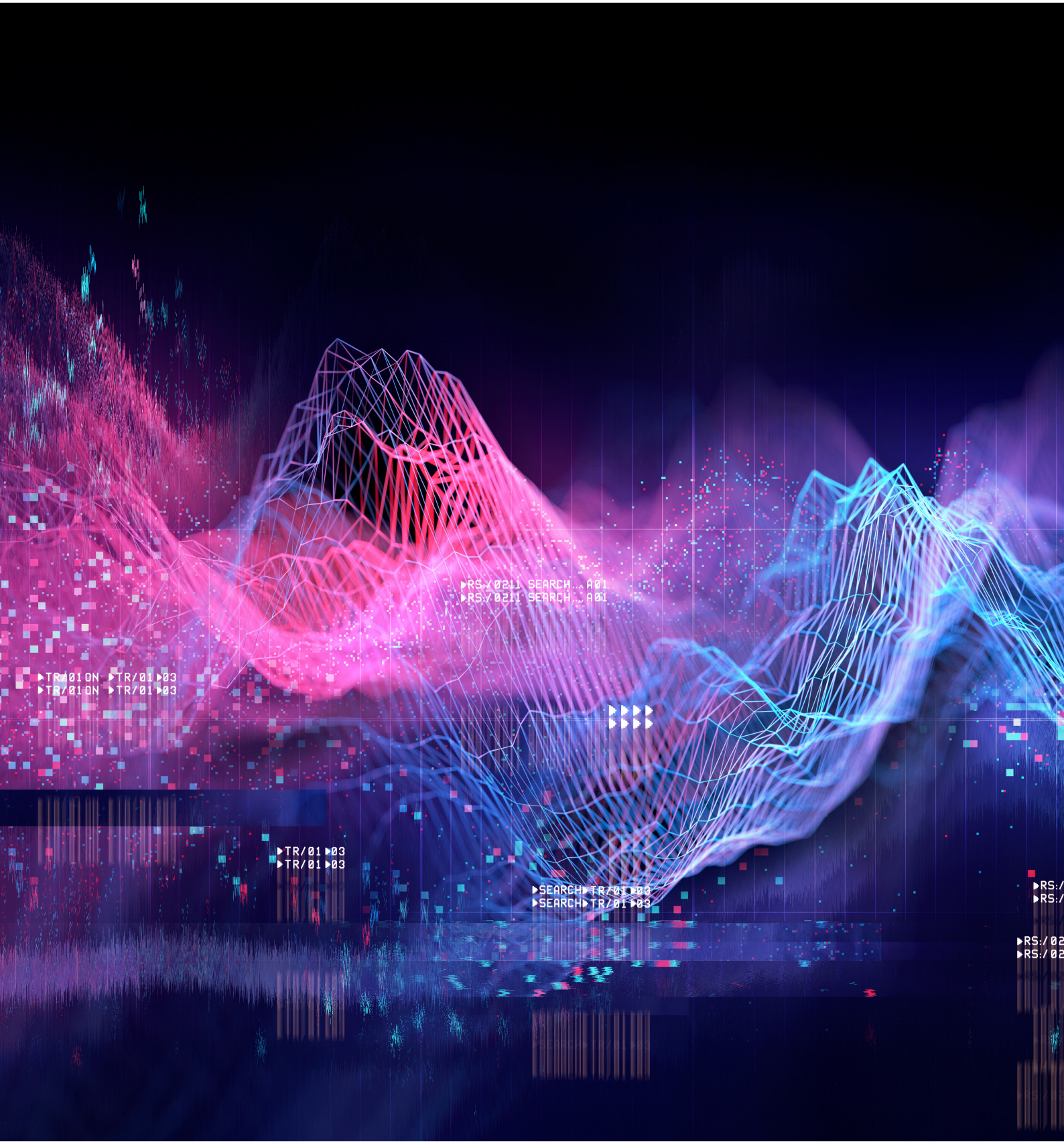
Increasing pharma quality and productivity using PAT.

Optimal
Industrial Technologies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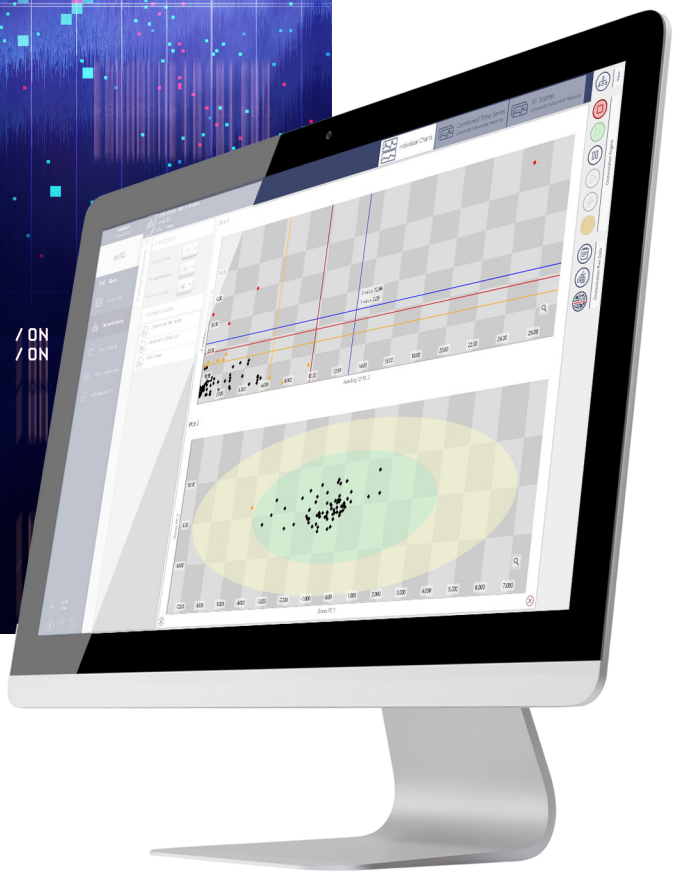
Process Analytical Technology (PAT) is a powerful quality assurance tool that can revolutionise the productivity of automated process manufacturing facilities. However, what is the reality behind the the buzzword, and where should prospective users start when implementing PAT?

Organisations that have successfully implemented a PAT based working structure are seeing production times fall from weeks to minutes using the same footprint.



The term ‘Process Analytical Technology’ or ‘PAT’ was coined by the pharmaceutical industry. It describes a method to measure quality and control in real-time the attributes that determine the quality and efficacy of a product. A scientific approach and process understanding are key to enabling PAT. The use of PAT enables users to establish a Quality by Design (QbD) approach, which aims to make a quality product that is verified in real time, rather than testing for quality after a process is completed. Therefore, by adopting a PAT enabled control strategy, it is possible to obtain a consistently high-quality product in a time, and cost-effective way.

How PAT works

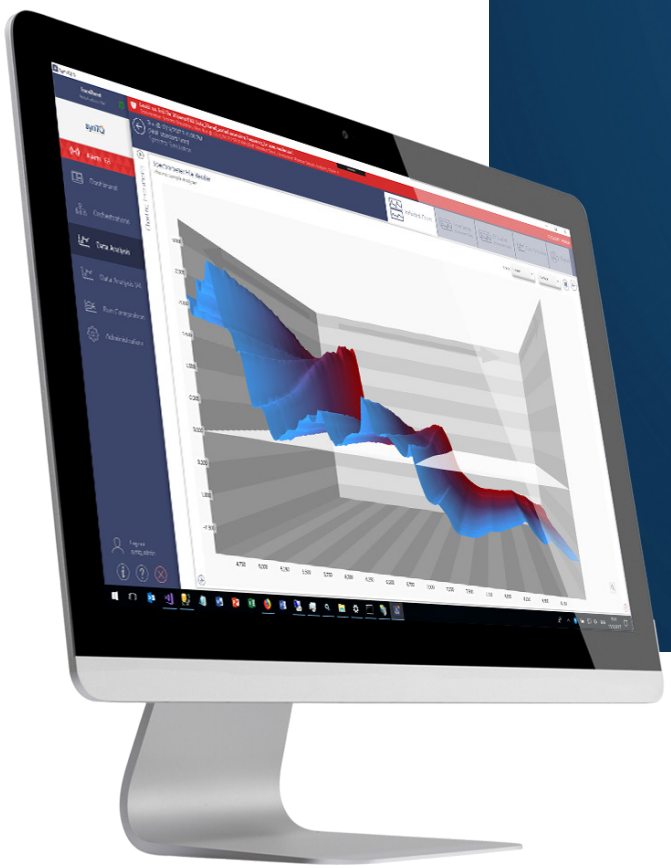
In order to measure critical quality attributes, a PAT system needs to measure product quality in a real time, non-destructive way, and this often calls for the use of spectral instrumentation such as Near Infra-Red (NIR), Raman, UV-Vis or other types of spectrometers. In order to 'calibrate' these instruments and convert the spectral responses to quality values, one or more multivariate prediction models are required. These models are statistical mathematical functions that can analyse the data, and predict the value of product quality attributes in real time.

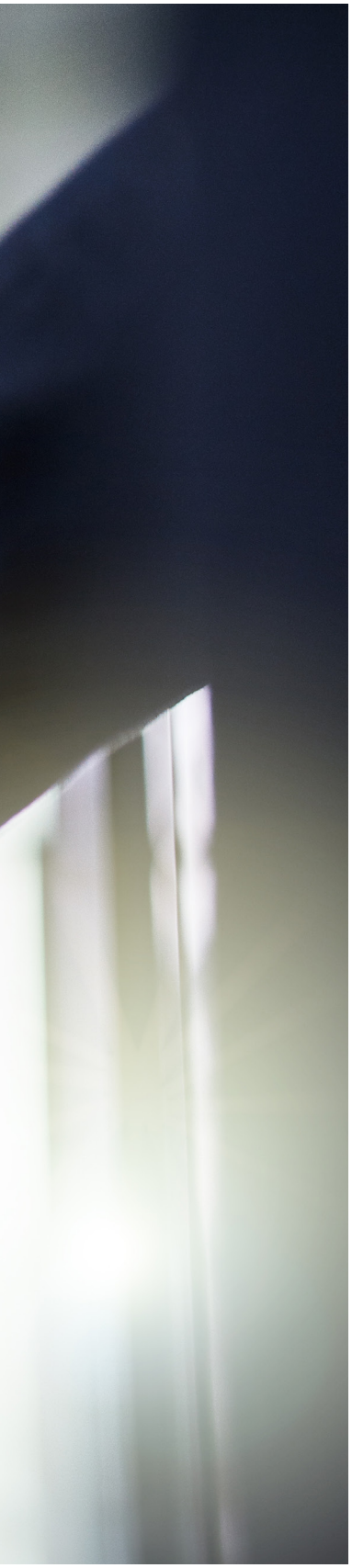
To build these calibration models during the development stage the use of 'traditional' laboratory analysis is required, however after the calibration models are built, then the reliance on traditional analysis is hugely reduced. Once you have the models built, you are able to execute more experiments and gain knowledge in relation to the process mechanistics – i.e. what input product and process parameters affect product quality, and in what way. This is what is meant by having a scientific approach to process understanding.

Having gained this process insight, it is possible to build control algorithms and then control the process in a way that delivers consistent, high-quality product. This automation approach is completely different to traditional process control. Traditional process control is based on empirically derived control formulae together with assumed raw material characteristics, with "Quality by Testing" being executed on process completion. PAT based control uses scientifically derived control algorithms that act on real time quality measurements that can take account of raw material and process variability – thus quality is assured at the end of the process.

The application of PAT early on in the development phase empowers industries to either have much reduced scale up challenges, or may eliminate them all together. The possibility of holistic, real time quality assurance also means that it becomes possible to change your processing methodology.

In particular, PAT provides the tools to move away from batch processing to continuous processing. The tedious manual "Quality by Testing" methods that characterise this manufacturing process can be substituted by more dynamic and responsive automated continuous quality assurance monitoring and control. While continuous processing requires a deep understanding of the production process, it can lead to a much more efficient production line that produces product with a much higher consistency of quality, with less scrap and rework whilst potentially removing all scaleup issues.





The way to implement PAT

Important aspects to consider before implementing PAT are determining the return on investment and assessing whether the instrumentation to measure quality attributes for specific products is available. However, the key challenge is not usually technological, but cultural. Many companies may require a complete change in their mindsets to move away from an existing manufacturing approach, which may have been in place for several years.

Once a PAT-friendly culture has been established, it is necessary to define the teams as well as the technologies required to implement the PAT strategy. In the first case, an organisation can look for PAT specialists either among its staff or from specialised third parties such as Optimal. Optimal for example has developed the market leading synTQ PAT knowledge management software platform, but also provides implementation support from turnkey system integration to training and ongoing 24hr technical support.

Concerning the technical equipment, a number of software systems are required, including MVA and Design of Experiment (DoE) programmes, as well as a knowledge management platform, such as Optimal's synTQ, that connects the IT system and the instruments together.

The next stage in PAT implementation consists in selecting a suitable project to apply this methodology to. Of course, succeeding in this first activity leads the way to the adoption of PAT on a larger scale, and on a range of different projects. Therefore, we always recommend starting your PAT journey in a modest way, so that the whole team can learn the techniques and demands of the technology on a process that is not too complex. Success with the first project is essential if your company is to adopt PAT! The goal is to then move from "islands" of PAT, where the technology is used to monitor and regulate quality attributes in an isolated way, to a "holistic" PAT approach, where quality is measured and assured from the raw materials entering the system, through the process to the finished goods exiting production.

PAT advances operational excellence in many industry sectors

Many of the large pharmaceutical manufacturers as well as businesses in other industry sectors have already adopted PAT. They have moved the technology from the laboratory, through pilot plants and eventually applied it in full scale GMP manufacture. Countless successful projects have been deployed in the field in a relatively short time period, delivering a fast, tangible return on investment - as well as improved and consistent product quality. It is safe to assume then, that the adoption of PAT will continue to accelerate.

synTQ

As well as providing the essential component in a PAT system – synTQ which is a PAT knowledge management software package, Optimal can provide a wide range of services to assist with the implementation of PAT projects. Optimal offers a single point of contact by being able to evaluate specific customers' requirements, assist in delivering the required PAT hardware, offering external expert teams for PAT implementation and providing the software – synTQ - to control the complete live PAT process.

Optimal Industrial Technologies has more than 30 years' experience in the automation and optimisation of control and data management systems for the pharmaceutical, biotech and life science industries.

The demands being placed on manufacturers in relation to production costs, product quality and business sustainability are ever increasing; hence, the company's primary aim is to deliver measurable improvements in all these target areas.

In addition to practical automation and system integration expertise Optimal Industrial Technologies has also developed a world leading PAT based data management software package – synTQ® which is used by over half of the world's largest pharma companies to improve quality, increase productivity and reduce time to market for large and small molecule processes using both batch and continuous manufacturing.

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