Temperature Sensors used in Pharmaceutical Industry and its application

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Abstract - *This document provides guidance on different types of sensors used in pharmaceutical industry in different areas like Walking chambers, laboratory incubators, deep freezers, oven and steam sterilizers.*

Specifically, for steam sterilizer T type thermocouples are used and study performed is elaborated for suitability of T type Thermocouples.

Key Words: Sensors, Steam sterilizer, Pharmaceuticals, Thermocouple

1. Introduction:

This article provides overview of the different types of sensors used in pharmaceutical industry and their suitable application for the calibration and mapping of controlled temperature chambers,
Deep freezers, refrigerated storage areas, Laboratory incubators and Steam sterilizes.

2. What are sensors and its importance?

A sensor is a device, module, machine, or subsystem that detects events or changes in its environment and relays the information to other electronics, most commonly on PLC, SCDA or computer devices.

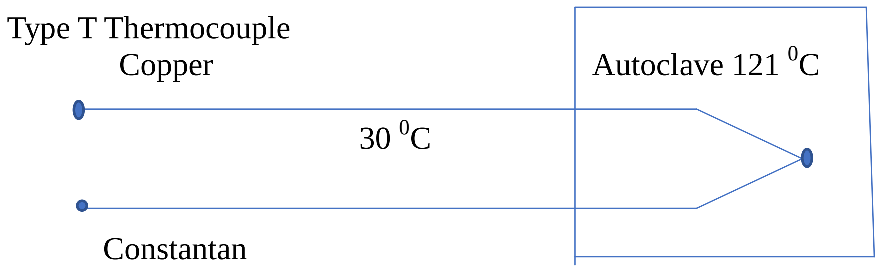
A sensor converts physical phenomena into a measurable digital signal, which can then be displayed, read, or processed further.

2.1 Different types of Temperature sensors used in pharmaceutical industry are as follows;

2.1.1 Thermocouple:

2.1.1.1 What is called thermocouple?

Thermocouple, also called thermal junction, a temperature-measuring device consisting of two wires of different metals joined at each end. One junction is placed where the temperature is to be measured, and the other is kept at a constant lower temperature.



2.1.1.2 What is the principle of thermocouple?

Thermocouples operate on the principle that when two metals are joined together, there is a potential difference, at the point of contact, that varies with changes in temperature.

What are the 2 types of thermocouple connectors?

Mini Plug (also known as SMP or sub-miniature plug),

Screw Terminal, and Terminal Block. Many of our thermocouple data loggers have different models available for each type of thermocouple connector.

2.1.1.3 Thermocouple Highlights and Limitations

Highlights

- Sensitivity
- Typical Measuring Range is wider i.e.-270 to +2000 °C
- Long-term Stability- Poor to Fair
- Repeatability -Excellent Poor to Fair
- Response Time -Short
- Response Type-Fast
- Linearity-Fair
- Undesirable Self-Heating -Excellent
- Tip Sensitivity -Excellent
- Low cost
- Dimension-small surface possible
- Connection cable-Thermo compensating cables
- Hot junction-connection point of two metals
- Cold junction-necessary

Limitations

- Lowered accuracy
- Less sensitive
- Relatively high drift-over-time
- Less stable
- Wiring is more expensive
- Accuracy-less accurate i.e. Good to Medium i.e. ± 0.05 0C

2.1.2 Resistance Temperature Detectors (RTD)

Resistance Temperature Detector

Resistance Temperature Detector (RTD) is a device with which its resistance varies with temperature.

2.1.2.1 What is the principle of RTD and thermocouple?

RTDs work on the principle of resistance, which happens uniformly with changes in temperature i.e resistance is directly proportional to temperature.

2.1.2.2 RTD Highlights and Limitations

Highlights

- Very high accuracy
- Outstanding sensitivity
- Excellent stability and repeatability (low drift)
- Response Time -Relatively long
- Connection cable-Copper cables
- Accuracy-Very Good
- Dimension-large sensor surface

- Consistency-very good
- Hot junction-over the whole length of the RTD
- Cold junction-not necessary

Limitations

- Narrow temperature range
- High Cost

2.1.3 Thermisters

Thermistors are a type of semiconductor that react like a resistor sensitive to temperature - meaning they have greater resistance than conducting materials, but lower resistance than insulating materials.

The main use of a thermistor is to measure the temperature of a device. In a temperature-controlled system.

2.1.3.1 What is the principle of thermistor?

The basic working principle of a thermistor is that its resistance is dependent on temperature. Its resistance is measured by an ohm meter, which is a device that measures electrical resistance.

2.1.3.2 Thermisters Highlights and Limitations

Highlights

- Response Time -Short
- Connection cable-Thermo compensating cables
- Accuracy-Good
- Dimension-small sensor surface
- Consistency-satisfactory
- Hot junction-connection point of 2 metals
- Cold junction-not necessary

Limitations

- Narrow temperature range
- High Cost

3. Application of appropriate sensors in Pharmaceutical equipment's

Which sensor is used in autoclave validation?

Either Thermocouple or RTD sensor to be used for autoclave validation.

Thermocouples are the most commonly used sensors but why?

- The thermocouple (TC) sensor is a voltage-generated device that changes its output based on the temperature changes detected.
- Temperature sensors are required to sense the temperature in locations in the chamber and load as specified in the tests. They may be either platinum resistance elements or thermocouples. Platinum resistance elements should comply with Class A of BS1904.
- Thermocouples should conform to BS4937: Part 4 (nickel-chromium/ nickel-aluminium) or Part 5 (copper/constantan).
- The calibration accuracy should be Tolerance Class 1 as specified in EN 60584: Part 2 (formerly BS4937: Part 20).

- The tolerance on Part 4 thermocouples (± 1.5 º C) is high when compared with that allowed for those in Part 5 (± 0.5 º C), and for this reason copper/constantan thermocouples are usually preferred for the test recording system.
- For selected wire this variation is typically (for copper/constantan) of the order of 0.015 mV which is equivalent to 0.4 º C at 20 º C and 0.3 º C at 134 º C.
- The wire should be single-strand, not exceeding 0.7 mm diameter over the covering of one core of a twin cable. Twin-core cable is usually preferred because it is easier to handle and more durable than single-core wire.
- The width of the cable should not exceed 2 mm.
- Thermocouples may be argon arc-welded or micro-welded. However, experience has shown that provided the wires are cleaned, they may be satisfactorily twisted together to form the hot junction. Brazing, silver brazing and welding with filler rods may be no more reliable in respect of accuracy than freshly twisted wires. Particular attention should be given to the condition of copper/constantan thermocouples when testing LTSF sterilizers. Thermocouples should not be fitted with a heat sink.

Reference: Health Technical Memorandum 2010 Part 3 (Including Amendment 1): Validation and verification Sterilization

Thermocouples are most suited for qualification of steam sterilizer because of below stated reasons,

Study performed by using RTD PT-100 sensors and Thermocouples placed at same locations of chamber and articles.

Note: Sensor Numbers mentioned are for information in actual sensor numbers are different however output is shown as is.

Table: -1 Location details of sensors for Heat Penetration Study with Variable load during Standard Process-I

Sr. No.	**RTD Sensors ID No.**	**Thermocouple Sensors ID No.**	**Location Description of the Sensors**	**Shelf/Location**
01	CH 0001	CH 0107	At the drain points of the chamber.	Near Drain
02	CH 0002	CH 0108	Inside media flask-1000 mL	Upper Shelf
03	CH 0003	CH 0109	Inside media flask -1000 mL	Upper Shelf
04	CH 0004	CH 0110	Inside media bottle-500 mL	Upper Shelf
05	CH 0005	CH 0201	Inside media beaker- 250 mL	Upper Shelf
06	CH 0006	CH 0202	Inside media bottle- 100 mL	Upper Shelf
07	CH 0007	CH 0203	Inside media flask-1000 mL	Lower Shelf
08	CH 0008	CH 0204	Inside media flask -1000 mL	Lower Shelf
09	CH 0009	CH 0205	Inside media bottle-500 mL	Lower Shelf
10	CH0010	CH 0206	Inside media beaker- 250 mL	Lower Shelf
11	CH 0101	CH 0207	Inside media bottle- 100 mL	Lower Shelf
12	CH 0102	CH 0208	Centre of the chamber	Lower Shelf
13	CH 0103	CH 0209	Near inbuilt sensor – T3	Near inbuilt sensor
14	CH 0104	CH 0210	Near inbuilt sensor- T5	Near inbuilt sensor

Table: -2 Refer to below summary results for Trial media cycle Run for RTD PT 100 sensors and T type Thermocouples are summarized below,

Channel No.	Total Duration	Delayed Time Duration	F0 Value (Minute)	Channel No.	Total Duration	Delayed Time Duration	F0 Value (Minute)
Summary of RTD PT 100 sensors				**Summary of T- type thermocouple sensors**			
CH0001	00:21:25	00:00:35	25.07	CH0107	00:22:05	00:00:10	30.04
CH0002	00:16:15	00:05:50	18.61	CH0108	00:21:35	00:00:55	27.60
CH0003	00:13:15	00:09:15	15.23	CH0109	00:21:30	00:01:10	27.87
CH0004	00:20:30	00:01:45	24.62	CH0110	00:21:30	00:01:10	29.66
CH0005	00:19:50	00:02:30	24.65	CH0201	00:21:45	00:00:55	29.98
CH0006	00:18:35	00:03:45	23.22	CH0202	00:21:50	00:00:35	28.14
CH0007	00:13:45	00:08:20	15.02	CH0203	00:19:10	00:03:00	25.33
CH0008	00:18:25	00:03:55	23.48	CH0204	00:21:35	00:01:00	28.73
CH0009	00:16:25	00:05:50	19.44	CH0205	00:20:10	00:02:10	26.05
CH0010	00:19:15	00:02:55	22.81	CH0206	00:21:10	00:01:10	28.08
CH0101	00:19:45	00:02:30	23.38	CH0207	00:21:00	00:01:20	27.06
CH0102	00:21:55	00:00:15	27.98	CH0208	00:22:15	00:00:00	31.46
CH0103	00:22:05	00:00:05	30.27	CH0209	00:22:05	00:00:10	30.47
CH0104	00:22:10	00:00:05	31.04	CH0210	00:22:00	00:00:10	29.17

Table: -3 Sensor Comparison

Parameter	**RTD PT 100**	**T-type Thermocouple**
Typical Measuring Range	-240 to +650 °C	-270 to +2,320 °C
Long-term Stability	Excellent	Poor to Fair
Accuracy	Excellent	Good to Medium
Repeatability	Excellent	Poor to Fair
Response Time	Good	Medium to Excellent
Linearity	Good	Fair
Undesirable Self-Heating	Medium to Excellent	Excellent
Tip Sensitivity	Fair	Excellent

- As compared to RTD with Thermocouple parameters, Response time and Tip sensitivity are better for Thermocouple and suitable for Autoclave qualification.

- Based on the above trial, it is demonstrated that the excellent response time of T-type thermocouple sensors reached the desired temperature quickly compared to RTD PT-100 sensors. In Autoclave during sterilization hold period steam pulsing is ongoing at a particular time that time is approximately in seconds and in this time Thermocouple sensing the temperature because of excellent response timing and RTD PT-100 is having adequate response time hence this type of sensors can't feel real-time temperature immediately.

- In the above cycle first sensor that reached 1210C is from Thermocouple (Sensor ID: - CH0208 at 15:24:15).

- Also, all sensors achieved 121°C in Thermocouple sensors at 15:27:15, and in RTD PT 100, all sensors achieved 121°C at 15:33:30.

- RTD PT 100 sensors CH0102, CH0103 and CH0104 are distribution sensors hence sterilization temperature reached earlier than penetration probes hence fo value is found to be higher for distribution probes i.e. 27.98,30.27 and 31.04 respectively. As response time is less in this type of sensors hence fo value is lower than RTD PT 100 sensors.

- T-type Thermocouple sensors CH0208, CH0209 and CH0210 are distribution sensors hence sterilization temperature reached earlier than penetration probes hence fo value is found to be higher for distribution probes i.e. 31.46, 30.47 and 29.17 respectively. As response time is higher in this type of sensors hence fo value is higher than RTD PT 100 sensors.

- Minimum fo value should be 15 for any media cycle, based on this concept both sensors are acceptable. Though sterilization hold time was found to be 00:13:45 for sensor CH0007 and fo value is 15.02 hence this cycle is also acceptable based on f0 concept.

- Because of good response timing RTD PT 100 sensors have less exposure to 1210C; however, in reality, 1210C temperature is already reached earlier in all sensors with a maximum lag time of 00:03:00 minutes; shows that steam sterilizer T-type Thermocouples are suitable for qualification.

Sensor locations wise evaluations:

Table:4 Locations of Distribution sensors

RTD Sensors ID No.	Thermocouple Sensors ID No.	Location Description of the Sensors	Shelf/Location
CH 0001	CH 0107	At the drain points of the chamber.	Near Drain
CH 0102	CH 0208	Centre of the chamber	Lower Shelf
CH 0103	CH 0209	Near inbuilt sensor – T3	Near inbuilt sensor
CH 0104	CH 0210	Near inbuilt sensor- T5	Near inbuilt sensor

Table 5: Summary of Distribution sensors

Channel No.	Total Duration	Delayed Time Duration	F0 Value (Minute)	Channel No.	Total Duration	Delayed Time Duration	F0 Value (Minute)
Summary of RTD PT 100 sensors				**Summary of T- type thermocouple sensors**			
CH0001	00:21:25	00:00:35	25.07	CH0107	00:22:05	00:00:10	30.04
CH0102	00:21:55	00:00:15	27.98	CH0208	00:22:15	00:00:00	31.46
CH0103	00:22:05	00:00:05	30.27	CH0209	00:22:05	00:00:10	30.47
CH0104	00:22:10	00:00:05	31.04	CH0210	00:22:00	00:00:10	29.17

Distributions sensors placed in three different locations,

At drain point, centre of chamber and Near inbuilt sensor.

- Drain is considered as coldest point hence delayed time found to be 00:00:35 in RTD PT 100 sensors and 00:00:10 in T type Thermocouples.

- In centre of chamber delayed time found to be 00:00:15 in RTD PT 100 sensors and 00:00:00 in T type Thermocouples.

- Near inbuilt sensor delayed time found to be 00:00:05 in RTD PT 100 sensors and 00:00:10 in T type Thermocouples. Delayed time is consistent in both type of sensors, here in RTD PT 100 sensors delayed time is less this may be because inbuilt sensors are also RTD PT 100 sensors and location is distribution sensors, because of this time already elapsed and stability achieved in the RTD PT 100 sensors.
  However, both readings are well within the acceptance criteria.

Table:6 Locations of Penetration sensors

RTD Sensors ID No.	**Thermocouple Sensors ID No.**	**Location Description of the Sensors**	**Shelf/Location**
CH 0002	CH 0108	Inside media flask-1000 mL	Upper Shelf
CH 0003	CH 0109	Inside media flask -1000 mL	Upper Shelf
CH 0004	CH 0110	Inside media bottle-500 mL	Upper Shelf
CH 0005	CH 0201	Inside media beaker- 250 mL	Upper Shelf
CH 0006	CH 0202	Inside media bottle- 100 mL	Upper Shelf
CH 0007	CH 0203	Inside media flask-1000 mL	Lower Shelf
CH 0008	CH 0204	Inside media flask -1000 mL	Lower Shelf
CH 0009	CH 0205	Inside media bottle-500 mL	Lower Shelf
CH0010	CH 0206	Inside media beaker- 250 mL	Lower Shelf
CH 0101	CH 0207	Inside media bottle- 100 mL	Lower Shelf

Table 7: Summary of Penetration sensors

Channel No.	**Total Duration**	**Delayed Time Duration**	**F0 Value (Minute)**	**Channel No.**	**Total Duration**	**Delayed Time Duration**	**F0 Value (Minute)**
Summary of RTD PT 100 sensors				**Summary of T- type thermocouple sensors**			
CH0002	00:16:15	00:05:50	18.61	CH0108	00:21:35	00:00:55	27.60
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CH0005	00:19:50	00:02:30	24.65	CH0201	00:21:45	00:00:55	29.98
CH0006	00:18:35	00:03:45	23.22	CH0202	00:21:50	00:00:35	28.14
CH0007	00:13:45	00:08:20	15.02	CH0203	00:19:10	00:03:00	25.33
CH0008	00:18:25	00:03:55	23.48	CH0204	00:21:35	00:01:00	28.73
CH0009	00:16:25	00:05:50	19.44	CH0205	00:20:10	00:02:10	26.05
CH0010	00:19:15	00:02:55	22.81	CH0206	00:21:10	00:01:10	28.08
CH0101	00:19:45	00:02:30	23.38	CH0207	00:21:00	00:01:20	27.06

Sensors placed in different volumes of containers, different types of containers and upper and lower shelf of chamber.

Reading observed in T type thermocouples sensors,

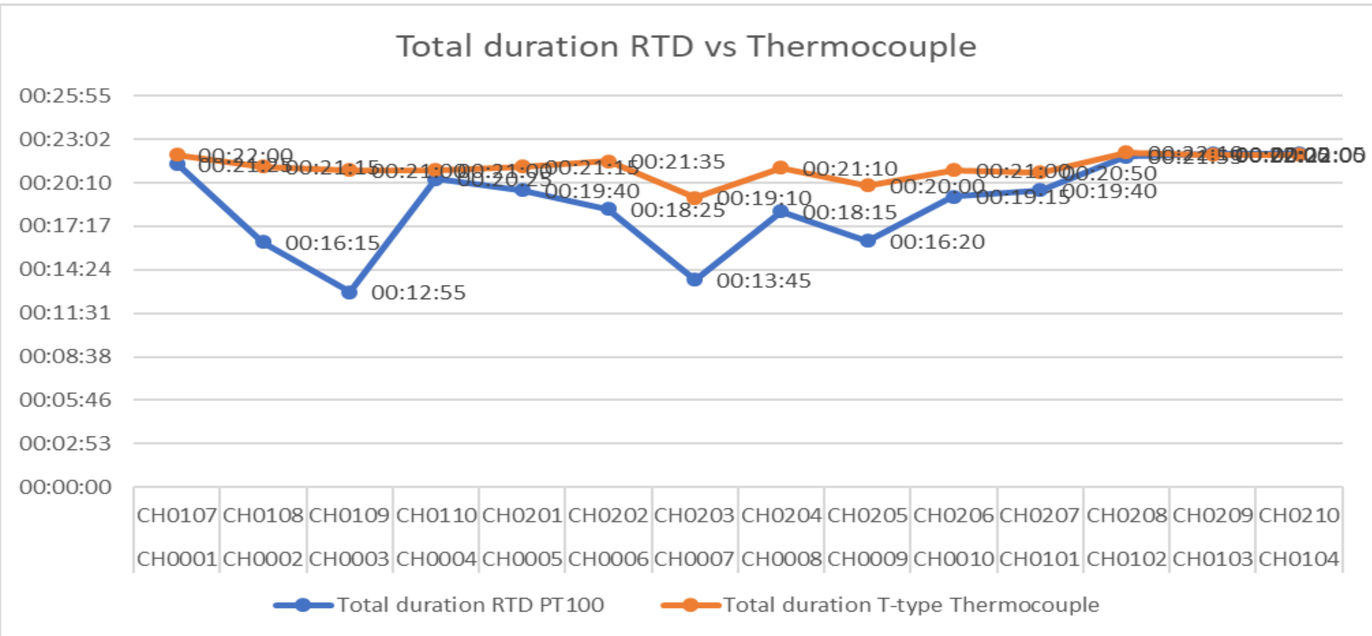
- Inside media bottle- 100 mL (upper shelf) delayed time observed as 00:00:35 and at lower shelf delayed time found to be 00:01:20.
- Inside media beaker- 250 mL (upper shelf) delayed time observed as 00:00:55 and at lower shelf delayed time found to be 00:01:10.
- Inside media bottle- 500 mL (upper shelf) delayed time observed as 00:01:10 and at lower shelf delayed time found to be 00:02:10.
- Inside media flask- 1000 mL (upper shelf) delayed time observed as 00:00:55, 00:01:10 and at lower shelf delayed time found to be 00:03:00 ,00:01:00.
- Media bottles requires light delayed time as compared to beaker and flasks because bottle surface is hard and requires time to heat hard surface.

Reading observed in RTD PT 100 sensors,

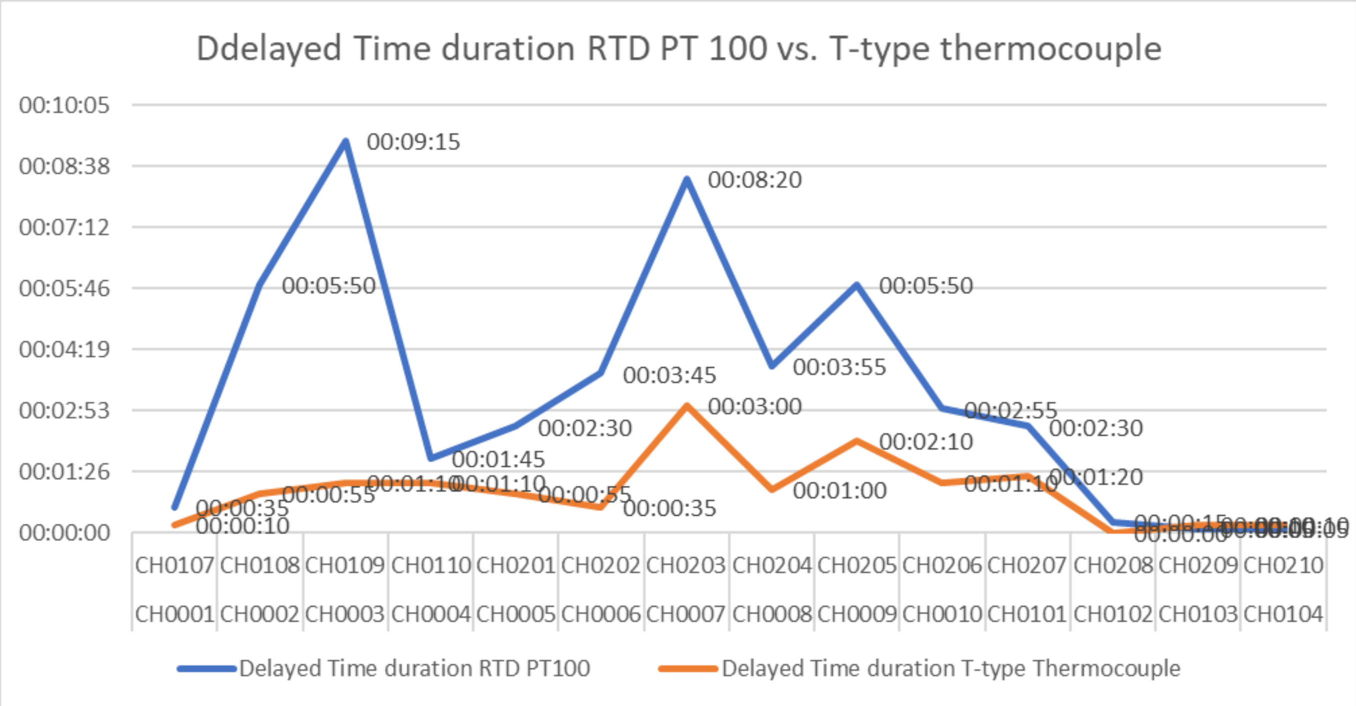
- Inside media bottle- 100 mL (upper shelf) delayed time observed as 00:03:45 and at lower shelf delayed time found to be 00:02:30.
- Inside media beaker- 250 mL (upper shelf) delayed time observed as 00:02:30 and at lower shelf delayed time found to be 00:02:55.
- Inside media bottle- 500 mL (upper shelf) delayed time observed as 00:01:45 and at lower shelf delayed time found to be 00:05:50.
- Inside media flask- 1000 mL (upper shelf) delayed time observed as 00:05:50, 00:09:15 and at lower shelf delayed time found to be 00:08:20 ,00:03:55.

Depending on location, sensor placement inside container response changes hence in this most time required as per container size i.e. for 100 mL flasks delayed time is more however, if you consider f0 value then cycle is pass.

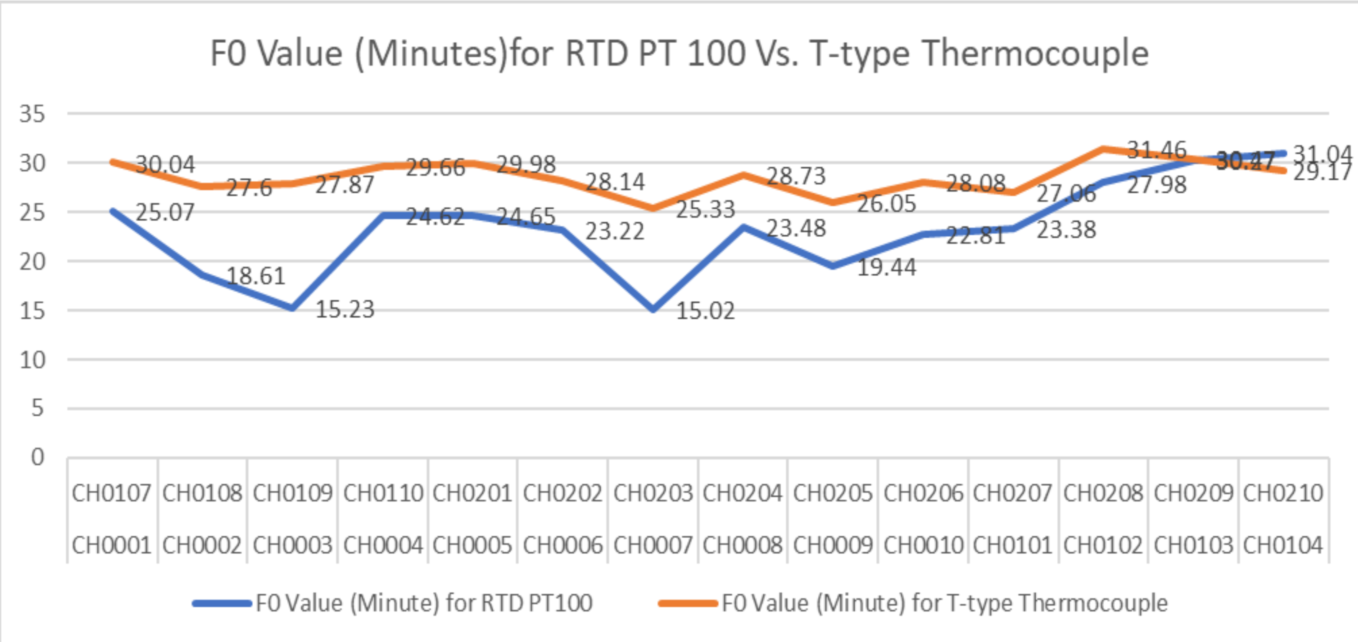
Graph 1: - Comparison of Total sterilization hold for RTD PT 100 Sensors Vs. T-type Thermocouple



Graph 2: - Comparison of Delayed Time for RTD PT 100 Sensors Vs. T-type Thermocouple



Graph 3: - Comparison of F0 Value (Minutes) for RTD PT 100 Sensors Vs. T-type Thermocouple



Overall conclusion:- T type Thermocouples are more suitable for steam sterilizer qualifications as, there is hold time for specific time period hence in this case response time is most important than stability and accuracy.

In case of Oven/Laboratory incubators and Stability chambers or cold rooms, where mapping is being performed for 24 Hrs and here response time is not important, stability and accuracy is important hence here we need to use RTD PT 100 sensors.

References:

1) Health Technical Memorandum 2010 Part 3 (Including Amendment 1): Validation and verification Sterilization
2) A Concept Paper by the ISPE Packaging Community of Practice April 2012 By ISPE
3) USP

BIOGRAPHIES

DR. NILESH SHAH

Dr Nilesh is accomplished Microbiologist professional with more than 18 years of experience in overseeing the testing of Pharmaceuticals industry. Worked in various MNC companies like Sandoz India, Navi Mumbai, Zydus Takeda, Navi Mumbai, SGS LSS, Navi Mumbai and currently working in Zydus Lifesciences Ltd, Ahmedabad. He has vast experience with development/validation of entire microbial testing program and providing guidance and direction to junior staff. Furthermore, he is expertise in Bioburden testing and MLT- Finished Products, Disinfectant efficacy testing, Bacterial endotoxin test by gel clot method and kinetic turbidimetric methods, Sterility Test, Microbial Assay of Antibiotics, GPT, Identification of Micro-organisms.

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