Lessons Learned: Choosing & Managing a CDMO

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PL Developments

Helping consumers live better lives through quality health and wellness products.

PLD is a premier manufacturer, packager and distributor of over-the-counter pharmaceutical products and consumer healthcare goods. This means, we create a great many of the high-quality health, wellness and NRT products for brands you know and trust nationwide.

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Avéma Pharma Solutions is a division of PL Developments

- Consumer and Supplier of Global CDMO services for both OTC and rX products.
- Currently managing 30+ CMOs
- More than 60 ANDAs
- Empathy & Experience creating good partnerships
- Focused on quality, efficiency & speed-to-market

Managing the Initial RFQ through a Rigorous Process

Is there a fit between needs and capabilities?

- Batch sizes vs. current capabilities

How can you prevent miscommunications and errors?

- Get as many details as possible about excipients, drug substances, process flow, parameters, development report
- Review scope of requirements
- Identify what questions are NOT asked.
- Discuss the “to market” strategy
- Understand and manage regulatory approvals

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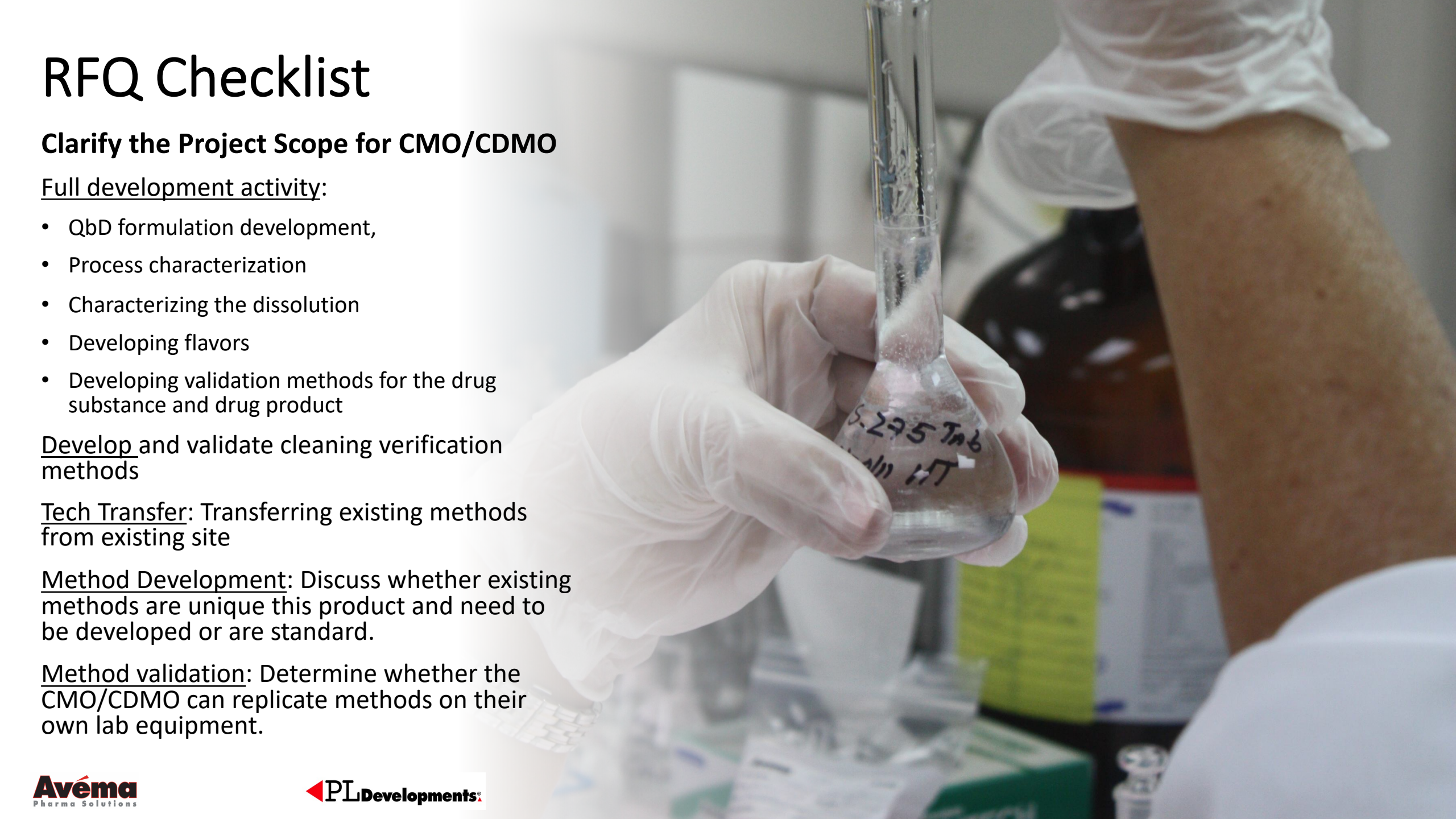
RFQ Checklist



Clarify the Project Scope for CMO/CDMO

Full development activity:

- QbD formulation development,
- Process characterization
- Characterizing the dissolution
- Developing flavors
- Developing validation methods for the drug substance and drug product

Develop and validate cleaning verification methods

Tech Transfer: Transferring existing methods from existing site

Method Development: Discuss whether existing methods are unique this product and need to be developed or are standard.

Method validation: Determine whether the CMO/CDMO can replicate methods on their own lab equipment.

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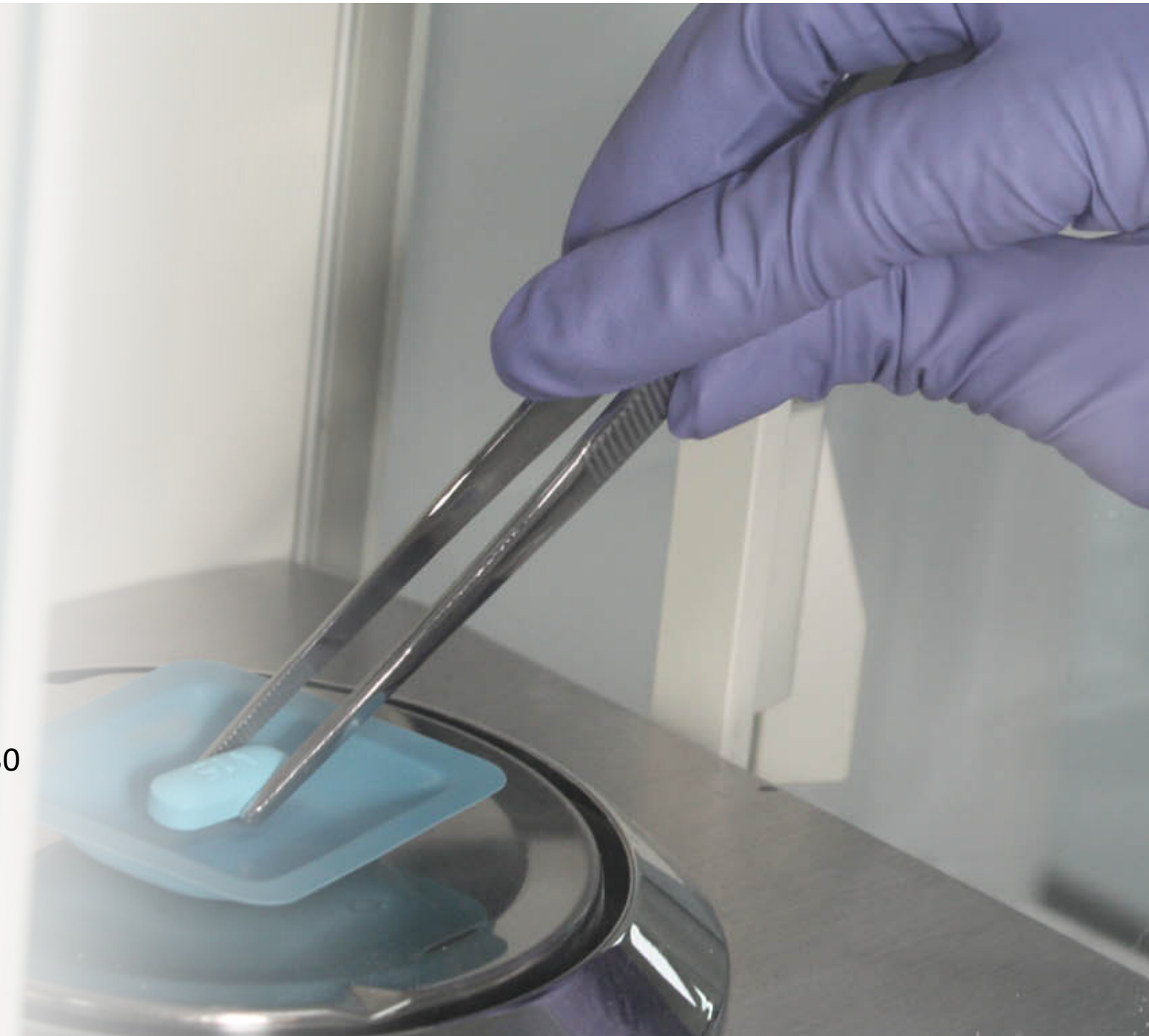
RFQ Checklist

Regulatory Strategy

- NDA, ANDA, CBE 30 or 505B2
  - Each has a different requirement and timeline
  - Identify what is “like for like.” Is the CMO/CDMO willing to invest in new equipment if necessary? What’s the timeline for that.
  - Preparation for a Prior Approval Inspection (PAI)
  - Discuss how changes could impact the timeline for the FDA review cycle. PAS would be longer review cycle vs. CBE 30
  - Prior approval supplement: what changed?



RFQ Checklist

Define CMO/CDMO Responsibilities

- Full turnkey: Concept to commercial, with CDMO handling everything from sourcing raw ingredients through packaging and serialization of the product.
- Conversion only: Customer supplies everything and the manufacturing is transferred to the CMO.
- Bulk only: CMO supplies the product (tablets, liquid, powder,) customer does the packaging.
- Early Stage ObD: Product and process development to support clinical and then transfer to customer for commercial manufacturing.

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RFQ Checklist

Customer Responsibilities

- Describe Drug Substance: Is it a controlled substance, hormone, small molecule, biological. Is any special handling required? Who sources it?
- Formulation: Is the formulation is already on production equipment? Is there an existing batch record available. What batch sizes are validated? Or, is it a concept that needs to be commercialized.
- API & Excipients: Who supplies them and what grade is required. Do they have existing suppliers. Is there a drug master file/DMF available
- Packaging components: Who provides the packaging? They would need to provide drawings, samples, or conceptual direction.

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RFQ Checklist

Project Kickoff timing

- Will all analysis/testing be done in house?
- If done by an external lab, how does that impact deadlines?
- What is the expected timeline?
- How long does the contracting process take? For supply agreement, quality and tech transfer. These are things that can extend the kickoff.
  - 1-4 months or longer depending on complexity to get a supply and quality agreement in place
- Who is the core team for the CDMO/CMO and customer?
- How will teams communicate and what is the frequency?

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RFQ Checklist

Project Definition

- Lab scale development
- Demonstration batches
- Exhibit batches
- Analytical support

Launch capabilities

- Small scale manufacturing – produced quarterly, for example, to reduce risk
- What is the scale up for commercial, time limitation from the introduction of API to FP, bulk holding time for packaging, shipping and storage conditions.
- Ramp up to commercial levels
- What are the tradeoffs in quantities, costs and market introduction?

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RFQ Checklist

Formulation and Process Definition

- Process flow chart – do they have one?
- Batch manufacturing records if it's a CBE 30 they are already making it and can it be evaluated in person by CDMO/CMO partner.
- Is the transfer from lab scale or commercial knowledge?
- Who manages API, excipients & packaging component qualifications and purchasing, CDMO/CMO or customer?
- Review executed manufacturing and packaging batch record for knowledge learning.

RFQ Checklist

Analytical Requirements

- Analytical methods/Drug substance specifications/Drug product specification
- Does the product require specific analytical equipment?
- Does the CMO need to acquire equipment or outsource something?
- Many CMOs don’t have a large range of analytical equipment and they use outside testing. Will that be a cost-effective and efficient strategy?
- From a CDMO perspective, we might invest in the analytical equipment if it supports both the customer’s needs and our long-term business goals

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RFQ Checklist

Quality by Design

- Following the FDA's mandate and following QbD techniques can significantly reduce FDA review times.
- Starting each project with DOE techniques can help identify critical quality attributes, develop a robust formulation and establish a process design centered around those attributes.
- Small batches with short turn times around allows for more characterization of the process through design of experiments that can help reduce review time by the FDA and lead to fewer information requests or a faster approval cycle.
- QbD also supports a stable supply chain for the customer with RFT and on time in full execution of orders.

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RFQ Checklist

Integration between R&D and Manufacturing

- Synergy with commercial scale up enhances speed to market
- The ability to develop product on small scale production equipment identical in specifications to the full-size commercial equipment eliminates delay and makes sure no information is lost during scale up.

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RFQ Checklist

Determine Market Launch Strategies

- Project commercial volumes by strength/count for first 3-5 years
- Discuss scalability of equipment at CDMO/CMO. The right size equipment is important so after the tech transfer, it’s ready for the customer’s growth
- Determine how to best run the product, including the degree of automation, bin size, etc.

RFQ Checklist

Questions to ask to ask a CDMO

- What investments have they made in new equipment?
- How do they manage technology transfer from R&D/Pilot to commercial manufacturing?
- Do they have pilot manufacturing equipment?
- How do they manage communication throughout the development process?
- Do they understand FDA requirements? What is their history with regulatory filings have they gone through this before?

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Red Flags

Cost variances because of incomplete information

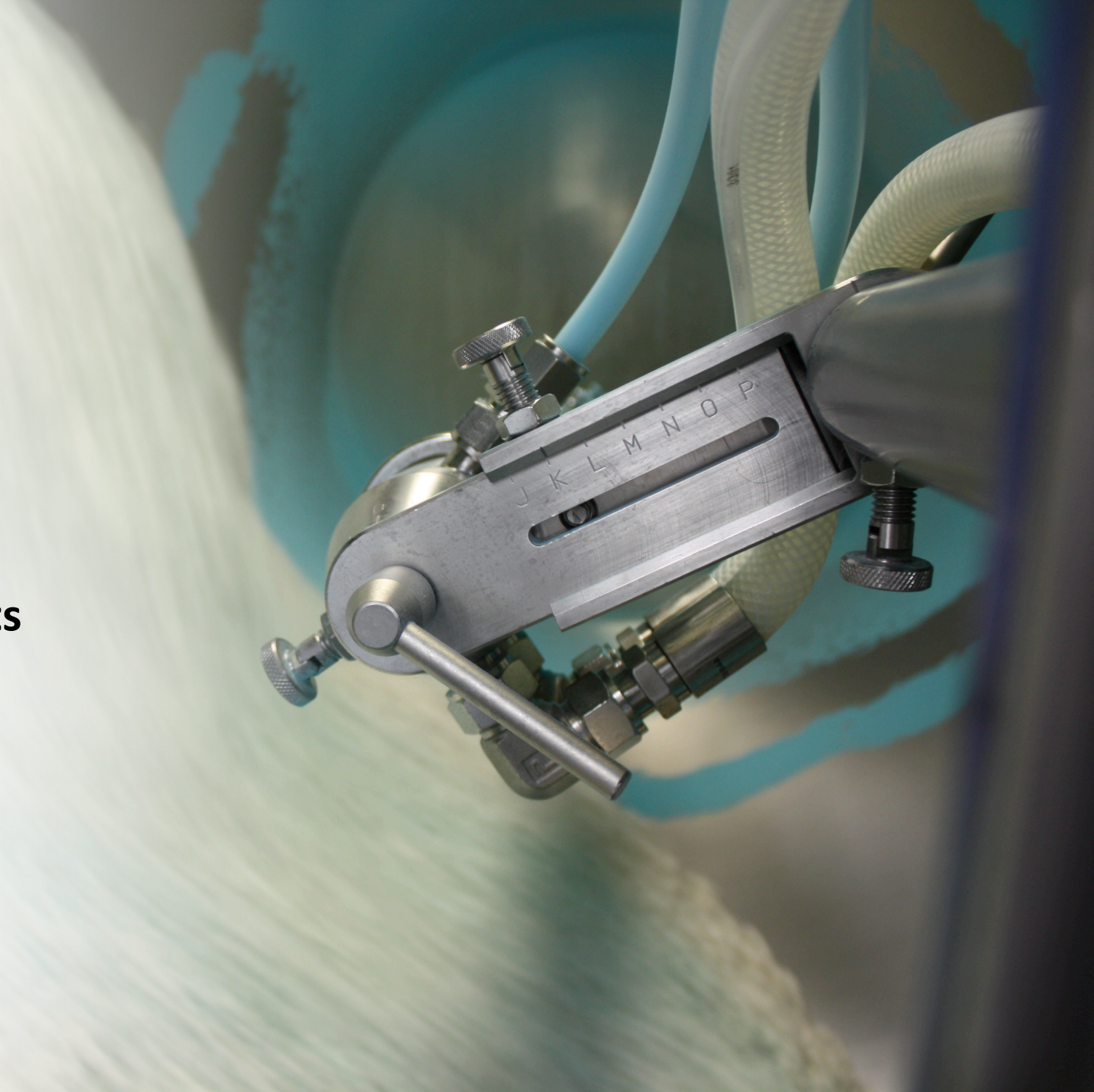
- Not enough detail on testing requirements can either increase or reduce costs

Time delays

- Outsourcing parts of the project can impact the timeline

Not understanding market requirements

- Share IMS, IQVIA market data to gauge demand
- Is there a need for the product or is that space already crowded?
- Is it a process we can/want to commercialize?
- Is the CMO I send this to viable for long term? What is the financial stability of the company?
- Does the nature of the API meet our handling requirements?



Addressing tough issues

Budgeting

- Changes of scope always occur. Be prepared for time and cost adjustments as the project evolves.

Time frame

- Estimated timelines need to be established for major milestones right from the start.
- If the customer is supplying the components, they need to say how soon can they have the API and when samples will be available for testing

Non-deliverables

- We add in extra batches on some quotes to account for the possibility of failures or even needing extra repetition of tasks to get it right. **We only bill for what is actually completed**.

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What can go wrong?

Stability issues

- Investigate equipment, methods, reagents.

Method dev/method transfer problems

- Methods aren't always robust for transfer and sometimes require modifications.
- Formulation refinement for flavors/mouth feel for ODTs can require several rounds of samples and even changes in flavors. A good flavor house with a robust library helps speed this up.

Process information that is not included in documentation

- Let the CMO team watch the process if the product is currently being manufactured to gain knowledge of the process that isn't in the documentation provided.
- Live stream calls with the customer or on-site visit during demo batches -- opens lines of discussion on process hints.
- Include the customer when training the operators and quality team to impart intimate knowledge of the manufacturing process and allow team to ask questions or identify parts of the process that create issues

What to look for in Manufacturing Capabilities

- Innovative, creative strategies to allow for faster speed to market
- Synergy with R&D and development
- Speed to Market with Scale Up
- Advantages of a company focused on speed to market
- What is the company's legacy? One of the advantages Avéma brings to the process is PLD's experience in the private label world where cost efficiency and speed to market are imperative.

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What makes a good CDMO?

- CMO/CDMO must be financially viable and poised for growth
- Must have new equipment and new capabilities
- The “right” size for your needs. Not so large that you are fighting for resources, not so small that resources are limited.
- Does the facility look clean, up to date
- Experienced personnel is another critical success factor.

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Long Term Relationships

- Once a site is approved and you go through the process of approving that vendor, through an onsite or virtual audit, you don't want to go through that expense and time, unless it's going to be a long-term relationship.
- Need to choose a CMO/CDMO that has the capabilities to support a product long term and which may be able to support other products.
- Will the CMO/CDMO invest in technologies/capabilities to support your product?
- Is the potential partner willing to be honest up front if there isn’t a good fit?

Questions?

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