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Custom Development & Manufacturing Organization (CDMO)

# Technology Transfer Documentation – What is Essential and Why?

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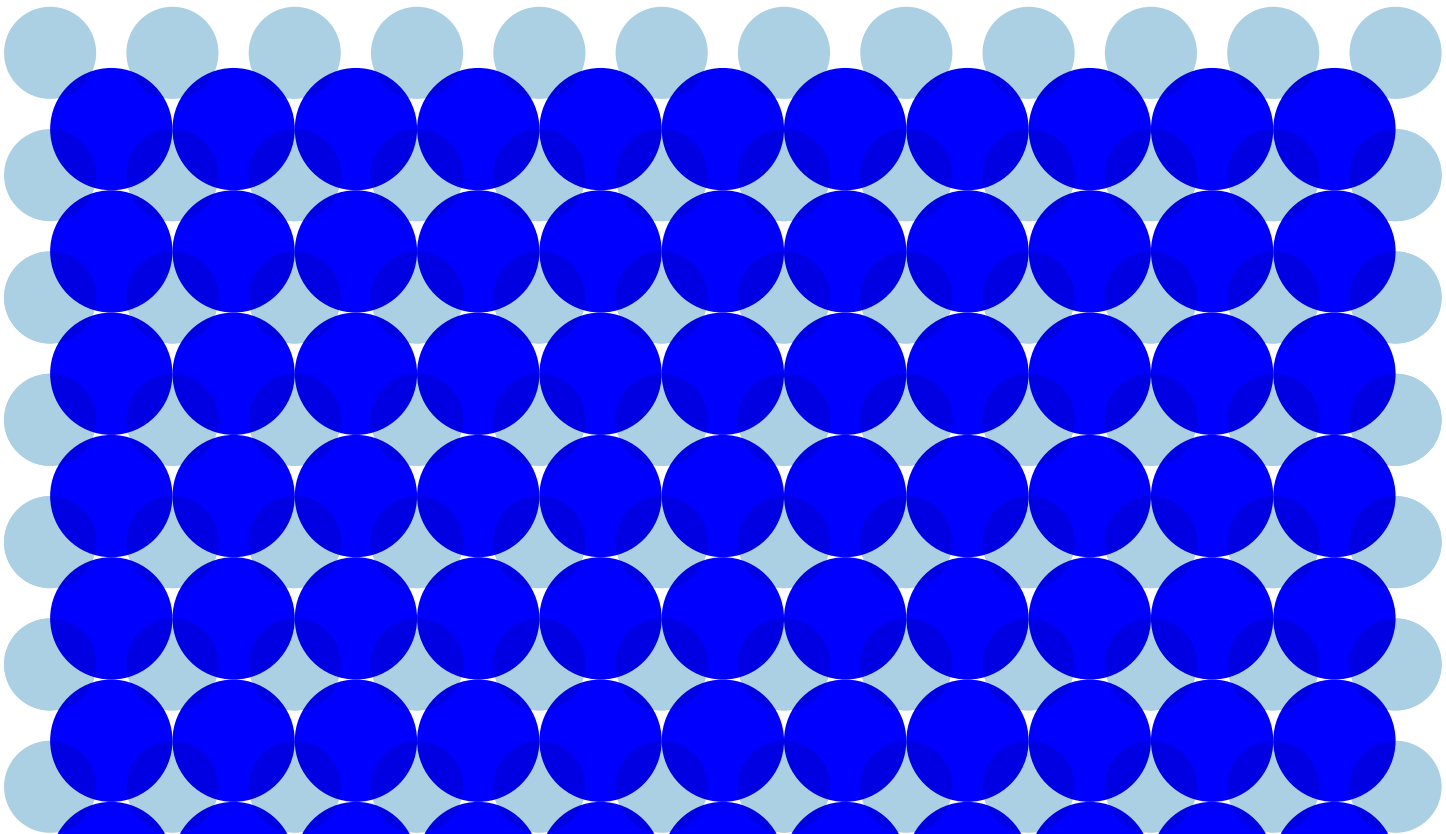
Unlock the potential of biotechnology CDMO services to expedite your product's journey to market. Our extensive coaching experience underscores the critical first step: crafting compelling technology narratives. By assessing your process and the completeness of your technology transfer package, you empower CDMOs to provide accurate price estimates and tailor their assistance to your project's needs. Whether your project is in its infancy or nearing completion, our guidelines aim to streamline documentation, reduce time-to-market, and elevate the success rate of technology transfers in the biotechnology industry.



## Technology Transfer Documentation – What is Essential and Why?

**Have you ever considered leveraging biotechnology CDMO services to bring your product to market? Drawing on our decades-long coaching experience, we highlight the initial step in this process – crafting technology narratives. It's crucial to assess what is known about your process and the completeness of your technology transfer package (TTP), then share this information with CDMOs to obtain price estimates. This enables CDMOs to realistically evaluate how they can assist with your project and under what conditions, facilitating a successful process transfer later on.**

**Depending on the stage of your project, technology documentation may be incomplete, contain inconsistent data sets, or focus on information not directly pertinent to the manufacturing process (such as detailed scientific descriptions of engineered metabolic pathways). We believe that by elucidating the guidelines outlined below, we can establish a standard within our industry, reducing the time-to-market for biotechnology projects and enhancing the success rate of technology transfers.**

What are the usual next steps that we and our customers take after our initial meeting? Following the execution of a mutual Confidentiality Agreement (CDA), the customer provides preliminary project and process details in the form of a document known as a Request for Proposal (RFP). This enables the CDMO to assess the project's technical feasibility, potential need for additional technology development one-time costs, CAPEX requirements, and timelines. Although the technology evaluation is a standardized process, it is iterative and necessitates effective communication between the parties during meetings that are typically technical in nature.

For startups and new business development initiatives, there are topics beyond just the production process that need consideration. Therefore, considering Arxada´s CDMO consulting services to focus on identifying critical points and determining the rationale behind initiating a feasibility study to gain insights into the production process and estimate costs for commercial production might be a wise decision.

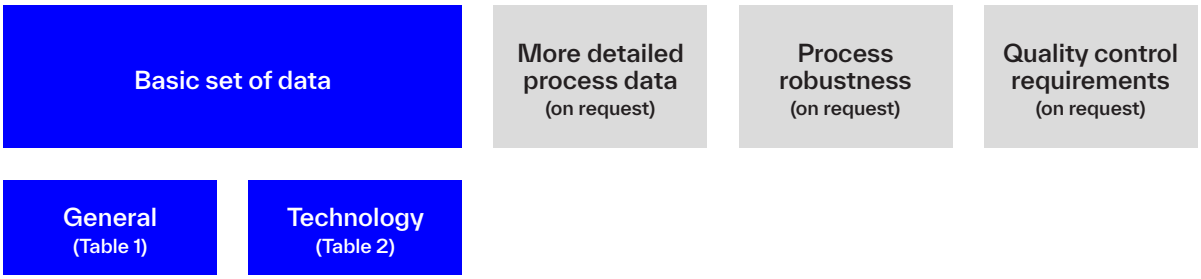
Already at this stage of technical feasibility evaluation Arxada CDMO can identify bottlenecks and potential technology scale up road blockers e.g.:

- Utilization of lab-grade, unreasonably pure or non-compliant (from regulatory perspective) raw materials, too many DSP (downstream processing) steps, sometimes arranged in a complex sequence (e.g., improper installation of an ultrafiltration (UF) membrane causing a suspended solids leak into the permeate and therefore additional depth filtration step was installed to clarify hazy UF permeate).
- Scale-up parameters do not considerably correspond to industrial ones (e.g. sterilization time, very low membrane load may dramatically change the nature of the process).
- High consumption of chemicals/generation of wastes (e.g. urea for protein solubilization if used at wrong place in the technology, extensive use of salts or solvents).
- DSP is developed using laboratory equipment not corresponding to the industrial set-up (e.g. bucket centrifuge vs. continuous disc stack centrifuge where the outcome can be very different).

*Figure 1: Scale-up parameters should be always watched carefully. E.g., grossly different membrane load at the customer's and CDMO's manufacturing scales in case of tangential flow filtrations can change the nature of the technology entirely. It is one of the main responsibilities in the project evaluation stage to uncover all such possible discrepancies.*

As illustrated in Figure 2, when drafting comprehensive technical documentation, information is typically organized into basic data, a more detailed set of process data, and details about process robustness and quality control requirements to ensure both mutual exclusivity and exhaustiveness.

*Figure 2: Classification of the information required for a cost estimate and the technology transfer. The detailed questions are in table 1 or 2, respectively can be received on request from myproject@arxada.com.*




At a minimum, answers to the questions within the initial basic set of data are necessary for preliminary, ballpark cost estimates (Table 1 & Table 2). However, to enhance the accuracy of the evaluation and reduce unexpected issues during the process, detailed responses are encouraged. This facilitates the provision of legally binding offers at the earliest opportunity.

**Table 1: General data needed for ballpark cost estimate.**

| Category | Question / Example Answer | Why is it important? |
|---|---|---|
| Project Objectives & Timelines | **What are the key objectives of the project, and what is the projected timeline?**<br><br>We are requesting a transfer of the current process into laboratories, optimization of downstream process, scale-up via pilot scale to 50 $m^3$ production scale, process validation and later in regular manufacturing campaigns.<br><br>Project timeline:<br>Q3/2024 Lab phase<br>Q1/2025 Pilot<br>Q3/2025 Validation batches<br>2026+ one production campaign every year | The aim is to understand the client's priorities and determine the focus areas, such as process development, scale-up, process validation at manufacturing scale, regular manufacturing, or further optimization. Should the focus be on any particular part of the process, such as upstream processing (USP) or downstream processing (DSP)?<br><br>Understanding the customer's timelines is crucial for assessing how to integrate the project into the current portfolio. |
| Campaign Size/ Timing & Outlook | **How are campaigns scheduled in terms of size, frequency, and outlook?**<br><br>2026 demand 5 000 - 10 000 kg<br>2027 demand 7 000 - 15 000 kg<br>2028 demand 11 000 - 22 000 kg<br>2029 demand 17 000 - 34 000 kg<br>Always 1 campaign per year | Does the customer prefer one campaign per year or a split into more campaigns throughout the year? Their outlook and possible scenarios help us with planning asset utilization and reveal potential conflicts with other projects we have in the pipeline. |

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| Product Nature & Regulatory Requirements | **What is the nature of the product. What regulatory requirements should be fulfilled?**<br><br>The product is “new-molecule-2-ol”, a small molecule with application as a nutraceutical. Manufacturing should be done under FSSC 22000. Kosher and Halal certifications are required. | CDMO manufacturers sometimes already have certification. In instances where certification is lacking, it's important to be informed beforehand so that an assessment can be made regarding the implementation of the missing requirements. |
| EHS Risks | **Are there any known environmental, health or safety risks associated with the technology?**<br><br>GMO biomass must be inactivated before disposal. Flammable solvent is used for product purification. Product has no associated health risks; a material safety data sheet is attached. | There are many potential risks associated with each technology. It is important to be aware of them as soon as possible to apply adequate safety measures. |
| Technology Readiness & Optimization Potential | **How ready is the technology for implementation, and what level of optimization is envisioned?**<br><br>The technology has been already scaled-up to 20-L volume (tens of experiments), some initial DSP development has been performed. Optimization is expected esp. in DSP, later also in USP with a further optimized strain. We expect to double the process productivity in 3 years from now. | The need is to understand which stage the work is to be taken over from the customers, along with their desired direction for future development. |

Table 1 offers a basic overview with example answers, serving as one component of the fundamental dataset for conducting ballpark cost estimations. Occasionally, certain aspects may not have been explored during feasibility or development studies. Nevertheless, Arxada CDMO conducts feasibility studies to uncover answers, allowing customers to share standardized technical transfer documentation with all considered CDMOs at that stage. The answers of table 1 are primarily valuable for determining technical feasibility: yes or no.

In addition to this general set of data, basic technological information (Table 2) is crucial for estimating production capacity and the required resources per day. These more quantitative answers enable the calculation of production costs.

**Table 2: Basic technology data for ballpark cost estimate.**

| Question / Answer | Why is it important? |
|---|---|
| **What microorganism is used as the production host? What is its biosafety level? Is it GMO? Is it sporulating?**<br><br>E. coli; BSL-1; GMO; non-sporulating. | A microorganism is at the forefront of any fermentation process. Biosafety level, genetic modifications and sporulation are important for understanding the nature of the process and associated safety risks. |
| **Which type of fermenter is used?**<br><br>Stirred tank. | Various configurations can be used by our customers, e.g., stirred tank, bubble column, airlift, solid state fermentation. Not all processes can be implemented in our facility such as solid-state fermentation. |

| | |
|---|---|
| **What is the bioprocess operation mode?**<br><br>Fed-batch mode with 2 feeds. | Various operation modes exist, e.g., batch, fed-batch, semi-continuous (also known as Repeated Fed-Batch or draw & fill), fully continuous, etc. Details need to be known to evaluate the process economics and fit into the existing facility set up. |
| **What productivity is achieved?**<br><br>The titer at the end of fermentation is 40 grams of the product per L of fermentation broth. The current DSP yield is just 50%, but we expect the yield increase to 70% with the optimized DSP process. | One of the key process performance characteristics. Productivity in terms kg-final product/$m^3$-fermentation broth (this number already includes DSP yield). Alternatively, the product titer after fermentation + DSP yield. It should be specified whether the titer is expressed per $m^3$ of the fermentation broth or per $m^3$ of the supernatant. In case the titer is per $m^3$ of the supernatant, also volume fraction of the supernatant in the fermentation broth should be stated. |
| **What is the duration of the main fermentation step excl. turn-around time?**<br><br>72 hours. | Another key process performance metric. Turn-around times are factory configuration dependent and difficult to assess by our customers, but easily assessable by CDMOs. |
| **What is the maximum filling of the fermenter at the end of fermentation?**<br><br>We are running the process with 70% filling. 80% could possibly be achieved as foaming is not extraordinarily strong. | Important but often omitted process performance metric. The higher the fermenter filling, the higher the output. Foaming is usually the most prominent constraint. |

After the agreement between the customer and the CDMO is reached and the contract is signed, the project moves into the next stage – execution of the technology transfer itself. Detailed TTPs are shared at this stage, but it is already a different story, which we will deal with in some of the following white papers.

**In summary, creating technical transfer documentation involves considering various aspects from both qualitative and quantitative perspectives. This is to facilitate prompt decision-making from a CDMO, either for a quick yes or no response, and then in case for providing a price estimation. Arxada's CDMO experts aim to guide you by asking targeted questions and advising whether to proceed directly to technical transfer or to delve deeper into uncovering hidden information through a customized feasibility study at the current stage.**

## Our offer

- **One stop shop CDMO services in the field of industrial biotechnology**
- **Engagement at any stage of product/process development stage**
- **Dedicated team for technical evaluation and consulting for your project stage**
- **Facility registered as food manufacturing site at FDA. Holding additional certification cosmetic manufacturing (EFfCI cGMP) and has certificates for ISO 9001:2015, FSSC 22000/HACCP, FAMI QS, Halal, Kosher and EFfCI**
- **Long lasting experience with high quality, speed, and strong focus on continuous process improvement**
- ***Focus on what matters to you***

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