

CDMO Project Execution

Driving Success by Being a Good Client

...and how to anticipate and proactively work to avoid issues

Other Side of the Desk

- CROs are in a very challenging and often “lumpy” business
 - Scarcity of capacity can sometimes drive price more than level of quality
- It costs real money to generate a proposal
- CROs and CMOs focus on doing what customers ask
 - Don’t expect them to stop you from making mistakes - It’s your Development Plan
 - Will they stop you from making process changes that affect impurity profiles or bioavailability?
- Development Stage vs. Commercial Stage CMO needs
- Differences between US, EU, India and China

Challenges CROs Face in Serving You

- CROs are a service business and you are one of many clients
 - CROs can be very service oriented but need to balance your project needs and changes with all those of all other clients
 - CROs do not always have resources, capacity and schedule availability to meet all needs exactly when required.
- CROs do not have unlimited surge capacity
 - Ability to add FTEs is limited
 - Ability to go back when there are significant technical hurdles or unplanned failures may not be immediate
- Lead times impact on responsiveness may not be their doing
 - RM not always available when required
- Flexibility is not always possible
 - The best CROs often don't have much flexibility
 - Clients that keep changing their mind create a ripple effect of cost
 - Be wary CROs offering too much flexibility!

Maximizing By Being a Good Client

- Success enablers often set before kick-off
 - Specificity - “Cocktail Napkin” RFPs / TIPs Cost You Money and Time!
 - Have realistic expectations of timing
 - Adequate internal resources for CRO guidance, oversight and to cover distance & cultural issues
 - Proactive management & metrics
- Planning - only certainty is that things will go wrong so plan accordingly
 - Plan with contracting and scheduling lead times in mind
 - Anticipate lead-times for problems and iterations for to-be-demonstrated technologies
 - Understand CMO need to balance multiple client schedules
- Execution
 - Early on-site involvement often means less time fixing things later
 - Clear PM roles and info flow BUT enable scientist-to-scientist interaction when needed
 - Strive to be easy to do business with while being clear and firm on your requirements
 - Understand how your changes impact the CRO

Quality Agreement for Clarity

- Clearly articulate technical and regulatory roles and responsibilities
- Phase-appropriate differences
- Integrated with Terms and Conditions, MSA or Supply Agreement
- Roles and Responsibilities matrix is more easily read and used by operating personnel than a legalese document but both are important
- Needed for GMP
- Not typical in US for GLP
- The devil is in the details so thinking through situations that may occur is critical

Quality Agreement R&R

Item	Issues & Responsibilities, Drafting, Review & Approval
<input type="checkbox"/> Org and Personnel	Be aligned on role of Quality Group and training
<input type="checkbox"/> Facilities	Commitment to compliance, access control, prevention of cross contamination
<input type="checkbox"/> Equipment	Qualification, cleaning logs & control
<input type="checkbox"/> Materials & packaging	Spec setting, testing, retention, approval of suppliers
<input type="checkbox"/> Production	Development, review and approval of MBR, BR, specs, deviations, reprocessing / rework, EM, retention, definition and handling of deviations
<input type="checkbox"/> Analytical	Specs, methods, sampling, OOS / Investigations, Turnaround time, validation, Right to participate in investigations
<input type="checkbox"/> QC	CofA, Product Disposition at various stages
<input type="checkbox"/> Label, Pkg, Ship & Storage	Label text, layout, retention, retest dates, storage conditions, shipping, inspection. Consider if need is more than 5 years and receiving at end of the period.
<input type="checkbox"/> Stability	Plan, reporting and approval
<input type="checkbox"/> Change Control	Clarity on how it will work
<input type="checkbox"/> QA	Complaints, recalls, MSDS, Auditing, Release, Timing of notifications
<input type="checkbox"/> Audits and Inspections	Access to facility for Audits, manufacturing oversight
<input type="checkbox"/> Regulatory Inspections	Notifications, Communications, timing
<input type="checkbox"/> Regulatory Filings	Initial, annual and ad hoc
<input type="checkbox"/> Expiry	R&R

Issues You Can Anticipate & Avoid

Issue	Comments
CRO “Performance” and commitment falls short	<ul style="list-style-type: none"> • Don’t always assume the CRO is motivated to deliver for you over an alternative • Invest time and effort up front in contracting and relationship management
Cost and delay of back and forth to get data	<ul style="list-style-type: none"> • Don't underestimate the effort required to complete a filing • Plan ahead for site and product specific post-run data checklists
Cost surprise on follow-on	<ul style="list-style-type: none"> • Consider separation of development / CTM to simplify earlier contracts but get ROM quotes based on assumptions
CRO has some IP or know-how that is needed in the future	<ul style="list-style-type: none"> • Protect your right to IP and know how to produce your product • rights to process and analytical methods and technology • The right to transfer the production technology and qualify other sites to produce the product
Need for unplanned technical work on a previously per-batch cost project	<ul style="list-style-type: none"> • Consider having that work charged on a transparent time and materials basis with the ability to review and cancel on 30 days notice.

Issues You Can Anticipate & Avoid

Issue	Comments
Delays in finalizing deliverables	<ul style="list-style-type: none"> • Consider Payment obligations that are triggered by acceptance of deliverables (i.e., reports, QA release, etc.) • Fixed pricing on each segment of the project as its scope becomes well defined (i.e., both parties are motivated to complete the work in a timely fashion)
Your time or cost constraints will be hard for CRO to meet	<ul style="list-style-type: none"> • Consider bonus payments for development and demonstration of specific process yields, which in turn tie to lower unit pricing for product supply
Stalemate on issues such as responsibility for failed batch	<ul style="list-style-type: none"> • Include terms which delineate the obligations of the parties in terms of communication and interactions, including arbitration
Cost increases when you feel there's no scope-creep	<ul style="list-style-type: none"> • Risk of surprise should decrease as project progresses • A step past which cost increases can not be passed on except for unforeseen and unavoidable technical issues is not unreasonable
Deviation and investigation report charges	<ul style="list-style-type: none"> • Should not constitute a scope change • Clarify up front in Quality Agreement or contract

Issues You Can Anticipate & Avoid

Bumping or Failure	<ul style="list-style-type: none"> • If CRO is fairly busy, the opportunity cost of their capacity is high. • Want to avoid ability to bump and then use “best efforts” to catch-up later and not be penalized • Penalty fees in general are a common practice and not unreasonable to include • Can trade-off some termination fee for equitable penalties for non-delivery based on things that they should to anticipate or control
Bumping or Failure – if it DOES Happen	<ul style="list-style-type: none"> • Consider the Pragmatic approach to the reality • Usually advisable to avoid forcing payment of fees from a CRO • Identify a win-win which maximizes the outcome and gain back time • Typically faster to recoup at contractor than to start over elsewhere • Have the contractor provide raw materials for another batch • Have contractor bump someone else in order to slot your work ahead • If CMO actions resulted in failure, CMO could redo at their cost • If results in significant timeline impact and work at a different CMO, consider RM at CMO’s expense or finished material for cost of materials alone without a processing fee

Metrics & Managing

- Keep metrics simple
- Understand how your demands change as you progress
 - Consider impact on the CMO
- Put in the effort to be a good client
- It's Your program – you need to lead the CMO
- Get on-site early
 - Less investment needed avoiding vs. solving

Summary and KSFs

Not rocket science but not easy either

1. A little planning & structure – it's NOT bureaucracy, its your friend
2. Honest understanding and documentation of yourself and your Requirements
3. The right internal expertise in the right amounts at the right time. Does not mean big infrastructure
4. Structured and forward-looking RFPs & Contracting
5. Its not hard to be a good client and anticipate understand what can go wrong. Many more things can be prevented than actually are!

We hope this was helpful!

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