OPTIMIZING CDMO TECH TRANSFER

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Many of the logistical, cost, and technical challenges associated with tech transfers can be overcome when the transfer takes place under one roof or occurs between near-identical facilities.

Technical transfers are a fact of life in pharmaceutical/biopharmaceutical development. Whether a process is being scaled for commercialization, transferred to another contract development and manufacturing organization (CDMO), or reproduced at the same scale at an additional site, pitfalls exist at every step when attempting to replicate a production process.

Companies transferring a process must focus on three key factors: the equipment, the process, and the employees' knowledge of the product. Obstacles to the smooth transfer differ, and some types of tech transfer are more complex than others. In this article, we discuss the challenges associated with tech transfers and share how Northway Biotech helps customers overcome such challenges at its twin facilities in Massachusetts (USA) and Lithuania (Europe).

TECH TRANSFER CHALLENGES

A technical transfer can replicate a single operation, a fully developed production process, or anything in between. Biotech companies may be seeking a CDMO with extra capacity to produce a particular drug substance or drug product or they may need material on an accelerated timeline. Other companies wish to increase the volume they produce at another facility, or they want to consolidate workflow – for example, a company working with four different CDMOs may want to trim its list of partners.

More importantly, companies planning a tech transfer prefer that a CDMO has experience scaling production from Phase 1 to Phases 2 and 3, should commercialization of their product become a reality. Often, biotech companies are adept in identifying new molecules or new mechanisms of action for drug targets and choose not to focus on current good manufacturing practice (cGMP) production for business and strategic reasons. Accordingly, their process as originally conceived may produce sufficient material to carry out initial studies, but it is not well-suited to scaling or robust enough to serve as a cGMP process.

Whatever the reason for the change to (or addition of) a new production site, biotech companies commonly encounter unexpected roadblocks to vital process transfer steps. Sometimes the organization whose process is being transferred or replicated simply refuses to cooperate. For example, the lab performing CRO tasks may have its customer locked into a master service agreement that prohibits transferring the process. More established CDMOs tend to be more up front in clearly communicating the master service agreement and ownership of the technology.

Other times, knowledge of the process being replicated is poorly transferred. In such scenarios, the process originator may not be accustomed to a smooth tech transfer, or they do not actively support the process due to various reasons. Usually in these cases, the process originator provides insufficient documentation. For example, if a customer is moving away from another CDMO – perhaps they are unhappy with that CDMO, it lacks the customer's required capacity/ slot availability, or it cannot produce enough material – that CDMO may be indifferent to the fate of the process leaving its hands.

However, it is more common that biotech companies or CDMOs transferring a process are support-

ive and facilitate an effective transfer of documentation. Typically, access to this documentation is a client right: since custom manufacturing is a service, the intellectual property (IP) belongs to the client, though exceptions exist. For example, while the customer may own IP on the process itself, we have seen a CDMO claiming that, because it added a proprietary step, it owns IP on the process. In other cases, a CDMO is not eager to share what it claims to be parts of its SOP, or gaps in documentation cannot be reconstructed because individuals responsible for the process have moved on from the company. In these situations, the new CDMO must essentially redevelop/redesign the process based on fragmented or minimal information.

Finally, tech transfers may be undermined by poor communication and coordination between partners. For example, most operational details about a process are recorded in production batch records. However, tacit or implicit process knowledge and best practices cannot be easily documented. Identifying and capturing this type of information presents a significant challenge. Therefore, CDMOs that provide comprehensive and integrated services with a highly skilled and experienced team are key to the success of tech transfer.

HOW NORTHWAY BIOTECH OPTIMIZES TECH TRANSFERS

Northway Biotech's success in tech transfers results from a combination of our facilities, processes, equipment, and experience. Our unique facility design concept — implemented in both Waltham, MA, and Vilnius, Lithuania — allows for total vertical integration and forms the foundation of the experience we provide to customers. Everything from cell line development to fill/finish is managed under one roof.

Consolidating in integrated facilities means Northway does not have to schedule the drug substance and the drug product at two different locations, and the client does not need to deal with separate CDMOs managing the drug substance and drug product. In such situations, sometimes the schedules do not match and cannot be changed, and the developer is forced to pay a penalty and/or experiences delays in their project timelines. Additionally, Northway Biotech's integrated facility approach inherently saves customers money and time — in our experience, six to eight weeks — by eliminating challenges associated with shipping between sites, release testing, and material quarantine.

In many cases, the formulation of a drug substance and a drug product are quite similar. If a completely different formulation buffer for the drug product is not used (i.e., with different excipients or a completely different concentration), the same qualification applied to analytical methods for the drug substance can be applied to the drug product, supporting product release without additional cost or effort for the client.

This effectiveness is further enhanced by the proximity of our facilities to most of our clients. As a global company predominantly serving customers in Europe and the United States, Northway Biotech has mirrored the facility design between its sites near Boston and in Lithuania. For example, the process development labs at each facility share the same selection of 200+ pieces of equipment (almost identical between the sites). Each site also maintains multiple pieces of equipment of the same model, ensuring customers do not have to wait for another customer to complete a project before kicking off their own program.

Identical equipment facilitates the usage of identical procedures/SOPs, as well. Ideally, the only difference between sites is the people, allowing for fast intra-company transfer from site to site. When Northway Biotech progresses from process development to GMP, or reproduces a process from another of its sites, no time delays or expenses are incurred changing procedures.

Manufacturing process scale-up or process transfer to a facility operating equipment different from the source site adds another layer of complexity to the tech transfer process. Still, Northway Biotech embraces such opportunities to evaluate precisely which process steps are viable for transfer and which ones require some redesign. If it is not a like-for-like tech transfer, we optimize the process in many cases, improving its ability to scale up.

Consider microbially produced biologics markets: many CDMOs operate in the low-volume and midsize range, but few excel in the high-volume range. Additionally, many CDMOs that offer 30,000- or 50,000-liter fermenters have equipment that is not suitable for biopharmaceutical manufacturing; it is used for food supplements, vitamins, or, in some cases, antibiotics (which require dedicated plants, per GMP requirements). Northway Biotech is among the few producers of pharmaceutical proteins who can produce low, medium- and high-volume batches. This ensures customers who partner with us from early process devel-

opment through commercialization can meet their production demand.

Northway has managed more than 100 international projects, many through commercialization, completing a typical tech transfer in three months. The first month, the project design phase, includes the exchange of any necessary process documentation, discussion between the Northway Biotech and customer teams, and procurement of raw materials. Thereafter, a tech transfer protocol is drafted before tech transfer and process confirmation runs are executed.

In addition, analytical method transfer protocols are drafted. Process development and analytical development are performed if required, with the performance of the newly improved process verified in demonstration runs. Readiness activities for non-GMP tox batches and GMP batches are executed early to ensure the technology transfer is smooth from the beginning to cGMP manufacturing. If these steps are successful, production of the drug substance begins in earnest.

Northway Biotech serves a worldwide customer base and draws on the global knowledge of our workforce. We enlist experts on each side of the Atlantic, all working with the same equipment and possessing a deep understanding of the biologics production processes they execute and transfer. To learn more about Northway Biotech, either for consolidating your operations or executing a seamless technical transfer, visit https://www.northwaybiotech.com/.

ABOUT THE AUTHORS

Vladas Algirdas Bumelis, Prof., is the Founder and CEO of Northway Biotech. He holds PhDs in both chemistry and biotechnology from Vilnius University and is a full member of the Lithuanian Academy of Sciences. Prof. V. Bumelis has extensive experience in the pharmaceutical and biotech industries, having previously served in senior management positions at international companies in the biopharma industry such as Teva Pharmaceuticals, Sicor Inc., Biofa, and Biotechna. His illustrious career has been recognized many times. In 2004, Prof. V. Bumelis received the Science Award of Lithuania in recognition of his achievements in the development and production of recombinant proteins, while in 2012, he was named CEO of the year in Lithuania. Vladas can be contacted at vladas.bumelis@northwaybiotech.com.

Dominic Chow, PhD, is the Sr. Director of Process Development for Northway Biotech's site in Waltham, MA. Dominic has more than 15 years of experience in the biotechnology and biopharmaceutical industry. He specializes in process development and characterization, technology transfer, scale-up, and manufacturing support for biologics (monoclonal antibodies, enzymes, and recombinant proteins) and novel therapeutics (antibody drug conjugates and mRNAs). He previously worked for Lonza Biologics, Bristol-Myers Squibb, ImmunoGen, and Moderna. Dominic has an MSc and a PhD, both in chemical engineering, from Northwestern University, and conducted his post-doc in biomedical engineering at Duke University. He can be contacted at dominic.chow@northwaybiotech.com.

André Markmann, PhD, is VP of Business Development for Northway Biotech since 2014. André has 19+ years' experience in the pharmaceutical and biotech industry, including employment with Sanofi-Aventis and DSM/ Patheon. He holds a PhD in biochemistry. André can be contacted at andre.markmann@northwaybiotech.com.

ABOUT NORTHWAY BIOTECH

Northway Biotech is a leading CDMO supporting customers worldwide. Its highly experienced, professional team executes projects at any stage, from cell line construction and process development to cGMP manufacturing of biopharmaceutical products. The company's wide-ranging expertise and vertically integrated service offerings translate to the ability to rapidly execute multiple projects from its state-of-the-art GMP facilities, while ensuring full process and product compliance at all stages of research, development, and commercial manufacturing. Northway Biotech is a privately owned company founded in 2004 and located in Vilnius (Lithuania) and Waltham, MA (USA).

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