Roundtable Session 2 - Table 16 - Challenges When Working with Contract Development Manufacturing Organizations (CDMOs)

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Abstract
Collaborating with Contract Development Manufacturing Organizations (CDMOs) has become a critical strategy for accelerating product development and scaling manufacturing in today's competitive landscape. However, these partnerships often present unique challenges that can impact timelines, quality, and compliance. This roundtable will explore the complexities of working with CDMOs, including communication barriers, alignment of technical standards, intellectual property considerations, and regulatory expectations. A therapeutic landscape leveraging novel modalities, can necessitate multiple outsourcing partners to leverage specialized expertise effectively, resulting in added complexity and alignment needs. Through interactive discussion, the roundtable will explore best practices for managing these relationships effectively, mitigating risks, and fostering collaboration that drives successful outcomes. Attendees will explore practical strategies to enhance transparency, streamline processes, drive quality alignment, and build resilient partnerships in an increasingly outsourced environment, while maintaining compliance standards.

Discussion Questions

1. What are the drivers for choosing to work with CDMOs as opposed to internal development?
2. What are the most significant challenges you've encountered when working with CDMOs, and how did you address them?
3. How do you balance maintaining quality and compliance while outsourcing critical development or manufacturing activities?
4. How often does utilizing a CDMO then lead to interfacing with multiple external partners (i.e. development versus manufacturing, manufacturing versus analytical)?
5. What practices have you found most effective for building trust and transparency with CDMO partners?

Notes

1. What are the drivers for choosing to work with CDMOs as opposed to internal development?
    - **Portfolio expansion via external assets:** CDMO use is often triggered when companies **in-license, acquire, partner on, or inherit assets through M&A**, especially when those assets come with established external manufacturing arrangements.
    - **Capability gaps:** Companies may lack specific **technical capabilities** internally (e.g., specialized process know-how), prompting outsourcing.
    - **Capacity constraints:** Even when capability exists, internal teams may be **outpaced by demand**, requiring CDMOs to expand throughput or support scale-up.
    - **Scale-up limitations:** Organizations may have early development capability but insufficient infrastructure for **late-stage scale-up** or GMP execution.
    - **Unique enabling technologies or materials:** Some projects depend on **unique cell lines** or proprietary platforms best supported externally.
    - **Complex supply-chain/ownership scenarios:** One example involved an asset acquired with an existing manufacturer; later, the asset was sold to another sponsor who brokered an agreement where the original company continued to **manufacture and supply within the asset's supply chain**.

2. What are the most significant challenges you've encountered when working with CDMOs, and how did you address them?

   Challenges were described as both operational and relationship-based, often rooted in misalignment between technical goals and business realities:

   - **CDMO strategic decisions that impact clients:** A major risk is when a CDMO makes **business decisions outside the sponsor's control** (e.g., shutting down a manufacturing site or pivoting away from a capability), forcing unplanned transfers and timeline disruption.
   - **Technical alignment vs. business friction:** Even when day-to-day technical collaboration is strong, misalignment among **finance/business development stakeholders** on either side can derail progress and weaken the overall relationship.
   - **Communication gaps and message inconsistency:** Several participants emphasized the need for **over-communication and deliberate alignment**, especially in strained partnerships. Tactics included:
     - Explicitly validating whether the CDMO team is receiving different direction internally
     - Surfacing fundamental operational differences early
     - Building trust through clarity and repeated checkpoints
   - **Contracting language misaligned with technical reality:** Issues arose when the **MSA/SOW/contract drafter** did not fully translate technical needs into specific contractual requirements. Participants stressed the importance of ensuring **regulatory, technical development, and business terms** are aligned—particularly around deliverables, timelines, change control, and responsibilities.
   - **Misinterpretation of sponsor requests:** One example highlighted a sponsor requesting the CDMO to pull a sample for testing. The CDMO treated it as hypothetical ("a test request") until the sponsor repeated it, illustrating the need for **unambiguous request pathways and escalation routes**.
   - **Quality outcomes that still fail sponsor usability:** In one case, a sponsor contracted for a **cell bank**. Even though the CDMO met QC criteria, the sponsor could not revive the cells upon receipt. This created significant tension and eroded trust, underscoring that **release specifications and real-world fitness-for-use** must be aligned upfront.

3. How do you balance maintaining quality and compliance while outsourcing critical development or manufacturing activities?

   Participants agreed that quality oversight must be active and structured—not assumed—when outsourcing key development or manufacturing steps:

   - **Sustained QA and Technical Development engagement:** Effective oversight depends on **continuous sponsor–CDMO communication**, including:
     - Strong technical interfaces (process, analytics, troubleshooting)
     - **QA-to-QA** engagement to maintain compliance alignment

       A recurring pain point: sponsor QA is not always engaged early enough.
   - **Audit access and audit receptivity:** Even when audits are specified in Quality Agreements, sponsors reported that some CDMOs are **not receptive**, creating practical difficulty in executing audits in a timely way.
   - **"Trust but verify," especially for late-stage assets:** One participant noted that when sponsors acquire late-stage programs and later file a BLA, they eventually "**descend onto the CDMO**" for deeper oversight. The consensus: build verification expectations early rather than escalating abruptly late in the lifecycle.

- **Relationship fundamentals that drive compliance behavior:** Simple actions were repeatedly mentioned as effective:
    - Reinforcing the mission and shared objectives
    - Recognizing what's working quickly
    - Helping the CDMO prioritize by clearly stating what matters most (e.g., "Please deprioritize Study A and prioritize Program B.")
- **Managing contractor motivation and accountability:** Participants discussed the challenge of influencing **loaned/embedded contractors** when internal sponsor reward systems don't apply. Suggested approaches included defining expectations early and creating appropriate feedback loops—even if formal recognition mechanisms are limited.

4. How often does utilizing a CDMO then lead to interfacing with multiple external partners (i.e., development versus manufacturing, manufacturing versus analytical)?

    The group noted that multi-partner ecosystems are common, particularly as programs mature:

- **"One-stop shop" claims don't always hold:** Not every CDMO truly offers end-to-end capabilities, even if they market themselves that way.
- **Capability gaps emerge over time:** Sponsors may discover gaps as the relationship evolves—especially because **development capabilities and GMP manufacturing capabilities are distinct** and not always equally strong within a single organization.
- **Cross-CDMO communication is often weak:** When sponsors split work across manufacturing and analytical testing providers, the CDMOs may **not communicate effectively with each other**, increasing integration burden on the sponsor.
- **Parent vs. new site inconsistency:** An example described auditing a CDMO's **new site** within a broader existing relationship. The audit did not go well—even from the accompanying scientific lead's perspective—highlighting that site-to-site variability can be significant even under the same corporate umbrella.

5. What practices have you found most effective for building trust and transparency with a CDMO partner?

    Trust-building was framed as an intentional discipline requiring structured transparency, stable communication, and expectation management:

- **Transparency as a prerequisite:** Participants emphasized building transparency into the partnership to enable **data review and candid questioning** without defensiveness.
- **Avoid constant "emergency mode":** A repeated theme: *"When everything is an emergency, nothing works."* Consistent prioritization and realistic planning improve responsiveness when true emergencies occur.
- **Set expectations internally—and protect the partnership when appropriate:** Sponsors must communicate effectively within their own organizations to:
    - Set realistic expectations
    - Build schedule buffers
    - Defend CDMO constraints when warranted
    - Avoid creating externally driven urgency that is not operationally feasible
- **Strategic communication:** Managing both internal and external expectations was viewed as essential—especially around timelines, changes, and decision points.
- **Enable collaboration within confidentiality limits:** If three-way conversations aren't possible due to NDA/confidentiality constraints, participants suggested using coordinated two-way conversations to keep parties aligned and to influence outcomes responsibly.

- **“Communication, communication, communication”:** Frequent, structured touchpoints—especially early—were repeatedly cited as the most reliable trust enabler.
- **Invest early and often:** Early engagement, clear governance, and proactive relationship-building reduce friction later when timelines compress or complexity increases.