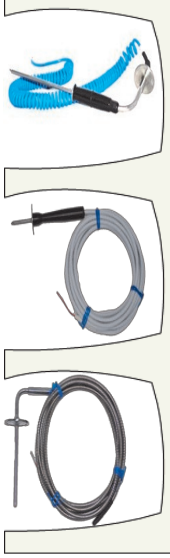

THERMOMETRICS CORPORATION

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Pharmaceutical Sensors.com

Addressing The Needs of Pharmaceutical Temperature Measurement

Thermometrics manufactures a full range of RTDs, thermocouples and thermowells that have been designed to meet the environmental, performance and surface finish requirements of the pharmaceutical and biotech markets. The sensors typically feature enhanced performance specifications and 316L stainless steel materials. Calibration certificates are also available. Designed specifically for the pharmaceutical, biotechnology and medical industries, Thermometrics Autoclave RTDs eliminate all of the problems associated with standard probes where the pressure and vacuum cycling of autoclaves forces moisture inside the probe, resulting in incorrect, low temperature readings and reduced life.

Helping you achieve your sterilization needs..

Our Autoclave RTDs are completely sealed. As a result, the entire sensor assembly of the Thermometrics, Autoclave RTD, including the probe and cables extending from the RTD, can be completely submerged in water without affecting accuracy or long-term stability.
Our general purpose sanitary RTD and thermocouple temperature sensors have been designed for food, beverage and dairy applications where sensor corrosion and product contamination are critical factors.

Call or e-mail us today with your requirements and learn why Thermometrics provides the fastest lead times and most cost effective temperature measurement solutions for any sanitary temperature measurement application.

MARKET NEWS

Today, pharmaceutical companies write elaborate calibration protocols that are consistent (and sometimes overly compliant) with FDA cGMP guidelines to maintain the reported process value integrity. This can result in extremely high cost for compliance with only a minimum ROI for improved productivity or product quality. For example, one pharmaceutical site in New Jersey conducts about 2,900 calibrations per month. Of those, about 500 are demand maintenance where the instrument has clearly failed as evidenced by a lack of signal or a digital diagnostic (catastrophic failures). The remaining 2,400 calibrations are scheduled per protocol. Of these, only about 400 calibrations find the instrument out of calibration. The majority, about 2,000 calibrations per month, find the instrument still working properly. Those at other pharmaceutical manufacturing facilities can check orders from the metrology department and obtain the exact ratio for their facility, and might be surprised to find similar numbers.[1]

Getting the most from your sensors.

"Quality You Can Sense!"

Validation of thermal sterilization process is a critical activity in the pharmaceutical industry.

FDA definition of Process Validation-

Establishing by objective evidence that a process consistently produces a result of product meeting its predetermined specifications.

In thermal sterilization processes "time at temperature" is critical to achieve required product sterility. Therefore temperature and time are the primary parameters used for validation of the sterilization process. The mathematical relation between "Time-at-Temperature" and the achieved level of sterility is exponential and makes it critical to have very accurate temperature measurements. The Lethality Rate L is calculated as follows:

$$L = 10^{\left(\frac{T-Tb}{z}\right)}$$

At a base temperature T_b = 121°C and z =10°C, the effect of 1°C error in measure temperature at T as 121°C results in approximately 26% error in lethality calculation.[1]

FDA's current thinking on the criticality of accurate temperature measurements:[2]
"For both validation and routine process control, the reliability of the data generated by sterilization cycle monitoring devices should be considered to be of the utmost importance. Devices that measure cycle parameters should be routinely calibrated. Written procedure should be established to ensure that these devices are maintained in a calibrated state.
For Example:
"Temperature monitoring devices for heat sterilization should be calibrated at suitable intervals, as well as before and after validation runs."

Overall Validation System Accuracy Required

The required process temperature uniformity in the chamber, according to regulations[3] and industry standards should be better than or equal to 1°C or 0.5°C depending on the application.

The validation instrument, including temperature sensors, used for validation measurements should be at least three times as accurate as the process variable measured[4]. This means that the Overall Validation System Accuracy should be better than or equal to +/- 0.33°C or +/- 0.17°C respectively. All components involved in the measurement are referred to as the "Measuring Chain".

Calibration compensates for systematic errors only. Random errors are not compensated for and can affect the results of a thermal validation study. Control and management of these variables require a good understanding of the underlying factors. The people who perform the validation study are responsible for the control and management of these factors.

Temperature Sensors

Type T thermocouples (copper/constantan) are the most commonly used sensor for temperature measurements in validation applications due to its high accuracy and low cost. Accurate temperature measurement with thermocouples requires proper design and installation of the thermocouple circuit.

Sensor Design

A sensor designed for measure the temperature in a LVP bag cannot be used for measuring the temperature in a 10ml vial. The thermocouple reports only what it "feels." This may or may not be the desired temperature of interest. Factors to consider when specifying the design of temperature sensors are: Size, Shape, Response Time, Heat Conduction, and Sensor Position.

Thermocouple Specifics

When using twisted bare wires, the instrument measures the temperature at first point of contact, i.e., the furthest point from the tip. Using a twisted thermocouple to measure heat distribution in a steam sterilizer not significantly affect accuracy. However, in a small vial, the error could be significant. Avoid this problem by reducing the junction to the smallest practical size.

References-
1. Pharmaceuticalmanufacturing.com
1[2]. Pda technical monograph
2. Draft Guidance Document "Steriile Drug Products Produced– Current good manufacturing practice, eqp, ctrl, inst calibration
3. cGMP, En 285, EN 554 4. EN 554

SMARTER SENSING: *Dry Heat vs. Wet Heat*

Wet Heat -is the most dependable procedure for the destruction of all forms of microbial life. Steam sterilization generally denotes heating in an autoclave employing saturated steam under a pressure of approximately 15 psi to achieve a chamber temperature of at least 121°C (250°F). The critical factors in insuring the reliability of this sterilization method is: 1) proper temperature and time; and 2) the complete replacement of the air with steam (i.e. no entrapment of air). Some autoclaves utilize a steam activated exhaust valve that remains open during the replacement of air by live steam until the steam triggers the valve to close. Others utilize a pre-cycle vacuum to remove air prior to steam introduction.

Dry heat-is less efficient than wet heat sterilization and requires longer times and/or higher temperatures. The specific times and temperatures must be determined for each type of material being sterilized. Generous safety factors are usually added to allow for the variables that can influence the efficiency of this method of sterilization. The moisture of the sterilization environment as well as the moisture history of organisms prior to heat exposure appear to affect the efficiency of dry heat sterilization..

Higher temperatures and shorter times may be used for heat resistant materials. The heat transfer properties and the spatial relation or arrangement of articles in the load are critical in insuring effective sterilization.

Conclusion- The advantage of wet heat is a better heat transfer to and into the cell resulting in overall shorter exposure time and lower temperature. Steam sterilization uses pressurized steam at 121-132°C (250-270° F) for 30 or 40 minutes. This type of heat kills all microbial cells including spores, which are normally heat resistant. In order to accomplish the same effect with dry heat in an oven, the temperature needs to be increased to 160-170° C (320-338° F) for periods of 2 to 4 hours.

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