

# PAT and ROI

## A holistic approach

Despite the advantages PAT offers to the pharmaceutical industry, many companies remain hesitant about its implementation due to high investment costs.

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By offering companies a chance to understand and control their processes, both at the R&D and manufacturing stages, PAT enables continuous quality verification and, with it, a chance to deliver consistent quality, lower costs, speed up product development and release, improve market responsiveness and reduce supply chain bottlenecks. Companies will also be rewarded by a lighter regulatory touch if they can gain PAT-led control of the product design space.

Nonetheless, many companies face difficulties in implementing PAT projects. An important building block is to develop a clear ROI analysis. Such an analysis delivers a number of benefits—the objectives and implications of PAT should become clearer for the company; it should provide a clear framework for investment and for evaluating outcomes; and the case for PAT could be articulated to top management and other key personnel within the company.

### Starting Point – The full ROI context

A vital starting point is for companies to consider the full context of PAT. Only by doing so can companies judge the true worth of PAT. This requires a consideration of the wider environment in which PAT will be

### The ROI context of pharmaceutical PAT projects

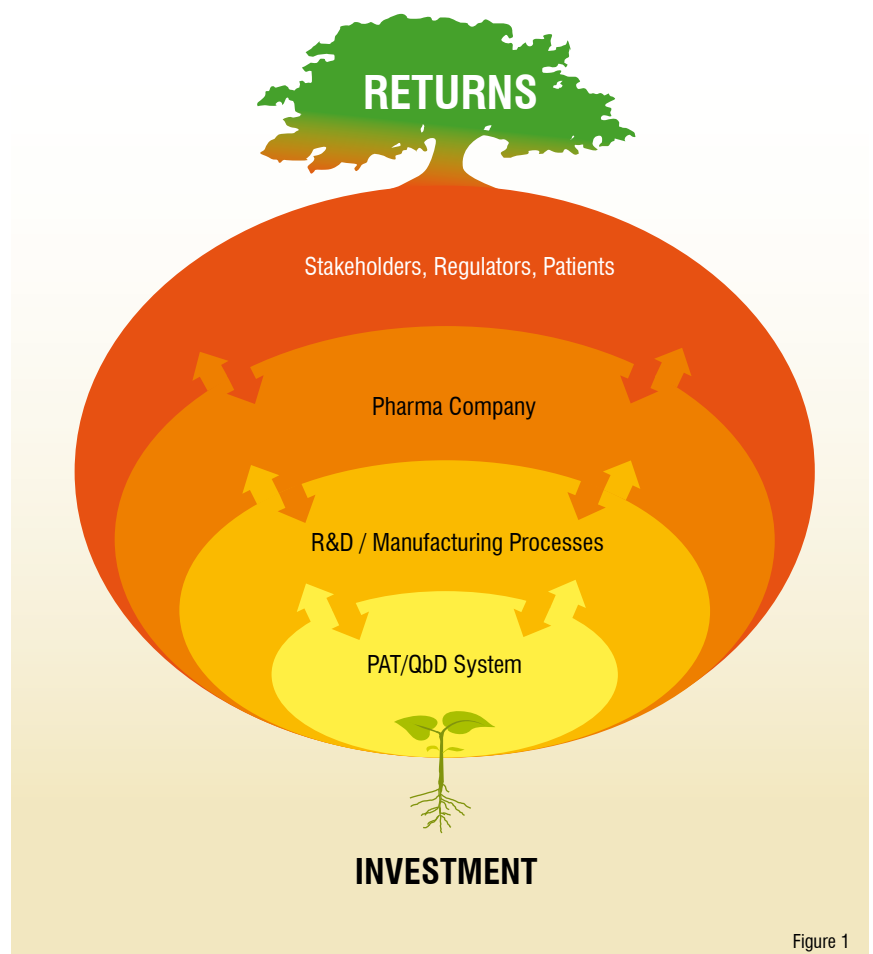


Figure 1

implemented (Figure 1), not just looking at quality and process control but going far beyond this to consider regulatory relationships, the needs of health-care organisations and, ultimately, the links with patients. An important part of the US Food and Drug Administration's vision for PAT, for example, is that the adoption of the technology by the pharmaceutical industry will help close the gap between drug product development and the patient. In the future, it is hoped that PAT will be part of a feedback loop that can enable companies to take account of how a specific drug is performing in specific patient contexts and adjust formulations and manufacturing accordingly.

In addition to these future visions, the development of PAT and decisions about the best roll-out of the technology needs to be taken in the context of a company's current and projected drug portfolio, reflecting the different manufacturing needs of products that are in the pipeline. In other words, decisions on PAT cannot be taken away from the context of the three key major elements—the company's future business and product strategy, its

organisational setting and external environment. However, in my experience, this consideration of wider external or internal context often does not take place when it comes to PAT projects in pharmaceutical companies. Companies frequently view PAT in exactly the opposite way, deciding to buy a couple of tools to replace existing lab measurement methods and see where that leads them.

This consideration of context outlined in Figure 1, in turn, leads to some of the parameters for the ROI analysis both on the cost and the benefits side. For example, investment in PAT should be expected to deliver tangible performance improvements in R&D and manufacturing processes, such as reduced waste, faster throughput times and, ultimately, the potential for real-time product release. At the same time, there will be wider company implications, such as retraining or redeployment whose costs will need to be fully factored in.

#### Rooting ROI in strategic ambition

The design and extent of the ROI analysis will be largely determined by

the extent of strategic ambition behind the PAT implementation. There is a big difference between a company that is seeking to develop PAT in a greenfield setting, aiming for full real-time product release, and a company that is seeking to improve an existing aspect of manufacturing, perhaps on a single unit operation such as drying. In many situations, companies can start with a small application of PAT on one part of the production process, for example on a single unit operation such as drying, before moving on to a more global view. A typical start point, for example, might be the establishment of an end-point detection for a dryer or granulator. Indeed, in our experience, the most common applications of PAT relate to online monitoring of blending, drying and granulation steps.

In all instances, the goal should be some clearly identifiable performance improvement. However, as discussed, many companies do not even start by identifying such clear change but instead fall into the trap of seeing PAT merely as an alternative to existing activities, for example investing in an in-line process analyser as a replacement

## Key ROI Questions

Companies need to identify the situations where PAT investment is most likely to be cost-effective and be clear about the purpose and scope of the project as well as how it helps the company to achieve its longer term manufacturing vision and strategy. The following series of questions can help in such identification:

**Strategic gain** – How does the PAT project fit with the company's wider product and manufacturing strategy? Also, what are the project's specific R&D or manufacturing benefits, such as operational savings, faster time to market, increased machine availability, less waste etc?

**Required investment** – How much investment, including capital expense, planning and deployment, training, and ongoing management and support, will the project require?

**Financial return** – What are the expected financial returns of the project, including ROI, savings and what is the payback period?

**Operational efficiency** – How will the PAT project contribute to overall enterprise efficiency? Is the enterprise and knowledge architecture in place to capture these gains?

**Risks** – What are the potential risks associated with the project? How likely are they and what contingencies need to be in place? What would be the impact on the financial return and strategic gains?

**Competitive and reputational impact** – What competitive advantage can be gained? What are the reputational implications of investing or not investing in PAT? How does the proposed investment compare with competitor's PAT plans?

**Accountability and ownership** – Who is accountable for the project's success? Is the project owned by top management? Is there sufficient leadership to deliver the change in working methods and culture that will be needed for the project to be successful?

for offline analysis in the laboratory. Such a narrow view of PAT is unlikely to prove cost-effective and, indeed, may fail to deliver sufficient ROI to be justified in isolation.

### The importance of integration

For any pharmaceutical company seeking to use PAT to achieve real-time product release or, indeed, to move towards the FDA's vision of closing the gap between drug development and the patient, the state and extent of existing infrastructure will be critical. Real-time product releases requires a PAT system that is linked to an electronic batch record and other support infrastructure. Integration of equipment is essential, otherwise the product may be ready but the next machine in the process may not be. Companies that already have such infrastructure in place will be able to achieve much faster ROI payback times.

Similarly, an important condition for being able to link clinical batch manufacturing and quality data to clinical outcomes, is the possibility to store data in the same format with the appropriate meta data / context data, so that different data sources can be combined and evaluated. Systems and data formats have to be aligned and be able to be merged. This puts the emphasis on common IT systems throughout the whole R&D process as well as on data mining tools to be able to discover relationships. The long-term benefit is that companies will be able to quickly gain insight and knowledge in therapeutic efficacies and mechanisms and how they are impacted by the manufacturing process. In fact, this is nothing new, as such principles have for long been applied in other industries, where customer satisfaction and product performance appreciation by customers is feedback into process development and improvement cycles.

One inhibiting factor in the development of pharmaceutical PAT has been the absence of software that enables the full integration of PAT tools and all information flows during processing and online comparison of process data with previous or historical data. This is now being addressed with the development of software that enables the collection of data and the full integration of all information flows during processing and online prediction calculations as well as comparison of the actual batch trajectory with the "golden batch" trajectory. Companies now have the important



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ability to have a common user-friendly interface for all PAT tools (process analysers, multivariate statistical tools, LIMS, MES, process control, historian etc.) and the ability to fully integrate PAT into the manufacturing and development architecture.

### The importance of leadership

As discussed above, any ROI analysis should take full account of the risks surrounding a PAT project. In doing so, companies should take care not to underestimate the less tangible, 'internal risk' that can occur if personnel fail to capitalise fully on the potential of PAT.

This can arise for a number of reasons such as inadequate attention to training, existing cultures that promote 'silos working' or other organisational inertia factors. PAT does require a greater focus on multi-disciplinary skills and teamwork than some pharmaceutical R&D and manufacturing units are used to. Different departments, such as regulatory affairs, quality control, process engineering and the manufacturing teams, need to work together on PAT. The potential of 'cultural drag anchors' to slow the progress of PAT is a very real project risk and can be minimised significantly by having clarity on the key ROI questions as outlined in the above box and the consequent leadership and backing of top management.

### Way forward

PAT projects are being developed by pharmaceutical companies in a wide range of circumstances, ranging from the development of greenfield future development and manufacturing facilities, to the fixing of specific snags in current manufacturing processes, such as end-point detection for a dryer or granulator. In all cases, the development of a clear ROI analysis will be important to the success of such projects. The best ROI framework needs to answer key questions that link the project to the company's wider strategy and environment. Those companies that succeed in bringing together a holistic view of the short and long-term are more likely to make PAT implementation decisions that deliver a more effective ROI. ■

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