

## STRATEGIC APPROACH TO SCALE-UP

Mark Warner, PE  
Founder, Warner Advisors LLC

The most common question I receive from companies working to scale-up advanced biotechnology is whether their process can operate at commercial scale. My common response is that it is not a question of whether it will work at commercial scale, but whether will work ***economically***. Advanced biotechnology has developed many impressive technologies and the focus of process scale-up needs to involve early stage strategic planning to concentrate on technologies that have a high probability of providing an economically viable process.

In my previous series ***“what makes scale-up of industrial biotechnology so difficult”***, I introduced the concept of ***not pushing the rope***. This notion involves identifying commercial scale equipment that can perform the process required and utilizing pilot testing to generate the data needed to select and design commercial equipment. The first step is to develop a concept for the commercial scale facility and use the pilot operation to prove out key parameters needed to build the process (i.e., “pull” the information needed from the pilot). Trying to simply replicate what has worked at pilot scale, without consideration of what is practical at commercial scale (pushing data forward), will not usually result in a viable process.

***The dollar test*** – the first test to use in evaluating process technologies for biotechnology scale-up is called the dollar test. Does the target product sell for dollars per gallon (commodity fuels and chemicals), dollars per pound (specialty chemicals or food proteins) or dollars per ounce (niche chemicals or pharmaceuticals). The value of the product will dictate which technologies have the best chance of making an economically viable process. For high value items like pharmaceuticals, the entire process toolkit is typically available. However, when making commodity chemicals or fuels that sell for a few dollars per gallon (or fraction of a dollar per pound), it is unlikely that many of the higher end process technologies will be viable. It should not be assumed that success of any specific technology is not possible, but it is worth pointing out that certain technologies are improbable to succeed and there needs to be expectations for a long development timeline.

***Look for footprints along the journey*** – when hiking in the snow, there is often a choice presented to use existing footprints to ease the journey or decide to forge one’s own path. Technology development is ironically similar and the determining factor is the same as hiking – is your destination the same as those that have gone before you or are you breaking new ground? This decision needs to be made for each process step. Just because you have an innovative organism or fermentation technology, does not drive a need re-invent the wheel on downstream recovery if an economically viable pathway exists. However, if the destination is different, forging a new path is a given and will need to be resourced appropriately.

***Placing your bet*** – scaling-up advanced biotechnology, by definition, is a valley of death activity. This is the chart that every entrepreneur has seen a thousand times that outlines the negative cash flow that needs to be overcome to reach commercial operations and profitability. Utilization of a strategic approach to scale-up is the best way to mitigate risks and minimize cash flow. When a tentative process

is selected for R&D, pilot and demonstration scale development, these activities will become the largest costs during technology commercialization. Selecting which path to move forward on is no different than placing a bet in Las Vegas, the best chance of a successful result is to understand the odds and corresponding risks, to make a decision that provides more reward than risk.

***There is always a chart*** – Attached is a chart that summarizes many of the common unit operations within advanced biotechnology and ranks them for applicability to a range of target products, from fuels to pharmaceuticals. Notice that there are not hard definitions such as “will not work” or “proven”, as each technology application is different and thus does not warrant hard lines. Instead, the technologies are rated against the specific products and determined either to be:

*Probable* – has a history of being used to produce products of this type and sales price category

*Possible* – technology likely to work to produce required separations, but may be challenged to be economically viable.

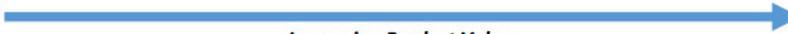
*Unlikely* – even if the technology works at small scale, the lack of availability of corresponding commercial scale equipment makes success unlikely to be achieved.

The fact that a technology has been used successfully in similar commercial applications is not a guarantee of success, but it is certainly a good place to start. Every investment advertisement starts with the disclaimer “past performance is not a guarantee of future success” and while I agree there is no guarantee, past performance is still one of the best predictors of success.

*Mark Warner is a registered professional engineer with 30 years of experience in process commercialization, focusing for the last 10 years on taking first-of-a-kind-technologies from bench-top to commercial operation. He has worked for four companies who have held the #1 spot in biofuels digest’s top company list, in a range of advanced biotechnologies including biodiesel, cellulosic ethanol, phototrophic algae, heterotrophic algae and innovative food products. He is the founder of Warner Advisors, providing consulting services and acting in interim engineering leadership roles for advanced bioeconomy clients. He can be reached at [mark@warneradvisorsllc.com](mailto:mark@warneradvisorsllc.com) or visit [www.warneradvisorsllc.com](http://www.warneradvisorsllc.com).*

## WARNER ADVISORS BIOTECHNOLOGY MATRIX

		Fuels	Commodity Chemicals	Specialty Chemicals	Food Proteins	Niche Chemicals	Pharma
Reactors	Anaerobic Digestion	?	✓	✓	✓	✓	✓
	Anaerobic Fermentation	?	?	✓	✓	✓	✓
	Aseptic Fermentation	?	?	?	?	✓	✓
Separation	Clarification	?	✓	✓	✓	✓	✓
	Separator	?	?	✓	✓	✓	✓
	Disc Stack Centrifuge	?	?	✓	✓	✓	✓
	Super G Centrifuge	X	X	X	?	?	✓
Disruption	Acid/Base Treatment	?	?	✓	✓	✓	✓
	Enzymes	?	?	✓	✓	✓	✓
	Bead Milling	?	?	✓	✓	✓	✓
	Homogenization	X	?	?	?	✓	✓
Sterility	Pasteurization	?	✓	✓	✓	✓	✓
	Sterile Filtration	X	?	?	?	✓	✓
	Irradiation	X	?	?	?	✓	✓
Purification	Solvent Extraction	?	?	✓	✓	✓	✓
	Distillation	?	?	✓	✓	✓	✓
	Crystallization	?	?	✓	✓	✓	✓
	Microfiltration	?	?	✓	✓	✓	✓
	Tangential Flow Filtration	X	?	?	?	✓	✓
	Chromatography	X	?	?	?	✓	✓
Drying	Spray Drying	?	?	✓	✓	✓	✓
	Fluidized Bed Drying	?	?	?	?	✓	✓
	Freeze Drying	X	?	?	?	✓	✓


  
**Increasing Product Value**

Likelihood of Technology Succeeding

Probable	✓
Possible	?
Unlikely	X

Disclaimer - Matrix is developed based on years of applying a broad range to advanced biotechnologies and is intended to provide strategic guidance in early stage process selection. It should only be considered a recommendation and actual testing needs to be conducted to determine applicability and viability of the technology.