐ Payment structure milestone based or over regular quarterly/half-yearly/yearly installments<br>☐ Intellectual property stipulations<br>☐ Royalty and licensing fees<br>☐ Allocated costs broken down by task in the quote<br>☐ Confidential Disclosure Agreements (CDAs)<br>☐ Participant to material transfer agreements (MTAs) | |

## Part 8. Other Factors to Consider

| Screening/Evaluation Criteria | Good Fit, Capacity, and In-house Expertise | Rating [ii] (Pass/Fail) |
|---|---|---|
| Location of the CMO | ☐ Convenience<br>☐ Same or different time zone | |
| Assess financial and corporate stability<br><br>(*Also seek external industry feedback*) | ☐ Corporate financials (credit check)<br>☐ Company's business structure and practices<br>☐ Assets and inventory<br>☐ Outstanding liabilities | |