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A Survey on Validation of Moist Heat Terminal Sterilization Product

Survey Data

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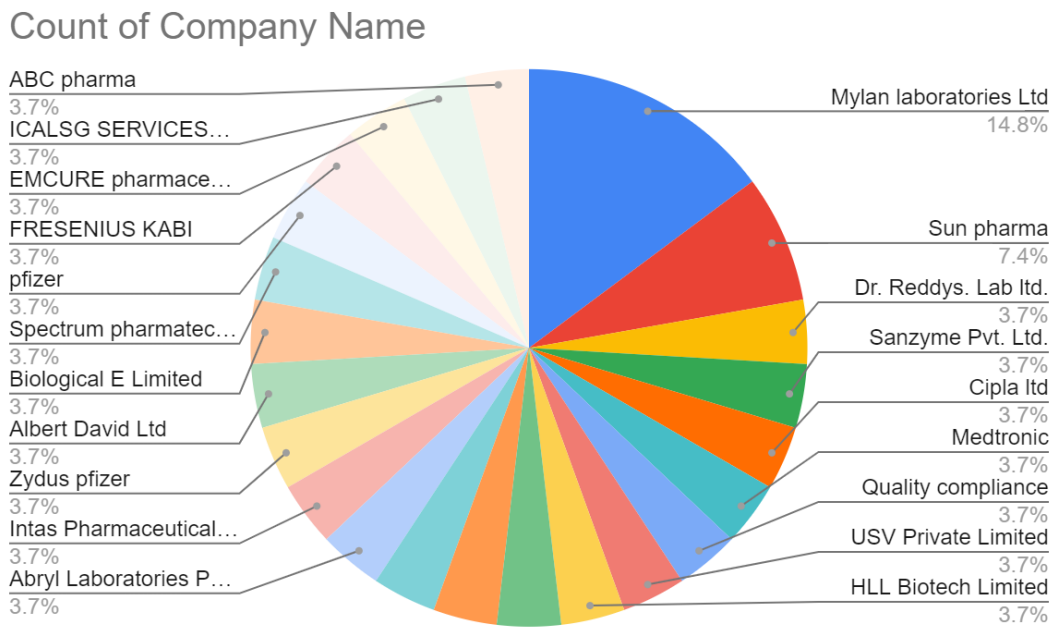
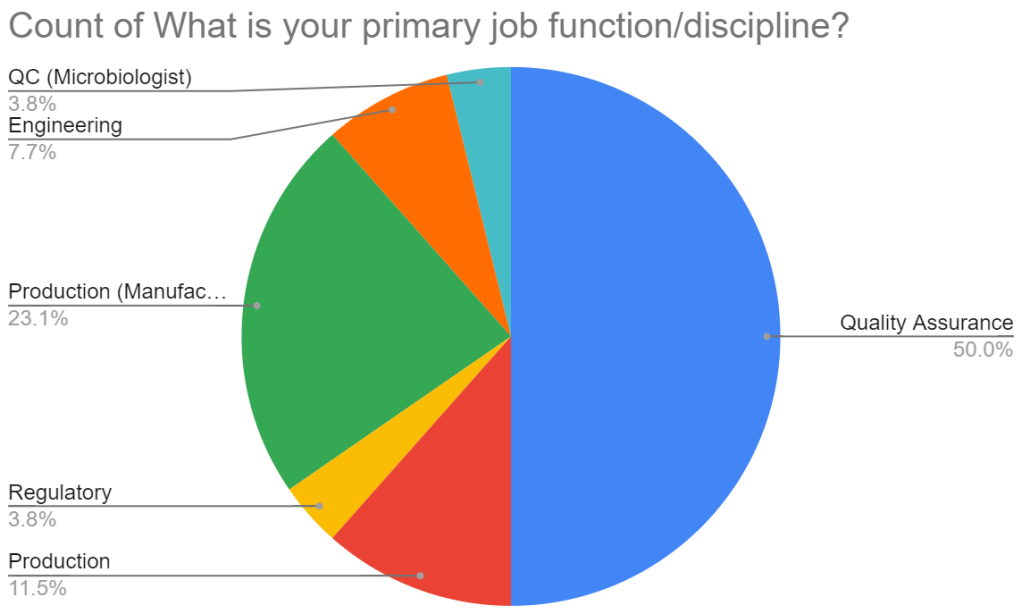
5-17-2020

We have conducted a thorough (phase one) review on the moist heat terminal sterilization process. We recognize and appreciate the contributions of all individual involved in this survey. We got excellent response from all number of Indian pharmaceutical organizations. This survey majorly focused on the understanding of practices of Indian pharmaceutical industry where as few Asia-Pacific organization response also considered.

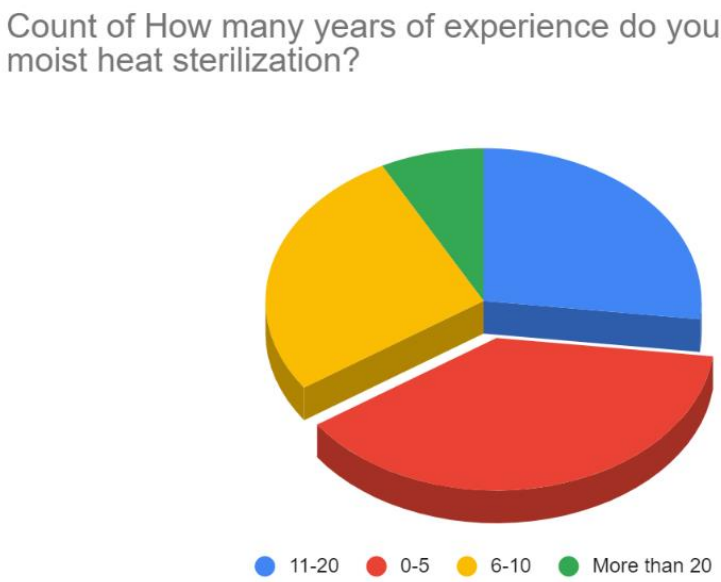
Let's see and analysis what are the response we have received, Personnel belongs to different pharmaceutical organizations are involved in the survey,



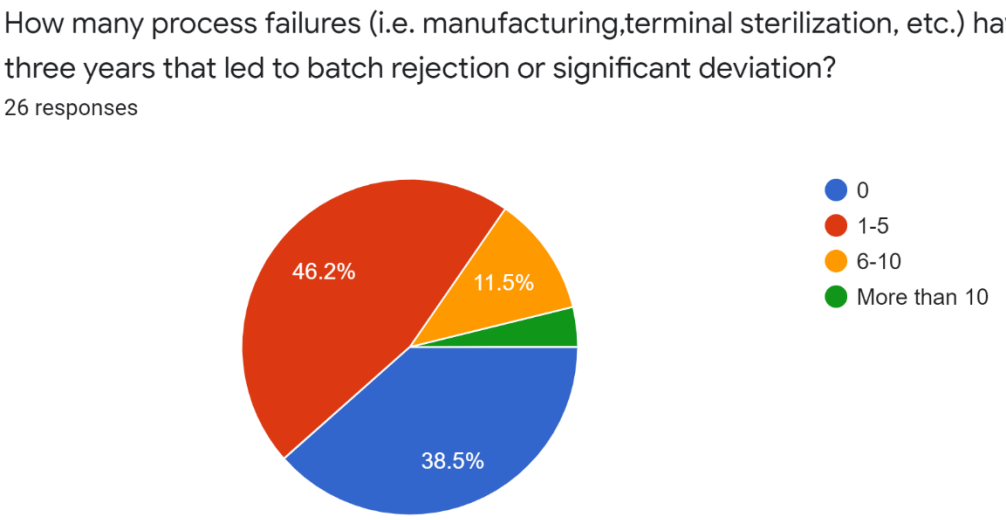
We received responses from following function,



People from different experience participated actively in the survey.



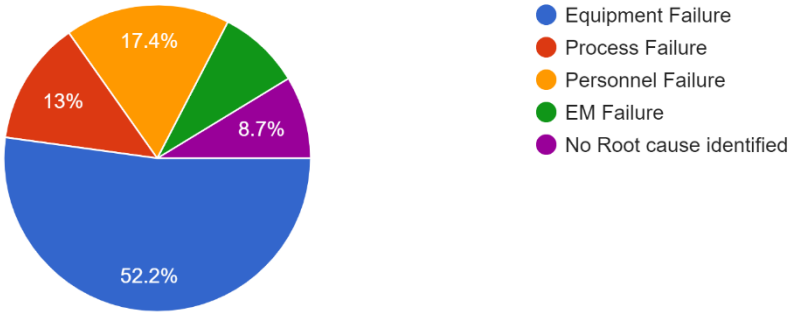
Majority of the participant from 0-5 Year experience, however people from different experience group are participated in the survey.



1-5 incident/3 year are recorded or observed due to failure. Next graphical presentation is going to state that which are the categories are contributing highest event.

For the majority of terminal process failures,what was the root cause related to?

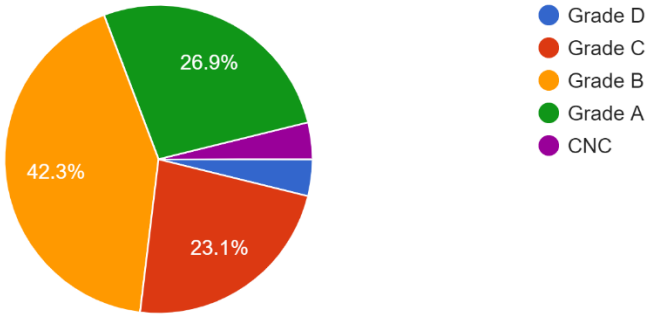
23 responses



Majority of the failure identified due to **Equipment failure** followed by personnel, process and environment failure.

What is the background environment use for filling and sealing activity ?

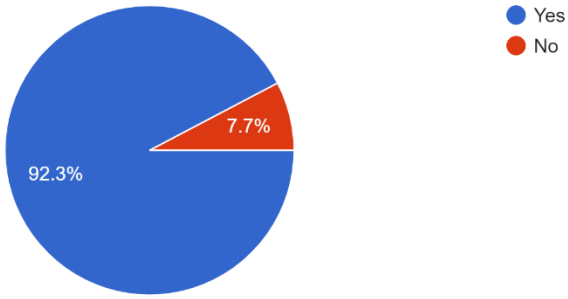
26 responses



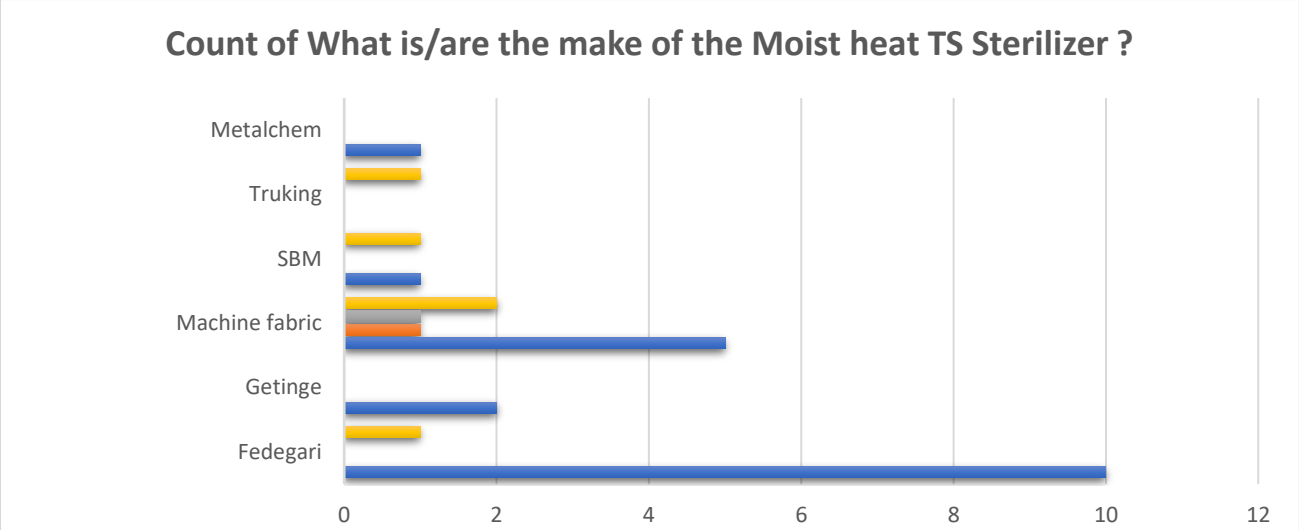
Majority of the filling background claimed as Grade B. But rare practices observed where filling performed with the background Grade D and CNC too.

Do you filtered the final compounded bulk with 0.2 micron filter before filling in to container?

26 responses



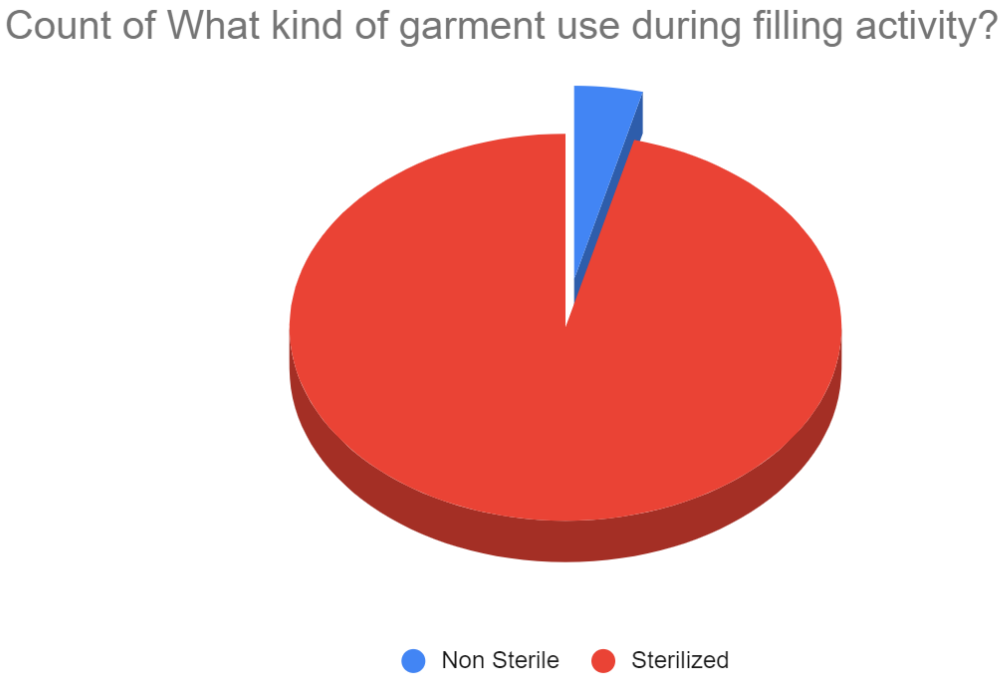
Majority of the manufacturer filtered final bulk with 0.2-micron filter before filling and sealing activity.



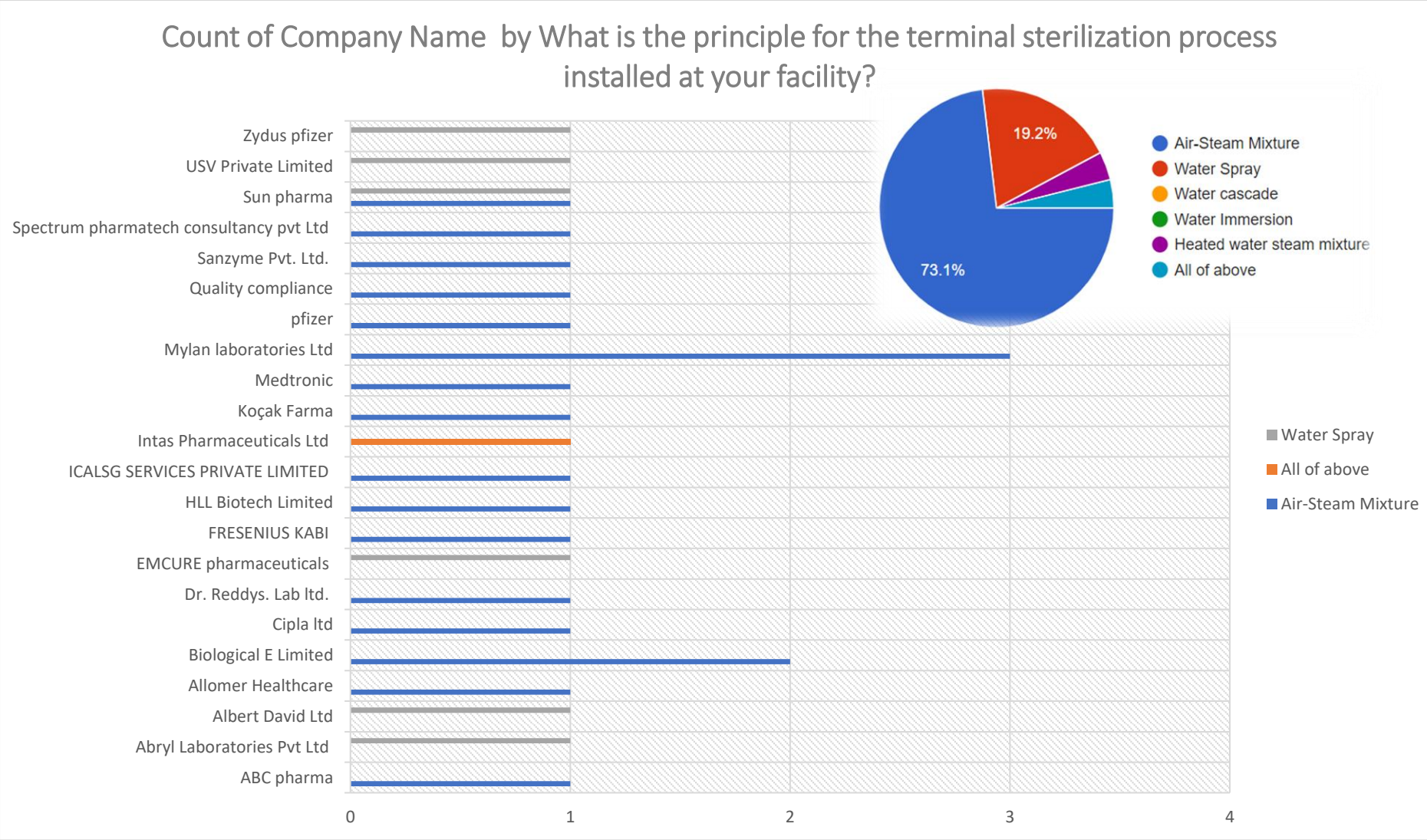
	Fedegari	Getinge	Machine fabric	SBM	Truking	Metalchem
Water Spray	1		2	1	1	
Heated water steam mixture			1			
All of above			1			
Air-Steam Mixture	10	2	5	1		1

Fedegari, Getinge and Machine fabric are the most used sterilizer brand identified through survey in India. A

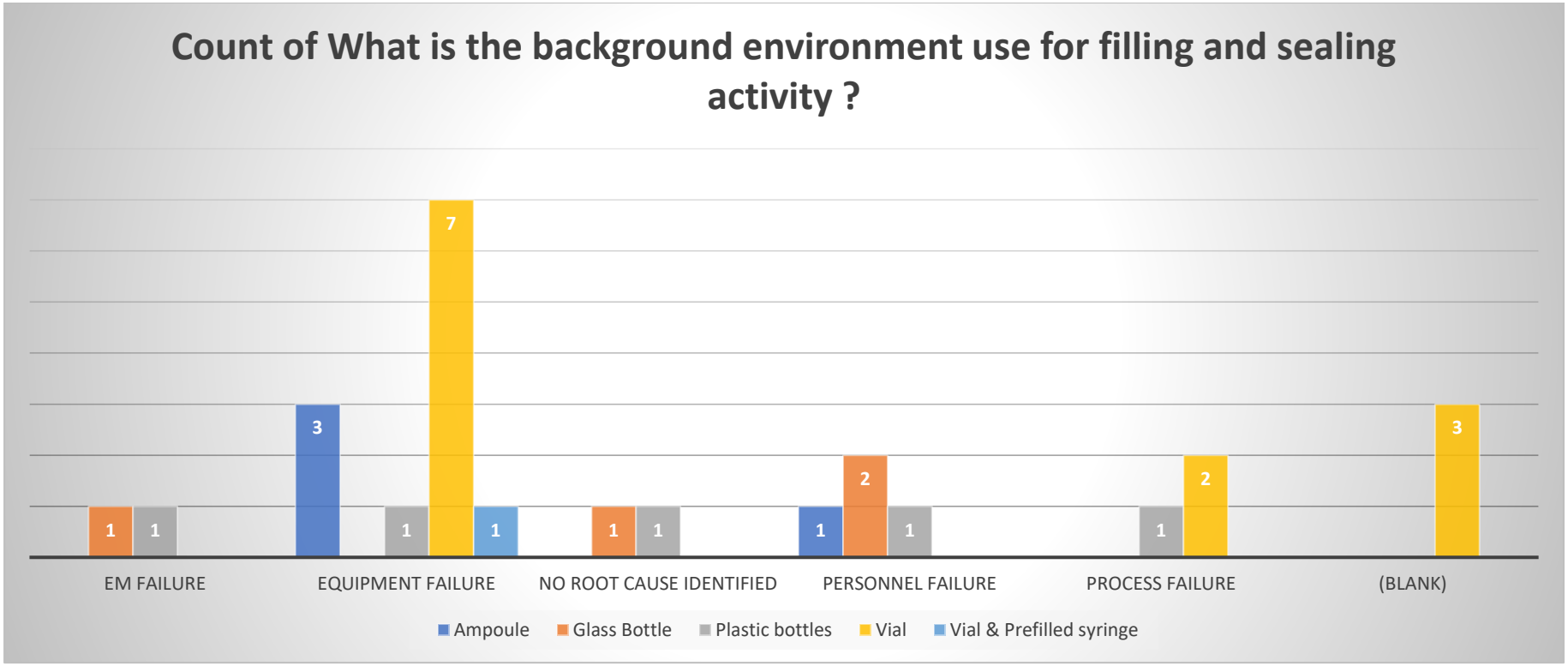
Note: We don't promote any sterilizer manufacturer brand, data was published here based on the responds received during survey. As all the details collected based on the voluntarily inputs received from industry expert as part of this survey therefore author/publisher of this report does not take responsibility on the reliability of the data presented here.

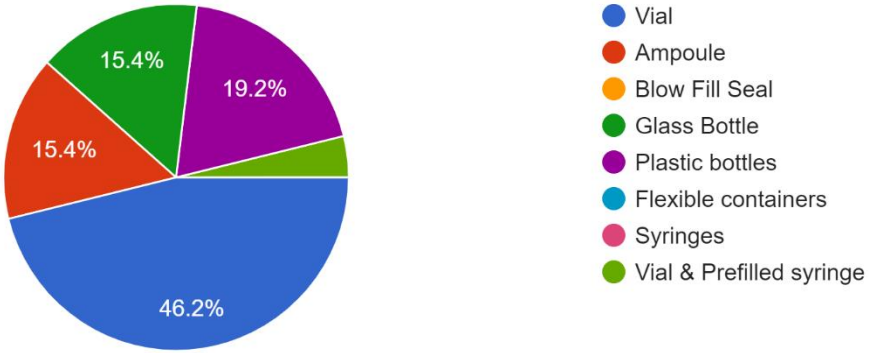


96% Organizations responded that they are using sterilized garment during filling and sealing activity.



It was identified that **Air-steam mixture** is the most applied technique used in the organization.



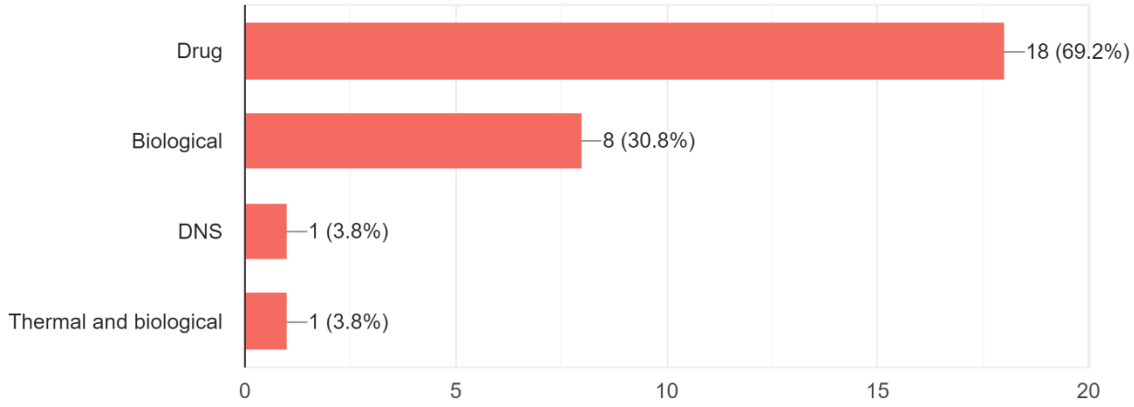


Filling and sealing of vials are the complicative process identified through this survey. Majority of the failure identified under equipment category. Although we should know that Vials are the largely manufactured product at industry as per survey.

#(blank) represent uncategorized failure event

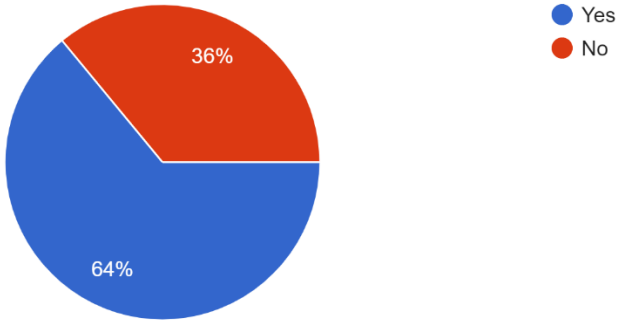
What types of products do you sterilize using the Overkill Cycle Design Approach? (Check all that apply)

26 responses



Do you use Parametric Release for TS Product?

25 responses



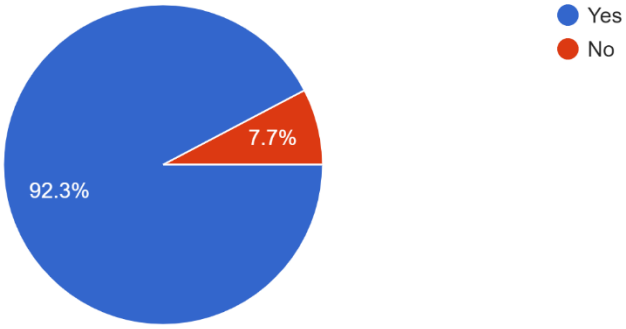
64% respond we received on the use of Parametric Release at Industry.

What is parametric release sterilization?

Parametric release is defined as a sterility assurance release program where demonstrated control of the sterilization process enables a firm to use defined critical process controls, in lieu of the sterility test, to fulfill the intent of 21 CFR 211.165(a), and 211.167(a).

Do you utilize the Overkill Cycle Design Approach for moist heat sterilization?

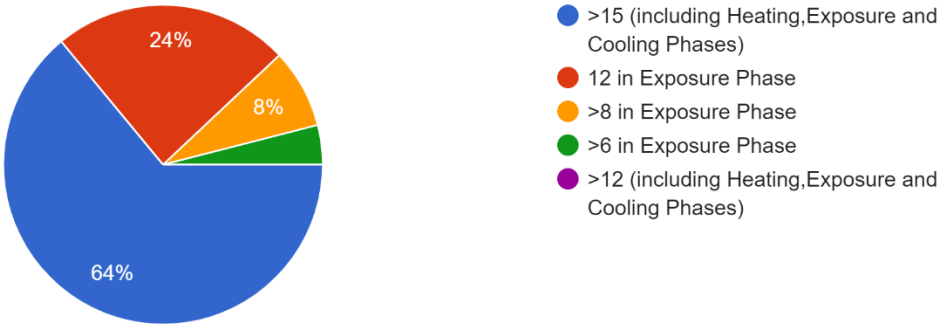
26 responses



92.3% response shows industry follow the principle of Overkill approach during sterilization.

What is the minimum F0 required for product heat penetration probes during qualification of your products sterilized with the Overkill Approach?

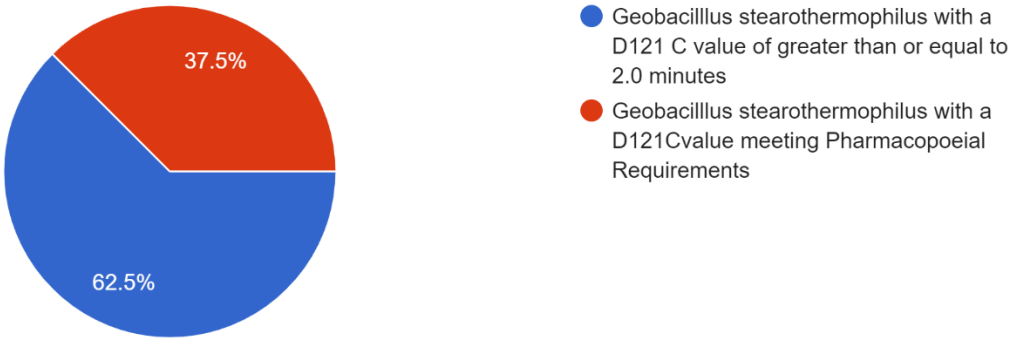
25 responses



64% survey support Heat Penetration (HP) F0>15 including Heating, Exposure and cooling phase consider as cycle design and qualification approach.

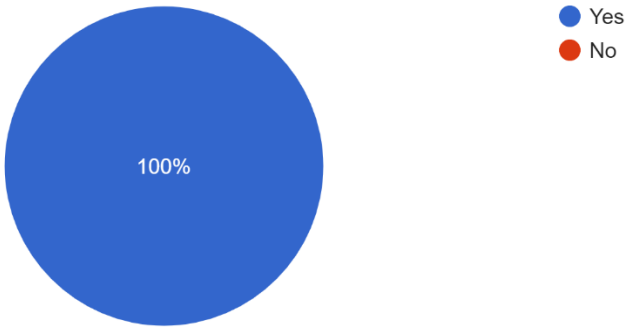
What is your requirement for Biological Indicators used to qualify the Overkill Process?

24 responses



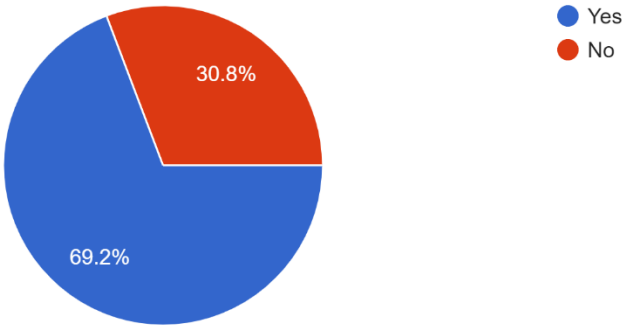
Is complete inactivation of the Geobacillus stearothermophilus biological indicator required for your Overkill qualification studies?

26 responses



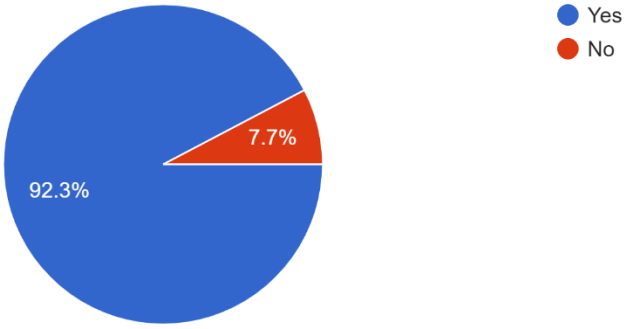
Do you calculate FBIO for your products sterilized with the Overkill approach?

26 responses



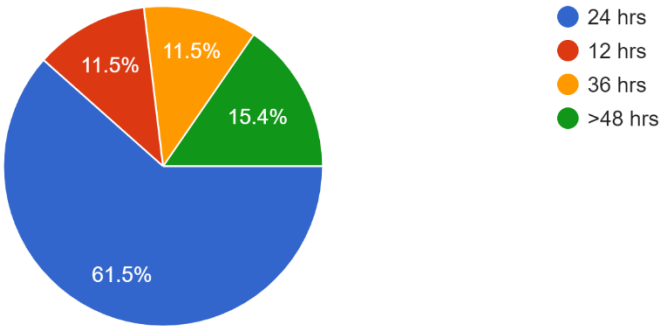
Do you filtered the final compounded bulk with 0.2 micron filter before filling in to container?

26 responses

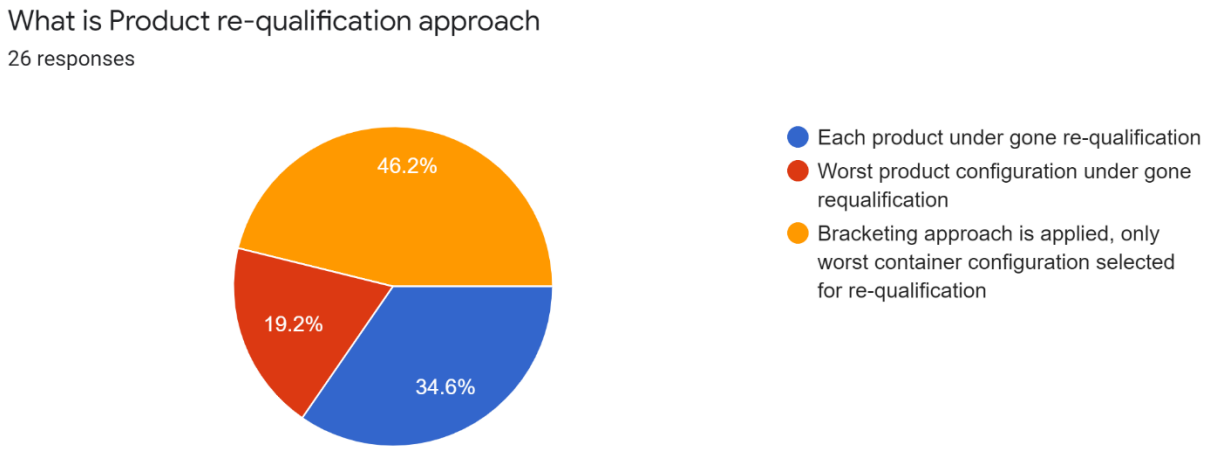


What is your established hold time (Adding of API for compounding to exposure to steam to product container with in the sterilizer)?

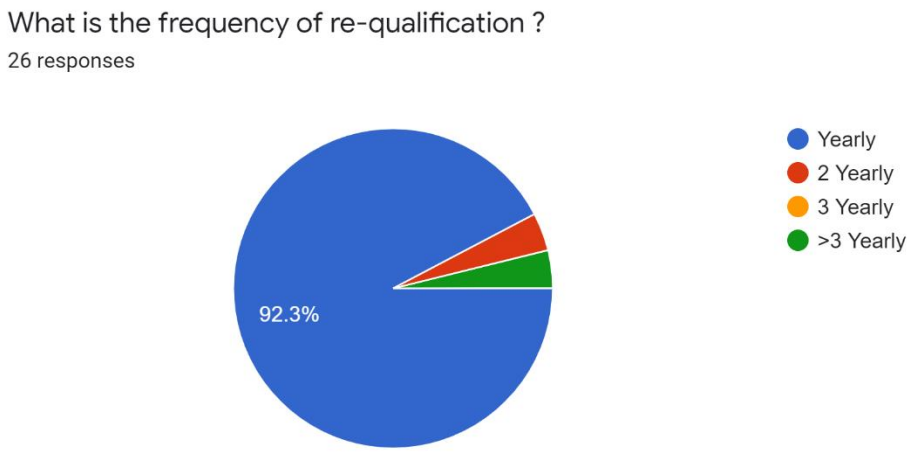
26 responses



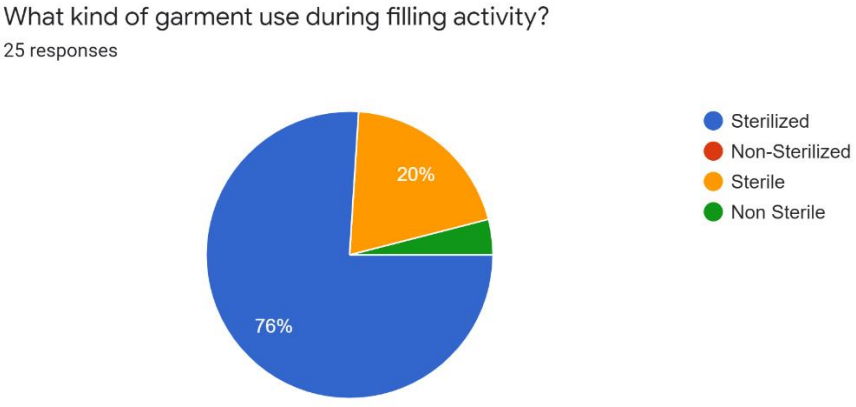
Mixed to sterilize time 12 hrs. to >48 hrs. use as a standard practice in the industry as per the survey result.



Majority people responded that they follow bracketing approach durign requalification. Although 34.6% respond suport qualifying each product container.

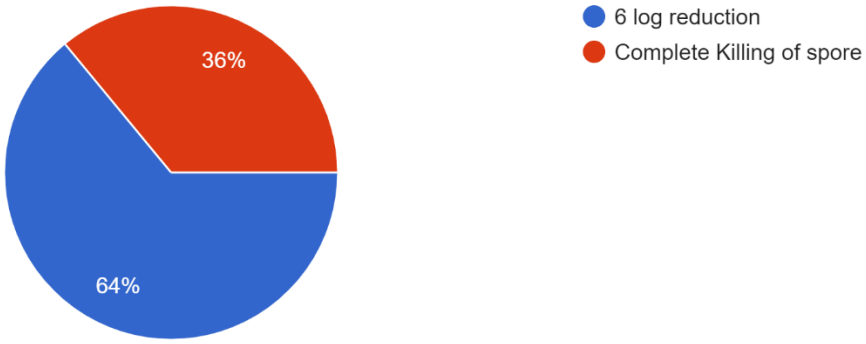


As our previous respond we got most of preffer breaketing approach and the frequency they select for requalification that is Yearly or annual. However covering all container configuration with in 2 or 3 year can be a additional chose based on risked based approach.



What are your requirements for inactivation of the BI during qualification studies with the Product Specific/Combined BI Bio-burden approach?

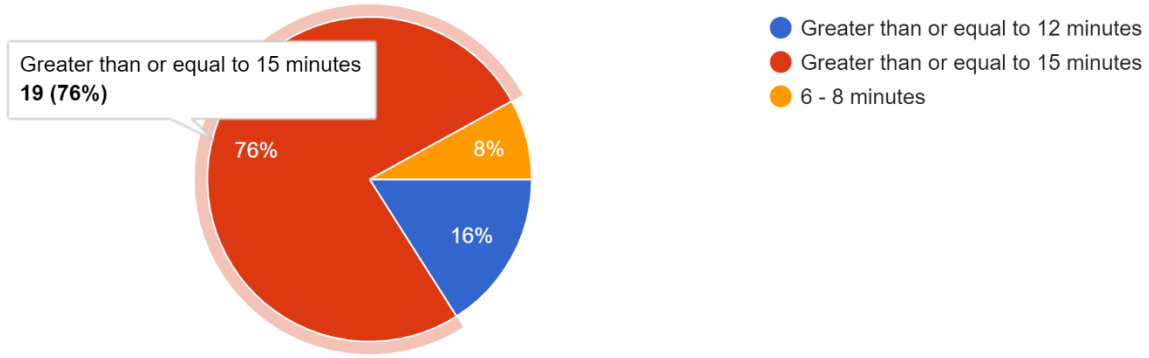
25 responses



6 log reduction of biological indicator (BI) approach was considered as conclusion of a biological inactivation during validation study against a complete killing of Bi's during process.

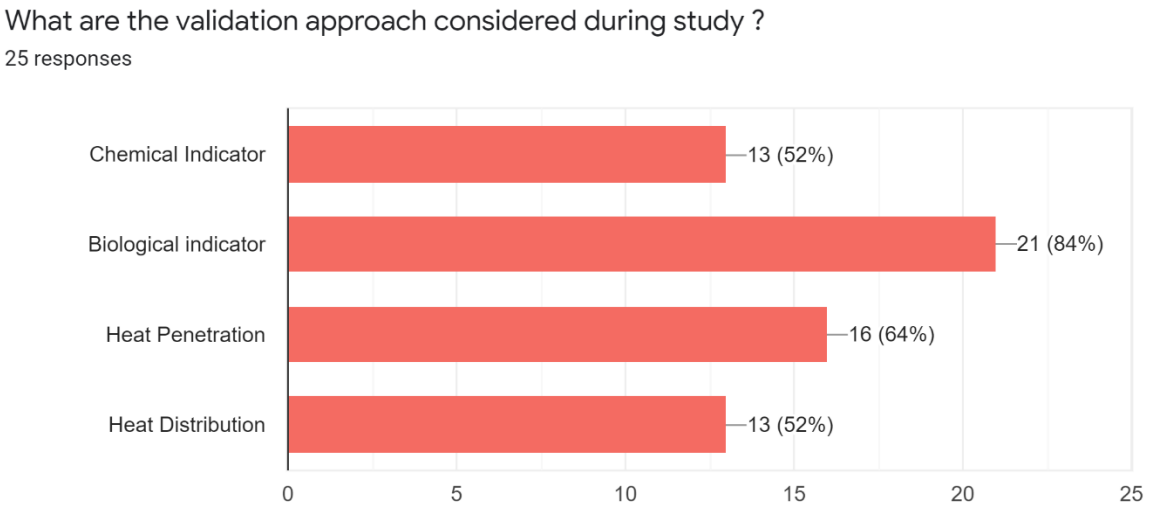
What is the minimum F0 required for product heat penetration probes during qualification of your products sterilized with the Product Specific/Combined BI Bio-burden Cycle Design Approach?

25 responses



F0>15 in Heat Penetration probe is consider as most preffered approach as part of our survey.

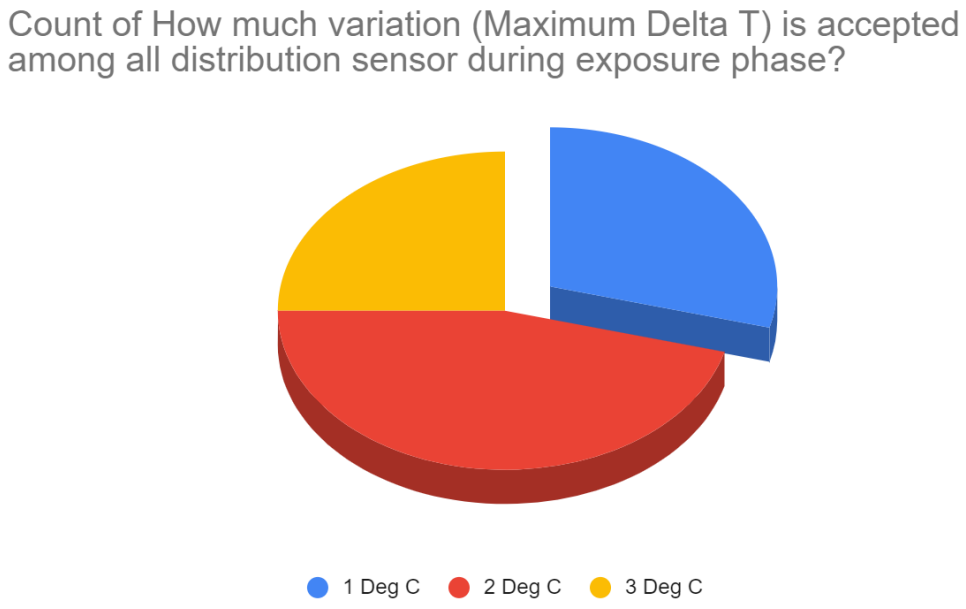
However EMA guidance **"Guideline on the sterilisation of the medicinal product, active substance, excipient and primary container"** discussed in detailed about the steam sterilisation and post-aseptic processing terminal heat treatment and corresponding data required in the quality dossier when 8>F0≥12 or F0>12.



52% of survey suport for using following technique as validation approach ,

- Chemical indication to indicate colour change during sterilization as per vendor COA
- Biological indicator to assure biological deactivation or calculate F_{BIO}
- Heat penetration (HP study) to know about thermal lethality or F_{PHY}
- Heat distribution (HD study) to know thermal profile with in the chamber during with actual load condition

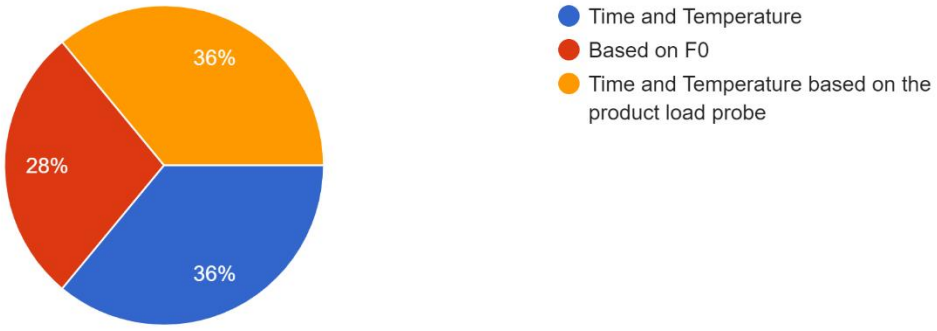
Although different approachs are also prefferd as validation approach as shown in the survey.



Maximum acceptable temperature difference (ΔT) across all the sensor during heat distribution was identfied 1 , 2 and 3 °C. 2°C is the highest temperature difference responded during survey.

How exposure period is controlled in the sterilizer?

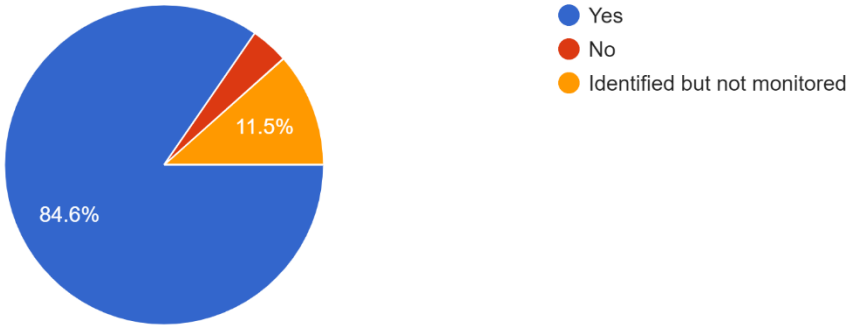
25 responses



In three mentioned technique, mixed respond received where three option selected equally during survey. Time and temperature based controlled is the most prefired technique during exposure/sterilization period control.

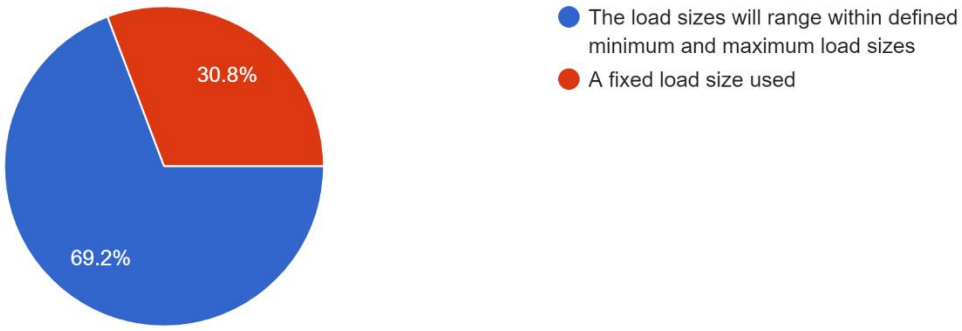
Do you identified and monitored the Cool zone?

26 responses



How the load pattern is design ?

26 responses



Maximum and minimum load qualification is the preferred technique during validation studies.