

# BATTLE FOR SURVIVAL

## PHARMA MANUFACTURING PRESSURES

- Growing influence of generic producers
- Government and intermediary buying power
- Rising costs of doing business

During the last 20 years, huge investments have been made in the pharmaceutical manufacturing industry. However, over last year a number of companies announced significant cuts in staff and plant closures. Maurice Parlane, director of New Wayz Consulting, has sound advice for companies intending to survive the next 20 years.

Today's pharmaceutical industry has come a long way since the days of the double-digit growth typical of the 1980s and 1990s, when there was an explosion in the construction of new manufacturing facilities and acquisition of new equipment. During 2007, five major pharmaceutical corporations announced significant cuts in staff and a number of site closures in efforts to streamline manufacture and improve efficiencies.

- January: Pfizer announces it will cut 10,000 jobs and close five plants by the end of 2008. Its five-year plan is to reduce its manufacturing plants from 93 to 48 by the end of 2008.
- February: AstraZeneca reveals plans to cut 3,300 jobs in its global supply chain. In July 2007, it confirms a further 4,300 jobs will be cut in areas, such as sales and marketing, business infrastructure and R&D.
- July: Johnson&Johnson says it will cut up to 4,800 jobs and close several production sites globally.
- October: GlaxoSmithKline (GSK) announces it will take £1.5 billion in charges to save as much as £700 million annually by 2010, a move that will include streamlining manufacturing, changing its selling model, improving efficiencies and job cuts.
- November: BMS confirms restructuring plans that 'includes workforce reductions in some areas and the rationalisation of some facilities'.

Statements made by GSK's outgoing CEO Jean-Pierre Garnier when announcing the company's plans, described the drivers

for these changes: 'We will be accelerating and expanding many initiatives to improve GSK's productivity.'

The current pressures on manufacturers come from a number of sources: there is increased price pressure on products from the growing influence of generic manufacturers,



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and from the buying power of governments and intermediaries. This is also a period where there are rising costs to doing business – compliance costs, taxes, energy and materials pricing are increasing in an environment where shareholders are focused on companies delivering returns in line with historical performance.

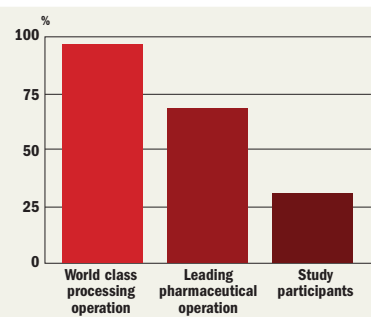
Contractions are how the larger organisations are reacting outwardly to demands to become more effective in delivering products to market. Meanwhile, there are significant changes occurring within manufacturing to meet the same objectives.

### Pharma challenge

The conversion of bulk-pharmaceutical products to something that is in a patient-ready dosage form has changed little in terms of the manufacturing operations in recent years, but the demands to yield lower cost, high quality products, faster and with less wastage are particularly evident. But there is room to improve. For some time there have been examples of inefficiencies when compared with other sectors of manufacturing, which for a long time were deemed a 'consequence' of the regulated nature of the industry. The popular view was that inefficiency was justified due to the need for quality-first approaches and the care required to counteract the potential risk products present to patients.

While this may be true in part, the situation was, and still is, that there are significant opportunities to improve efficiency in pharmaceutical manufacture. Data published as recently as 2007/6 illustrates this. Figure 1 shows how overall equipment effectiveness (OEE) in a UK pharmaceutical benchmarking study compared with world class manufacture in the process sector.

Figure 1. Manufacturing OEE benchmarks



### Harnessing opportunities

Today's challenge to manufacturing is to reduce cost in order to remain competitive. The industry as a whole is responding and is in a period where opportunity exists for process improvements by leveraging areas both outside and within operations. These opportunities exist due to the following factors:

- Regulators – regulations are becoming harmonised globally and recent changes allow appropriate levels of regulatory relief.
- Equipment vendors and service providers – suppliers are developing smarter and faster production equipment and support systems. They can provide a wide range of goods and services. Specialised contract manufacturers are more prevalent and provide cost-competitive alternatives to in-house manufacturing of difficult or non-proprietary product lines.
- Manufacturers – there is rapid adoption of advanced manufacturing practices focused on operations and processes.

### Regulatory environment

Regulatory authorities now recognise they have a role to play in the delivery of more cost-effective medicines, in particular, the compliance arm of the regulatory body is more aware of its role relating to these wider health issues. This has led to a developing paradigm for application of risk-based compliance practices, where rigour in regulatory oversight is applied according to patient risk, rather than at a consistent level across an operation. In this context manufacturers with well developed risk assessment and management strategies can operate their processes and quality systems with degrees of resource and effort based on the level of risk that aspects of their operations present.

There has been a recent shift in regulatory thinking to permit alternative compliance strategies where processes are well developed and characterised and a 'design space' exists. Regulators are accepting that well behaved, scientifically and technically sound processes can be self-evident as compliant.

Recent developments in instrumentation and control technologies has led to acceptance that process analytical technology (PAT) is now possible. PAT is the application of systems that reduce or remove the need for post-operational QC – the compliance of the process is evident and controlled in real time. Much of the focus in PAT has been for new processes, however, manufacturers realise it is possible to develop an operational space around existing processes and apply PAT to these based on historical data.

There has been increased cooperation between regulatory authorities and industry in recent years, particularly

through industry groups. The frequency of interactions has not only increased, but the openness and candidness of these interactions has been beneficial to both parties developing a better understanding of each other's requirements. This has led to the development of new regulatory guidances, with wide industry acceptance, and in some cases, the interaction has led to withdrawal or clarification of existing rules and guidance that were problematic.

Additionally, individual companies are forging closer relationships with regulatory authorities, enabling more open dialogue to take place on a specific level, which is proving beneficial to resolution of compliance issues.

### Equipment vendors

The ability to improve manufacturing processes is generally limited to increases in speed, capacity or reduction in waste. These benefits tend to be associated with demand increases – the capacity and reject rates for most processes show only small opportunities for improvement.

There are some technological improvements on offer, such as smarter monitoring and in-process control systems and rapid test methods. These benefits are evolutionary and to some extent have always occurred.

Vendors and suppliers, particularly those specialising in the pharmaceutical market, have recognised the demands on their clients and have responded to this by providing



Survival of the fittest: pharmaceutical companies must adapt to prosper.



Specialised contract manufacturers are providing cost-competitive alternatives to in-house manufacturing of difficult product lines.

a wider range of support. It is common to now see an integrated supply relationship, where life-cycle activities or responsibilities may be contracted to the supplier under a technical agreement. This type of relationship benefits both parties. The supplier has the opportunity to gain added value from their business and the manufacturer is able to divest of some of the cost previously associated with managing this. Advanced examples of this type of relationship see a level of integration of the supplier and client's quality management systems (QMS) and sharing of responsibilities for quality.

This kind of support can be as simple as provision of qualification, but often extends to suppliers assuming direct responsibility for quality such as acceptance testing, and often will include collaborative arrangements where supplier's staff are trained in the operations and procedures of the client company and interact with them directly.

**Service providers**

Contract manufacturing/outsourcing has become a common way to optimise production schedules, particularly where difficult, infrequent or non-proprietary lines are concerned. Service providers have assisted this practice to flourish by setting up facilities that operate as specialist providers for particular types of product or process, and provide the manufacturer the opportunity to free up capacity for new or higher value product lines where the opportunity exists. Contract manufacturing/outsourcing also provides the opportunity to rationalise expertise and remove difficult or unusual, but otherwise profitable products or those requiring disproportionate resources or overheads from their manufacturing schedules.

The outsourcing of manufacturing brings a new set of challenges and responsibilities. Contract manufacturers are often cost competitive, and may not approach the manufacture and quality assurance for products in the same way as contract providers. Successful outsourcing needs the contract provider to be prepared to accept an additional level of risk through the separation of accountabilities and provide systems to manage this.

The management of third party manufacturing requires a balance of commercial and quality assurance in dealings with the contractor, which is different to that required in the control of internal manufacturing operations. It is not an opportunity to contract out of responsibility for difficult or low value product lines. Those companies that do not recognise this often find the outsourcing experience less than fruitful. Those organisations that are positioned to manage outsourcing find it an effective

practice in the management of costs and competitiveness.

**Manufacturing practices**

A number of manufacturing practices, which were seldom encountered in the past, are now commonplace. These include:

- An increased focus on development and technical transfer for new processes to bring about a higher degree of knowledge and permit quality by design
- Focus on competencies of an organisation either to rationalise similar products or operations into centres of specialisation (offshoring), or contracting out

- (outsourcing) to remove incompatible or inefficient processes
- Within larger organisations, performance measures are more visible and healthy focus on key performance indicators encourages internal competition, which can be harnessed positively
- Collaboration between organisations, mainly through industry groups has become widespread – providing a platform for benchmarking best practice

By far the greatest opportunity for operational improvement exists where organisations apply best practice from within and outside of the pharmaceutical industry. The uptake of advanced manufacturing practices such as Six Sigma, lean manufacturing and statistical process control is now readily adopted to improve efficiencies, where previously such practices were not commonly found in pharmaceutical manufacture.

The key to realising efficiency from these approaches is to diffuse these practices throughout the business to remove the 'silos' that exist in terms of functional responsibilities, for example, through the use of live process data from manufacture for process monitoring and improvement initiatives, but then implementing feed-forward and feedback of the results and trends into validation and to quality assurance programmes as a product quality review on a continual basis. Also, the application of lean principles driven by manufacturing (such as, on-time in full delivery and added value per employee cost) across business functions, resulting in improvements in manufacturing operations and in all functions supporting supply.

**Character change**

The pharmaceutical manufacturing organisation today comprises facilities, equipment and unit processes that are similar technologically to 10-15 years ago. However compared with process engineering practice there are some significant differences. Companies that are to remain competitive have a clear focus on harnessing process-improvement opportunities. A modern well-run pharmaceutical manufacturer intending to survive the next ten years needs to exhibit a number of characteristics not often seen in the past. **WPF**