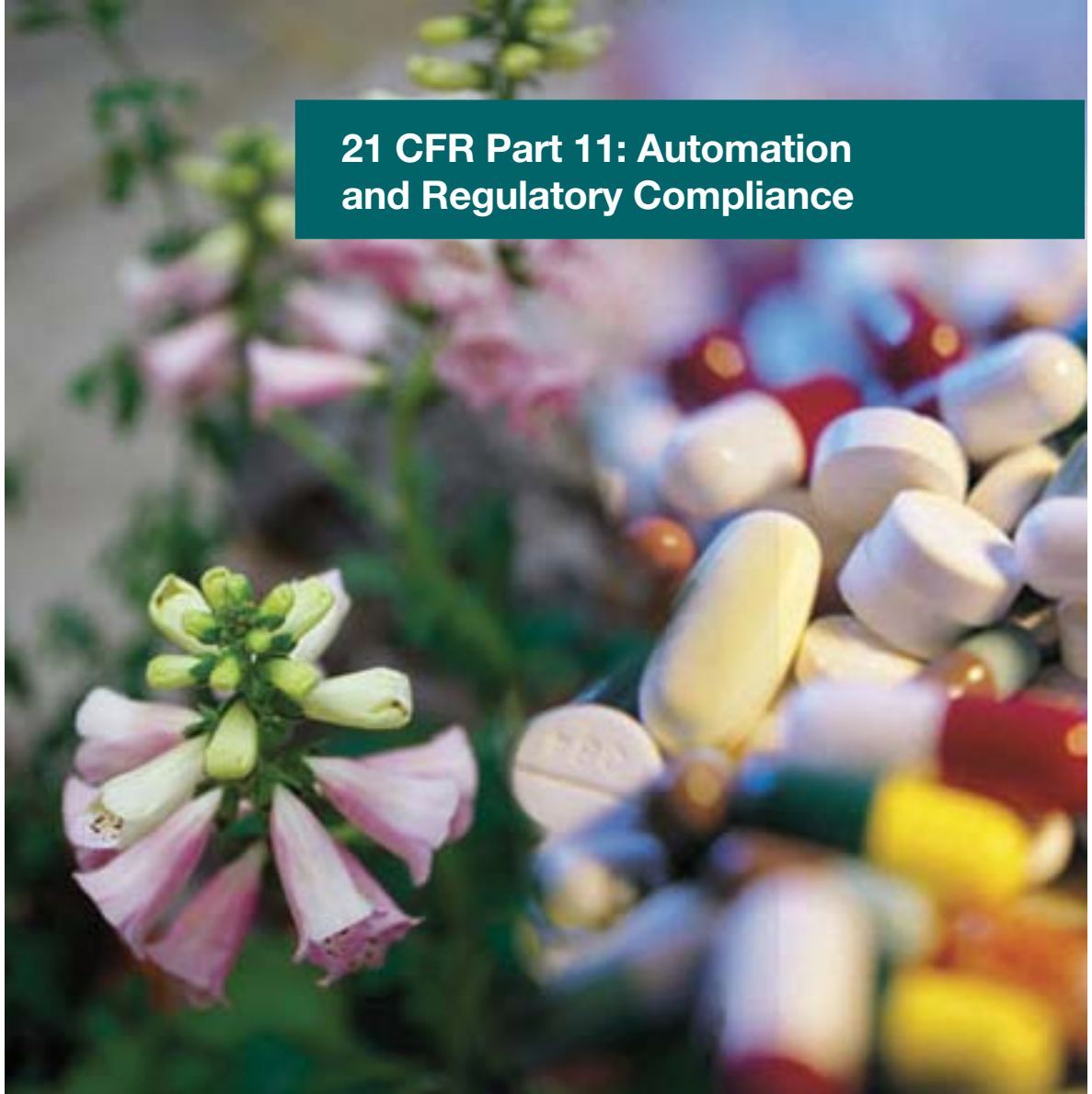


Industrial^{IT} Solutions for the Life Sciences Industry

**21 CFR Part 11: Automation
and Regulatory Compliance**



As part of ABB's Industrial^{IT} strategy we have invested considerably in the development of advanced solutions and services in the Life Sciences industries.

System 800xA facilitates regulatory compliance

One of the most recent regulations relevant to pharmaceutical manufacturing is 21 CFR Part 11, issued by the U.S. Food and Drug Administration. This rule applies to all products manufactured in the United States, and also to products manufactured elsewhere but distributed in the United States, which gives it international relevance.

21 CFR Part 11 has two main areas of enforcement: electronic records and electronic signatures. Moving to a paperless world with fully electronic data handling promises cost savings from improved efficiency and reduced physical handling and storage. Electronic signatures are given legal equivalence with traditional "wet ink" signatures on paper.

In Life Sciences companies, 21 CFR Part 11 is applied to automation or computer system applications that manage product-related data such as:

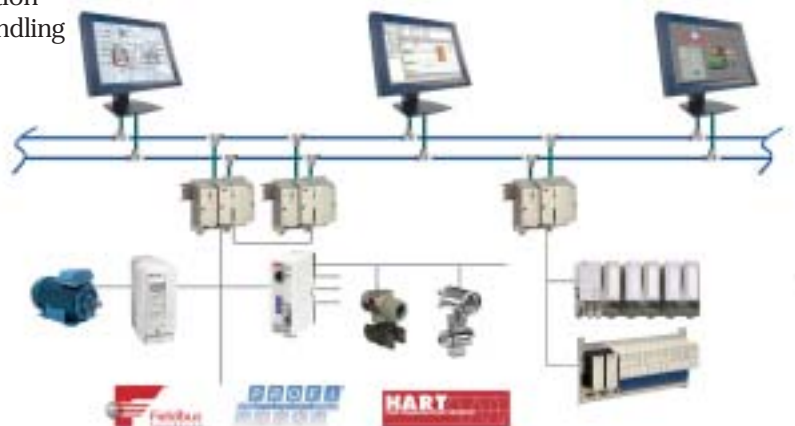
- Calibration and maintenance
- Cleaning automation
- Corrective actions
- Critical equipment and instrumentation
- Facility and building automation
- HVAC controls and alarm handling
- Manufacturing instructions
- Material traceability
- Recipes and formulations
- Packaging automation and labeling information
- Security access control

The Industrial^{IT} Extended Automation System 800xA facilitates compliance with the rule with features like system security, secure data management and reporting, electronic records and signatures, and the automated electronic recording of changes.

Core system functions that support regulatory requirements are:

- Access control
- Authentication and re-authentication
- Alarm and event management
- Audit trail
- Batch control and management
- Electronic recording
- Electronic signatures
- Event reports
- History and archiving
- Trends
- Redundancy
- Sequential function charts
- Shift, production and batch reports
- Infrastructure and network security

System 800xA makes automation and regulatory compliance easy.



System 800xA automation technology facilitates compliance with FDA 21 CFR Part 11 and integrates electronic records and electronic signatures as core system functions.

Limiting system access to authorized individuals

Our technology combines the efficiency of electronic record keeping with the security of authenticated electronic signatures.

System, engineering, manufacturing and product data are protected throughout the system's life cycle from unauthorized access, modification or deletion in order to ensure accuracy, consistency, and completeness.

We utilize the Microsoft® security system and extend it to meet the demands of automation applications for Life Sciences industries.

Users and user roles

Standard procedures to limit physical access are the responsibility of the pharmaceutical company. ABB's system security functions support these procedures and allow many combinations of individual users and user groups. User roles may include general permissions for administration, configuration, tuning and operation, or specific permissions for security configuration and for first and second digital signature.

Access control

For login, authentication and electronic signing, two component security codes apply. Every combination of user identification and password is unique. Minimum password length, password aging, and rules against re-using recent passwords are all configurable.

Access can be controlled from the system level down to the object level (for example a single valve or a range of cleaning equipment or an entire ingredient list). Access to functional inputs can be limited, including the right to open a single valve, or start a CIP process, or schedule the next batches and campaigns. Operators must identify themselves both at login and before an input is accepted; for example, before a motor is switched on or a cleaning process is started.

Change control

In addition to authority checks, the system gives pharmaceutical manufacturers control over which changes are made. Using electronic signatures, system users can be held accountable and responsible for actions initiated. This could apply, for example, to the configuration of control applications, including all embedded logic and I/O functions for release to production.

The system records any changes made to it or to devices and applications. Time-stamped audit trails show managers as well as inspectors:

- When changes were made
- Which changes were made
- Who made the changes, and why

System 800xA makes automation secure, and tracks changes automatically.



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CGMP regulations also apply to production of dosage forms that incorporate botanical drug substances. The botanicals displayed are either starting materials for the production of active pharmaceutical ingredients or drug substances for use as ingredients in dosage forms.



Operational efficiency

You can reduce data error, enhance process control, and improve data recording by replacing obsolete or inefficient equipment with automated 800xA technology. The introduction of a new control system with integrated information management will facilitate compliance and help reduce paperwork.

Relevant information at your fingertips

800xA human-system interface terminals can operate as integrated control system interface, or can serve as the central operation and record keeping system coordinating connected programmable logic controllers.

A single click of the right-hand mouse button accesses further information about a signal, a mixing motor, a plant component or any other "object." The information, called aspect, is connected to the object and includes:

- Graphic displays with real-time data from your process
- Faceplates to operate and control the tags and I/O points
- Pre-configured trend displays
- Alarm and event displays
- Trend, alarm and event history
- Device calibration history
- On-line help

Sequencing of steps

System 800xA can enforce permitted sequencing of steps and events, as applicable. Sequential function charts offer a graphical method of organizing the control logic and manufacturing steps. Transitions are used to move from one step to the next; assigned actions are automatically initiated and interlocks are automatically monitored.

Manufacturing instructions

System 800xA improves security through operational checks also for manual operations. Manufacturers can replace paper records by on-line instruction sheets, a proactive way to ensure the sequencing of steps to be taken.

The operators follow the interactive operation procedures or instructions line-by-line, supported by the system. All operator actions are automatically logged into the system audit trail. For critical settings, re-authorization can be mandated before the system will accept the change.

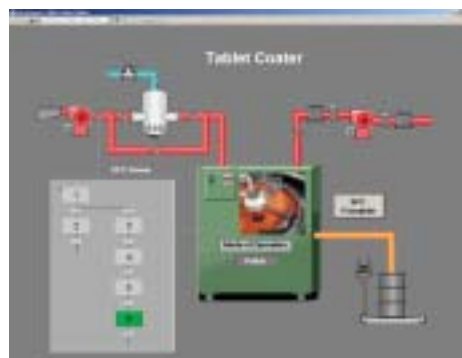
Electronic batch records

By replacing paper records by electronic 800xA batch records, manufacturers are able to keep an accurate history and save huge amounts of paper records. You also gain a further method of sequencing steps and increase consistency from batch to batch.

System integrated 800xA Batch Management is built to ISA S88 standards. Batch procedures describe how pharmaceutical products are manufactured.

Information on the status of process and batch operations is easily accessible through integrated batch scheduling, control and reporting features.

Batch and signature events are an integrated part of the system audit trail.





Consistent performance

Alarm and event management

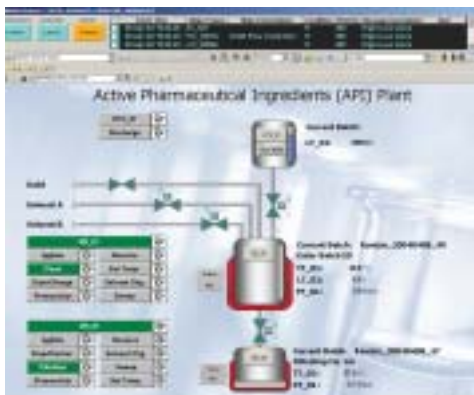
On the technical side, 800xA alarm and event management is another compliance element to ensure consistent intended performance. Audible and visible alarms will enable the operator or initiate automated actions to quickly correct out-of-tolerance conditions. For example, the system will alarm in the event a low water level is reached if this had been determined to be critical from the thermal processing stand point.

The alarm and event management is system-wide and incorporates complete audit trail functionality. Alarms are typically generated when an object has an abnormal state; they are messages that the operator must acknowledge. Events inform operators about changes and interactions. All alarms and events can be automatically logged into the historian.

Audit trail

The integrated system-wide audit trail lets authorized users view and filter:

- User login, logout and change events
- Configuration changes
- Operator actions and inputs
- Alarm events
- System and device events
- Calibration alarms and events
- Batch alarms and events
- Signature events



All time-stamped audit trail events contain information about the object or file changed, the change itself and the action's owner. System 800xA also logs the reasons for the change and optional comments that the user has entered.

Electronic signatures

Critical operations in a process or critical changes of machine settings might require significant authentication steps to ensure that the correct persons have the rights and authority to perform certain actions.

Pharmaceutical manufacturers who decide to use additional security checks before users are allowed to download setpoints or issue commands rely on the 800xA human-system interface. The user will be required to provide username, password and new value and, if necessary, comments or a supervisor signature before the change affects the process.

Documented

The access to, and use of documentation for system operation and maintenance is outlined in 21 CFR Part 11.

On-line help is part of our system, and includes guidance on configuration, operation, field device and asset management, and batch control or information management. All ABB documentation is fully version controlled in accordance with our quality procedure.





Record protection and retrieval

Archiving

Archiving is a further requirement of 21 CFR Part 11. System 800xA allows users to archive process data and system configuration, as well as standard operation procedures.

History and reporting

The Information Management functions collect, store and retrieve historical product, manufacturing, process, batch or audit trail data. Reporting is easy. Reports present recorded data in human readable form.

The computer-generated records can be printed out, for example:

- Process data records listing the times, temperatures, pressures, and other critical factors
- Alarm records, listing alarm events and violations of alarm conditions noted during the process

Regular or daily audit trail reports, shift, calibration or batch reports can be scheduled using pre-configured templates. Templates can also be customized in the familiar Microsoft Windows® desktop environment using Excel or Crystal Reports. ODBC, OLE DB and SQL provide additional access to the archive.

Full 21 CFR Part 11 support applies to the Information Management functions, such as access control, electronic signing of reports, data protection and integrity.

Infrastructure

The 800xA system infrastructure ensures accuracy, reliability, integrity and confidentiality of inputs and outputs. The network is based on TCP/IP over Ethernet and utilizes built-in error detection mechanisms. Supported fieldbus standards include communication and data security mechanisms. The network also supports the operation of devices from different manufacturers.

Redundant network communications are supported for all communication levels.

Quality assurance

The whole system, including communication design and network security, is verified against the development and system requirements in accordance with ABB's quality procedures. Tests are applied to individual modules and to the entire system. The system is also designed and tested against the customer's specific needs, such as 21 CFR Part 11 support.

We develop automation technology that fully meets validation and regulatory requirements. Compliant Industrial^{IT} solutions are delivered and supported by our validation and compliance professionals, ensuring seamless integration into regulated and quality controlled processes.





Professional skills

Automation systems are becoming increasingly essential to pharmaceutical production. Whether our control products are embedded in process equipment or function as a stand-alone system, they are critical to achieving product quality. Our unique integration of 21 CFR Part 11 support into our technology makes it easy to build compliant applications.

Freedom of choice

Our Industrial^{IT} 800xA technology offers you a faster path to manufacturing efficiency. Take advantage of system 800xA and choose the functional area you need, without concerns about compliance. All our products – visualization, batch or information management, maintenance, fieldbus devices, maintenance and calibration integration, or package unit and OPC server connectivity – come with built-in 21 CFR Part 11 support. They all use the same system security features, offer the same authorization and signature support, and log events to the same audit trail.

An experienced validation partner

Are your quality assurance and validation managers under pressure to deliver greater assurance with smaller teams? Do they increasingly rely on the active support of other parts of the organization and suppliers to meet regulatory needs?

ABB offers an industry leading capability in the validation of all computer systems. With our considerable track record in managing automation technologies and projects, we can deliver both regulatory compliance and optimal business benefit.

Our specialists are experienced practitioners who have dealt with issues similar to those you currently face. Building on this hands-on experience and our knowledge of regulatory needs, we can help you to understand and manage your validation issues.

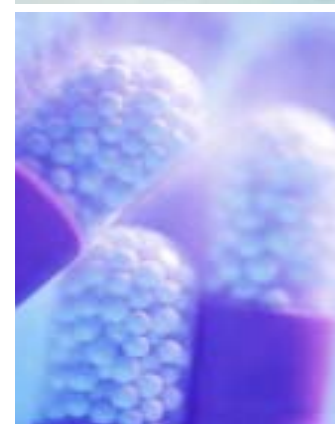
We are known for flexibility in our approach. We are able to cover in depth all aspects of regulatory compliance from R&D (laboratories and LIMS) to production (facilities and process equipment), business systems (MRPII and MES) and warehouses.

Industrial^{IT}

ABB is more than an equipment and automation provider. We are your complete Industrial Information Technology partner. Changing market demands require faster turnarounds, greater customization, smaller lot sizes, and lower overall costs. With the Industrial^{IT} Extended Automation System 800xA, ABB provides you with the technology to extend productivity gains by:

- Fully integrated FDA 21 CFR Part 11 support
- Delivering control and I/O to meet entire plant needs
- Optimizing plant asset availability and performance
- Improving batch consistency, quality and cycle time
- Integrating information for improved visibility

With Industrial^{IT} you are always in full control.



Industrial^{IT} for the Life Sciences Industry



An overview of Industrial^{IT} products and services for the Life Sciences Industry

Analysis and Instrumentation Equipment

- Raw material identification
- On-line monitoring of API manufacturing process, and solvent recovery process
- On-line moisture analysis
- At-line analysis of powder blend homogeneity, and solid dosage from content uniformity

Automation

- Discrete control and visualization systems
- Process control systems
- Fieldbus technology and asset management
- Engineering and optimization software
- Batch control and management

Manufacturing Execution Systems (MES/EBR)

Robot-based Manufacturing

- End-of-line packaging cells
- Robots to pick, pack and palletize

Validation and Compliance Services

- Risk assessment
- Computer systems validation
- Laboratory systems validation
- Equipment and facilities qualification
- Business systems validations
- Quality systems and standard operating procedures

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