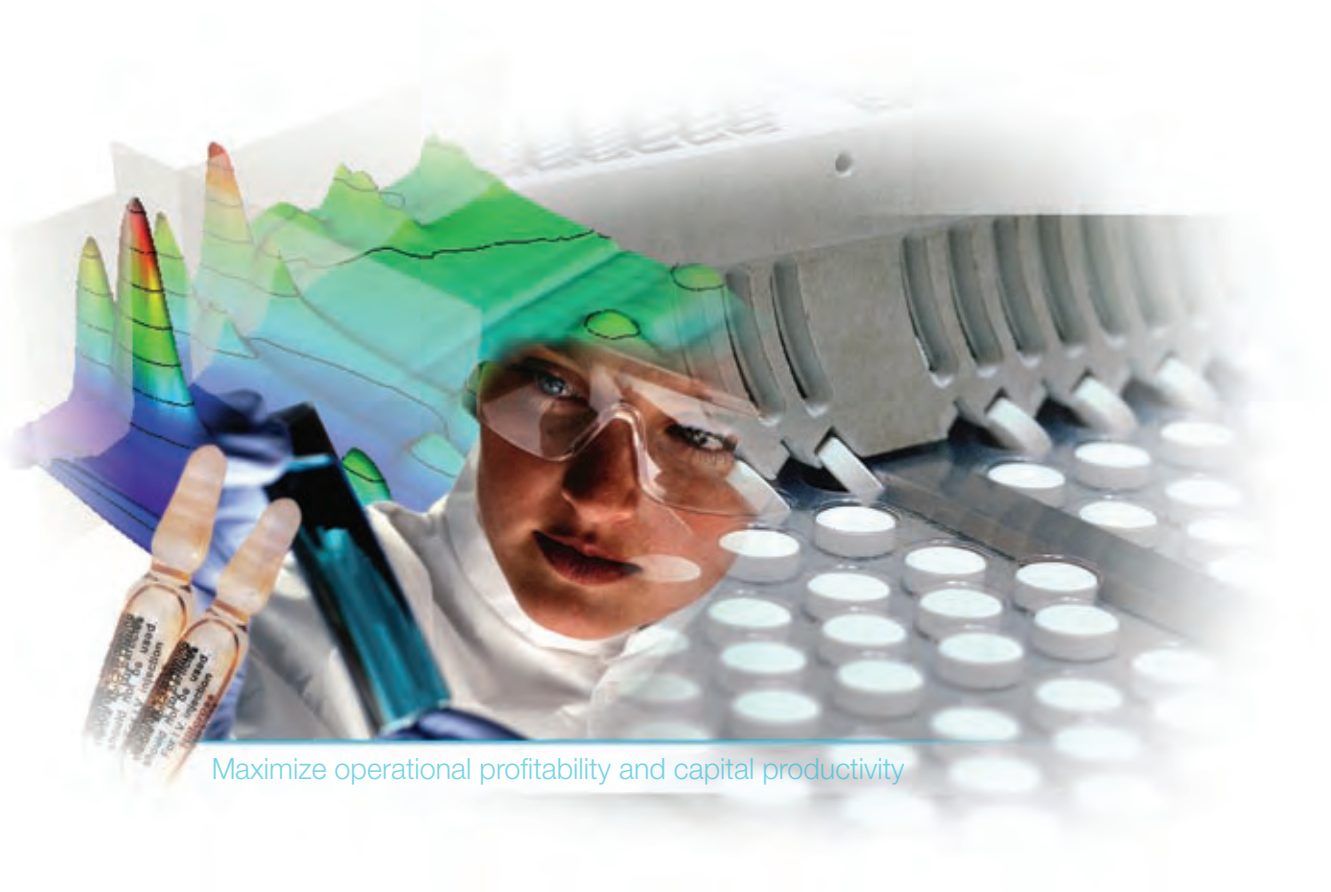
Industrial^{IT} for Process Analytical Technology

Supplying the complete scope required for the introduction and operation of Process Analytical Technology (PAT) to the Life Sciences Industry.



Maximize operational profitability and capital productivity

ABB

The right mix of consultancy services, products and lifecycle support

A Quality By Design approach using Process Analytical Technology (PAT) requires more than a collection of analyzers and models. It requires people who understand the Pharmaceutical Industry, the right products that allow data to be captured, processed and stored in a regulatory compliant manner – plus lifecycle support to enhance the benefits of the capital invested.

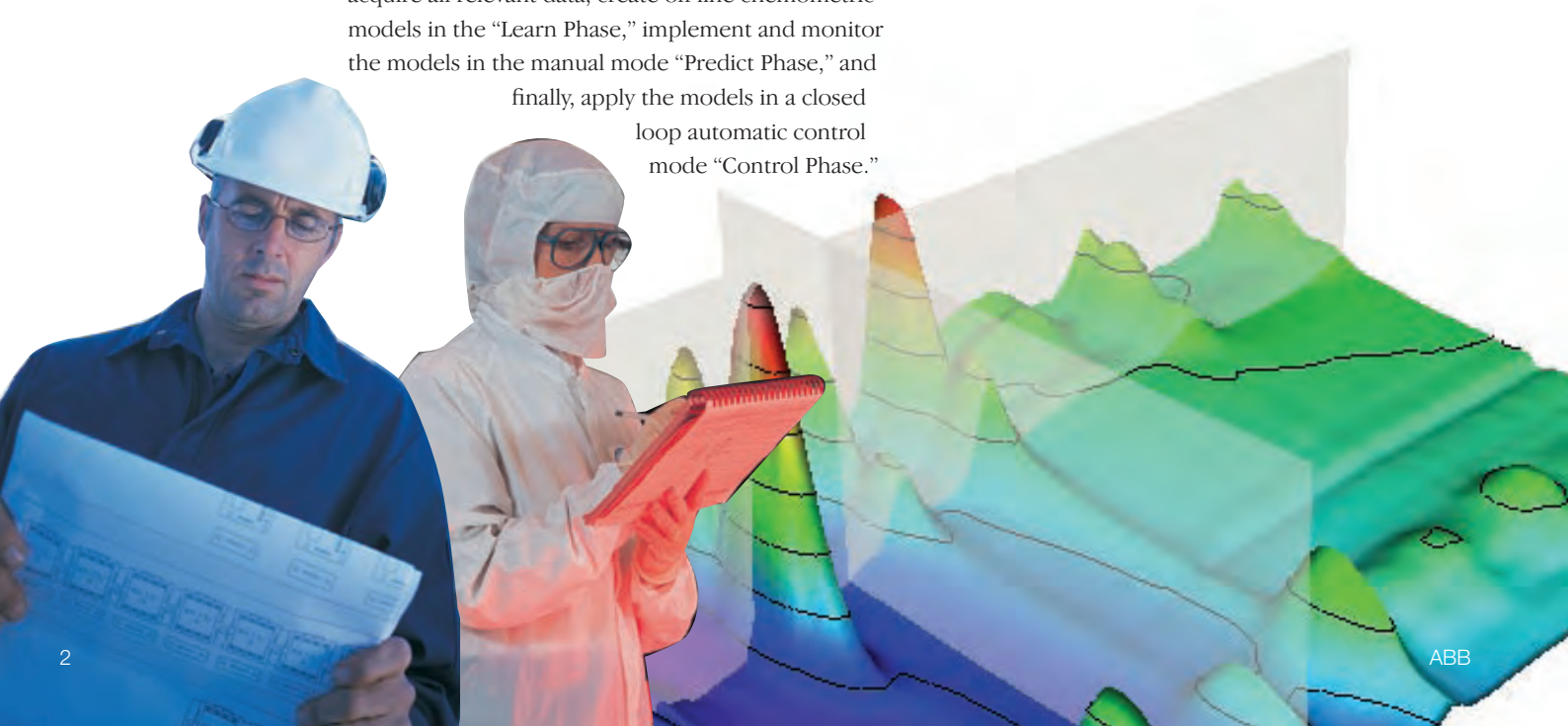
ABB provides a single, scalable, integrated solution for PAT that supports not only ABB analyzers but also those of other companies. The Industrial IT for PAT solution provides process visibility, analysis, warehousing and archiving of data, including spectral, chromatographic, histogram, imaging, quality attributes and process data. The ABB PAT solution is scalable, from a single analyzer and process assessment on a single process unit to multiple analyzers on multiple process units covering a complete process train.

Supporting the concept of "Real Time Product Release" based on the clear understanding of the process variability, the ABB PAT solution allows you to acquire all relevant data, create off-line chemometric models in the "Learn Phase," implement and monitor the models in the manual mode "Predict Phase," and finally, apply the models in a closed loop automatic control mode "Control Phase."

Through the use of ABB's products, analytical experts and process engineering services consultants, we can assist you in the process assessment of where the product variability comes from, and identify how we can reduce product quality issues and cycle time.

Similarly, our consultants can work together with you to break down any internal interdepartment issues and build interdisciplinary relationships.

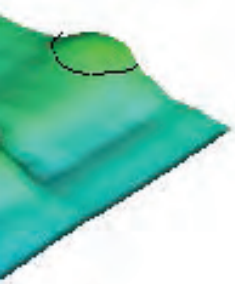
The ABB PAT solution is part of our ongoing commitment to the Life Sciences Industry. The solution supports interfacing to non-ABB process control systems, and is available as part of an ABB Industrial IT 800xA extended automation system providing process, facility and electrical automation.



Understanding the issues surrounding a PAT installation

A single company to support you taking advantage of PAT, providing:

- Assessment of the opportunities to use PAT
- Variability identification assistance
- PAT implementation strategy planning
- Validation support
- PAT submission strategy
- Scalable system
- Multivariable data acquisition, analysis equipment and expertise
- Training on analyzer technology, applications and chemometrics
- Consultative services



There is potential for the systems landscape to become very complex, costly to maintain, and an impediment to the flexibility called for in a development environment. Experience in other industries points to the need for consolidating tools in a common environment, and to the use of best-in-class tools to ensure maximum benefits are derived from the applied technologies. In addition, the drive for a common development/manufacturing platform to facilitate technology transfer will place conflicting pressures for flexibility and information management rigor on the systems. There is a need for a minimum number of simple configuration interfaces.

Translating data into information and knowledge requires a range of tools from information management and archiving to advanced multivariate statistics methods, and needs the integration of process control and modeling toolkits which are often new to the pharmaceuticals sector.

Client risks are reduced by Industrial IT – enabling features, and testing carried out by ABB using cGMP on the different analyzer interfaces. The use of ABB as the total scope supplier eliminates the barriers between consultants, engineers and the suppliers of data mining and analysis programs. ABB is well positioned to provide a single company responsibility for a PAT solution.

By having a single environment based solution, users can look to optimizing the models through better visualization of the process and the causes of product variability. Improved operational profitability can also be achieved by incorporating other common process industry functions such as ISA-88 compliant batch management, facility automation and electrical control. All of this is can be accomplished while meeting the requirements of FDA 21CFR part 11. Having a common data format minimizes pre-processing and eliminates inconsistencies.

Having a single company responsible for all components of the PAT solution simplifies lifecycle support of the facility. ABB offers reliability and maintenance services for the installation, including the third party components (analyzers, interface SW, etc.) This approach ensures that that the quality of the installed solution is always maintained for peak efficiency, while reducing overall maintenance costs.

Utilizing online analysis as part of the manufacturing process to:

- Reduce typical cycle times by up to 40%
- Reduce production costs by up to 30%
- Improve consistency of production
- Improve right first time production levels from 90 to 99.9%
- Reduce the non-value added time in laboratory testing and associated paperwork by 50%
- Lower compliance costs through an integrated PAT and control system solution

Supporting a full range of analyzers from ABB FT-IR/NIR to Zeiss UV-Vis

ABB PAT analyzers offer the following features:

- Provide the acquisition parameters to start collecting the data through a preconfigured configuration (or method)
- Perform mathematical calculations on the data to generate physical or chemical value predictions
- Locally trend the results and provide alarms/warnings
- Accept process data through I/O links (usually OPC)
- Collect all vector data (spectroscopic analyzer raw data) and scalar data (process data as well as scalar results obtained from the analyzers) and publish them through a standard communication protocol to the control network

For many years, pharmaceutical companies have installed PAT analyzers to generate data in order to better understand individual unit operations. The next challenge is to gather information from separate unit operations to ensure predictability of the end product quality. This is not possible without an integrated and flexible IT environment. When all analyzers have different user interfaces and data formats it is almost impossible to have timely access to analyzer and plant data. There is a need for new tools to execute complex PAT methods that will integrate and dictate the operations of multiple analyzers for controlling several end product Critical Quality Attributes (CQAs), using a standard and PAT-friendly interface.

The ABB modular software suite provides a complete solution for easily applying analyzer technology and process control applications. This software supervises real-time spectra acquisition and property determination as well as on-the-fly spectral diagnostics. It supports appropriate data-processing algorithms and is compliant with pharmaceutical PAT guidelines. FTSW800 provides a local interface for data trending and operator interaction, and full connectivity to DCS or PLC. The built-in multilevel security manager provides password protection to all functions and provides different access levels for each operator. All measurements, events and operator actions are tracked in a full audit log for traceability and diagnostic purposes. This software has already been used for controlling over 700 ABB FT-IR/NIR process analyzers across several industries, including typical PAT applications like reaction monitoring, dryer monitoring and control of blend uniformity.

ABB has now extended the concept of FTSW to multiple PAT analyzers including third party instruments. It is designed to manage communications and data flow with one or several PAT analyzers. The ABB PAT Data Manager will then archive analyzer data collected through FTSW800 as well as the Critical Process Parameters (CPPs) from different sensors, using unique identifiers provided by the local control system.

The data is organized in an S88 compliant manner and can be queried to display scalar and vector data. Data from multiple batches can be mined for further process understanding and continuous improvement. Data can also be exported for use in a multivariate data analysis package in order, for example, to determine the root-cause of a process outlier.

One of the strengths of the architecture is the redundancy of raw data, results and configuration databases. Methods will be centrally stored and replicated locally throughout the PAT environment. This enables the system to operate under normal conditions even if the network is momentarily down. The other major advantage of the ABB PAT solution is to provide a simple approach to PAT method design and configuration with minimal operator programming needed to make the system fully operational. This, in turn, provides for a reduced validation effort.

FTSW is designed to manage communications and data flow with one or several PAT analyzers such as:

- ABB FT-IR/NIR
- Agilent HPLC
- Bruker FT-NIR
- Mettler-Toledo FBRM
- And more

Industrial IT for PAT offers a scientific, risk-based approach to regulatory compliance

An ABB scalable platform for common visualization for multiple analyzer manufacturers offering:

- Consistent data format with a modular structure
- ALL vector and scalar data - PAT and plant data historization
- Organized in a batch structure
- Date / time aligned
- Open and flexible communication in real-time for control
- 21 CFR part 11 compliant

ABB's PAT solution provides critical integrated, scalable, analytical capabilities. These includes connectivity with common data warehousing, data mining and visualization tools, as well as root cause analysis that can integrate batch, LIMS, process and analyzers from ABB and third party companies. The Industrial IT for PAT solution, coupled with the project, engineering and consulting services that ABB can provide greatly lowers the risk of implementing a PAT solution.

The ABB solution consolidates those tasks within the PAT environment where centralization and common data management processes and structures lower risk. The solution includes out-of-the-box tools for the integration of multiple manufacturers' analyzers. Common architecture allows the user to develop control models for test purposes with minimum additional configuration.

Tightly integrated best-in-class tools from companies such as Umetrics and Matlab drive analysis and modeling, give open access to a range of functionality to allow the system to grow, expand and implement new technology as it is developed.

Building a database of process information from such techniques is key to identifying patterns and forming hypotheses to explain process and product behavior. Linking multiple measurements and related process data and laboratory input within a unit operation can be challenging in terms of relating common batch and time stamped information which may be temporarily delayed or held in different or embedded formats. Tackling this task across multiple unit operations multiplies the potential issues many fold.

ABB's solution offers a blend of open architecture and tools integration which allows the user to:

- Consolidate those tasks within the PAT environment where centralization and common data management processes and structures are of benefit. This includes out-of-the-box tools for the integration of multiple manufacturers' analyzers.
- Develop control methods for test purposes with minimal additional configuration.
- Tightly integrate best-in-class tools to drive analysis and modeling from companies such as Umetrics and Matlab to give open access to a range of functionality to allow the system to grow, expand and implement new technology as it is developed.
- Benefit from common data formats to minimize pre-processing and inconsistencies.

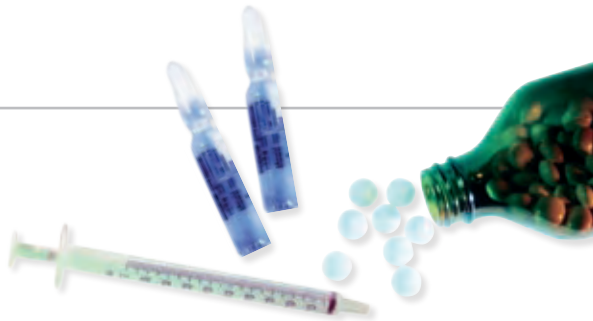
Facilitating the connection of many, varied analytical measurement systems to a common platform simplifies the data handling issues and provides for integration of data to facilitate the task of data mining – using the tools of customer choice. This avoids a range of potential problems associated with data warehousing and duplication of records which can lead to regulatory issues.

Building process understanding is likely to be a key role of pharmaceutical development groups employing DoE techniques with measurement and data management to deliver robust process models. These groups require the flexibility to reconfigure systems on-the-fly to capture data from a range of experiments and scenarios. Minimizing configuration requirements and providing common mechanisms for data management will be key to ensuring the completeness of data sets, minimizing development costs and maximizing the flexibility of the systems for the scientists.

ABB PAT Technology Partnership
assisting you in your corporate implementation program

Scalable products, services, solutions and lifecycle support.

Corporate Vision	PAT Program Design	Technology Selection	PAT Project Design	Regulatory Liaison	Change Management Program
Client	Client / ABB	Client / ABB	Client / ABB	Client / ABB	ABB / Client
■ Appoint steering committee ■ Define PAT strategy and vision ■ Set objectives ■ Define key milestones ■ Approve investment program	■ Appoint technology champions ■ Recruit necessary knowledge and competencies where necessary ■ Devise PAT role in R&D ■ Devise PAT role in tech transfer and scale-up ■ Devise PAT role in manufacturing license application ■ Prepare time to market scenarios	■ Develop corporate high level requirements specification ■ Evaluate vendor technologies ■ The technology is new – choose a vendor willing to invest and jointly develop and improve systems ■ Consider ability to support global implementations and support ■ Consider wider knowledge transfer and technology support capabilities ■ Develop agreement	■ Set up global and local organizations and facilities ■ Establish core processes ■ Establish procedural frameworks and controls ■ Agree roles, responsibilities and skills / competency map ■ Define validation/ quality procedures, and controls ■ Define risk assessment and management framework (peer review) ■ Produce program	■ Meet with regulators / share vision and objectives ■ Communicate the following via a comparability protocol: ● Quality procedures – scientific integrity measures ● Internal audit and peer review processes ● Analytical / experimental design ● Competence frameworks and competence assessments ● Proposed formal reporting and review framework	■ Develop communications and targeted training program ■ Define measure and report KPI's for the technology introduction program ■ Define, develop and deliver training programs ■ Value and reward key contributions and behaviors ■ Evaluate and report successes / breakthroughs ■ Form focused improvement teams



Experimental Design / Piloting

Client / ABB

- Mathematical modeling design and ongoing optimization
- Sample system design
- Analytical method design
- Analytical method validation
  - Accuracy
  - Precision
  - Repeatability
  - Robustness
  - Process coverage
- Calibration model maintenance and change control
- Ongoing verification
- Data and metadata management

Information Management

Client / ABB

- Devise data and knowledge safety, integrity and archiving systems / procedures
- Devise data sorting and management systems
- Devise data mining systems and competence
- Develop core skills and systems to derive the process models and quality models from data assessment
- Use findings to influence future experiments

Stage 1 Validation

ABB / Client

Initial validation of the PAT system

- Validation master plan
- ABB analytical instrument validation package
- ABB 800xA streamlined documentation covering:
  - User requirements specification
  - System specification
  - Design reviews
  - System engineering
  - FAT / SAT
  - IQ
  - OQ
  - Summary reporting
  - Start-up training
  - Core use and technical SOP's
  - Full scope PAT system validation

Stage 2 Validation

Client / ABB

Validation and QA of the ongoing use of the PAT system

- Regulatory liaison
- Performance qualification
- Experimental design and review
- Start-up training
- Design verification
- Analytical method validation
- Statistical model verification and maintenance
- Periodic review
- Auditing and peer review frameworks
- Change control and configuration management
- Documentation generation and management: QA, SOPs, instructions

Ongoing Support and Maintenance

ABB / Client

New projects

- Technical innovation
- Project collaboration
- Completed / ongoing projects
- Maintenance strategy development
- Reliability centered engineering and maintenance program implementation
- Fast response support agreements
- Collaborative technology / system development support
- Ongoing validation support

Drive for Continuous Improvement

ABB / Client

- Review technology performance
- Operate key client user / interest group forum
- Maintain focus on key industry needs / drivers
  - Regulatory
  - Applications
  - Advanced control
  - Biotechnology
- Continue to invest in the solution and improve productivity

Supporting you from variability recognition in the lab to full process scale-up

Many companies are going to want to start small, when implementing a PAT solution. ABB's Industrial IT for PAT allows companies to start with a single controller on a single process, and add additional controllers or steps in the process once the initial objectives have been achieved.

PAT solution for optimum dryer control:

- Reduce cycle time for earlier release of product
- Cut production costs
- Implement process flexibility

The ABB PAT Data Manager maintains the PAT method and manages the collection and storage of data from analyzers and the DCS in a regulatory compliant manner. This information is then available to the various process models and operator interfaces.

Chemometric models which link a number of analytical sources together can be developed and the data used for monitoring, analysis or closed loop control.

PAT solution for the scaled-up process

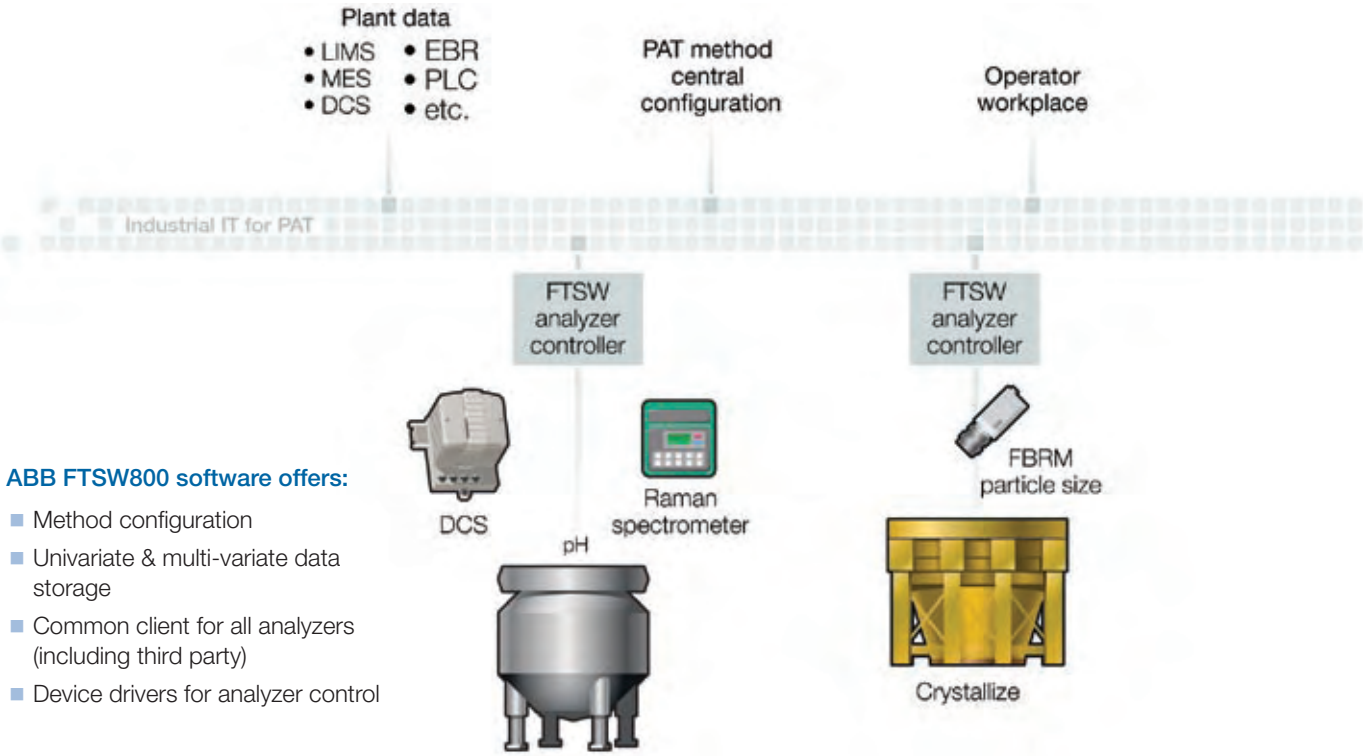
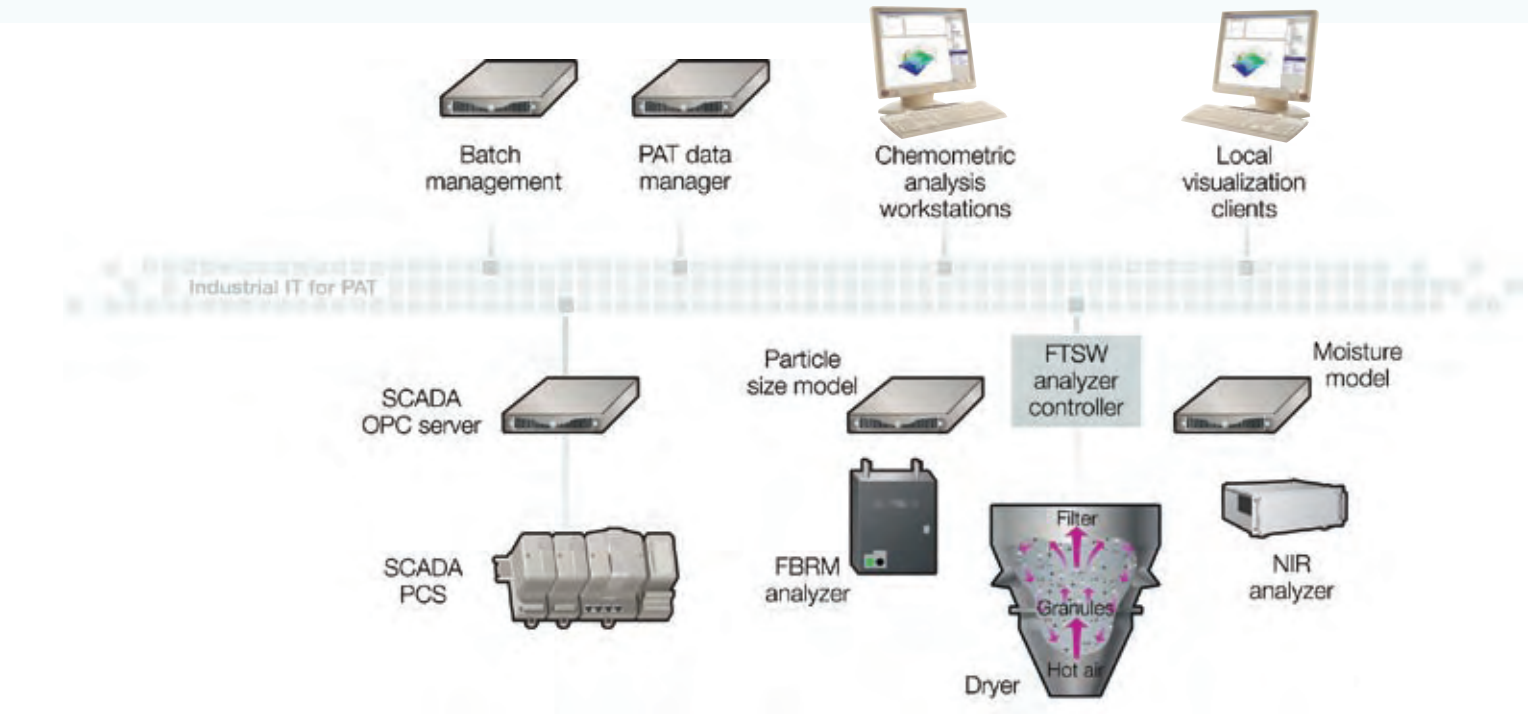
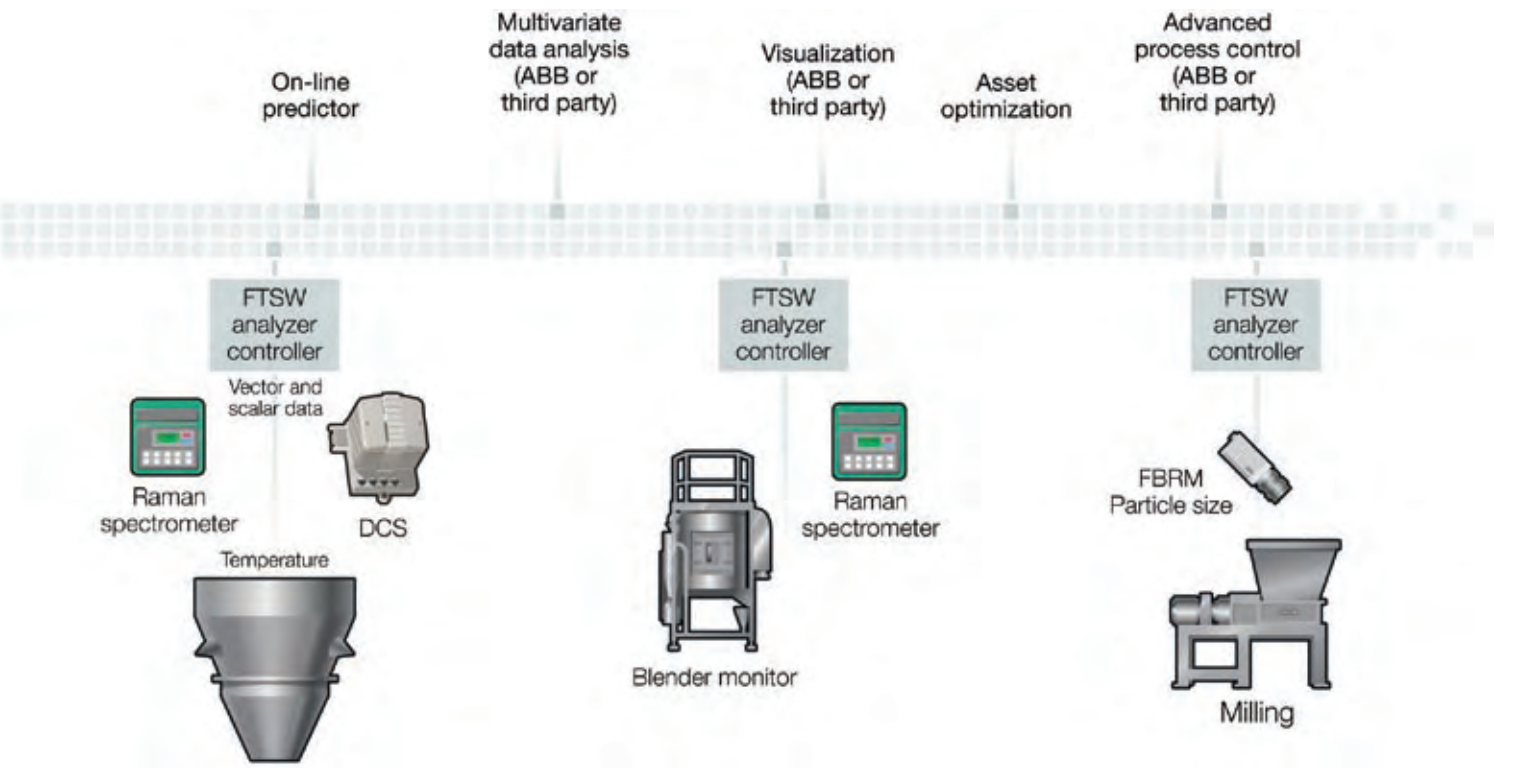


ABB FTSW800 software offers:

- Method configuration
- Univariate & multi-variate data storage
- Common client for all analyzers (including third party)
- Device drivers for analyzer control


Batch management
PAT data manager
Chemometric analysis workstations
Local visualization clients
Industrial IT for PAT
SCADA OPC server
Particle size model
FTSW analyzer controller
Moisture model
SCADA PCS
FBRM analyzer
Filter
Granules
Hot air
Dryer
NIR analyzer


On-line predictor
Multivariate data analysis (ABB or third party)
Visualization (ABB or third party)
Asset optimization
Advanced process control (ABB or third party)
FTSW analyzer controller
Vector and scalar data
Raman spectrometer
DCS
Temperature
FTSW analyzer controller
Raman spectrometer
Blender monitor
FTSW analyzer controller
FBRM Particle size
Milling

Offering you world-wide service and lifecycle support

World-wide footprint

As a fully supported ABB solution, users are assured of global assistance, that future system upgrades will be easy to implement, and that the system has lifecycle support throughout the life of the plant/ installation.

Users are assured that combining analyzers from multiple companies will work together, and as each company, in turn, upgrades its analyzers / interface SW that the solution will continue to function. By removing customized site solutions, and relying on ABB with its centers of excellence and competency your risks and costs are minimized.

ABB is experienced in delivering its solutions globally, using a network of centers of excellence and competency. This knowledge-sharing process allows for consistent, world-wide support based on shared implementation know-how, and not on specific individuals or regional specialization alone.

Consultancy

Developing an understanding of PAT often begins with an application of measurement and control techniques varying from analytical instrumentation to inferential measurement. Integrating PAT fully into the manufacturing and development environments is a major task involving fundamental change in working practices, application of sophisticated and high technology equipment, and development of expertise in chemometric analysis and advanced control.

Approaching such change in an exploratory fashion is to be recommended as opposed to “Big Bang” applications with potentially high risks. A better approach involves scalable solutions which are flexible enough to enable fast reconfiguration and frees the scientists to build a knowledge base, while providing robust industrial performance to facilitate deployment in manufacturing, as well as allow direct technology transfer with a common systems base.

ABB has its own Engineering Services organization providing consultative services across many areas of the Life Sciences Industry. It provides PAT expertise in the validation, safety assessment, and business processes to enable the different disciplines to work together as is required for a successful PAT implementation. You can be assured the solution will utilize best practices to cGMP throughout the life of the installation, and assist you in scale-up of NCE’s (New Chemical Entities) in the lab and pilot plants to full production facilities.

Through the early involvement of ABB consultants, an understanding of monitoring, product variability and cultural issues can be identified and addressed within a validated environment. From this front-end work, clients can decide on the best use of their investment:

- Product quality issues
- Reducing cycle time
- Improving process visibility

The use of ABB Industrial IT for PAT solutions ensures that the analytical equipment, data mining and visualization, plus consultancy services minimize interface and start-up costs.

Data mining

Faced with a wide variety of data, the aspiring PAT development or manufacturing business must organize and manage the data, and provide and integrate multiple data sources and formats from LIMS, process historians, PAT instrumentation and raw material information, including traditional single point data and multivariate data arrays. Without consistent data formats in open standards, the task of identifying meaningful relationships requires extensive data pre-processing and becomes difficult to complete repeatedly (due to complexity and the range of data treatments) and prone to errors from data reconciliation.

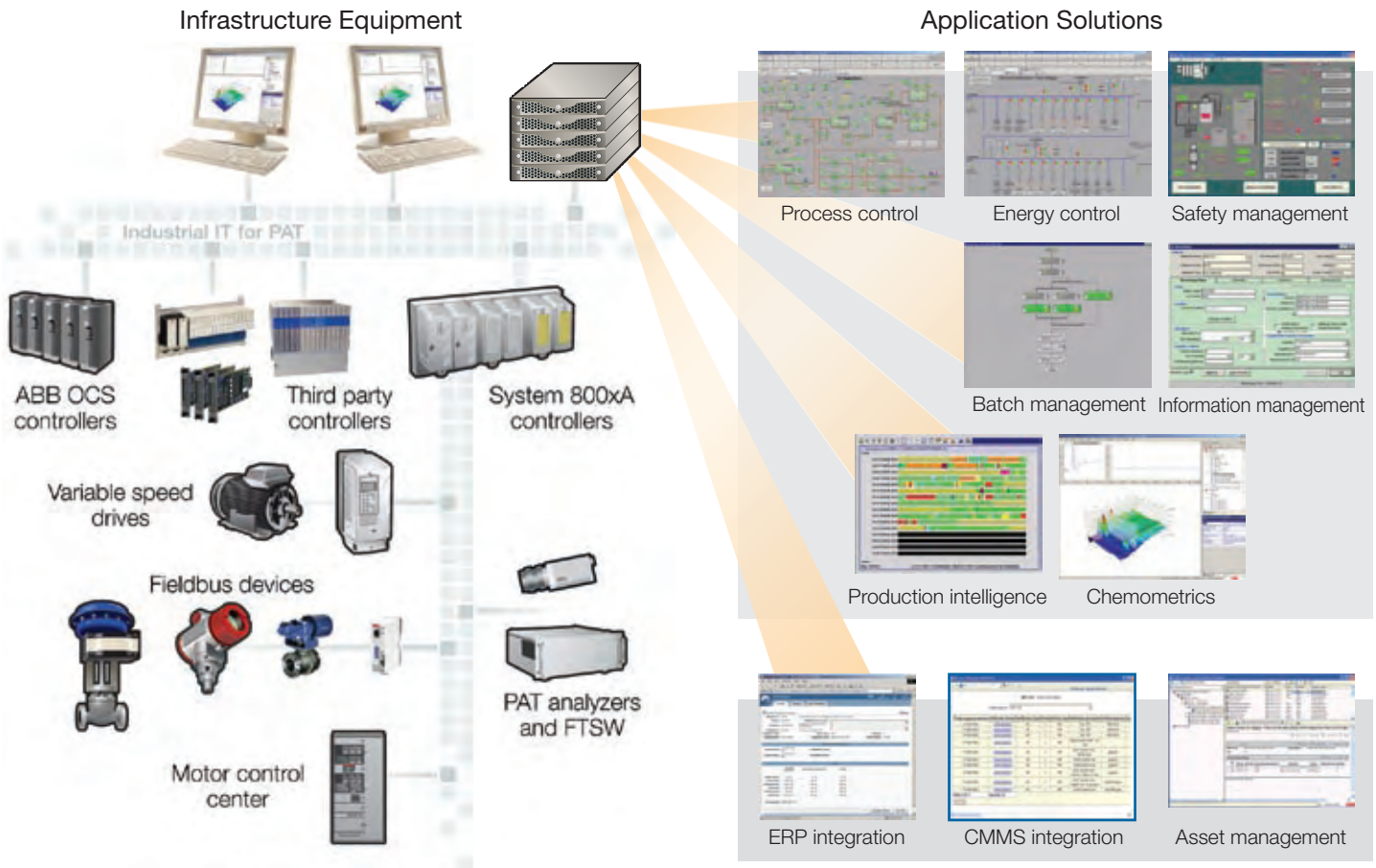
Having a large amount of contextualized data allows scientists to extract trends and patterns, provide root cause analysis, and to further the knowledge of the process.

Industrial IT

ABB's PAT solution is part of the Industrial IT and 800xA suite of products and services. The ABB 800xA platform is industrially robust and implemented throughout the Pharmaceutical Industry, giving reliable and proven operation in a single integrated environment. 800xA, with its Aspect Object technology and fully integrated Safety Instrumented System (SIS), internal Asset Management Software (AMS), fieldbus support (FF and Profibus), motor control, drives and other automation and electrical devices, provides many operational benefits while reducing cost and risk. The use of 800xA for process, PAT, and facility automation at both the process unit level and plant-wide gives pharmaceutical users advantages for production, safety, and maintenance management while maintaining compliance to the recommendations of the FDA.

Integration to other business functions is achieved by the ABB Enterprise Connectivity Solutions (ECS) package, a solution that is compliant with ISA-95 for Manufacturing / ERP integration.

The Industrial IT solution for PAT



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www.abb.com/lifesciences

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