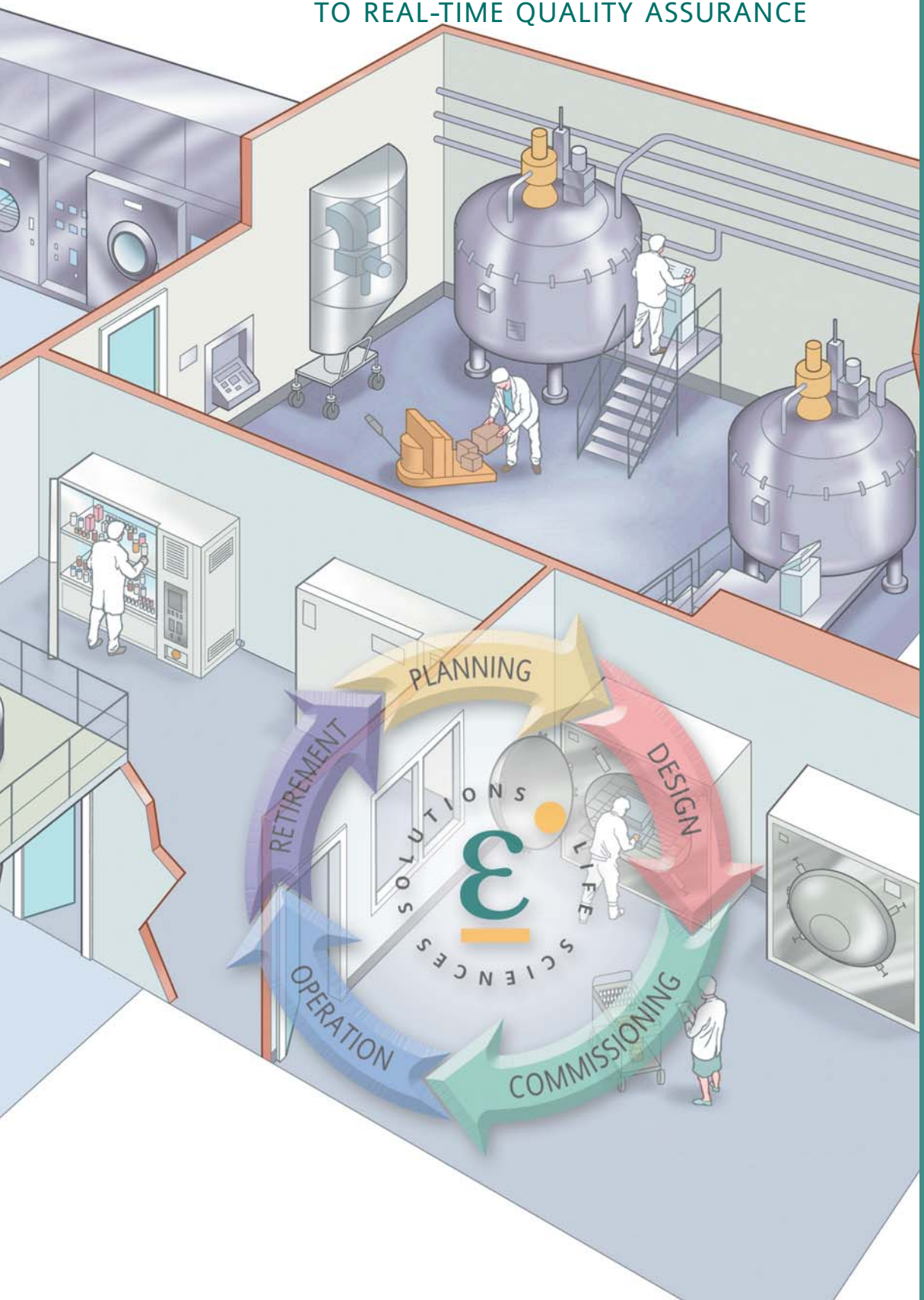
EUROTHERM® FLEXIBLE SOLUTIONS

PROCESS ANALYTICAL TECHNOLOGY

A SCIENTIFIC RISK BASED APPROACH TO REAL-TIME QUALITY ASSURANCE



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Process Analytical Technology - PAT

PAT is a flexible regulatory path for innovation in manufacturing and post approval changes. It represents the FDA's vision for future pharmaceutical product development and manufacture. As pharmaceutical development and manufacturing evolves from an art form to one based on science & engineering, the FDA will use the knowledge developed in PAT to establish product specifications and evaluate manufacturing processes. This is an opportunity to create improvement in the productivity of both manufacturing & regulatory processes. (ASTM standardisation news, May 2004)

What is PAT?

PAT final Guidance was published September 2004. Its aim is to encourage the voluntary development and implementation of innovative pharmaceutical development, manufacturing, and quality assurance.

"A system for designing, analyzing, and controlling manufacturing through timely measurements (i.e. during processing) of critical quality and performance attributes of raw and in-process materials and processes, with the goal of ensuring final product quality."

PAT is based on the principal that "quality cannot be tested into products; it should be built-in or should be by design."

Why PAT?

Conventional Manufacturing

- Generally inefficient with long cycle time, utilisation <15%
- Scrap & rework 5-10%
- Lab testing on collected samples, generally long waiting time
- Variable materials resulting in variable quality of product
- Generally low level of automation
- Perceived rigid regulatory requirement: Once validated try to avoid any change.
- Minimum innovation
- Generally "time defined" end point

EurothermSuite® PAT Solution

EurothermSuite's PAT solution is made up of the best-of-class "PAT tools", designed to address the Life Science's PAT requirement. It is a tightly integrated package which incorporates all the necessary tools for a PAT based manufacturing application.

EurothermSuite is by nature a modular DCS system which is ideal for the Life Science applications that often consists of a series of Unit Operations. These features allow the application of PAT to Unit Operations individually and therefore ensuring quality at every stage of the manufacturing process.

EurothermSuite's PAT solution will help you to establish

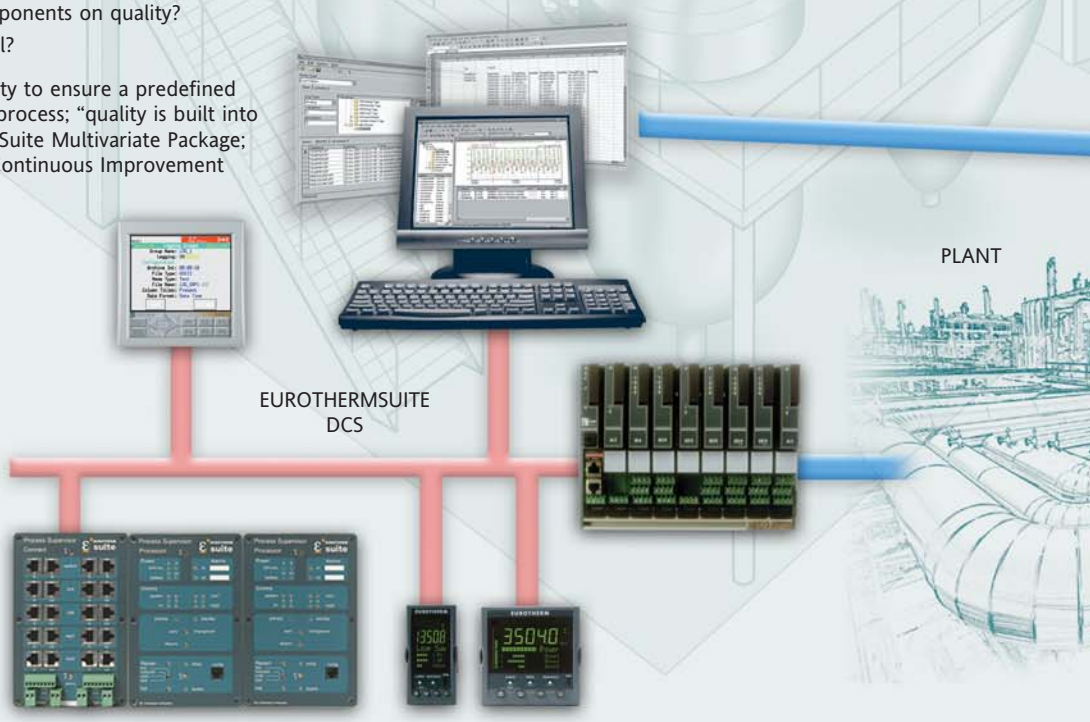
- What are the effects of product components on quality?
- What sources of variability are critical?

It will enable you to manage the variability to ensure a predefined quality at the end of the manufacturing process; "quality is built into your product". It includes the EurothermSuite Multivariate Package; Process Analyzers; Process control; and Continuous Improvement and Knowledge Management.

Process Control

EurothermSuite DCS solution has been widely used in the Life Science industry. With its high accurate analogue control it is ideal for monitoring and ensuring effective control of all critical attributes of the Process and ensuring operation in the desired state at every Unit Operation stage. It is ideal for providing advance control strategies including Feed Forward & Back, Predictors, Time Delays.

EurothermSuite DCS system is tightly integrated with the Multivariate package. Generally Process End Points are determined by the Multivariate package. At every stage of the process, once a Process End Point has been achieved, the EurothermSuite DCS system will take the necessary action to move to the next stage until the final Product has been accomplished.



PAT based Manufacturing

- Reducing production cycle times by using on-, in-, and/or at-line measurements and controls
- Preventing rejects, scrap, and re-processing
- Continuous real time quality assurance, real-time release
- Increasing automation to improve operator safety and reduce human errors
- Improving energy and material use and increasing capacity
- Facilitating continuous processing to improve efficiency and manage variability
- Physical/Chemical/Biological attribute end point

What is involved in a PAT based Manufacturing?

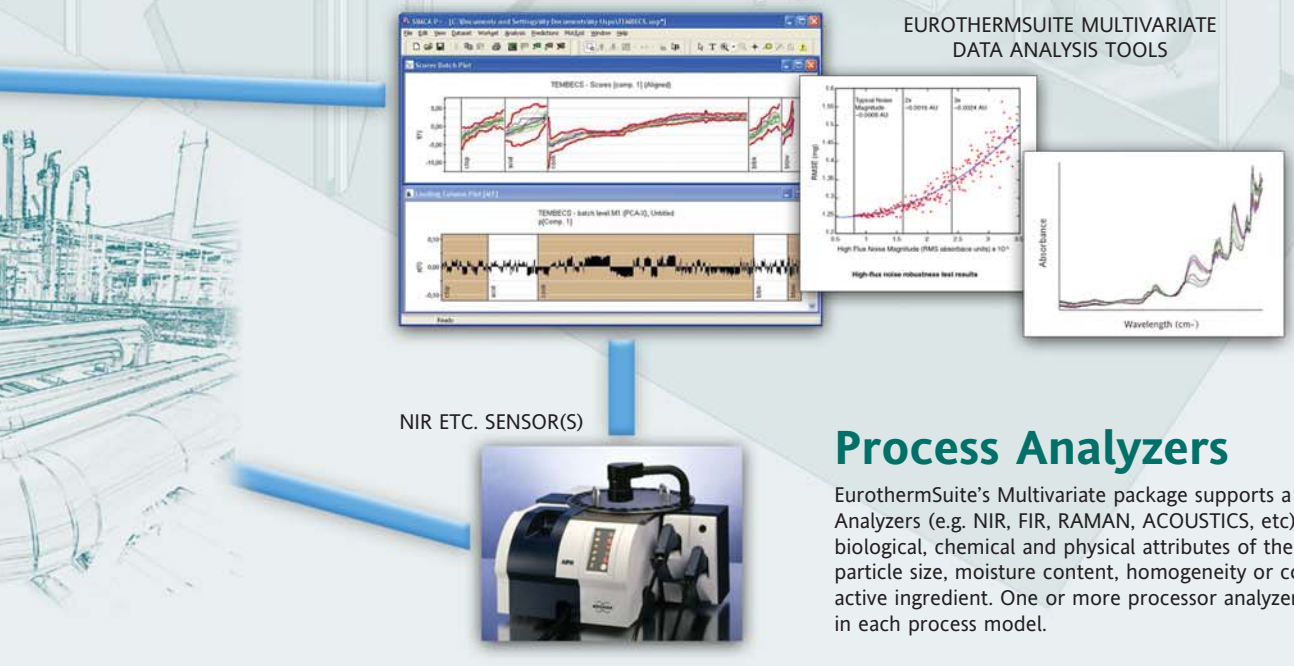
- Understanding the process and all its critical sources of variability
- Timely measurement, i.e. during processing (on-, in-, or at-line)
- Control of critical quality and performance attributes including in-process materials (e.g. using process endpoints)
- Continuous improvement and knowledge management.
- Continuous validation (every lot is a validation lot) versus discrete 3-lot exercise.

Continuous Improvement & Knowledge Management

The use of Design of Experiments (DoE) to build a comprehensive model that captures the understanding of the process allows for many new opportunities. It becomes a simple procedure to scale up from a pilot production to full production. The model may also be used to determine other possible outcomes resulting from: variation in ingredients that could allow the use of lower cost materials, or alternative strategies in the control of the process e.g. fastest, lowest power consumption etc. A system validated by the FDA according to PAT principles may take account of future technological advances to improve efficiency and product quality without complete re-validation as there is a better understanding of the process and its variability is managed. As the principle of PAT is extended, so eventually the ultimate goal of real-time release may become a reality.

EurothermSuite Multivariate Package

EurothermSuite Multivariate Package provides for the (DoE) to build a better understanding of the process and thus determine the safe production window. DoE allows a model to be built that incorporates the relationship between the measured variable and the critical quality attributes of the process. Data acquisition of both multivariate and univariate data for electronic data records is built-in to enable compliance to 21CFR Part 11. The analysis and prediction engine uses the model from the DoE to predict the critical quality attributes of a process and to accurately determine Process Endpoints. With direct interfacing to the process control system it is able to effect control over the process in real-time to manage the inherent variability.

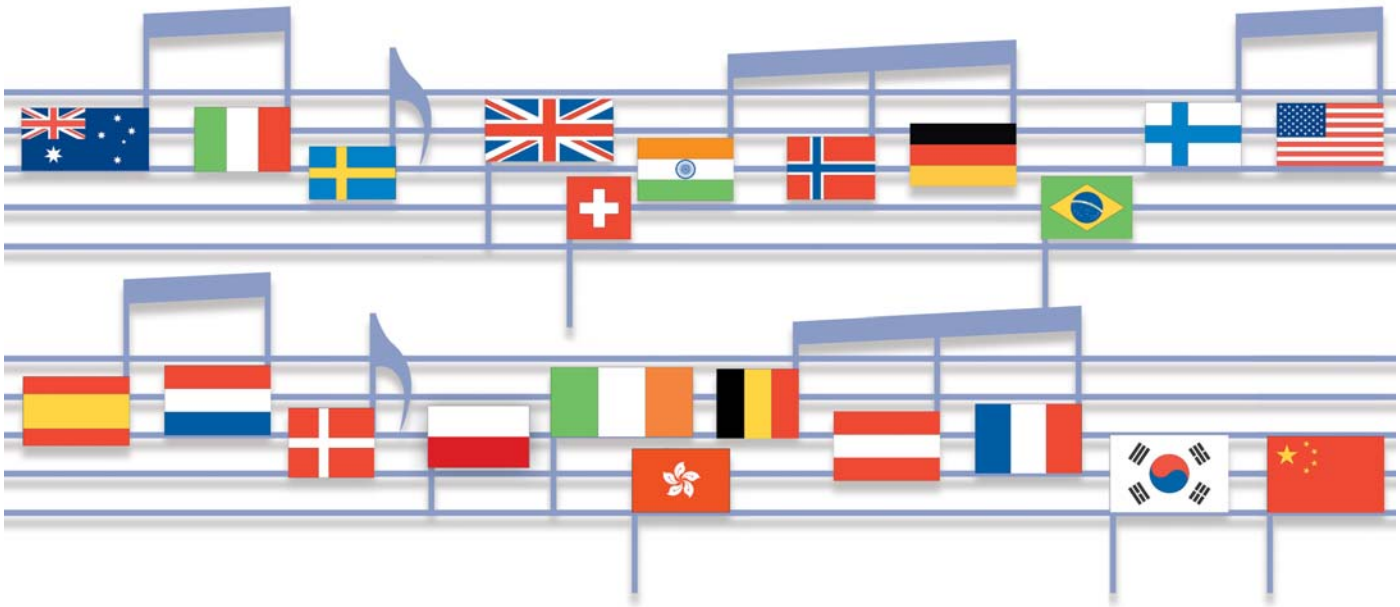


Process Analyzers

EurothermSuite's Multivariate package supports a number of Process Analyzers (e.g. NIR, FIR, RAMAN, ACOUSTICS, etc) to measure biological, chemical and physical attributes of the process such as particle size, moisture content, homogeneity or concentration of active ingredient. One or more processor analyzer may incorporated in each process model.

Eurotherm: International sales and service

Understanding and providing local support is a key part of Eurotherm's business. Complementing worldwide Eurotherm offices are a whole range of partners and a comprehensive technical support team... to ensure you get a service you will want to go back to.



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Part No. HA029104 Issue 3

Printed on recycled paper in England 06.07