WHAT IS CONSIDERED CONFORMING PRODUCT FOR UNDERDOSED RADIATION-STERILIZED PRODUCT?

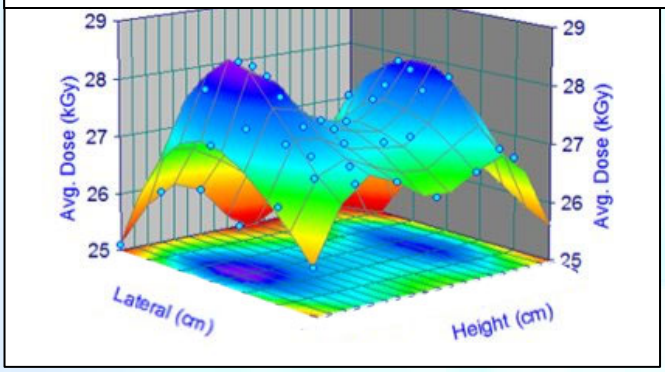
RISK-BASED FACTORS TO CONSIDER

Question:
D_{ster} = 25 kGy, dose delivered = 24.8 kGy
Is the product conforming to 10^{-6}?
Is there any potential impact to patients?

How do we define sterile product?
Typically: 10^{-6} SAL — What is meant by 10^{-6}?
Does $10^{-5.95} = 10^{-6}$? — Does $10^{-5.5} = 10^{-6}$?
ISO 11137-2 does not specify significant figures (e.g., 10^{-6}, $10^{-6.0}$ or $10^{-6.00}$).
Considering all variables, SAL 10^{-6} might be possible even when D_{ster} is not achieved during processing.

Understanding VD_{max}^{25}
Verification dose allows ±10%
Example: 300 CFU = target dose of 8.6 kGy, range of 7.7-9.5 kGy
Delivered dose from initial or recent verification dose: 8.1-9.1 kGy
Max dose of 9.1 → Could be target dose of 8.3 kGy = 24.7 kGy
(AAMI TIR76 VD_{max} Calculation Tool)
Therefore: data might support D_{ster} of 24.7 kGy for 10^{-6}.
Also consider current bioburden with TIR76 tool

What percentage of product receives the min dose?
Typically quite small: if 10% of a product box was underdosed, is it possible that the products still achieved an SAL of $10^{-6.0}$ overall? Can individual boxes in irradiation container be segregated?



What SAL must be met with the product?
Is SAL of $10^{-5.95}$ acceptable from risk assessment?
Total Log Reduction = TLR — Product Bioburden = BB
Delivered Dose = DD — Average D value = D_{10}
$SAL = TLR - Log_{10}BB$ and $TLR = DD / D_{10}$
Combined: $SAL = (DD / D_{10}) - Log_{10}BB$
Then: $D_{10} = DD / (SAL + Log_{10}BB)$
→ Solve for D_{10}
→ Use D_{10} with DD to calculate SAL obtained (SAL_O)

BIOBURDEN COUNT

DD	1 SAL_O	10 SAL_O	100 SAL_O	300 SAL_O	1,000 SAL_O
24.9	6.0	6.0	6.0	6.0	6.0
24.8	6.0	5.9	5.9	5.9	5.9
24.7	5.9	5.9	5.9	5.9	5.9

Takeaway:
24.9 kGy might give an acceptable SAL

If 10^{-6} is required (i.e., not $10^{-6.0}$)

DD	1 SAL_O	10 SAL_O	100 SAL_O	300 SAL_O	1,000 SAL_O
24.9	6	6	6	6	6
24.8	6	6	6	6	6
24.7	6	6	6	6	6
24.6	6	6	6	6	6
24.5	6	6	6	6	6
24.4	6	6	6	6	6
24.3	6	6	6	6	6

Other questions to consider:
Why did the product receive <D_{ster}?
Investigation may still be warranted.
Do you usually obtain 0 positives?

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