ABB MEASUREMENT & ANALYTICS | APPLICATION NOTE

Water purification in the pharmaceutical industry

Providing independent verification and validation of the water purification process for compliance with the latest regulations and GAMP guidelines

Measurement made easy

GAMP compliance from ABB's paperless chart recorder range

Introduction

The conditions for water purification in the pharmaceutical industry are subject to stringent standards. Satisfying these requirements is essential for companies wishing to prove that their products have been safely produced and are suitable for sale both at home and overseas.

When it comes to the use of electronic equipment in water purification, the de facto standards are set by the International Society of Pharmaceutical Engineers' (ISPE) Good Automated Manufacturing Practice (GAMP) guidelines. Adopted by countries worldwide, these guidelines set down the main requirements that need to be considered when planning and implementing computerized system in pharmaceutical applications. Figure 1 on the next page shows the standard drivers associated with the current GAMP guidelines.

As the world's largest market for pharmaceutical products, the US has led the way in developing its own interpretation of these guidelines, with the Food & Drug Administration's (FDA's) good practice rules setting the standard for companies worldwide.

Particularly important are the FDA's Predicate Rules, which set stringent requirements for the manufacture, processing, packing and storage of pharmaceutical products.

The rules

The specific predicate rules relating to pharmaceutical manufacturing are:

- 21 CFR Part 210, stipulating current good manufacturing practice in the manufacture, processing, packing and storage of pharmaceutical products; and
- 21 CFR Part 211, setting current good manufacturing practice for finished products

These rules include guidance on which aspects of pharmaceutical production need to be recorded, including any process control settings, details on checking of recorded data and specific requirements relating to the collection of batch production and control records.

Where these records are collected electronically, then 21 CFR Part 11 also applies, which aims to give electronic records and signatures the same weight and trustworthiness as their paper-based counterparts. A key aspect of 21 CFR Part 11 is its focus on security, particularly relating to the prevention of data tampering and the ability to identify specific individuals and events involved in the production and / or data management processes.

The application

Water is a major commodity used by the pharmaceutical industry. Different grades of water quality are required according to the pharmaceutical process.

The United States Pharmacopoeia (USP) and the European Pharmacopoeia (EP) are the governing bodies that issue guidelines for the manufacture of drugs to their respective markets. Amongst these guidelines are regulations, legally enforceable by the FDA and European equivalents (such as the MHRA), for the purification of different grades of water used in the pharmaceutical processes:

- Purified water – is used in preparation of medicinal products other than those that require the use of water to be sterile.
- Highly purified water – intended for use in the preparation of products where water of high biological quality is needed, except where water for injection is required.
- Water for injection – the purest grade of bulk water monographed by the USP and EP and is found in the manufacture of parenteral, ophthalmic and inhalation products.

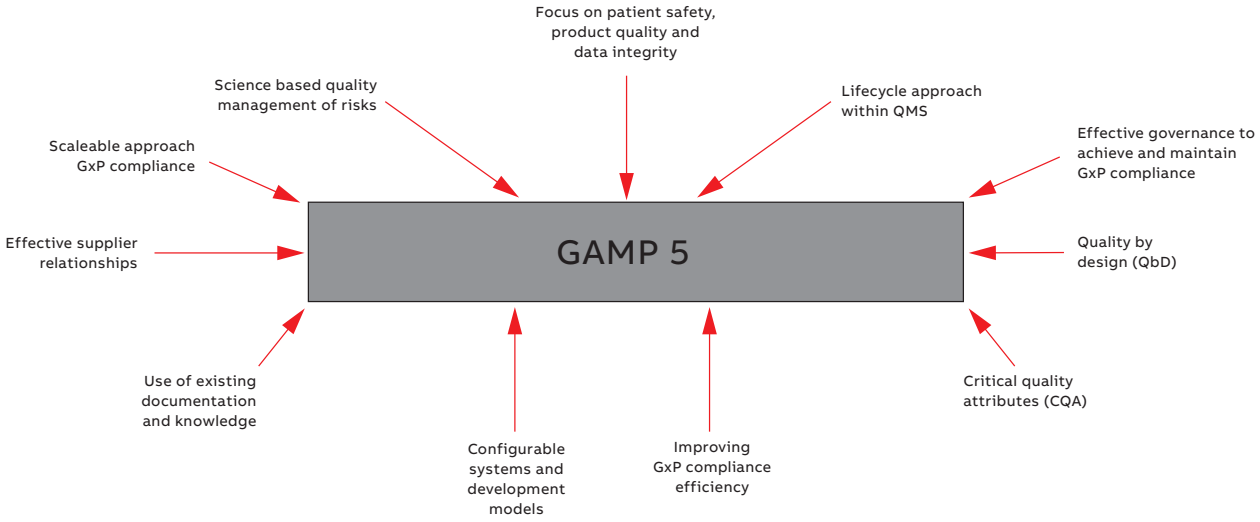

Figure 1 GAMP 5 sets the main requirements for the use of computerized systems in pharmaceutical applications.

The challenge

The validation and qualification of water purification systems are a fundamental part of Good Automated Manufacturing Practice (GAMP) and form an integral part of the GAMP inspection.

Different grades of water are produced according to USP and EP requirements, usually by:

- distillation
- reverse osmosis
- deionisation
- ultrafiltration.

All of these processes must be validated and recorded according to specific standards.

Each set of guidelines outline legal requirements for the chemical content of each grade of water, including a three stage conductivity test for inorganic compounds that will determine pH and total organic oxygen (TOC) levels. The FDA states that implicit in the term “Purified Water” is that it has some reasonable, objective level of purity. TOC testing allows for evaluating impurities in water besides those which are inorganic anions and cations.

Although there are no absolute microbial standards for water (other than water intended to be sterile), GAMP regulations require that appropriate specifications be established and monitored. Action or alert limits must be based upon validation data and must be set low enough to signal significant changes from normal operating conditions.

In all these instances a range of instrumentation is required to meet GAMP guidelines, including conductivity meters, pH meters, temperature sensors and recording equipment. An independent monitoring and recording system should therefore be put in place to provide sufficient and secure data to ensure these processes meet the various specific standards.

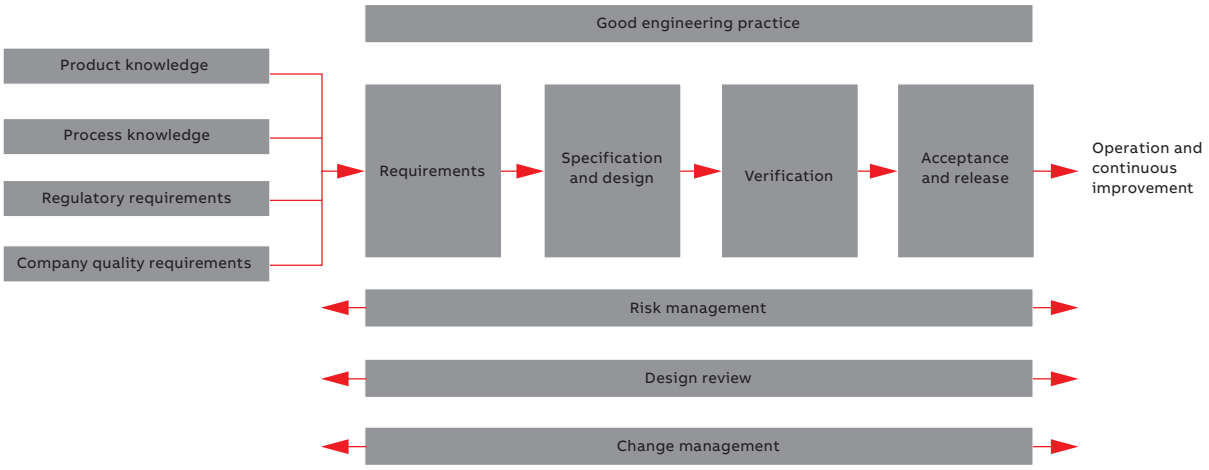

Figure 2 GAMP 5 illustrates the specification, design, and verification process.

Security

In order for recorded data to be accepted as valid proof of compliance with the various standards relating to water purification, it is necessary to eliminate any potential for unauthorized adjustment or tampering with that data.

Whereas tampering with paper charts can be easily spotted, it is less obvious where electronic data is concerned. For this reason, any electronic data recorder must incorporate a full range of security features, including:

- Data Access restricted to authorized individuals only
- Password protection to protect against unauthorized access
- Audit trail facility to independently attribute a time and date every time a record is created, modified or deleted
- The ability to protect against unwanted loss of recorded data
- Use of digital signatures to show that the device has only been used by authorized persons

It is also necessary to ensure that recorded data cannot be altered when downloaded to a PC or other device for review.

The solution

As there are a number of methods for producing purified water of different grades there are also a variety of different parameters must be monitored and controlled, including conductivity, pH, temperature and pressure, amongst others. It is important to perform a regular calibration check and to be able to perform full calibration adjustment for the system inputs, as it is important to verify that the measurements made are reliable.

The system that records the data should also independently trigger warning and active alarms, should the accepted process parameters be exceeded. These often incorporate a time delay and / or a hysteresis. This only triggers the alarm once the parameter has exceeded acceptable levels by a certain amount of time, which helps prevent nuisance alarms.

The provision of Ethernet connectivity will also allow historical recorded data and alarm and audit trail information to be relayed automatically to a central database where archive and analysis, if required, can take place.

The use of independent recorders for production of purified water allows specific, independent and easily validated processes to be monitored without the requirement of validating an entire complex Distributed Control System (DCS). It shows exactly what has happened, together with details of any alarms in real-time.

What can ABB offer?

ABB offers a full range of products and expertise that can help operators comply with the requirements for water purification.

ABB offers GAMP validation templates with its SM series of videographic recorders, compliant with 21 CFR Part 11, that will follow the unit's life through delivery, calibration, production and can even extend to its end of life disposal. ABB can offer a range of validation documentation services in accordance with the required application, such as instrument configuration sheets to help document the User Requirement Specification (URS) and aid the production of the Functional Specification (FS), as well as Installation Qualification (IQ) and Operational Qualification (OQ) documentation.

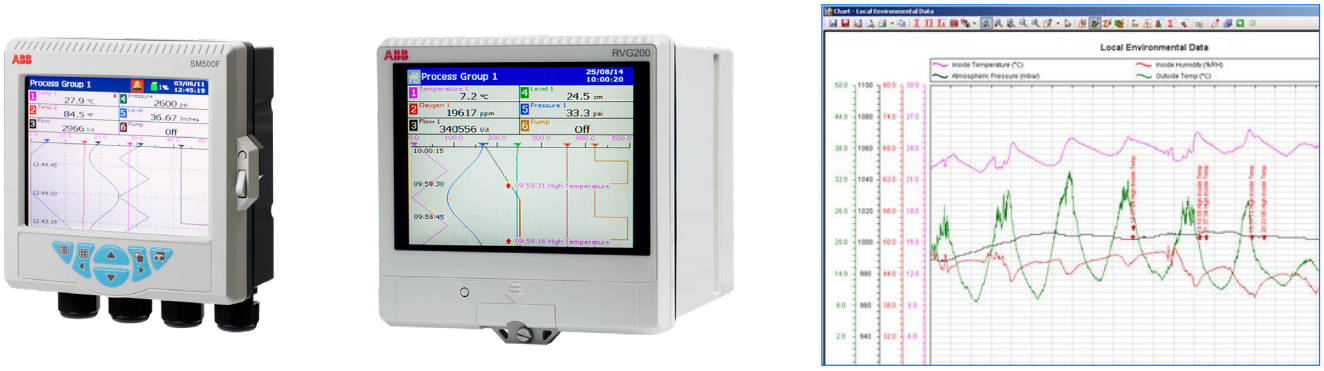

Figure 3 ABB paperless recorders and data review software

… What can ABB offer?

SM500F

The world's first field-mountable videographic data recorder, the SM500F can be part of a fully compliant 21CFR11 system - the FDA's (Food and Drug Administration) regulations concerning electronic process data collection. Process data is displayed clearly to the local operator through a variety of display formats, including chart, bargraph and digital indicator.

With two totalizers per input, the SM500F allows even greater control of data. One totalizer can be left to run for the life of the recorder to give a complete history of the data measured; the other can be reset when necessary to measure certain parameters or time periods. The SM500F offers up to seven analogue inputs, enabling multiple sensors to be connected. This is accompanied by 12 recording channels that can each record process and communications inputs, math block results, digital signals and other values, providing additional detail and functionality.

The SM500F comes with a choice of Ethernet or RS485 communications. Ethernet allows link-enabled historical data to be remotely downloaded to a PC for subsequent analysis via ABB's DataManager Pro software. It also enables a web browser view and connection to a SCADA or PLC system using the Modbus TCP protocol. The RS485 option gives Modbus RTU in either three- or five-wire configurations. These protocols provide the ideal opportunity for integration of third party equipment into the display and recording systems by OEMs.

The SM500F can send email notifications whenever an alarm occurs to ensure that any potential problems are promptly addressed. Users can also choose to receive email status reports at any time.

The SM500F now also provides users with greater functionality for batch recording processes. When a new batch is initiated on the control system, the SM500F will automatically start to record the batch, including any associated batch information. This eliminates the need for the operator to duplicate the data entry process on both the recorder and the PLC, saving time and reducing the chance of any potential errors.

Figure 4 SM500F field-mount paperless chart recorder

RVG200

The RVG200 recorder takes the established operating and security benefits of the ScreenMaster range one step further. Features include touchscreen 'swipe' operation, front and rear USB ports for connecting peripheral devices (including a barcode scanner and keyboard) and Ethernet and RS485 communications. Up to 24 process signals can be connected to the RVG200's analog inputs or transferred to it via digital communications.

As with all devices in the ScreenMaster paperless recorder range, the RVG200 features extensive security measures to protect against unauthorized tampering with process data, compliant with FDA 21 CFR Part 11 requirements. Standard security features include the ability to configure and allocate multiple users with individual password and access rights. All recorded data is also securely stored by the RVG200's 256 MB of internal flash memory that can be expanded to 2 GB if required.

DataManager Pro

ABB's DataManager Pro analysis software offers a powerful tool for reviewing recorded data. Using the software, operators can review data from multiple recorders. Functions include the ability to compile graphical charts comparing multiple parameters, plus a dual cursor function enabling operators to review data for specific periods of time and specific recorders.

ABB's ScreenMaster series paperless recorders feature Ethernet communications, allowing users to access the recorders from any web browser. Information can be automatically retrieved and placed in DataManager Pro for further analysis.

DataManager Pro also offers a range of presentation possibilities, including the ability to annotate specific alarms and present recorded data as a combined graph accompanied by tables and statistics.

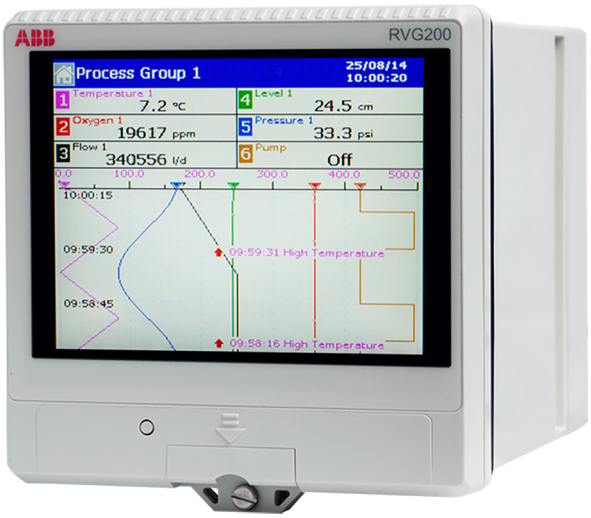

Figure 5 RVG200 paperless recorder

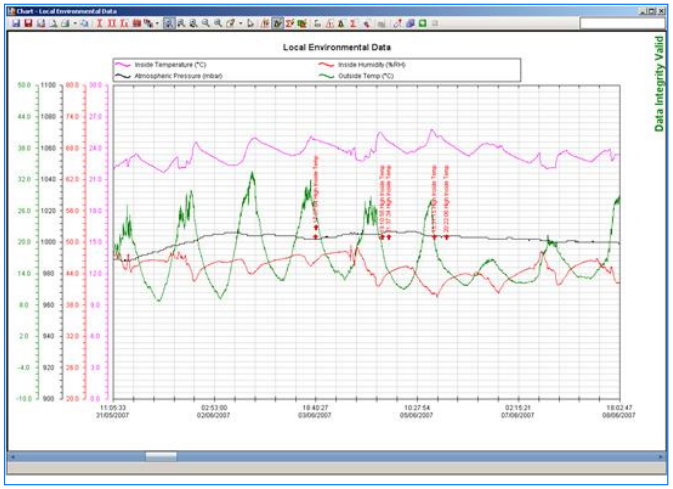

Figure 6 DataManager Pro data review software

ABB Limited
Measurement & Analytics
Howard Road, St. Neots
Cambridgeshire, PE19 8EU
UK
Tel: +44 (0)1480 475 321
Fax: +44 (0)1480 217 948
Email: instrumentation@gb.abb.com

ABB Inc.
Measurement & Analytics
125 E. County Line Road
Warminster, PA 18974
USA
Tel: +1 215 674 6000
Fax: +1 215 674 7183

abb.com/measurement

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