Navigating the Small and Virtual Business Landscape

CMC Considerations for Managing More with Less: CMC Paths to Patients for Small & Virtual Biotechs

CASSS WCBP Conference, January 2025

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Topics

- Enterprise Level Considerations
- CMC Considerations

Enterprise drivers shape CMC strategy

- Leadership: first time CEO? Venture Capital funding?
- Disease or platform technology focus?
- Longer term vision: academic PoC, build-to-buy, FIBCO?
- Financial Resources: runway, “value creation” timeline
- “Virtuality”

- Target Product Profile
- USA-only or worldwide ambitions (regulatory compliance)

CMC Module 3 needs plenty of help

Which functions to hire or rent and when?

- Process & Analytical Development (well-char starting materials, fit for purpose assays, potency early,…)
- Early Stage Manufacturing
- Quality Control
- Quality Assurance
- CMC Regulatory Affairs
- Early Stage Clinical Manufacturing
- Supply Chain & Logistics
- Late Stage Clinical & Commercial Manufacturing

For some or all:

- Build internal capability
- Collaborate with a Fully Integrated Biotech Company/Big Pharma
- Hire a contract development & manufacturing organization (CDMO)

CDMO contract terms

Probe CDMOs via RFP and meetings

- Range of services offered; automation
- GMP suite model
- PIP
- Exclusivity
- Commitments
- Proprietary
- Quality Agreement
- Pricing
- Timelines
- Change Orders
- Project Management

Things to consider (assess, weight, rank)

Plan for at least 6 months from RFP to signed contract

- Total Price (including capex; overall fair and reasonable?)
- Business Model & Financial Risk (D&B)
- Customer Service (operational flexibility, PIP, schedules)
- Proposal timeline & supply capacity
- Equipment and facilities
- Technical capabilities
- Proposal adherence
- Compliance record and audit status
- Other (tax, IP, strategic considerations)

All CDMOs are not the same

- Established big name, multi-site with many approved products, mature systems, may be less flexible, may offer proprietary technology
- Start-up CDMO with experienced people but no "institutional" knowledge, immature systems, flexible
- Single offering (e.g., outsourced QC or can only supply one of many components) versus one stop shop
- Academic core facility stopping before pivotal

Oh, yes, there's a product…
Example: engineered autologous cell therapy

- Remember that TPP? It drives QTPP → CQA → CPP, CMP and also the product Specification
- Effective process development requires fit-for-purpose assays
- Start doing potency assay(s) experiments early
- Keep in mind what's "phase appropriate" in relation to Enterprise drivers/timeline and ultimate approved patient treatment – possibly toughest ongoing trade-off
- Plan for changes = Comparability!

Context is everything

- FDA: phase appropriate = some flexibility
- Enterprise: time and money priorities
- CMC for small and virtual companies: case by case
- Patients will be able to get the drug, if
  - it can be shown to be safe & effective relative to benefit:risk
  - it can be made reliably (and tested to confirm this)
  - & if all of the above happen within the constraints of the sponsor

How to Navigate the Small and Virtual Business Landscape & Manage More with Less?

- It depends (”case by case”)
  - Enterprise drivers drive CMC approach
  - Focus on patient needs to balance speed, money, rigor