Fritsch Bioprocess
engineering | consulting

About the importance of conceptual thinking in technology commercialization

Bioprocess engineering itself is a multi-dimensional field. As was concluded earlier[1] the shortened development cycles furthermore put spotlight towards DSP, scale-up and commercialization related topics. This even more underlines the importance of a broad and balanced, TEA-driven, risk-mitigating, conceptual design thinking from early stages in development. This conclusion in general isn't new as many industry leaders have been emphasizing to begin any such venture with "*the end in mind*"[2] [3]. However, in the past this key lesson was mainly considering the "classic" CAPEX expensive approach from lab to pilot to commercial, performing most steps inhouse or at least under own leadership but over a longer time span. It follows a good engineering practice. A lot of best practices on that topic were shared before and are highly recommended to study. However emerging companies with new technologies haven't gone through these learnings themselves yet. It is hard to picture any "*end*" if your small company primarily consists of a few subject matter experts.

Additionally, in case of the "modern" approach using external CRO / CDMO facilities you need to be aware of the differences towards the "classic" route, its intrinsic side-effects, uncertainties and potential lack of transparency, and the general complexity, interdependency and dynamics of each of the project phases onto commercialization.

Both the "classic" and the "modern" approaches demand for diversified and experienced project teams, but the structure or assignment of the teams can be greatly different. A short overview is provided by Table *1*.

What we are seeing now is that larger tasks (relatively and in total of overall program size) are to be performed at external partners. This directly effects the path to commercial positively and negatively:

- Facilities have individual strengths and can provide access to important knowhow
- External partners are constrained by their individual circumstances, interests and regulations and are not completely controllable
- The CDMO (and much more the CMO[4]) market is tightening, making it more difficult to get scale-up/manufacturing slots at preferred sites. Larger facilities are becoming a potentially critical resource from a schedule and knowhow perspective, especially if non-standard DSP or regulatory requirements are involved
- The degrees of freedom and flexibility might increase short term at the smaller scale compared to building inhouse capabilities but might decrease in the longer term at the larger scale. This is because of the different business model of the CDMO / CMO as they have to deal with several projects at the same time and need to minimize interference between them

[1] See paper "Shifts in technology commercialization strategies - Causes and consequences"

[2] https://www.genomatica.com/wp-content/uploads/2017/01/20160421-Industry-Lessons-Lievense.pdf

[3] https://www.genomatica.com/wp-content/uploads/2017/01/20160614-Alex-Patist-AIChE-PD-June-2016.pdf

[4] https://www.biofuelsdigest.com/bdigest/2021/04/19/the-coming-apocalypse-will-industrial-biotech-flourish-or-flounder/

Table 1: High level comparison of the classic and modern commercialization strategy

	"Classic" route	**"Modern" route**
Products	# Mostly commodities (low-value, high volume, industrial use) # Few niche products	# Niche biochems (high-value, low-volume) # Trends into larger-volume segments (regulated)
Technology development	Mostly inhouse (USP+DSP)	USP inhouse, DSP partially external
Piloting / Scale-up	Inhouse (purpose-built pilot/demo facilities)	External (CRO/CDMO/vendors)
Biomanufacturing	Inhouse or licensed to others	External
Process engineering	Internal resources and external partners	Limited internal resources
Cost to commercial	Higher	Lower
Time to market	Longer	Shorter
Typical risks	# Changes in market environment # Operational costs and negative surprises during demonstration ("Valley of Death")	# Many critical external success factors # Limited depth of process technology (USP+DSP) # Limited long-term production perspective

Naturally most ventures are focusing on strain & fermentation design. In some cases however it seems that the overall importance of DSP development, logistical, regulatory and scale-up topics on any steps to follow are undervalued or belatedly addressed. The utilization of external facilities can further create challenges if not addressed early on in a sufficient manner. Awareness can drift and key scale or facility dependent technological or operational aspects remain blurry during a critical phase of commercialization. All this could mean that the way towards "*the end*" in the "modern" route might be even less predictable and harder to describe from the beginning, as many more external factors and interests are to be considered (or to be accepted). On the opposite however a lot of knowhow and experience is also getting accessible by working with external providers.

Imagine your technology would be developed primarily using external facilities for piloting/demonstration. Even under your leadership/support many decisions would have been triggered simply by the circumstances around the chosen facility, e.g.:

- Available timeslots
- Suitability of equipment
- Local regulations
- Resource issues
- Expertise and experiences
- Local network of service providers
- Cost and contract conditions

Outsourcing of activities is done for good reasons nowadays, however we sometimes observed that less emphasis was put in before to those topics on which process engineers would have been typically involved during the “classic” commercialization approach. Fundamental questions such as expected cost (drivers) or technology boundaries at full commercial scale (maybe at a different CMO or again at own purpose-built plant), the representativeness of certain works performed or questions related to the behavior of intermediates and product might easily fall below the radar. The expertise of the external party, its technical fit, transparency in collaboration and ability to manage and understand your project targets can directly determine your overall commercial success. Not to mention the importance of its trustworthiness as you are going to share your most sensitive piece of technology (the strain).

Not many companies in our field proved to have such a broad scientific, technical, commercial and project management knowhow available and exemplify a holistic process development with TEA and stage-gate driven decisions. The available knowhow at some external providers could at least add some part of this critical insight. Such facilities could provide true development partnership and key knowhow in a B2B environment instead of primarily being service providers for defined tasks or partners in public funded development projects. This could bring up operational, logistical, scale-up or DSP related topics to a much greater awareness earlier in the path. But it depends how collaboration is managed.

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.

Contact us:
Fritsch Bioprocess | Engineering | Consulting
markus@fritsch-bioprocess.com
https://fritsch-bioprocess.com

Date of last revision: September 21st 2021