Life Sciences

INDUSTRY

- **Alarm management**
- **21 CFR Part 11**
- **Data storage**
- **Reports**
- **Scalability**

Pharmaceutical Environmental & Stability Chamber Monitoring

Application Note

Monitoring of storage and production environments has become an important issue within the Pharmaceutical Industry. The FDA and other regulatory bodies require not only accurate measurement and storage of room parameters but if the storage medium is electronic then the methods used must comply with 21 CFR Part 11.

Stability Monitoring of medicinal products is an area also addressed by the ICH (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) and the ICH final guidance (agreed Feb 2003), is now being adopted across Europe, Japan and the United States.

The FDA also states in its 21 CFR part 203 section that manufacturers, authorised distributors of drugs and their representatives shall store and handle all drug samples under conditions that will maintain their stability, integrity and effectiveness, and ensure that the drug samples are free of contamination, deterioration and adulteration.

With environmental chambers, temperature, humidity, particulate counts, differential pressure, lighting, gas levels and other environmental conditions can be controlled. This can be extended to equipment required to detect toxic gases and fume hood positions.

Regulatory bodies require that stability facilities have to meet the following criteria:

- Proper documentation, including SOPs and periodical reports
- Chambers and rooms have to be equipped with multiple sensors spread evenly throughout the controlled area
- Generous multilevel shelving providing orderly storage and proper exposure to the controlled environment
- Acceptable monitoring equipment (probes, recorders, etc.)
- Continuous recording of data and full traceability
- Corrective action taken when stability factors go outside the specifications

Alarms and excursions

Detecting and announcing abnormal conditions is a key requirement for the environmental monitoring systems.

Pharmaceutical companies have adopted various methods for capturing and announcing abnormal conditions. These include:

- Alarms if monitored values go outside a predefined value.
- Alarms on excursion conditions being breached (usually a set temperature or humidity for a particular time).
- Intelligent alarms (e.g. “alarm immediately if it is silent hours, after a period if it is during the day” or “delay the alarm if the room door is known to be open”).
- Alarms based on rolling yearly MKT.
- SMS or e-mail alerts triggered by alarms or events

Mean Kinetic Temperature (MKT)

Measurement and recording of temperatures is vital to the storage of perishable goods, but there is more than one way to record an average.

The ICH defines the mean kinetic temperature as being “a single derived temperature that, if maintained over a defined period of time, affords the same thermal challenge to a drug substance or drug product as would be experienced over a range of both higher and lower temperatures for an equivalent defined period”.

MKT expresses the cumulative thermal stress experienced by a product at varying temperatures, during storage and distribution. It differs from other means (such as a simple numerical average or arithmetic mean) in that higher temperatures are given greater weight in computing the average, thus, recognising the accelerated rate of thermal degradation of materials at higher temperatures.

The mean kinetic temperature is calculated as being:

$$T_k = \frac{\frac{-\Delta H}{R}}{\ln\left[\frac{e^{\frac{-\Delta H}{RT_1}} + \cdots e^{\frac{-\Delta H}{RT_n}}}{n}\right]}$$

T_K being the mean kinetic temperature in Kelvin
ΔH is the heat activation in kjoule per mole
R is the universal gas constant in kjoule per mole per Kelvin
T_1 and T_n are the temperature samples for periods 1 and n, respectively
n is the total number of periods in the calculation

There are a number of interpretations of how this calculation is achieved using real samples:

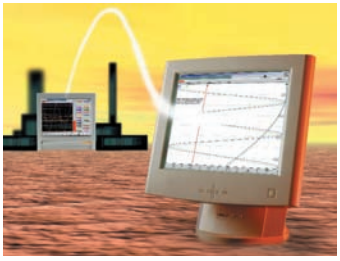
- All sample values fed into formula
- Maximum/minimum samples fed into formula separately (recommended by the FDA)
- Arithmetic mean of maximum and minimum fed into formula (recommended in the US Pharmacopeia and by the UK MCA)

Eurotherm® offers all the above methods with

- A choice of stability testing period (hourly / daily / weekly)
- A choice of sampling frequency (from 1 minute to 1 hour)
- Option to remove individual probes from calculation (e.g. during a calibration process)
- Corrective action in case stability is out of specification
- Secure and low cost custom reporting
- Significant reduction of the cost of ownership

Eurotherm Scalable and Flexible Solutions

Eurotherm offers a comprehensive range of scalable and flexible solutions which will satisfy the requirements of environmental and stability chamber monitoring for Pharmaceutical and Bio-Pharma industries. These solutions unify the environmental and security data from the manufacturing area for presentation to plant or laboratory managers and operators.



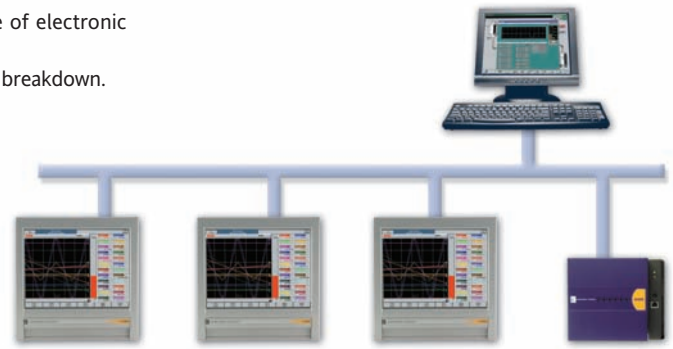
Single room monitoring with 6000 series Data acquisition system

- Meets requirements of 21 CFR part 11
- Single data recorder
- Local storage
- Maths capability including Mean Kinetic Temperature
- Bridge software for remote access and monitoring
- Report software via MS Excel™ Add-in option

Multiple room monitoring with local logging capability

Networking the 6000 series recorders to a central PC for long-term storage of electronic records and remote monitoring of the individual recorder.

The main feature of this offering is security of data in the event of a network breakdown.



- Meets requirements of 21 CFR part 11
- Multiple data recorders
- Local storage
- Optional local display
- Maths capability including Mean Kinetic Temperature
- Not dependant on network
- Bridge and Report software via MS Excel Add-in option
- Time synchronisation

Multiple room monitoring with central logging

This offering includes the EurothermSuite SCADA package combined with T2500 distributed I/O. T2550 I/O units distributed around the plant communicate with the supervisory system via MODBUS TCP/IP (MODBUS over Ethernet).

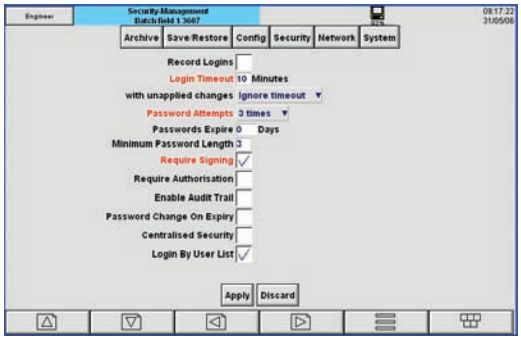
- Meets requirements of 21 CFR part 11
- Accurate continuous and sequential control
- Extensive Maths and Logic libraries (e.g. delay alarms if the room door is open)
- Maths capability including Mean Kinetic Temperature
- Report generation via MS Excel Add-in option
- Cost effective multiple room solution
- Sophisticated alarm functionality
- Time Synchronisation

Fulfilling the Requirements of 21 CFR Part 11

Eurotherm data recorders and process control systems have Electronic Signature and Electronic Record capability. The controllers have a lockout feature that permits changes through a 21 CFR part 11 compliant operator station, thus providing the necessary audit trail.

Tamperproof electronic records

- Process Values and Audit Trails (Alarms, Events, Electronic Signatures)
- Date and Time stamping
- Time Synchronisation
- Viewable in human readable format
- Export conversion facility to MS Excel



Electronic signature

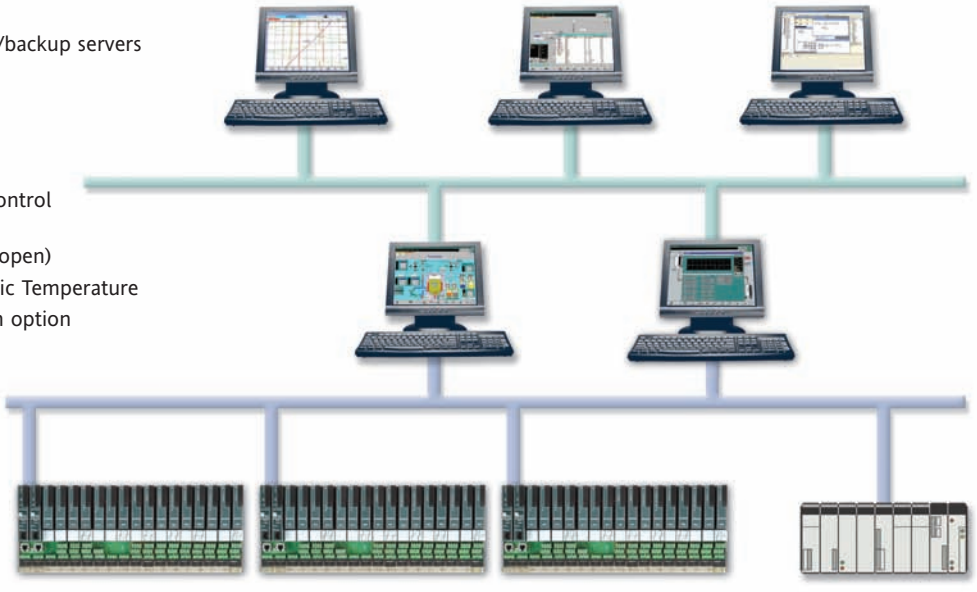
- User actions with Signing and Authorisation
- Unique signatures
- Automatic log-off
- Minimum length password
- Access control according to authority level
- Automatic password expiry
- Traceable audit trail (e.g. in case an attempt is made to gain unauthorised access)

6000 Series data acquisition and management

- Meet requirements of 21 CFR part 11
- Multi-batch recording
- Network-ready via a range of Ethernet protocols
- Maths capability including Mean Kinetic Temperature Calculation
- High precision displays for accurate operator reading
- Remote viewing via Bridge software
- Time synchronisation
- Offline data viewing via Review software
- Report generation via MS Excel Add-in option

EurothermSuite® operation server and viewer

- Meet requirements of 21 CFR part 11
- Client/server architecture with master/backup servers
- Defined display structure
- Trending
- Sophisticated alarm functionality
- Single global database
- Accurate continuous and sequential control
- Extensive Maths and Logic libraries (e.g. delay alarms if the room door is open)
- Maths capability including Mean Kinetic Temperature
- Report generation via MS Excel Add-in option
- Time Synchronisation



T2550 Process interface

- Distributed scalable I/O system
- Live plug-in modules
- Direct wiring on a DIN rail mounting
- High accuracy modules
- Standard communications protocols
- Individual module and channel status indication

Eurotherm: International sales and service

Understanding and providing local support is a key part of Eurotherm 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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