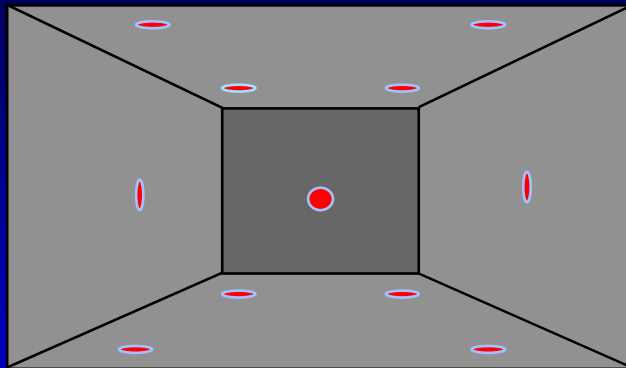


Distribution Studies Thermal Mapping



Thermocouples are distributed geometrically in horizontal and vertical planes in the sterilizer.

Distribution Criteria

- ◆ **GMP'S** **Uniformity should be $\pm 1^{\circ}\text{C}$ of the mean or average temperature**
- ◆ **EN554** **All temperature within sterilization band with upper limit sterilization temp. plus 3K**
Do not differ from each other by more than 2K
Do not fluctuate by more than 1K

Penetration Studies

- ◆ **Conducted to assure that the coolest container within the load will consistently be exposed to sufficient heat for proper sterilization of the drug.**
- ◆ **A product is considered sterile when the probability of survival of any micro-organism is reduced to 10^{-6} regardless of the number and resistance of the microorganisms.**

Penetration Studies

- ◆ **Evenly distribute probed containers between pallets or layers, ensuring coldest spot in vessel is represented**
- ◆ **For solutions use maximum fill volume**
- ◆ **Microbiological Challenge Studies using calibrated biological indicators, (min 10) positioned adjacent to probed containers**

Penetration Studies

- ◆ **Calculate lethality for probed containers using normal production cycle**
- ◆ **Under minimum and maximum loads**
- ◆ **For each product and container size or type**
- ◆ **Repeat test to ensure repeatability**

Instant Lethality Calculation

Z	10	T °C	F _o
T _b	121.1	116.0	0.31
		117.0	0.39
		118.0	0.49
		119.0	0.62
		120.0	0.78
		120.1	0.79
		121.1	1
		122.1	1.26
		123.0	1.55
		124.0	1.95

Instant Lethality Calculation

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		122.1	1.26
		123.0	1.55
		124.0	1.95

Validation Equipment Accuracy Requirements

HTM 2010

- ◆ **6.16 The repeatability of the test equipment should be $\pm 0.25^{\circ}\text{C}$ or better, and the limit of error of the complete measurement system (including sensors) should be no more than 0.5°C .**

Validation Equipment Accuracy Requirements

EN 285

- ◆ **26.4.5 The limit of error between 0°C and 150°C shall not exceed $\pm 0.25\%$...**

Validation Equipment Accuracy Requirements

EN 554

- ◆ **4.6.2 The accuracy of test equipment shall be not less than the accuracy of the instruments fitted to the sterilizer, and shall exceed by at least a factor of three the accuracy of measurements required to judge the performance of the sterilizer.**

Validation Equipment Accuracy Requirements

EN 554

- ◆ **A.2.6 The factor of three was chosen because it provides approximately a 1 : 10 guarantee that any error noted in readings is not caused by the inaccuracy of the test instrument.**