



Myth or Facts ?

Exposure of 3 min at 300°C necessary
for Depyrogenation in Tunnel (Dry heat)
Performance Qualification?



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- Not less than a 3.0 log reduction in recoverable endotoxin is used as a standard for process validation. The log reduction is calculated by determining the measured log of recoverable endotoxin in the unprocessed item minus the measured log of recoverable endotoxin remaining in the processed item.
- F_D value: Calculation of an F-Value at each probe location may be useful tool to help in assessing process comparability , evaluation process repeatability, or location of cool areas. There is no minimum FH value acceptance criteria for depyrogenation. Endotoxin inactivation efficacies cannot be accurately correlated with standard dry-heat lethality conventions (F_D) which rely upon a linear destruction model.
- Depyrogenation processes typically operate at a range of temperature from approximately 220°C and 400 °C. $F_D = 1$ is defined as the depyrogenation effect achieved by 1 min of heating at 250. *(see the calculation slide)*

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- Considering different time and temperature set point during thermal study will provide variation in delivered F_D value.
- Demonstrating ≥ 3 log reduction endotoxin with reduced time-temperature condition from those utilize in routine processing will consider as a successful depyrogenation. The F_D value achieved during the study can be compare with periodic F_D value to ensure system operated in a validated state of control and there no significant nonconformance during the process. Therefore, F_D active with the validated recipe and predefined equipment setting (e.g. time and temperature , belt speed, Air velocity and differential pressure etc.) can be consider as critical control for review during routine batch processing.
- It is important that every article in the tunnel be exposed to at least the stated temperature for not less than the stated time.

How to calculate F_D for dry heat depyrogenation (reference USP1228.1)

The F_D approach is used as a means to compare dry heat depyrogenation effects produced by processes that operate at varying temperatures. Basic mathematics can be used to calculate the depyrogenation effect produced at temperatures other than 250° to determine equivalence to that provided at 250°.

Using a reference temperature of 250° and an assumed z-value of 50°, the F_D calculation can be determined:

$$F_D = \int_{t_1}^{t_2} 10^{\left(\frac{T-250}{50}\right)} dt = \sum_{t_1}^{t_2} 10^{\left(\frac{T-250}{50}\right)} \Delta t$$

F_D = accumulated destruction

t_1 = process start time

t_2 = process end time

T = temperature at each time increment

Δt = time interval between temperature measurements

F_D Calculation considering 300 °C minimum set temperature :

$$F_D = \Delta T \sum 10^{(T-250)/Z}$$

$$F_D = 3 \times 10^{(300-250)/50}$$

$$F_D = 3 \times 10^{50/50}$$

$$F_D = 3 \times 10$$

$$F_D = 30$$

If tunnel hot zone maintain minimum 300 °C for 3-minute during dynamic condition F_D will be more than 30.

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- **Definitions:**
 - **depyrogenation process:** series of actions or operations needed to achieve the specified requirements for removal or inactivation of Pyrogens
 - **Depyrogenation:** validated process designed to remove or inactivate pyrogenic material, by a specified quantity, which is monitored by inactivation of endotoxin
 - **Inactivation:** loss of ability of microorganisms to grow and/or multiply
- **References :**
 - 5.1.12 Depyrogenation of item for parenteral preparation , European Pharmacopoeia 10.3
 - TR 3 Rev2013
 - ANSI/AAMI/ISO 20857:2021
 - USP <1228.1>

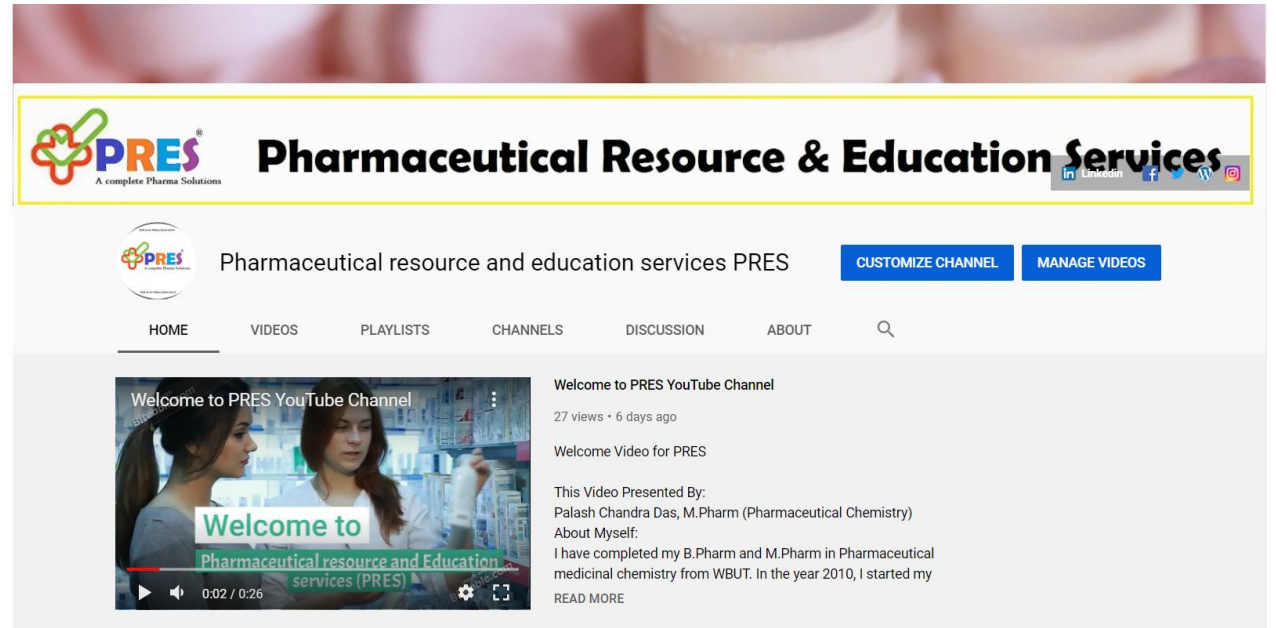


Conclusion

- Exposure of 3 min at 300°C necessary for Depyrogenation in Tunnel (Dry heat) Performance Qualification?
 - Consider as myth , A 3-log₁₀ reduction of a standard endotoxin challenge is typical; however, a lower level of reduction can be validated, provided that a programme is in place to ensure that pyrogen levels are controlled to the validated limits.



Thank You



The screenshot shows the YouTube channel page for Pharmaceutical Resource & Education Services (PRES). The channel name is "Pharmaceutical resource and education services PRES". The channel banner features the PRES logo, which consists of a stylized green and red cross with the text "PRES A complete Pharma Solutions" and "Pharmaceutical Resource & Education Services". Below the banner, there are navigation tabs for HOME, VIDEOS, PLAYLISTS, CHANNELS, DISCUSSION, and ABOUT. A search icon is also present. The main content area displays a video titled "Welcome to PRES YouTube Channel" with a thumbnail showing two women in a laboratory setting. The video description includes the text: "Welcome Video for PRES", "This Video Presented By: Palash Chandra Das, M.Pharm (Pharmaceutical Chemistry)", "About Myself: I have completed my B.Pharm and M.Pharm in Pharmaceutical medicinal chemistry from WBUT. In the year 2010, I started my", and a "READ MORE" link.



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