

New System Integration

A new type of System Integration offering...



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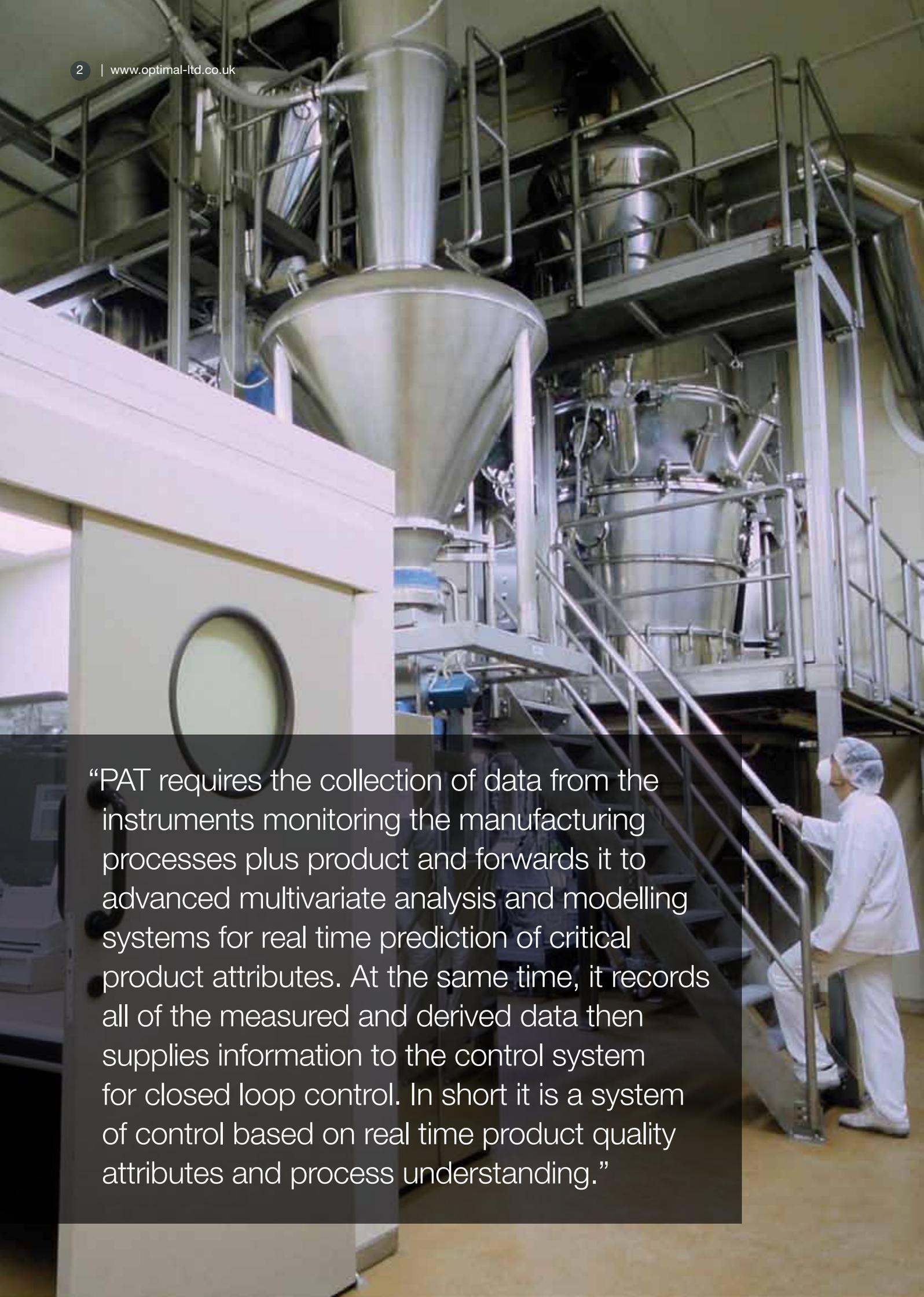
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PAT

News on the latest Pharmaceutical automation projects designed, developed, manufactured and implemented, with full software development and integration.

Whether you are extending an existing production line, upgrading process equipment or building an entirely new plant, this is the essential read to ensure that your upgrade delivers on production, efficiency and reporting targets.

A photograph of a pharmaceutical manufacturing plant. The scene is filled with complex stainless steel machinery, including large vertical tanks and funnels, connected by a network of pipes and walkways. A worker in a white cleanroom suit and hairnet is seen from the side, walking up a set of stairs. The lighting is bright and clinical. A semi-transparent dark grey box containing text is overlaid on the lower-left portion of the image.

“PAT requires the collection of data from the instruments monitoring the manufacturing processes plus product and forwards it to advanced multivariate analysis and modelling systems for real time prediction of critical product attributes. At the same time, it records all of the measured and derived data then supplies information to the control system for closed loop control. In short it is a system of control based on real time product quality attributes and process understanding.”



What is synTQ?

synTQ (synchronised total Quality) is a PAT Knowledge Management software package. It is a unified software platform with which users can gain new levels of control over manufacturing processes, even when production is spread over several different sites. It is highly scalable so can be used in laboratory scale development systems, then seamlessly transferred to production operations.

PAT is becoming increasingly popular in the process industries such as life sciences, pharmaceuticals, oil and gas, chemicals and food. It is not only the manufacturing companies that are adopting it; PAT is also proving popular with industry regulators.

“PAT meets two pressing - and often conflicting - challenges in a wide range of modern production processes,” says Optimal Technical

Director, Dave Richards. “It improves the degree of control over manufacturing processes, and coordinates production over remote facilities.”

One of PAT’s major attractions is that it allows pharma companies to move away from end-of-line and end-of-process testing and inspection, replacing it with efficient on-line and in-line analysis and closed loop control.

As Dave explains: “synTQ collects data from the instruments monitoring the manufacturing processes plus product and forwards it to advanced multivariate analysis and modelling systems for real time prediction of critical product attributes. At the same time, it records all of the measured and derived data, supplies information to the control system for closed loop control. In short it is a system of control based on real

time product quality attributes and process understanding.”

Importantly synTQ manages all data from one central point, which greatly simplifies model management and enables the sharing of models between different sites. Data archiving is also very much simplified.

As users scale up from laboratory or a pilot scale process to global production, synTQ solutions ensure that products manufactured at multiple sites all use the most up-to-date models and controls. Users can also integrate their synTQ systems with those of their contract manufacturing partners.

Other advantages of synTQ systems include enhanced data visualisation modules, web connectivity, high speed, ease of use, real time analysis and real time control.

Cutting edge PAT system delivers a huge increase in production efficiency

Improvements in product quality, process reliability and manufacturing efficiency can be achieved by switching from batch processes to continuous production in the pharmaceutical industries.

A continuous manufacturing line typically requires a more sophisticated control system than batch production, and in pharmaceuticals the control requirements are particularly demanding, including the need for precision ingredient handling, absolutely complete mixing and 100% accuracy in record-keeping for traceability purposes.

To meet these stringent demands many pharmaceutical companies are turning to Optimal, with its deep understanding of process analytical technologies (PAT)-based control systems.

Typically, installation of a state-of-the-art PAT system delivers a huge increase in production efficiency. It also ensures regulatory compliance – a critical issue for pharmaceutical manufacturers and increasingly important in many other industries.

Optimal's excellence in the field has led to the development and constant refining of its synTQ® PAT implementation management software. This is coupled with the company's 26 years of systems integration experience in the pharmaceutical sector.

Encouraged by regulators, there is considerable interest across the pharmaceutical industry in

the adoption of PAT and closed-loop control strategies in order to improve quality, process reliability and manufacturing efficiency. The potential advantages of the approach include shorter cycle times, reduced reject rates and improvements in the way energy and materials are managed.

Production-level PAT implementations can require considerable computing power, and many may require the installation of several high-powered servers. In one recent Optimal installation three servers are used to control the operation of high-speed near-infrared (NIR) spectrometers, which collect data on the condition of the product in real time during manufacture.

This data is processed and passed on to a dedicated synTQ® server, which compares the results to expectations and makes appropriate adjustments to process parameters to optimise the quality of the product. Other servers within the system are used for data collection, distribution and reporting, both on-site and remotely, via a secure web-based interface.

Shop-floor interactions with the system are made using human machine interfaces (HMIs). One HMI, for example, is located in the dispensary, where staff will check the condition of raw materials using an automated probe. The synTQ® system stores that data and makes use of it to adjust control parameters when that



batch of materials is introduced into the manufacturing process.

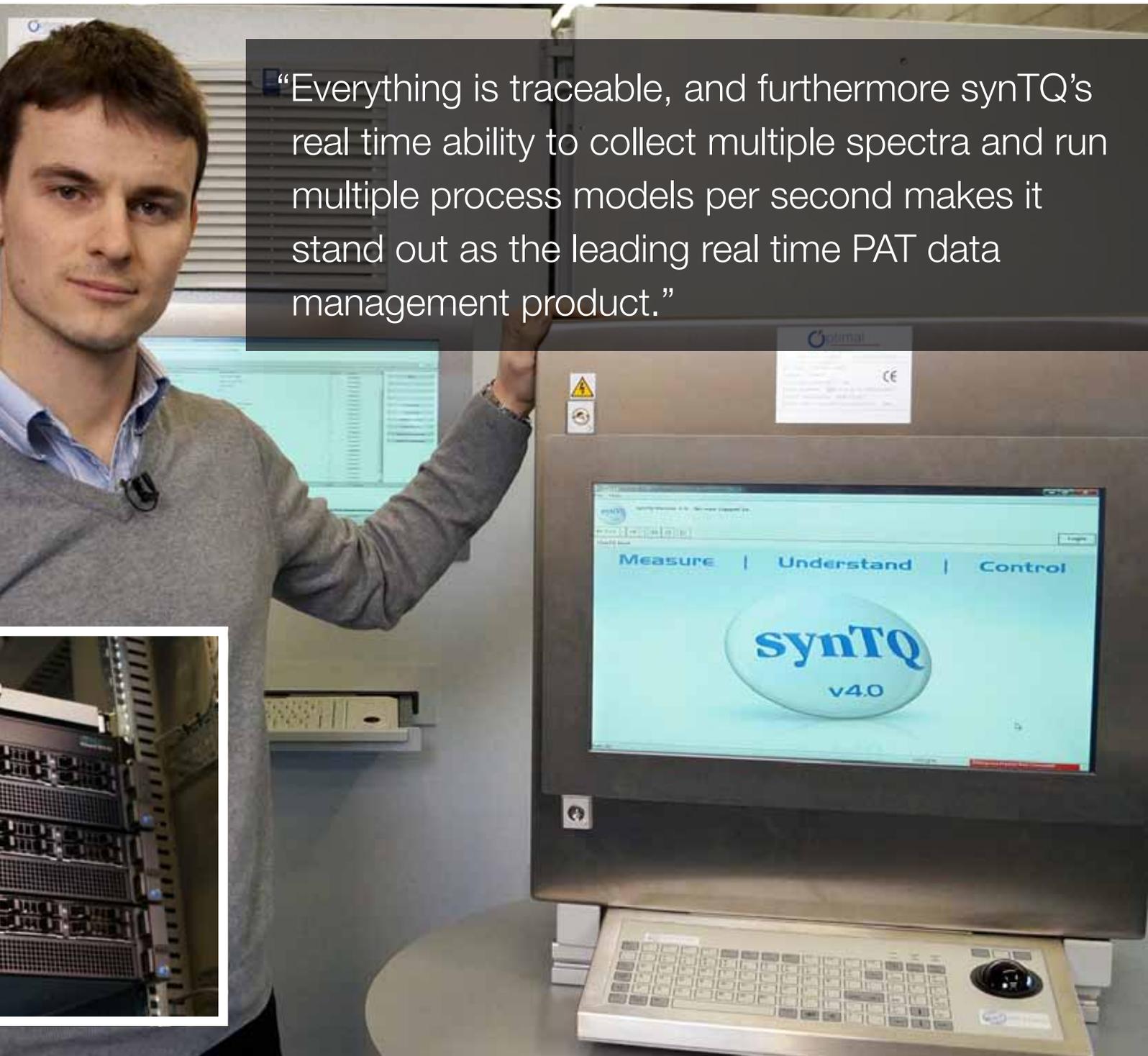
Like all synTQ® applications, the new system has been built to be fully compliant with FDA (Federal Drug Administration) guidelines on the traceability of manufacturing data. Complete records are retained within the system for audit purposes, or to facilitate ongoing continuous improvements to the production process.

“The idea is that you design your PAT process and methods within synTQ® and then run the configured PAT system in real time when the process is operational. Every time you run that process, it uses exactly the same configuration, until you decide that you need to improve it. At which point, all those changes are audited and stored within the system,” explains Paul Gillham, Optimal’s

technical lead on the project.

Continuous production is an important goal for many pharmaceutical companies. As Optimal is both a systems integrator and the developer of the synTQ® software, it can take customers’ requirements, work with the machinery vendor, produce the required PAT hardware and provide the software to control the complete system.

“Everything is traceable, and furthermore synTQ’s real time ability to collect multiple spectra and run multiple process models per second makes it stand out as the leading real time PAT data management product.”



PAT will bring new drugs to market faster, while improving quality and reducing costs

Some potential users of process analytical technology (PAT) see it as expensive, complex and too time consuming to integrate. But Martin Gadsby, a director of PAT specialist Optimal Industrial Automation, says that PAT is the way forward if the pharmaceutical industry is to deliver new drugs to market, faster, with improved quality and at reduced cost.

Pharmaceutical manufacturers usually have a choice between improving product quality, enhancing manufacturing or reducing costs. PAT, however, offers the possibility to deliver all of these while also providing a rapid return on investment.

The heart of a PAT system is PAT Management software, which ties all the disparate pieces of equipment and software together to provide a simple way to develop and maintain process (and control) models in a regulatory-compliant way. The

software also forms a framework that ensures that all data is gathered, arranged, stored, analysed and presented to prediction engines in a cohesive way.

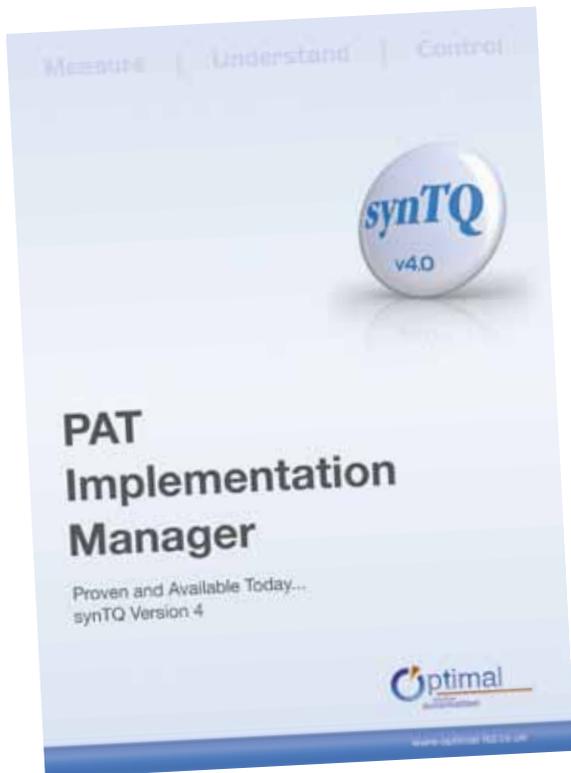
The benefits of PAT can be summarised as:

- Increases process understanding with more data and analysis.
- Causes of product variability can be identified and managed.
- Increases understanding so will reduce development and scale-up time.
- Increases patent life of new and existing products.
- Reduces production cycle times.
- Reduces work in progress.
- Identifies alternative (less expensive) raw materials.
- Reduces wastage and rejects.
- Improves in quality and consistency of quality.
- Enables rapid release of product.
- Improves energy and material use.
- Facilitates continuous processing.
- Reduces manufacturing cycle times and staffing.
- Reduces the manufacturing facilities required.
- Creates potential for skid-/cell-based manufacturing for rapid deployment as pre-built systems.
- Meets the new FDA Process Validation Guidance.
- Reduces development, manufacturing and quality costs.

All of these benefits are delivered by a PAT data manager, which is in effect a real-time coordinator that controls the process(es) and/ or passes the data onto a third party control system in a timely and regulatory-compliant manner.



Brochures explain synTQ® options



Brochures are now available describing the features, benefits and range of application for all the modules in synTQ® V4.0, the software suite for process analytical technology (PAT) implementation in the life sciences, food and petrochemical sectors.

For copies please call Optimal's Sales department on +44 (0)1454 333 222 or download them from www.optimal-ltd.co.uk.

synTQ® V4.0 is a single, robust and proven software platform with which users can develop, deploy and manage PAT from the research laboratory to the production network. It consists of four modules: synTQ® Lite, synTQ® Flexible Manufacturing, synTQ® Reporting Services and synTQ® Enterprise Master.

There is a brochure for each module, plus an overview brochure which explains the concept of PAT and details the complete synTQ® V4.0 suite.

“synTQ® V4.0”, says Optimal Sales and Marketing Director, Martin Gadsby, “improves control over manufacturing processes, and also manages an increasingly widely distributed production footprint. Its modular design offers a clear path through PAT development from the research laboratory to global production networks.”

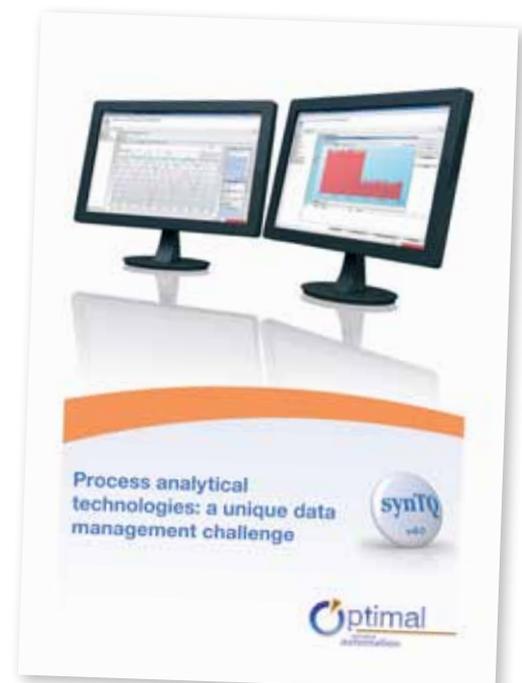
White paper on PAT for pharmaceutical manufacturing

Optimal has published a white paper to explain how to create a unified framework for data collection, model development, process understanding, process control and continuous improvement. It is entitled: *Process Analytical Technologies: a unique data management challenge* and can be downloaded from http://optimal-ltd.co.uk/white-papers/optimal_white_paper_dec_2012.pdf

Process Analytical Technologies (PAT) have the potential to revolutionise pharma manufacturing, by compensating for input variability, tightening finished product specifications and cutting production cycle times.

However a successful PAT implementation requires users to master new skills and new technologies, including the synchronisation and collection of large and complex analytical datasets and archiving of data and models for complete traceability. Alongside these are the commercial requirements of product quality, rapid time to market and ROI goals.

Author, Martin Gadsby, says: “The paper looks in detail at each of the skills and technologies required, and makes the case for the use of a dedicated PAT implementation software environment, such as Optimal synTQ®.”



Reducing energy use while improving drying control

Optimal Industrial Automation software has played a vital role helping scientists improve both the performance and energy efficiency of a drying process widely used in the production of pharmaceuticals.

Researchers from the University of Puerto Rico at Mayaguez and the Universidad de Atlantico, Barranquilla, Columbia have worked together to assess the performance of a fluidised bed dryer. They have demonstrate that closed loop control of the dryer's temperature and air flow rate can optimise the drying process while simultaneously reducing energy consumption by up to 60%.

During the research programme, Luis Obregón, Leonel Quiñones, and Carlos Velázquez set up a system based on an inline near infrared (NIR) sensor together with real time control models. They then ran a series of tests using both open and closed loop control regimes and measured the results.

Within the system, synTQ® was used to control the inline NIR sensor that analysed the material being dried. The spectra recorded by the sensor were passed to an analysis package (SIMCA QP), which generated data about the real time moisture content of the material. This data was then passed back to the synTQ® package, which processed it and, in turn, passed it on to the dryer's Delta V control system, using the OPC protocol. Delta V then used the predicted data to alter the inlet temperature and air flow rate in the dryer, according to an empirically

derived process model.

Encouraged by regulators, there is considerable interest in the pharmaceutical industry in the adoption of process analytical technologies (PAT) and closed-loop control strategies in order to improve quality, process reliability and manufacturing efficiency.

The researchers' findings, published in the learned journal *Control Engineering Practice*, also showed how such an approach can effectively handle process variables such as initial moisture content or grain size.

In the tests, the closed-loop control model was able to achieve the desired state of dryness with substantially lower energy consumption than could be achieved using traditional open loop techniques. Also of great significance for pharma

companies, the researchers tested the robustness of the system by altering the granulation and moisture content of the test ingredients without adapting the control model parameters. In this test, the closed loop approach was still able to achieve the desired level of dryness, albeit without such dramatic improvements in energy efficiency.

"This project is a great demonstration, both of the power of model-based control to improve pharmaceutical manufacturing, and of the power of synTQ® to enable that process," says Optimal Sales and Marketing Director, Martin Gadsby. "Leading pharmaceutical research and manufacturing organisations are now using synTQ® systems at every scale, from lab based research projects like this, all the way up to the control of multi-site, multi-country manufacturing operations."



“This project is a great demonstration, both of the power of model based control to improve pharmaceutical manufacturing, and of the power of synTQ® to enable that process,”



News from synTQ user conference underlines a shift in development and production technology for the pharma industry.

Attendees at this year's user conference for market leading PAT knowledge management software synTQ expressed a clear intention to continue the application and roll-out of PAT (Process Analytical Technology). This affirms that users are now working in line with the FDA's guidance on PAT and reaping the benefits of this technology which has promised so much for so long for the whole drug development and manufacturing lifecycle.

Process Analytical Technology when correctly applied can revolutionise drug production by reducing development and manufacturing times whilst simultaneously improving quality and reducing cost. This applies equally to batch and discrete manufacturing techniques, but also puts the operating framework in place to realise continuous manufacturing and real time release, which will amplify the already significant improvements that are now possible.

The synTQ User Group (SUG) conference was held in Washington DC from 29th – 30th January 2015 directly following the global PAT conference IFPAC. synTQ users, developers and application experts joined with technical support operatives from synTQ's software creator Optimal to discuss the use of what has now become a market standard solution for PAT implementations, including continuous drug production and real-time release via a PAT framework.

Conference attendees enjoyed presentations on 'real time automatic advanced control of continuous pharmaceutical tablet manufacture' from Dr. Ravendra Singh from the Department of Chemical and Biochemical Engineering, **Rutgers University**, USA, plus, user experience case studies from **Vertex Pharmaceuticals**, **Bristol-Myers Squibb**, **Sun Pharma** and **the Janssen division of Johnson & Johnson**.

Martin Gadsby, Director at Optimal and one of the speakers at the event commented on how industry attitudes have crystallised and action is now being taken, 'There is no doubt that Process Analytical Technology (PAT) is the key emergent process technology in the pharmaceutical drug production industry today. The savings in time-to-market for development and the speed of production, once the operational model is transferred, are breathtaking. As an example we have seen production processes that previously took weeks using batch production methods reduced to a matter of minutes'.

"Enthusiasm for a PAT enabled production technique has been there in the market for a decade, the difference now however is that a number of the major global pharma companies and generics manufacturers have bought into synTQ and are seeing the potential turn into a reality. The user conference, combined with rising sales of course, is a litmus test for us on where the industry is at in terms of PAT; the range of questions we were asked and the enthusiasm for technical development to provide new tools and feature updates showed this year that the industry is indeed changing as adoption of this way of working takes off."

The IFPAC exhibition and conference that directly preceded our event, which we were also involved with, served to underline the fact that the pharmaceutical

industry is making the step change from the stricture of slow, inefficient and cumbersome batch production techniques, to fully integrated regulatory compliant PAT based production including continuous technology.

We have exhibited at IFPAC for over 10 years and are used to the discussions surrounding theoretical PAT implementations. However this year things were different in that the discussions were in relation to real projects where it was recognised that data and knowledge management needed resolution, these being key challenges to successfully applying the technique.

This for us clearly demonstrates that if not a paradigm shift, then there is certainly a substantial change in the way that drugs are being developed and produced. PAT-enabled batch and continuous production isn't the end of the changes that are happening though, for many, real-time release of drugs is the end goal, this having a huge additional impact on the industry.

Realising a PAT enabled project

To be able to use all the data streaming from lab and production equipment sensors and instruments, in real-time, to develop a PAT based production process for a new drug, or an existing one, means that there is a huge amount of data to manage. There are many disparate instruments and sensors to configure and co-ordinate, one



or more MVA models to run and maybe control algorithms to run, this being in real time and not after the fact.

These are the typical requirements of a PAT based system; however, you need an effective data & knowledge manager such as synTQ in order to achieve it. One that can keep-up with the myriad of data sources and process the vast amount of data in real time, load it into multiple complex multivariate models; gather and act on the calculated Critical Quality Attributes and make changes and adjustments to the process on the fly, in real-time. Additionally

it has to convert the data to knowledge to facilitate the process understanding, plus record, collate and report on all the information in a way that is compliant with regulatory body guidelines in order to achieve real-time release.

By effectively allowing all the skilled key players in a PAT implementation to work together using the same operational software platform, the application of a PAT enabled development and production process using an easy to configure, graphically based data management solution such as synTQ is proving irresistible to the industry, especially now that

many of the significant market players have adopted it as their PAT Knowledge Manager of choice.

The good news for consumers and patients is that medicines in the future may well reach the market faster and represent a more consistent and even higher quality standard than is being achieved right now. Furthermore the decreased cost of development and manufacture may filter down to reduced drug costs, creating the uncommon scenario where you can deliver a product faster, to a higher quality and at a lower cost.

Optimal's dedicated synTQ PAT software website goes live



Optimal has launched a dedicated synTQ web site and synTQ Assured product support portal for users of its synTQ Process Analytical Technology (PAT) Knowledge Management software.

Now with its fifth generation in development, the software has become the default choice for many of the pharmaceutical majors, as PAT based real time monitoring and control manufacturing techniques are revolutionising drug production.

In response to these trends, the new synTQ website www.synTQ.com provides all interested parties from system integrators to end users with a comprehensive public knowledge base for both synTQ and PAT. It also provides a gateway to the synTQ user site, MyPortal.synTQ.com for further detailed information, plus the synTQ Assured product support portal for dedicated 24/7/365 support for synTQ Assured clients.

The public access areas of the site provide valuable insight into the practical application of PAT principles and methods.

PAT and synTQ can be applied to all areas of drug manufacture from R&D and the laboratories through pilot plants to full manufacturing facilities. Consequently, the technology is making huge changes to how many pharmaceuticals are produced.

Optimal's synTQ has steadily been gaining traction as the preferred choice of PAT Knowledge Management software for many of the global majors – designating synTQ as a key component in their PAT implementation strategy. This trend was further highlighted at the popular PAT conference IFFAC and subsequently at Optimal's synTQ User Group meeting.

The synTQ web site provides common user data for all aspects of the synTQ software, plus the

MyPortal and synTQ Assured login areas for the ticketed 24/7/365 support area. The authorised users for this area can enter and track any issues, search FAQs, download software applicable to the licences that they have purchased, plus all related upgrades and patches – including the latest major releases whilst their support programme is in place. A vast wealth of technical knowledge is also accessible - incorporating knowledge-based articles from experts; details associated with a client's specific installation, how-to and troubleshooting articles.

The new synTQ website and synTQ Assured portal are therefore important pillars in the growing infrastructure around PAT – dedicated to serving the industry with vital knowledge to make the most of a customer's synTQ system. As with any new technology, guidance and knowledge are vital to its transmission within the industry if a paradigm shift is to be truly achieved. With the launch of the synTQ website and support portal, Optimal is dedicated to not only providing the tools – but also a service and knowledge centre so others can gain from this technology.

The public synTQ website is located at: www.synTQ.com and prospective synTQ Assured Customers can contact Optimal through the website, by email enquiries@optimal-ltd.co.uk or by phone +44 (0) 1454 333222 to request a quotation for synTQ Assured support and access to the dedicated support portals.