ThermoFisher SCIENTIFIC

CDMO TIMEBOMBS

FIVE WAYS THE WRONG PARTNER CAN LEAD TO TROUBLE DOWN THE ROAD

- API
- BIOLOGICS
- VIRAL VECTOR SERVICES
- EARLY & LATE PHASE DEVELOPMENT
- CLINICAL TRIAL SOLUTIONS
- LOGISTICS SERVICES
- COMMERCIAL MANUFACTURING

patheon

INTRODUCTION

BIOLOGICS ARE COMPLEX. MANAGING THAT COMPLEXITY SHOULD NOT BE.

In the evolving biopharmaceutical industry, there is one thing you can count on: Unpredictability. It is in the nature of large molecules generating complex biological activity as scientists seek the right combination of purity, potency, safety and stability – from cell lines to commercialization.

Overcoming the technical challenges of developing and manufacturing biologics is a tall order. You need cutting-edge technology, razor-sharp data analytics and streamlined processes to establish a quality product, navigate high regulatory standards and meet ever-changing market demands. These challenges make choosing the right CDMO partner critical.

THE RISKS OF THE WRONG CDMO CHOICE

Working with a manufacturing partner who cannot manage the complexities of your biologic can cause problems both large and small – in the near term and the long run. Whether it is a batch failure, clinical hold or production shortfall, any delay can lead to missed milestones, unexpected costs or worse. The wrong CDMO can put your next level of funding, or even the future of your company, in jeopardy.

Tick-tick-ticking timebombs

What happens when a CDMO partnership goes awry?
Beware of these five cautionary tales inspired by true events:

1. **Promises made, promises missed**
   An accelerated timeline slows the works
2. **Know-how vs. “No, how?”**
   Technical expertise matters now more than ever
3. **A steeper scale-up**
   Falling behind by not thinking ahead
4. **Strong proposal, wrong priorities**
   A partner that does not live up to the hype
5. **Get with the program**
   When operational excellence is anything but

TIMEBOMB 1: PROMISES MADE, PROMISES MISSED

After meeting with several manufacturers for its IgG4 molecule, Biopharma A selected the CDMO that promised the first GMP batch within eight months, and costs within their budget.

Biopharma A's molecule appeared on track during upstream development. However, problems soon arose because the CDMO did not properly vet the scope of work or capture enough early data, forcing significant scope changes and cost increases.

The CDMO cut corners in an aggressive attempt to hit the approaching deadline, evaluating an inadequate data package during development that caused analytical characterization issues and manufacturing problems down the line.

TICK-TICK-TICK

The CDMO rushed to produce the first GMP batch to meet their timeline, resulting in:

- Purity concerns and poor viral clearance performance
- Failure to meet regulatory requirements for IND approval
- FDA applying a clinical hold, and a program delay of 12 months

HOW TO DEFUSE

Your CDMO should not compromise quality for an approach that risks timeline delays and surprise costs. Choose a partner with:

- A realistic plan to produce GMP material within 12 months
- Strong early-phase development experience
- Established platforms to anticipate problems and accelerate production

+ Seek a CDMO that seamlessly integrates analytics, enables real-time data access and evaluates molecules with proven platform methods.

TIMEBOMB 2: KNOW-HOW VS. “NO, HOW?”

The emerging Biopharma B was working on a recombinant therapeutic protein with its first manufacturing partner, a CDMO offering a solid development background, dynamic project team and low fee – but no biologics experience.

The CDMO relied on techniques and technology that could not handle challenging formats and highly complex biological materials. This poor platform fit created stability, purification and production complications throughout development.

The CDMO’s scientists missed a trend in dissolved oxygen that resulted in a failed cell culture. Their engineers did not recognize a problem with the packed chromatography bed during qualification. They were slow to address a lingering precipitation issue. Quality control concerns added up fast.

TICK-TICK-TICK

The CDMO lacked the technical expertise needed for complex molecules, resulting in:

- Multiple batch failures and clinical trial delays
- Unexpected and increased costs
- A new CDMO getting hired, and a 15-month program reset

HOW TO DEFUSE

Your CDMO should have the right biologics know-how from development through commercialization. Choose a partner with:

- An experienced team of industry experts
- Talented scientists and engineers
- Proven processes for recognizing and resolving complex molecular challenges

\+ Seek a CDMO that embraces cutting-edge technology to streamline development and enhance manufacturing.

TIMEBOMB 3: A STEEPER SCALE-UP

Hoping to gain expedited IND approval for its vaccine, Biopharma C engaged a small CDMO known for early-stage biologics success – and steep fees. The decision paid off. Efficient cell line development and purification processes led to swift IND filing and Phase I clinical trials.

Yet the CDMO did not look around the next corner and failed to create a workable scale-up plan for expanded trials and commercialization. They used exotic raw materials that worked well at 200 liters but were prohibitively expensive at larger scale, making the cost of goods too high.

The CDMO's lack of scaling experience also caused substantial supply chain and volume concerns, all while erasing the timeline gains Biopharma C made early in the program.

TICK-TICK-TICK

The CDMO's near-term development focus did not address future demands of scaling, resulting in:

- Higher raw material costs due to a faltering supply chain
- Slower scale-up due to more batches needing to be run
- Significant production and commercialization delays, and a flawed vaccine roll-out

HOW TO DEFUSE

Your CDMO should think several milestones ahead and prepare for commercialization from day one. Choose a partner with:

- An approach that balances fit-for-purpose with fit-for-future
- A strategy that aligns development and production processes
- Strong supply chain experience and relationships

\+ Seek a CDMO with capacity to scale production, a network of flexible manufacturing facilities and a large stockpile of commonly used raw materials.

TIMEBOMB 4: STRONG PROPOSAL, WRONG PRIORITIES

In a rush to bring its gene therapy drug to market first, Biopharma D partnered with an up-and-coming CDMO that put together an engaging proposal featuring an aggressive schedule, impressive claims and big technology investments.

However, the CDMO lacked real know-how to lead a biological molecule through late-stage development and commercialization, delivering an inefficient program that produced poor quality, serious safety concerns and missed milestones.

Ultimately, Biopharma D's drug product failed process validation steps and fell short within several key studies, including an inability to demonstrate clearance of impurities and inadequate bioburden control strategies.

TICK-TICK-TICK

The CDMO's bold proposal belied a critical scarcity of experience and knowledge, resulting in:

- Key analytical missteps throughout development
- Ill-informed process characterization leading to ill-fated validation
- 11-month filing delay prior to FDA approval, and Biopharma D not being first to market

HOW TO DEFUSE

Your CDMO should value experience and expertise over excitement and extravagance. Choose a partner with:

- Proven biologics experience and pressure-tested technical expertise
- The know-how to set realistic development and production timelines
- The ability to manage regulatory reviews, clinical trials and commercialization

+ Seek a CDMO with end-to-end capabilities – one team that can seamlessly guide your product from upstream to downstream to the commercial market.

TIMEBOMB 5: GET WITH THE PROGRAM

Biopharma E engaged a CDMO with renowned scientists and a strong biologics background to develop its allergen immunotherapy product. Unfortunately, the new partner's inexperienced project management team ran a flawed manufacturing program.

Challenges arose quickly. The CDMO did not use templated documentation to streamline processes. They collected insufficient early data, which impacted verification stages later. Their scale-up proposal proved inadequate for production.

Instead of guiding Biopharma E's drug product from one clinical milestone to the next, the CDMO put out process fires at every step. Before long, their flawed program turned into a failed product.

TICK-TICK-TICK

The CDMO struggled to identify problems, address gaps and handle key logistics, resulting in:

- Timeline delays and missed milestones
- Inconsistent production and volume shortages
- Substantial quality control concerns and repeated clinical failures

HOW TO DEFUSE

Your CDMO should never settle for good enough when it comes to the success of your biologic. Choose a partner with:

- An effective continuous improvement program
- Dedicated operational excellence resources
- Templated documentation and real-time data management

+ Seek a CDMO with a collaborative project team that focuses on quality and excels in everything from process development to global logistics.

AVOID A TIMEBOMB. CHOOSE THE RIGHT CDMO.

Now that you have read these tales, seek the true story from your current or prospective CDMO by asking: do they have the right approach and capabilities, process and programs, expertise and experience?

Partnering with the wrong CDMO – whether they break big promises, lack deep know-how or fail to look around the next corner – can create a potential timebomb for your biopharma. From increased costs and production missteps to delayed approvals and missed milestones, you could put your drug product at risk.

HOW TO MAKE THE RIGHT DECISION

Ultimately, managing the complexity of biologics is simple: hire a CDMO with proven experience in upstream and downstream development and manufacturing. An organization with the technical expertise, advanced technology, platform processes, end-to-end network, program management and robust resources to meet your biologic's needs. A partner with a flexible, forward-thinking approach to guide you through clinical trials, efficiently scale production, adeptly navigate commercialization and successfully launch your product.

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