Managing Service Partnerships

The Unexpected and Often Unplanned Management Needs

Avoiding pitfalls that could derail your project. *This is the third of a four-part series of articles addressing best practices for a successful relationship with your service partners.*

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In this third installment of our four-part series, we will discuss the day-to-day requirements and activities that happen before and after your production scheduled slots and areas where poor planning or experience could derail your program.

In the first installment,[1] we discussed how to start the partnership, and in part two,[2] we covered some of the areas where early intervention will go a long way in keeping your programs on track and on budget.

During preparation for the first campaign or production of cGMP materials, there is a lot of expected work related to tech transfer, batch records, and other cGMP documentation required to be successful. This effort is typically well supported by both parties as it is expected, well understood, and required for all cGMP production activities. However, once production is completed, there are many more activities that require the attention of subject matter experts and management. Some examples of these activities include:

- Executed documentation review and approval
- Non-conformance review and approval
- Investigation plan and execution
- Change controls
- IND/BLA annual reports
- Post marketing commitments and/or requirements
- Master record amendments
- Continued process verification
- Stability pulls, testing, and reporting both to the client and to the agency

- Decisions about storing or disposal of high-cost raw materials, such as resin, filters, media, etc.
- Decisions about storing samples, drug substance handling, and shipping
- Financial matters related to all the above, many often not part of routine production

Small and/or early-stage companies—both CDMOs and sponsors—are often naive to the efforts required in addressing all the above and therefore do not properly resource the talent, costs, and time required to be successful. Although strong project managers can understand and manage what must be done and by when, the decisions and resources must often come from subject matter experts and senior leadership.

One major deviation that requires a full investigation could delay your entire program. An event like this should be expected and planned for during any campaign.

So how can you possibly know what you need? It can be difficult, but leaning on others with experience will help. Here are some thoughts on how to best plan for the ongoing CMC development activities:

1. If your process is unproven at scale or it is the first time at scale with a new supplier, you must assume there will be many deviations and/or change controls to write, review and manage. These will occur due to lack of process knowledge, lack of experience and training with the process, human error events, supply chain mishaps or delays and potential equipment challenges. Plan for extra time, costs, and talent support.

2. If your process was manufactured at the same site previously, make sure you pull out the old records and update them with lessons learned. Make sure that the analytical methods are updated. Verify that raw materials, special reagents, and other process requirements are not expired and are released. If it has been greater than eight months, make sure the operators and analysts review/retrain on batch and analytical documentation.

3. Stay on top of stability pulls. The CDMO manages multiple clients, and several have multiple production stability lots. Make sure you review how they manage the complicated pull dates, the OOS process and, if one occurs, the reporting timing. Ensure you have visibility to all the stages of the stability program and can provide support if needed.

4. Make sure there are enough retains and other extra samples to allow for retesting. Things go wrong in the lab as much as they do in production. These extra samples could save a batch. However, do not over sample without careful planning. These samples require oversight and storage space. It is costly for the CDMO to keep too many for too long. Eventually, the sponsor will have to decide on the disposal of these as well. You will need to have a mutual agreement on when it is time to discard.

5. Shipping, labeling, storage, and other logistics are often overlooked and require resources and planning and subject matter expertise.

6. Reference standard and critical reagents are often overlooked and impact release and stability testing. If you don't have reference standard or critical reagents, it doesn't matter if you have retains or stability samples, you won't be able to test.

In our experience, it is mission critical that a sponsor has a dedicated resource to manage external partners. That resource must have authority to draw on subject matter experts within the organization or have the budget to pull in consulting experts from outside, if needed. There is no substitute for experience.

It is also critical that the CDMO provides a project manager (PM) who has the time to support your program during these in-between times. Often these PMs will be moved off a program to lead an active production campaign with a different client. There is not much a sponsor can do except to know this upfront and work with the CDMO to ensure you have a strong resource at the site. The sponsor will likely be paying for these resources, so make sure they are accessible and competent.

If there are long gaps between campaigns, make sure to visit the site prior to the next one to re-engage key leaders, provide some extra incentives and pep-talks, i.e., a lunch and learn on the program and indication. You want all employees at the CDMO engaged. These folks do not enjoy the same upside incentives that sponsor employees do, so they need extra attention and some free food!

This list could go on and on, however, the point of this part three is to remind folks that the work for both parties is not done once the product is in the final container. Sometimes, the hardest work is yet to come. **CP**

References

1. *https://www.contractpharma.com/issues/2023-06-01/view_features/contract-service-providers-part-of-your-process/?widget=listSection*
2. *https://www.contractpharma.com/issues/2023-11-01/view_features/overcoming-stressors-in-knowledge-transfer/?widget=listSection*

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