Supplier Innovation Is an Imperative

Five Steps to Achieving a Competitive Advantage

by Jennifer Maynard

In the increasingly competitive biopharmaceutical industry it is critical to be resilient and ready for constant change. Facing mounting pressures to improve performance and decrease costs, many manufacturing sites are finding it imperative to achieve operational excellence. The focus of most operations is no longer to push product out the door, but rather to achieve the highest operating capacity at the lowest cost. For many sites with existing products and processes this may seem easier said than done, and achieving a sustainable competitive advantage can prove to be difficult. Organizations have to be creative with cost-cutting strategies and extend their enterprises to attain more rigorous results. Process value improvement goals (process innovations) are nowadays 10 to 20 times higher than achieving just a price discount. In a fast-moving environment, innovation is the most sustainable competitive advantage (**1**).

Responding to the Pressures of Competition

Although the biopharmaceutical industry has been hard for some to penetrate because of patent life, regulations, and time to market, shifts in developing geographies and market entries have set a new horizon and have forced the industry to be more competitive. New regulations such as EMEA's guidelines on similar biological medical products (**2**) have even accelerated this shift in the industry. In comparison, for other industries such as the automotive industry these driving forces hit hard more than 10 years ago, and they have left behind proven concepts to build from. One such concept is that of the *extended enterprise*, in which a value chain (an extended supply chain) partners with suppliers as an integrated team (**3**). Although the biopharmaceutical industry is far from reaching virtual and physical integration, its suppliers have created an ideal atmosphere to begin this process. Many now offer total service packages starting with initial assessments and providing follow-up support in validating their recommendations. The supplier innovation "bucket" is one of the easiest buckets to pull from and is typically the least costly, least risky, and fastest to market (**1**).

One reason to leverage supplier innovation is that suppliers are the experts on their own products and applications. Biopharmaceutical organizations can then focus on their core competencies while still innovation and making high-quality products. Rather than approaching every application as an adaptive challenge, they can leverage existing technical solutions.

Another reason is the difference of slope in the manufacturer-versus-supplier innovation curve (Figure 1). Supplier innovation occurs exponentially in comparison with manufacturer innovation. New applications or significant variations of processes can appear weekly for suppliers through in-house R&D or through acquisitions, whereas biopharmaceutical product innovations occur annually, at best. Because most blockbuster drugs have long lifecycles, several renditions of process innovation are necessary to continue

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reducing costs and driving revenue throughout the life of a drug. One biotherapeutic can leverage thousands of products from a supplier's portfolio to provide it with the optimal solution.

The following sections provide five steps to guide your way through process innovation (Figure 2).

Select the Systems or Product Lines to Focus on

Organizations should look at improvement initiatives strategically: What product lines need to be "leaned out" the most? What areas are feeling the most pain? Where are the highest value losses? Tools such as value stream maps and sites gap analysis may be a good starting point to identify and prioritize which product lines or areas where to start the optimization effort. After an organization performs an internal site assessment, it should create a team with an appropriate sponsor to have oversight of the total effort and follow the project throughout its lifecycle. That team should be cross-functional (8–10 core members, including the sponsor). The sponsor should be at an appropriate level in the organization to influence

Figure 1: Comparing biomanufacturer and filter supplier innovation curves (number of new product launches within each year)

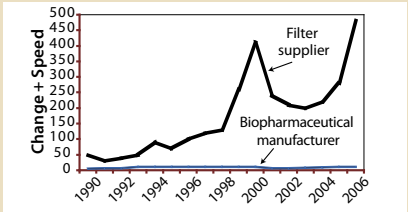


Figure 3: Shifting focuses, upstream and downstream

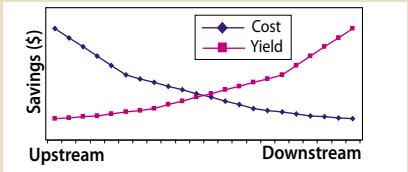
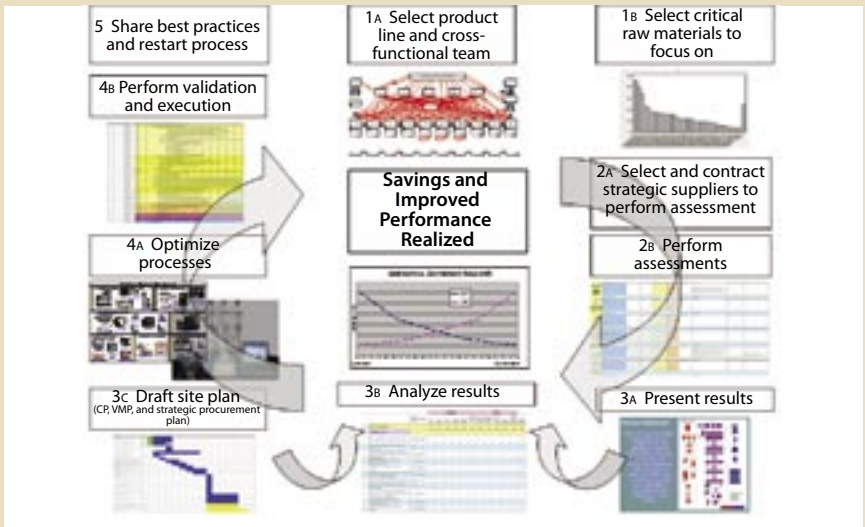


Figure 2: Supplier innovation implementation flow



change and decision making — at least a vice president of a division. If a project crosses multiple divisions, a higher-level team member is required.

This approach is critical because it drives alignment with corporate initiatives and ensures that innovation is focused in the right areas and is not creating bottlenecks. The sponsor also ensures that the initiative gains appropriate resources, visibility. and cross-departmental buy-in.

Within the Product Line, Determine Major/Critical Components and Raw Materials: The team should start by looking at the spread of raw materials and components across the site, looking at largest areas and volumes of expenditures and the biggest potential problems and/or risks. Using simple tools such as Pareto analysis, the team can narrow down and prioritize its efforts. One group of components that is typically expensive for biopharmaceutical companies is filters: not only the price of filters, but also potential yield losses due to unspecific adsorption, hold-up volume, or insufficient throughput. Because this is a high cost area offering many opportunities for optimization, I offer filtration examples as a case study here.

Table 1: Cost savings example

Savings of Media Filter Application				
	Before Optimization (nondisposable)		After Optimization (disposable)	
Filter Element Cost				
Quantity	5 × 20″		1 × 30″	
Pre		$275		$850
Quantity	4 × 20″		2 × 10″	
Final		$350		$550
Total		$2,775		$1,950
Operations Hours				
Prep Lines	90 min		5 min	
Cleaning	150 min		10 min	
Sanitization	510 min		0 min	
Teardown	45 min		5 min	
Total		$775		$25
Processing Time	~4 hours		< 2 hours	
Total		$3,550		$1,975
Validation Costs				
Total		$1,242,500		$691,250
Capital Costs				
Pre		$3,500		$150
Final		$2,500		$150
Total		$6,000		
Total		**$1,248,500**		**$691,250**
Savings		**$557,250**		

Select Strategic Suppliers for Focus of Site Assessment

Site assessments are a service most suppliers provide at no cost to identify the largest areas of opportunity for which they can provide solutions. This is an ideal situation because it immediately provides mutual benefits. The customer gets an overview of the best equipment possibilities for specific applications available for its needs, and the supplier has an open audience to share its newest innovation.

This requires advance planning. Usually the team selects the top two or three suppliers in a category and brings them on-site to assess the entire manufacturing process. Seeing every process step and learning the process

Table 2: Example of transactional costs

Supplier Audits (based on two auditors and two sites/supplier)				
Audit labor	$85/hr × 20 hrs		$1,700/site	$6,800
Prep/Follow-up	$85/hr × 20 hrs		$1,700/site	$6,800
Travel	$2,250/site			$9,000
Room/Board	$1,000/site			$4,000
Procurement				
Business meetings	$85/hr × 5 hrs/month × 3			$15,300
Purchase orders				
	5 hrs/order	$85/hr	$450/trans	$5,400
Shipping/Handling				
	$500/order			$6,000
SAP p/n maintenance				
	2 hrs/part	20 parts	$85/hr	$20,400
Total Annually				**$73,700**

parameters allows each supplier to provide an optimal solution — and the team can compare multiple assessments for risk mitigation. This approach also removes bias and allows all critical suppliers selected to perform an assessment with the same opportunity to review the process and propose solutions. Once its assessment is complete, a supplier can provide a formal report and presentation to highlight possible solutions. From such assessments the team can prioritize efforts further and set timelines and milestones for each effort.

That allows suppliers to observe the total process and provide a total train solution rather than cookie-cutter improvements that optimize only single process steps, providing subpar results.This enables critical evaluation of an entire process as the focus shifts from upstream to downstream. In the examples used here, the cost of upfront filtration are typically high and can be optimized with the least regulatory impact and cost of implementation. However, cost savings shift as you move downstream toward yield, which provides a different focus and opportunity for savings (Figure 3).

Taking a holistic approach across the product line with one team leader monitoring the portfolio allows the team to look at the total opportunity from a total-cost-of-ownership approach (Tables 1 and 2). Taking this approach allows all goals to be achieved including bottom line cost savings and cost avoidance. Benefits that can be achieved include

- >30% bottom line savings
- Increased speed and efficiency — improved flow rates
- Improved throughput
- Reduced square footage of filter
- Reduced inventory levels
- Reduced preparation time
- Improved operator safety and ergonomics
- Reduced hold-up volumes
- Improved yields — improved nonspecific adsorption
- Disposable applications
- Reduced cleaning time
- Higher capacity use.

Additional benefits come in planning for regulatory submissions, validation,

Table 3: Diagram showing the relationship of benefit and effort

				Benefit						Effort			
		Project type	Supplier	Tier 1 savings	Tier 2 savings	Tier 3 savings	Customer service	Quality and safety	Total benefits	Probability of success	Validation impact	Regulatory impact	Risk to business
ID No.	Level of Importance Identified Goals			0.25	0.10	0.10	0.10	0.45	1.00	0.20	0.20	0.20	0.20
1	Same filter media — reduced surface area	Media	Supplier 1	3	3	1	9	3	2.5	1	3	1	3
2	Different filter media type and reduced surface area	Media	All	3	3	1	3	3	2.5	1	9	1	3
3	Different filter media type and reduced surface area — keep separate but move prefilter to capsule	Media	Supplier 1	3	9	9	3	2.8	1	9	1	3	4
4	Combined pre- and postuse filter — eliminate prefilter	Media	Supplier 2	9	9	3	3	3	4.8	1	9	3	3
5	Combined pre- and postuse filter in capsule	Media	Supplier 2	9	9	9	3	3	5.4	1	9	3	3
6	Combined pre- and postuse and 0.1-µm final filter to improve safety	Media	Supplier 2	9	9	9	3	9	8.1	1	9	9	1
7	Same filter media — reduced surface area	Cell sep	All	9	1	1	3	3	3.8	1	3	1	3
8	Different filter media type and reduced surface area	Cell sep	All	9	3	3	3	3	4.2	3	9	1	3
9	Different filter media type and reduced surface area — keep separate but move prefilter to capsule	Cell sep	Supplier 1	3	3	3	9	3	2.7	3	9	1	3
10	Combined pre- and postuse filter — eliminate prefilter	Cell sep	Supplier 2	9	3	3	3	3	4.2	3	9	3	3
11	Combined pre- and postuse filter in capsule	Cell sep	Supplier 2	9	3	9	3	3	4.8	3	9	3	3

Table 4: Example filter-optimization checklis

Check	Exp. Comp.	Responsibility	Study Level	Test to Quality/Validate Sterilizing-Grade Filters
☐		Supplier	Q	1 Filter Selection and Characterization
☐		Supplier	Q	1.1 Test for determination of filtration media and materials of construction
☐		Supplier	Q	1.1.1 Polymers (cellulose ester, nylon, polyesters, polyetraflouroethylene,
☐		Supplier	Q	polyvinylidene fluoride, polycarbonate, polypropylene, polyethersulfone),
☐		Supplier	Q	and polysulfone); other properties may be considered
☐		Supplier	Q	1.1.2 Minor components add to filter media to render them hydrophilic or
☐		Supplier	Q	hydrophilic
☐		Supplier	Q	1.1.3 All filter components should meet applicable compedial requirements
☐		Supplier	Q	1.1.4 Processing Capacity and Filtrate Quality
☐		Supplier	Q	1.1.3.1 V_{max} System Sizing Experiment
☐		Supplier	Q	1.1.3.2 Filter Volume
☐		Supplier	Q	1.1.3.3 Flow Rate
☐		Supplier	Q	1.1.3.4 Pressure Differential
☐		Supplier	Q	1.1.3.5 Temperature
☐		Supplier	Q	1.1.3.6 Chemical characteristics of soultion
☐		Supplier	Q	1.2 Filter Configuration for sterilizing-grade filters
☐		Supplier	Q	1.2.1 Flat Stock Membranes
☐		Supplier	Q	1.2.2 Preassembled Capsules — including end connections
☐		Supplier	Q	1.2.3 Membrane Cartridge Assemblies — including end cap design
☐		Supplier	Q	1.2.4 Effect of and effect on associated lines
☐		Supplier	Q	1.3 Particle Shedding
☐		Supplier, Customer	Q, V	1.4 Extractables
☐		Supplier, Customer	Q, V	1.4.1 Prove nontoxic — considering product and process physical and chemical characteristics
☐		Supplier, Customer	Q, V	1.4.2 Impact of Sterilization cycles
☐		Customer	Q	1.5 Chemical Compatability
☐		Supplier, Customer	Q	1.6 Absorption — solution specific, prove it is not a problem affecting solution characteristics
☐		Supplier	Q	1.7 Thermal Stress Resistance — filter and support structures remain stable under process conditions
☐		Supplier	Q	1.8 Hydraulic Stress Resistance — pressure differentials do not adversely affect filters
☐		Supplier	Q	1.9 Toxicity Testing — prove no toxic chemicals present could adversly effect product quality
☐		Supplier	Q, V	1.10 Bacterial Challenge Testing — use product or solution to be filtered, validate sterilizing-grade filters
☐		Supplier	Q	1.10.1 Bacteria retention/integrity test relationship data
☐		Supplier, Customer	Q, V	1.10.2 Bacteria retention Water, SLB and Product
☐		Supplier, Customer	Q, V	1.10.3 Bacteria retention/integrity test methodology
☐		Supplier, Customer	Q, V	1.11 Physical Integrity Testing
☐		Supplier, Customer	Q, V	1.11.1 Integrity Test Methodology and Selection
☐		Supplier, Customer	Q, V	1.11.2 Integrity Tests — Water/Solvent or product specific
☐		Supplier, Customer	Q, V	1.11.3 Effects of Chemical Compatibility on Filter Integrity
☐		Supplier, Customer	Q, V	1.11.4 Effects of Sterilization Methods on Filter Integrity
☐		Supplier, Customer	Q, V	2 Performance Qualifications (Physical and Mechanical Characteristics)
☐		Supplier, Customer	Q, V	2.1 Flow Rate/Filtration Rate/Clog Rate/Throughput
☐		Supplier, Customer	Q, V	2.2 Fluid/Tubing or Piping
☐		Supplier, Customer	Q, V	2.3 Fluid/Filter
☐		Supplier, Customer	Q, V	2.4 Physical and Structural Limitations — Pressure and Temperature Resistance
☐		Supplier, Customer	Q, V	3 Filter Sterilization
☐		Supplier, Customer	Q, V	3.1 Capsule Filters — Gamma Radiated/Ethylene Oxide (ETO)

strategic procurement, supplier relationships, and risk mitigation.

Regulatory Planning: Comparability studies can be drafted in advance to lay out the regulatory requirements upfront. This allows the portfolio manager to provide an accurate cascading timeline with built-in levels of regulatory communications.

Validation: Because of the site-wide holistic approach, the entire filtration project on-site can be laid out in the site's validation master plan to ensure alignment and prioritization with other validation projects. Monitoring and tracking can be performed in a controlled system.

Strategic Procurement: Cross-functional involvement from procurement is a necessity. A filter supplier strategy can be developed after the initial assessments to be used for strategic planning and negotiations. Once each supplier brings its value to the table, the team can determine the best strategic direction (reducing supply base, driving volume with strategic suppliers, rewarding good performance, reducing transactional costs, and so on). This allows the TCO approach to be used in full so that strategic decisions can be made while considering transactional costs. Although such savings are difficult to quantify, they are real savings and should be considered when making initial decisions about which supplier to bring in to narrow down the path for filterability trials.

Supplier Relationships: Once an initial selection is made, the assessment allows suppliers to be judged on an equal playing field. This removes bias and allows filters to sell themselves because the data cannot be disputed. Although customer service and transactional costs are also considered, it removes personal relationships and provides a more institutionalized trust and consistency. Because the decision process is built into decision matrixes (Table 3) and a team approach is taken, the overall supplier relationship can be improved and driven across the organization, ultimately strengthening the relationship with strategic suppliers.

Risk Mitigation allows for side-by-side validation and for alternative sources to be validated in the same resource effort. This again takes the total cost of ownership into account. Avoiding costs by leveraging supplier validation resources removes a large portion of the pain usually associated with filter validations. Cost avoidance depends on the choice of filter application, but filter validation can cost >$25,000. Often that can be reduced by >50% through leveraging supplier resources.

Present Business-Case and Launch-Site–Wide Projects

Each project milestone has critical decision points such as supplier selection and awarding of business, testing, and validation needs. It is critical to ensure availability of all cross-functional resources. Decision matrixes are good tools for ensuring that the cost-of-ownership approach is being taken and that personal bias is removed.

Value analysis must be reviewed to determine what ideal solutions need to be implemented. Filter cost savings may be passed up for savings in labor. For example, moving toward disposable applications typically increases filter costs by >30% but can save significant labor hours per day due to reductions in cleaning time, prep time, and tear-down. Those savings may be desired over the filter costs savings if the objective is to reduce overhead or cycle time.

Check sheets can be used to identify roles and responsibilities. The site-wide team can determine what role a supplier needs to take in the follow-up activities after the assessment, and strategic procurement can negotiate costs with the suppliers before final selection and execution of studies.

Optimize Process Using Supplier Solutions for Valued Results

Optimizing systems that have not been improved in the past three years typically yields >30% saving. The key to any improvement is driving true value into the network. This should be tracked to ensure that targets are being met and maintained. Savings can often be lost if projects go out of scope or are diluted by piggyback projects. Front-end value creation starts with bringing suppliers in for bench-top studies to confirm initial opportunities. This starts with small-scale trials that are then scaled up to intermediate pleated devices and then large-scale runs and validation (Table 4). Most suppliers including filter suppliers provide a range of total services to support small- and medium-scale filterability testing and validation services. Filterability trials are often performed by suppliers either at no cost or at discounted rates, whereby process validation studies, if performed by a supplier, are a cost to the customer. However, the benefits of such validation services are obvious because the validation expert teams are able to both reduce overall validation costs and speed up the validation process. Because validation resources are often a constrained resource for site project priorities, this is one way to move strategic projects forward without draining critical internal resources.

Share Best Practices; Restart

Once the team has achieved proven results, it is critical to share them with other sites or product lines. Global organizations can leverage changes across the entire organization. Taking a more strategic approach allows organizations to focus their business with suppliers that provide the most value, allowing the purchasing and supplier management organization to be more efficient and successful in reducing total expenditures even with standard supplier pricing increases. This allows organizations also to approach the regulatory submission process with a strategy and defined approach. Comparability studies and other approaches can be taken to speed this path and ensure that all bases are covered and communicated.

A Strategic Imperative

Supplier innovation is the fastest and least costly innovation that biopharmaceutical companies can pull from. Using filtration as an example, it is apparent that significant changes in filtration technology over the past ten years have steadily increased filtration capabilities and rendered many filters obsolete. Any changes to systems that are more than three years old can provide significant savings and opportunities. Companies can fill in resource gaps by leveraging suppliers' total service options. These costs are often already built into the costs of the

filters or other products and thus are essentially wasted by manufacturers that do not choose to leverage them.

As shown in Figure 2, supplier innovations can be leveraged by a standard process that can be further developed based on the needs of the organization. The key to this flow is to start it and continue to repeat it. Supplier innovation is truly an imperative in the modern-day biopharmaceutical industry and should be taken into account during strategic planning and prioritization.

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