

This article explores the need for a more strategic approach to outsourcing decisions in clinical materials management.

# Strategic Value of Clinical Supplies

by Colin Andrews

## Background

A previous article in *Pharmaceutical Engineering*<sup>1</sup> described the dynamic and changing business environment for drug discovery and development. This article concluded that – due to a potential step increase in drug discovery – execution processes such as Clinical Materials Management (CMM) are becoming more critical to competitiveness than ever before.

A key area of focus in CMM has been about the development of outsourcing in this area of activity.<sup>2,3</sup> For some firms, this may be the only viable option for effective CMM. For others, outsourcing may be appropriate in selective cases. Indeed, the growth of CROs in the last three years<sup>2</sup> demonstrates the growing demand for this service.

However, it is equally clear that the decision to outsource is frequently taken *arbitrarily* rather than for *strategic/tactical* reasons, for example, “we haven’t the capacity to do ‘this’, ‘now.’” Given the increasingly central position of CMM in determining a company’s competitive capability, too many short-term decisions can weaken its overall competitive performance. The discussion is too often “We don’t have the capacity so we’ll have to outsource...” The discussion should be “What are our strategic priorities?” Are these reflected in our core competencies and capabilities? What must we do ourselves and what therefore should we outsource?”

The growth of the outsourcing of execution activities has been a feature of many other

industries. There are lessons to be learned and shared. Equally, there are distinctive features of the pharmaceutical development industry that must be taken into account.

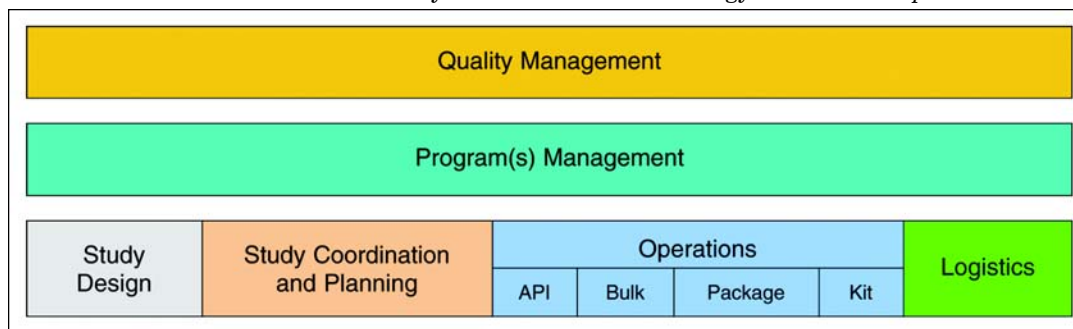
This article develops a framework for understanding where the firm is deriving *strategic* value from its clinical materials processes in order to help organizations formulate appropriate strategies for developing their CMM capability.

## Supply Chain Learning from Other Industries

Other industries, such as the electronics industry, have followed a development path that is analogous to the pharmaceutical industry, albeit with relatively more compressed market life cycles. In the early growth stages of the industry, firms were strong innovators. As no one could provide them with the specialist skills and services they required, they were developed in-house. Many organizations became highly vertically integrated.

As the industry developed, more and more specialist suppliers emerged, or were spun off. Original Equipment Manufacturers (OEMs) began to focus on core competences in areas such as design, assembly, and marketing. The specific competencies developed depended on the OEMs’ particular competitive strategies. Some organizations pursued a strategy of *differentiation* where design and new product introduction capabilities were core. Others pursued a strategy of *lowest-cost producer* where

Figure 1. Clinical Materials Management competencies.



design competencies were about following trends and core competencies for competitive advantage were in manufacturing and distribution.

Toward the end of the growth phase, the typical electronics producer would have a number of design 'centers of excellence.' Production/execution would be via regionally based manufacturing centers focused on assembly operations with core expertise in managing the supply chain. Relationships were established with Tier One suppliers who shared the OEMs global reach. Each Tier One supplier would have a network of secondary suppliers in each region for the provision of required materials.

With the market essentially mature in many areas of electronics products (VCRs, television, personal stereos, computers), the OEMs are stepping back from supply chain operations. Their competitive area of focus is now on product design and marketing.

The automotive industry has followed a similar although less extreme pattern. The OEMs still tend to assemble the vehicles, but this is not exclusively their preserve. Major components and sub-assemblies such as engines, gearboxes, and even body shells are produced by partner organizations. These may be suppliers. They may actually include other OEMs, for example, sharing engines and gearboxes.

In both these industries, close involvement with many aspects of the suppliers' operations is seen as critical to maintaining and developing competitive advantage for the OEM.

## Make or Buy in CMM

The decision to outsource Clinical Supplies can be seen as a classic 'make or buy' issue. For some businesses, such as 'virtual' corporations or bio-technology start-ups, there may be no other way to access the necessary expertise. For other firms, the complete outsourcing of CMM is a dangerously simplistic option that ignores the many linkages between CMM and other development activities such as study design, formulation development, and manufacturing process specification. It is a common complaint within CMM organizations that the trial's personnel assume that materials are available 'off the shelf' to meet any trial requirement at any time.

One of the unique features of clinical materials is that they come in many forms. Not all of these forms are equally 'valuable.' By the time a drug development program has reached Phase III, clinical supplies can include:

- the 'drug' being trialed - likely to be in short supply and highly valuable
- a suitable comparator - possibly difficult to source, but of lesser value than the drug
- a placebo - simple to produce and low in value

Issues of blinding in the study will restrict how differently these groups of materials can be managed.

It is also necessary to consider sub-divisions of the whole supply process. Figure 1 describes a simplified supply chain for CMM.

Any one of the above supply chain steps can be outsourced. It also is possible that only parts of each step may be outsourced, for example, bulk production of placebo. These are important decisions with implications for business performance, and such decisions are not to be taken arbitrarily.

Another dimension of complexity in CMM is the phase of clinical trial being considered, i.e., Phase I – IV. The different phases have very different requirements both for the volumes of clinical supplies required, and in terms of the level and types of controls required. The clinical phase also has a significant impact on the nature of the manufacturing capability required.

With this complexity, it can be challenging for firms to manage CMM processes clearly and consistently. It is unusual to find a consistent approach across multiple clinical trials within a single organization. Clearly, some form of strategic reference-point for these activities is essential.

The issue is less of a simple and often (capacity determined) arbitrary choice between in-house operation and outsourcing. The real issue is where most benefit can be derived from outsourcing and what competencies provide greatest benefit to the company if developed and maintained 'in-house.'

## Value in the Clinical Materials Supply Chain

It is generally easy for organizations to see the costs involved in the supply chain for clinical materials. Equally, there is an inherent logic that any facility within a single company set up to cope with a peak of large Phase III trials will be under-utilized at other times. Similarly, the complexity described above suggests that any company aiming to maintain a broad capability in CMM, for its own competitive advantage, must retain a significant level of redundancy in its Clinical Materials supply chain.

A focus on costs tends to push any outsourcing activity into a price sensitive transaction-by-transaction equation. There is anecdotal evidence that this is the case within CMM.<sup>4</sup>

Counter-balancing the positive financial attractions in outsourcing are concerns about the reliability of supply from contractors, and worries over assuring the quality of those supplies. These concerns are often based on personalized experiences of specific projects and often lack appropriate review of the causes of 'wrong' outcomes. The end result of this is a tendency to frequently move suppliers, and to impose significant levels of intervention in the outsourced processes.

The costs of outsourced clinical materials supply tend to make up only a small proportion of a typical Phase III trial's budget. While significant differences in cost *between* suppliers may only change the overall budget by a few percent, different levels of performance *from* the supplier (quality, delivery, responsiveness) may negatively impact the whole study significantly. Therefore, there is a need to get back to basics and consider where the 'value' in the supply chain resides.

The following elements are suggested as potential areas of value-add for the development company. In turn, these should begin to form the framework for the 'make or buy' decisions

referred to earlier. Figure 2 describes a 'virtuous circle' of added value from the elements described below.

## Product Knowledge

Throughout the development process, there is 'learning' about how the 'end product' production scales-up. Benefiting from this 'learning' is an underlying driver for 'concurrent engineering' in other industries. The objective is that – by tackling production issues during the development stage – new products can be introduced to market more quickly and with better quality. As medicine becomes more 'niche' and personalized, and the development process more transparent with earlier 'me-too' products, well-managed product knowledge will be essential for sustained competitiveness.

This knowledge is of most value to the eventual producer of the drug product. Where arbitrary decisions are made about the production of clinical supplies, the producer of the drug during trials is not necessarily involved intimately enough in the later specifying of production processes. This makes it difficult to transfer any learning regarding the unique characteristics of the specific product.

It is a particular feature of pharmaceuticals that it is difficult to make changes to a production process once it has been validated for approval. Early optimization is not just a 'nice to have,' it is an essential in the new competitive environment. It is also too important to leave to chance.

In general, the management of knowledge regarding the end product can become critical at key stages in the development. Typical of the types of problems seen are difficulties with Methods Transfer. These difficulties can arise between the development organization and the contractor, or just within the development organization itself. Such difficulties can cause significant delay in the program. At their worst, they can jeopardize the whole program by introducing concerns over the robustness of the product that may or may not in fact be valid.

Problems with this knowledge management can lie undetected and may not be recognized until late in the development program – for example, if there are queries regarding submissions to regulatory authorities.

## Supply/Lead-Time Flexibility

It is a fundamental of clinical trial experience that clinical materials supply is not a 'critical-path' activity for study start. Indeed, it has been identified that fewer than 5% of clinical studies are delayed by late clinical materials.<sup>5</sup>

However, there are still significant elements of value in *reliably* reducing the clinical materials lead-time. Research at the Tufts Centre for the Study of Drug Development has identified that reducing the development lead-time by half will reduce total costs by approximately 30%.<sup>6</sup> This reduction comes from a myriad of savings, but even from a restricted CMM viewpoint, the longer materials sit on the shelf, the more effort is required to maintain and coordinate expiry dates, the more resource required to identify and manage stability issues, and greater volumes of storage required (significant if refrigerated, or specialist storage is required).

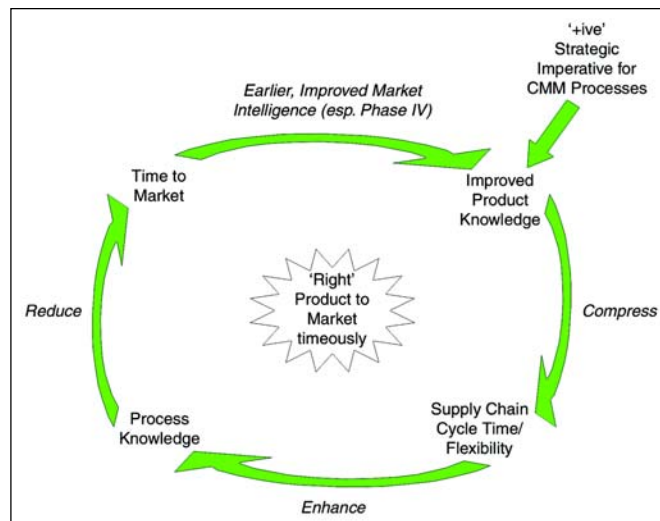


Figure 2. Added value in CMM.

Intangible benefits also can come from reducing supply lead-times. The shorter the lead-time, the greater the opportunity there is to fine-tune details of study protocol. Provided this is well managed, the end result will be a better study. An example of how this may work is allowing the study sites to have more input, or input closer to the study start, thereby improving investigator ownership of their tasks and reducing the number of issues to be addressed during the study operation.

## Alternative Use

Active Pharmaceutical Ingredient (API) is often in very short supply during the development process. The ability to change the trial destination of API can be crucial to bringing the best product to market quickly.

One of the mantras often cited for efficient drug development is 'kill early, kill often.' Benefit will only be gained if the resources that are freed up can be redeployed in a timely and purposeful manner.

This may be simple in principle. However, in practice, the delays and potential for mistakes in retrieving a batch of material from one site and re-releasing and/or transferring to another can, and does, make this course of action impractical for some organizations in some cases. Enhancing product and process knowledge is essential to achieving these levels of organizational competence.

## Responsiveness to Trial Results

Clinical trials often require 'fine tuning' during their run. Patient recruitment may be markedly different from expectations (country, demographics, quantity etc.). Patient retention may be better or worse than anticipated. Survival rates may be higher or lower. Results may show un-expected outcomes. Each of these can impact the nature of the clinical materials required, and the mechanisms used to manage existing supplies.

Extended, complex or poorly thought out supply chains can make change expensive and time consuming. In the worst case, CMM activities may influence decisions on the develop-

# Outsourcing Clinical Supplies

ment process. For example, as an extreme case, an otherwise promising drug program may fall into the 'kill early' category due to the failure of CMM processes to cope with difficulties in the running of the clinical trial.

## Process Knowledge

Deriving value through process knowledge is an over-arching case of all the above elements. The automotive and electronics experience is that quality improvement over a multitude of projects comes from the active involvement of suppliers rather than from 'intervention' and policing.

Sometimes it is possible to look at a pattern of supply difficulties and make a single coordinated change to produce a step improvement in performance. Often, it is more practical to make many small, incremental improvements. Experience from other industries is that this can result in real performance benefits in the long term.

## Patterns of Outsourcing

As indicated previously, other industries have had to address comparable issues with their own supply chains. There is a generally recognized hierarchy of outsourcing from transaction-based relationships to risk sharing partnerships - *Figure 3*.

### Transactional

In a transactional relationship, it is assumed that all suppliers' offerings are comparable and so price dominates. The outsourcing process involves publishing invitations to tender, getting a number of quotes, and selecting the cheapest credible quote.

In this relationship, costs are believed to be closely controlled. The reality is that significant levels of negotiation are

required, based on a contract document, to avoid creep in either costs or requirements.

### Preferred Supplier

In preferred supplier relationships, it is recognized that some suppliers better fit the company's requirements than others. Suppliers are selected based on some form of pre-qualification, perhaps including some elements of 'unit pricing' for the services provided. Typically, a limited number of suppliers will be identified for a specified range of services.

This benefits both parties by reducing the cost of each transaction. The contracting company also benefits through shortened lead-times.

In this type of relationship, the costs of services for a single project are less tightly controlled. However, costs are well defined and predictable.

### Partnering

Partnering relationships develop where it is recognized that the supplier has specific competencies that complement the contracting company's. Clearly, before any supplier competence can be described as 'complementary,' one must first understand one's own (required) competencies.

The partner supplier is likely to be closely involved in the specification of work required and in the planning of projects. The cost of service is secondary although it must be related to the value of the input. A partner supplier would typically be expected to share in the risks of the development in some way.

### Alliances

This is appropriate where core competencies are mutually understood within a meaningful strategic framework.

Alliances tend to occur where the 'supplier' has key skills

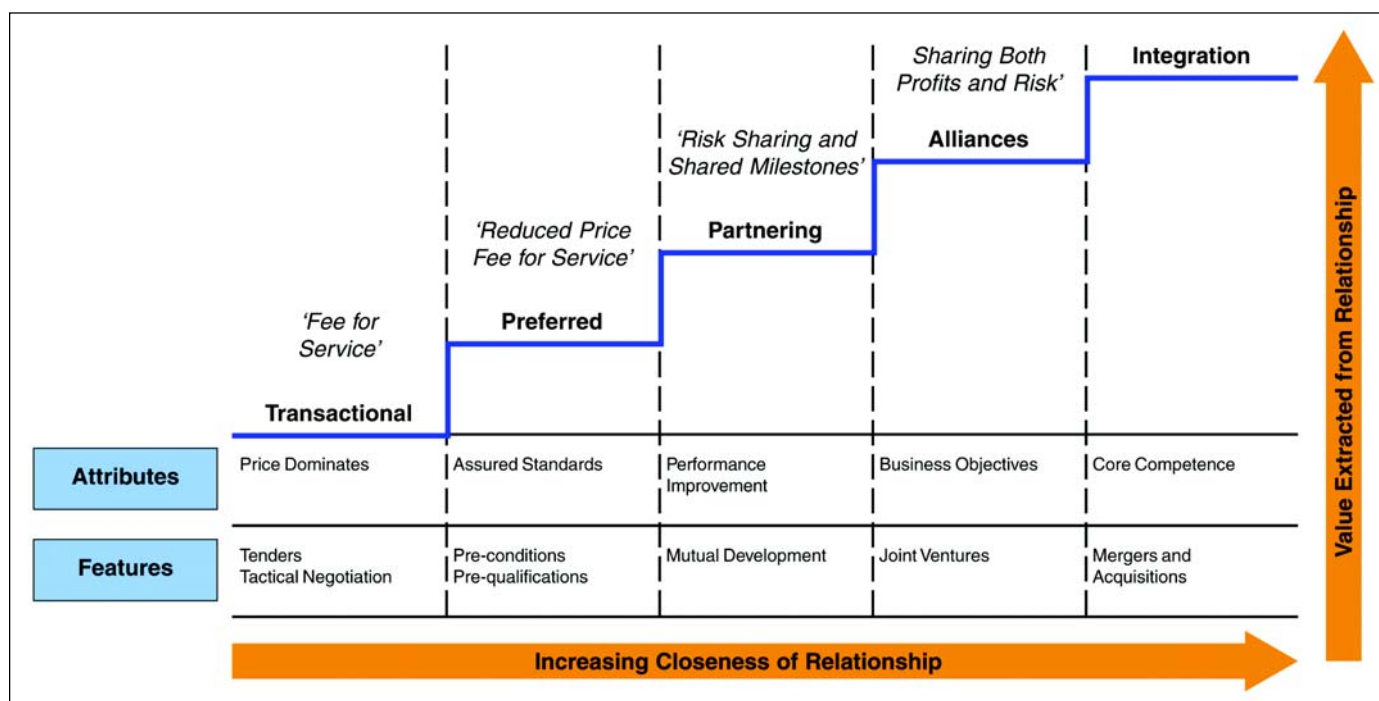


Figure 3. Development of customer – supplier relationships.

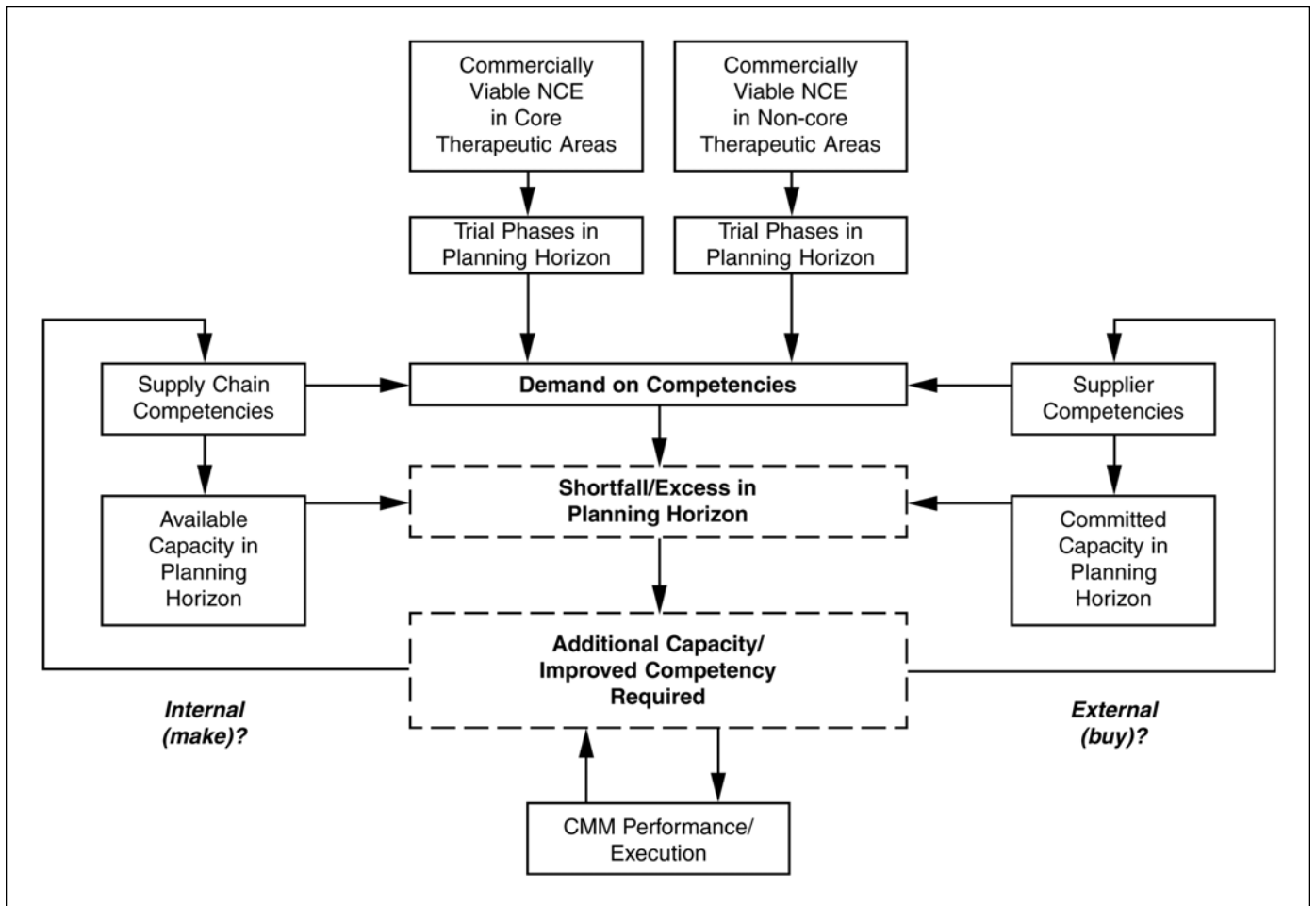


Figure 4. Influence map strategic choices in Clinical Materials Management.

that are required by the OEM. The supplier will be solely responsible for certain deliverables within the project.

It is not unusual for the companies involved in an Alliance relationship to be nominal competitors.

In Alliance relationships, the costs are a joint responsibility and liability. Any profits from the venture are split between the OEM and supplier according to pre-agreed arrangements.

### Integration

This is the extreme of close customer-supplier relationships. The closeness of the relationship, and the mutual dependence of each party, means that it is appropriate that the supplier becomes part of the same organization as the customer. Logic determines mutual benefit from combining core competencies in a single business entity for compelling strategic reasons.

This development hierarchy is shown as a series of steps. In reality, it is more of a continuum and there can be significant friction between the customer and supplier when there is a mismatch of perceptions about where the relationship stands.

The most important consideration is to recognize that as the relationship gets closer, and the value invested in the relationship gets greater, so the core competencies that are

required by both parties changes.

At the transactional level, the core focus for both organizations is to manage the contract. Procurement and sales departments are the main points of contact. In a partnering relationship, the focus has moved away from the contract to consider what performance improvements can be achieved by operational changes. Line management functions become the main point of contact.

### Planning CMM Strategic Value

How then can companies make appropriate *strategic* and *tactical* decisions about the configuration of their CMM processes? The goal is to have a clearly defined framework that eliminates the arbitrary nature of outsourcing decisions. The objective is to ensure that the core competencies required internally are fully developed, and that qualified outsource capabilities are available when required.

Among the key dimensions that must be considered by this framework are:

- The market opportunity represented by an NCE. What annual sales value is projected for the end drug?
- The fit of the NCE to core therapeutic areas for the company. What level of risk does the development represent?
- the Phase of Clinical Trial being considered

These first three elements set the requirements necessary of CMM. The business also must consider the competencies and capabilities that are to be deployed to meet these requirements:

- Core CMM competencies. Where does the company add most value – managing the programs, designing studies, coordinating supplies, policing quality, producing pharmaceuticals etc?
- Available capabilities. Essentially, a combination of supplier management and internal performance management. In both cases, appropriate capabilities for different Clinical Trial situations must be available to the company.

The choices open can be illustrated on an influence map in Figure 4. The following statements describe how the influence-map (or framework) might be deployed:

*'NCEs within the core therapeutic areas will have all active clinical materials produced and managed in-house for all Phase I, II, and III clinical work.'*

*'CMM operations for NCE opportunities in non-core therapeutic areas that become available to the company for development/exploitation will be outsourced from Phase III to our partner CRO supplier.'*

*Our internal CMM competencies are:*

- supplier quality assurance
- program management
- study design
- bulk product production

*The following activities will always be outsourced to our Partner suppliers:*

- placebo and comparator production and material management
- end use packaging
- logistics

*'The requirement for capacity in CMM will be assessed annually and any external capacity required will be placed with partner CROs.'*

Establishing such a strategic framework places some practical demands on CMM organizations. They must:

- understand their core competences as determined strategically
- understand their effective operating capacities
- operate a Capacity Planning regime that is flexible enough to accommodate a variety of scenarios
- deploy appropriate Planning and Scheduling tools to manage processes tactically for optimum performance

## Summary

This article describes the complex environment within which CMM processes operate. Outsourcing is a valid mechanism for reducing that complexity. However, any business intending to outsource such processes must understand where value in its CMM is derived. If outsourcing is used solely to drive down the cost of individual clinical trials, or to 'plug' short-term arbitrary capacity holes, competitive performance will, over time, be eroded.

Important areas of value that are embedded in the supply chain include:

- management of product and process knowledge
- increase responsiveness of the organization to clinical trials
- 'portfolio' management of new entity opportunities
- fundamental competitive strategy of the business

Organizations cannot now leave the configuration of CMM as an arbitrary decision taken on a project-by-project basis. There must be clear alignment to business strategies, and a focus on developing competencies and capabilities in the resultant 'execution' processes.

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## About the Author



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