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Fundaments of project success

If you are heading towards an external piloting or manufacturing campaign two phases should receive the highest attention both from client and contractor due to their importance for project success: The technical and commercial contract initiations (CI) & the tech transfer phase (TT).

This is a lesson which we have been confronted with repeatedly. Wrong or undiscussed expectations, a flawed understanding of the clients' process, product requirements, project targets or even an unawareness of the technical limitations of the contractors' facility will either yield a bumpy project start or greater turbulences later on. Even if gaps are available, openly addressing them from both sides is of great value as it shows the need to give them attention as the project proceeds. Mature companies with process and piloting experience are stressing these two project stages. Less experienced ones under timely pressure sometimes tend to short-cut and undervalue their importance.

Technical and commercial contract initiation (CI)

Developing a service contract can take 3-9 months, depending on the technical and commercial complexity. Ideally the CI discussions involve commercial *and* technical key personal from the very beginning. This phase provides the chance for "*having the end in mind*" even though just for this single project between client and service provider and not the overall technology commercialization. A proven way to do so is to jointly develop one consecutive set of conceptual documents, including:

(1) Sufficiently detailed process and analytical descriptions
(2) The scope of services, scope of deliverables and expected quality of results/data
(3) An execution concept summarizing which equipment shall be used, a preliminary schedule and mass balance estimate
(4) A scale-up concept (scale-up criteria) incl. a thorough technical due diligence on the key equipment critical to scale-up or production
(5) The service (or manufacturing) contract

It is also important to agree if separate future-term targets need to be considered for planning and execution of a distinct trial phase, even if those could significantly add cost or time[1]:

- If it isn't considered that scale-up and trial work (typically fee for service / time based) shall later be transferred into a manufacturing work (cost per kg), the trials likely won't consider each operational/logistical aspect. The focus would be the trials success but not its efficiency. Thus delays/further cost should be expected if production trials become necessary after all
- If the trials shall generate engineering data without a written concept available which/how critical data shall be collected, you should expect negative surprises as critical probes/meters,

[1] In this phase it is only needed to conclude if this is becoming important or not. How the requirements would be fulfilled in detail will be worked out later in the project

calibration protocols, sampling points, the possibility to run extended trials or to take very frequent samples could be different to your expectation

All that work is time consuming, but certainly a good investment as areas of concern can be identified before damage is unavoidable. Even if the project will be stuck later on to whatever reason (cost, scale-up surprises, technical fit, availability of timeslots etc) the outcome of this conceptual work likely was a good exercise as some type of larger-scale feedback on the clients' technology or contractors' project approach is to be expected. Its value shouldn't be underestimated. On a good start a successful project is more likely - or at least a positive mutual mindset for the more difficult project phases to come.

Kick-off and tech transfer (TT)

Once the contract is signed a kickoff meeting and the tech transfer phase are about to follow. This is the chance to build trust and confidence in each other and into the specific technology. From now on only the technical teams are needed, whereas both parties project managers are responsible to execute the works under the contractual framework provided. Besides the key personal that participated in contract initiation already other project members from both sides should be brought in, to make them familiar with the counterparts on the other side and the actual project.

The kickoff meeting is typically about organizational items and used to reconsider the key aspects of the project. Frequency of progress meetings, communication rules, secure data transfer etc. are typical points to address. Decisions should be clearly documented (throughout the project). Furthermore it makes sense to combine the kickoff meeting with the paper-based tech transfer.

The tech transfer phase (TT) intents to establish key parts of the process and necessary analytical methods to follow it at the service provider. Quite often the practical TT only focuses on the fermentation and initial DSP steps. Depending on the complexity and type of project TT can be multistage and performed on different sites. Duration of this phase typically sums up to 3-8 weeks, even longer, depending on

- The status of technology documentation
- The complexity of the process (fermentation with or without DSP) and regulatory requirements
- Readiness of equipment and analytics (technical adaptations needed?)
- Availability of people at service provider (maybe still limited if preceding project interfering)
- Number of repeats for crossvalidation trials (process + analytics)
- Sample logistics between service provider and client

The costs of visiting the site of the other party are a fair investment as a visit provides insights that documents or web conferences never could give. Not mentioning the importance to have a chance for team building after a long day of discussion.

If not already accomplished before in a satisfying manner, TT should also be used to discuss details on key equipment of the service provider including technical, logistical and operational constraints that might impact the piloting or manufacturing works. Using this information and the available process description the scale-up & operational approach for each unit operation can be fixed.

Table 1: Work split during tech transfer

Tech-Transfer Phase	Content	Responsibility of client	Responsibility of service provider	Location	Comment
Theory	Process details & analytical methods	# Provide (and update) process description, analytical methods & process data set (range of trials, not only best case) # Develop questionaire on remaining itemson providers' equipment # Answer open questions to service provider # Request detailed information of providers key equipment # Jointly agree on a scale-up approach	# Critical review of clients information package (understanding, completeness for takeover at own plant) # Develop questionaire for remaining items on clients process # Provide detailed information of key equipment (if not already done during technical contract initiation) # Jointly agree on a scale-up approach	At client (or web-meeting)	# "Scale-up" goes beyond individual scale-up criteria for unit operations. It also implies logistical and operational aspects/limitations that need to be considered if they could impact the results, cost, timeline or risk-profile of the USP/DSP work
Practice I	Demonstrate key unit operations	# Perform process and analytics under the eyes of service provider # Provide samples of test run for analyses at service provider	# Observe # Discuss potential differences to potential conditions at home facility # Analyse samples of test run (after analytical crossvalidation)	At client	# Should be mandatory if process is completely unknown or unusual. Optionally if process is simple or relatively standard # Typically only fermentation or initial DSP steps covered # Typically bench-scale, but can be different # Ideally combined with theoretical TT sessions
Practice II	Analytical cross validation	# Define procedure of crossvalidation and success criteria # Provide standards / reference samples	# Establish method and perform validation program	At service provider	
Practice III	Demonstrate key unit operations	# Observe # Analyse samples from test run	# Perform process and analytics under the eyes of client # Provide samples of test run for analyses at client	At service provider	# Clients company preferred to provide 1st hand feedback on site # typically bench scale or max scale that client already successfully tested # The trials scale can be different to the clients TT run (often at larger scale), as long as the there is sufficient confidence/ data available that supports such a change
					*) preferred

About the author

Dr.-Ing. Markus Fritsch is a bioprocess engineer and has been working in the Industrial Biotechnology sector on R&D, engineering, scale-up & biomanufacturing assignments. In particular he enjoyed the last ten years, in which he was managing projects in various positions at the interface of an industrial scale multi-purpose plant that acted as a gateway for commercialization projects.

Markus repeatedly experienced the challenges and dynamics arising out of different perspectives and requirements from customers, technology-, engineering- and service providers, end-users and financial institutes. Now he is providing independent engineering and consulting services for technology ventures, service providers and other stakeholders of the bioeconomy.

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