Global Pharmaceuticals
and Life Sciences Industry Group

Manufacturing, R&D & IT

Aligning current demands with a Pharma 2020 vision:

the role of technology*

Taking big leaps or small step changes

Foreword

The PricewaterhouseCoopers Pharma 2020 thought leadership series paints a challenging and compelling vision of the sector at the end of the coming decade. It will be a decade where, increasingly, all medicines which receive approval will be approved on a real-time basis, with live licences contingent on the performance of extensive in-life testing, including trials in specific patient subpopulations, and a predetermined schedule for reviewing each set of results. It will be a decade where the nature of pharma products will become more diverse, with the advent of combination therapies, diagnostics, biomarkers and treatments targeted at patients with specific disease subtypes. The technologies used to manufacture some of these new therapies will become much more complex. It will be a decade where many agencies will share safety and efficacy data to create a broader picture of how medicines perform.

A more connected, fitter pharma

Technology and IT developments will be central to all these aspects of the future. A key challenge for companies is how best to prepare for this future while also addressing the pressures of today. One of the big strides that pharma companies will need to make is to create much better connectivity and interfaces between different parts of their value chain – crucially between R&D, manufacturing, the supply chain, the patient and, also, the regulatory sphere. Silo working remains a strong characteristic of many companies. This is reinforced by the fact that much of the technological architecture is in the form of separate standalone systems – one for one part of R&D, another for another part, a quite different one for manufacturing and so on. This is rapidly becoming unsustainable and will be completely so by 2020.

Technological and IT changes in R&D and manufacturing, for example, are already pressing if companies are to embrace the full potential of the FDA's cGMP for the 21st century initiative and new draft process validation guideline. They are equally pressing if companies are to succeed in reducing drug development times. Well-judged technological innovation in manufacturing can also radically reduce costs by minimising waste and re-work. Investments such as quality by design, process analytical technology (PAT) solutions and product lifecycle and knowledge management tools are all important ways in which companies can prepare well for a future based on live-licensing while, also, addressing the pressures of today. Such investments can help companies deliver more flexible manufacturing, reduce costs, respond to the regulatory goals being flagged up by the US Food and Drug Administration (FDA) and begin to bridge the gap between R&D and manufacturing and, as a result, reduce drug development times.

For example:

Product and process lifecycle management systems (PLMs) - pharmaceutical companies sometimes get mired in the amount of information they produce or even lose the information. At worst, knowledge gets lost throughout the product lifecycle at each key stage. At best, knowledge is not shared fully across different stages of the product lifecycle, thus slowing, for example, the transfer from R&D to development to manufacturing. PLM systems have not been widely applied in pharma so far. Companies will need to accelerate the implementation of such systems if they are to respond successfully to various new initiatives. These include:

- the publication of the FDA process validation draft guidance (November 2008);
- the ISPE PQLI (product quality lifecycle implementation) initiative;
- live licensing (as described in the FDA critical path initiative document);
- the upcoming mandatory request from FDA for submissions based on e-CTD (Common Technical Document) from July 2009 (and no paper based submissions);
- ASTM E55 continuous quality verification standard;
- continuous improvement throughout the product life cycle (PAT and QbD FDA guidance) from September 2004;
- ICH/FDA is pushing pharma manufacturers towards complete and detailed information control related to product during the whole product lifecycle. Product data includes anything related to product requirement, product active mechanism, product testing, product definition, product manufacturing, product retailing, pre sales data (pre-clinical and clinical data), post-sales data (adverse events) as time goes by, for any region and for all regions. ICH/FDA/EMEA wants a more continuous data exchange about the above data between pharma industry and drug agencies.

Built-in quality through process analytical technology (PAT) - Quality by Design (QbD) in R&D reduces process development, upscaling and tech transfer time while process analytical technology (PAT) in the manufacturing plant delivers a more stable process with much greater manufacturing productivity at lower costs. The FDA's cGMPs for the 21st Century initiative and Process Analytical Technology Guidance calls for the design of effective and efficient processes to assure product quality and performance; product specifications based on a mechanistic understanding of how different formulations and processes affect product performance; and continuous real-time assurance of quality. Although it is now five years since this initiative was launched, pharma companies have been slow to implement PAT. In many cases, when they are doing, they are implementing in a narrow way, replacing existing testing with an automated analyser or in-line sensor rather than realising the full potential of the technology to build process knowledge and control processes in a flexible way to always produce right first-time quality products. In terms of manufacturing, PAT gives companies the opportunity to move from the current typical 70 to 90% yields to near zero wastage or defects.

These are two essential building blocks for companies wishing to become more connected and in control of the knowledge needed for R&D, fast transfer from R&D to manufacturing and move towards a situation where they can deliver continuous improvement using feedback from patients that is linked directly in to the development and manufacturing process. Companies have the opportunity to reduce costs, build-in quality and gain the flexibility needed for demand-driven manufacturing and small batch production. Using smaller production units will enable companies to avoid the inefficiencies of having large plants that, typically, only currently utilise around 40% of their capacity and, ultimately, to produce drugs when they are needed to match personalised or small segment patient profiles.

Many of these changes can not wait. Already, for example, regulatory changes are changing the interaction needed with regulatory authorities. Regulators are now requesting or soon will request insight on produced batch information. Indeed, produced batch data may need to be available for clients, such as distributors, pharmacists or physicians. This change will impact the choice of technological solutions. Electronic Batch Records (EBR), PAT systems, Data management and storage solutions, Laboratory Information management Systems (LIMS), Manufacturing Execution Systems (MES), ERP (Enterprise Resource Management) or Product and Process Lifecycle management (PLM) systems will need to be configured and secured in such a way that safe and efficient data exchange with authorities and clients is made possible. In the other direction, feedback from clients and suppliers towards manufacturers will offer opportunities for product improvement and development. As such, internet portals and CRM systems will need to be developed to capture the feedback (product quality, issues, improvement, etc.) from distributors, hospitals, pharmacists, physicians, etc. Today several US states have also passed product pedigree laws, and many others are contemplating such legislation. These laws will ultimately apply to every contractor in the worldwide supply chain, including active pharmaceutical ingredient manufacturers.

Judging the best technological moves

Companies need to assess the best way to make the technological investments that will be necessary for 2020 preparedness while also delivering answers to current pressing demands. Should companies be making 'big leap' rather or small step changes? How can companies judge how best to prepare for the future development and manufacturing strategy and infrastructure? How fast and how far should they move? What are the cultural and behavioral changes that need to accompany technological change? How to build up the business case?

Many companies are seeking to implement change, based on today's competitive challenges, but are doing so in sub-optimal ways that do not maximise benefit for the company. This is because, often, changes are not being informed by a clear vision or a broadly evaluated business case. Such a vision must address the regulatory, market, scientific, and technological forces that will shape pharmaceutical R&D and manufacturing in the future. The outcome of this type of process will be a view about what type of R&D and manufacturing strategy and plant the company needs in a more medium to long term timeframe, say five to ten years time which, in turn, can frame the steps they take now. The answer may be different from plant to plant and many companies are likely to need to plan for a mix of scenarios.

The technological change roadmap needs to be shaped by calculations of ROI (return on investment) or expected net present value (NPV) and risk evaluation, ensuring a route to the final 2020 destination as well as an effective answer to the more short to medium term five, ten and fifteen year challenges along the way. On the manufacturing front.

For example:

- The short term future - today and in the coming five years, most companies will invest in their existing manufacturing facilities to upgrade to a state with lower manufacturing costs, increase safety, comply to actual regulatory demands, increase quality, etc. This can be by the implementation of a higher degree of automation, integration of equipment and systems and the introduction of new technologies.

- The mid term future - within 5 to 10 years, companies will move away from batch manufacturing with 'after the event' offline product testing to fully automated and integrated continuous manufacturing with quality designed into the process. This will allow manufacturing on a smaller footprint.

- The longer term future - within 10 to 15 years, companies will also be mindful that a possible trend towards more personalised medicines will increase manufacturing complexity and, in turn, pose challenges for manufacturing execution systems (MES) and quality systems. A larger variety of products and variation of the same products will require greater flexibility of production as well as closer integration along the whole pharmaceutical chain - R&D, manufacturing, supply chain, sales and the end customer. Highly flexible, high density R&D pilot facilities will also serve as manufacturing environments, supported with process and product lifecycle management tools as knowledge repositories.

For further information

Contact:

Ingrid Maes, Director

PricewaterhouseCoopers
Generaal Lemanstraat 67
B-2018 Antwerpen

Tel.: +32 (0)3 259 33 05
Fax: +32 (0)3 259 30 99
Cell: +32 (0)499 55 89 93

E-Mail: ingrid.maes@pwc.be

About PricewaterhouseCoopers

PricewaterhouseCoopers' (PwC) Global Pharmaceutical and Life Sciences Industry Group is dedicated to delivering effective solutions to the complex business challenges facing pharmaceutical and life sciences companies. A global leader in serving the pharmaceutical and life sciences industry PwC has extensive experience working with companies on industry-specific strategic, operational, and financial issues. Our expertise includes assurance, tax and advisory services, as well as specialised capabilities in regulatory compliance, risk management, performance improvement and transaction support. In helping our clients, we draw on the full knowledge and skills of PwC's professionals. More than 155,000 people in 153 countries connect their thinking, experience and solutions to build public trust and enhance value for clients and their stakeholders.

www.pwc.com/pharma