Title: Tissue Disinfection Process Characterization and Validation – Determining Log Reductions for Microorganisms and Viruses – The Science Behind the Testing and Case Studies

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Background: In establishing a tissue disinfection process it is critical to understand how the various parameters of concentration, temperature, time, and other factors play a role in the log reduction capability of the process for both microorganisms and viruses. Even determining the proper mixture of antibiotic types and relative concentrations can be difficult and can influence years of future tissue to be processed. There are a number of factors to consider when characterizing and then validating a tissue process.

This presentation is intended to describe the science and concepts behind tissue disinfection process characterization and validation. Although case studies will be referenced, the primary focus is on the science, not the data. The presentation will include critical factors to assess, provide guidance on setting up a process characterization and validation, and help describe proper interpretation of data. Other topics such as establishment of acceptance criteria and using data received over time to look back and adjust criteria will be addressed. Lastly, case studies will be shown including troubleshooting particular aspects of characterization and validation.

Hypothesis: This presentation is intended to provide concepts and details for tissue disinfection process characterization and validation rather than providing data from a specific study. Thus, there is not a specific hypothesis except that these types of studies are used to fully understand the capabilities and limitations of tissue disinfection processes.

Methods: As part of the presentation some methods used to determine log reductions of microorganisms and viruses will be described. These include methods such as inoculation, extraction and enumeration, and calculation of log reductions.

Results: In the presentation, results will be provided to be used as examples for calculation of log reductions, including issues that can arise depending on the data that are gathered. Since the focus of the presentation is on the process of evaluating data, rather than evaluating results from a specific validation, the results to be used as examples are not provided as part of this abstract.

Conclusions: The presentation will describe approaches to making conclusions based on the type of data obtained and will describe situations where additional testing might be warranted or where changes to the disinfection process might be appropriate.

Ethical Considerations: There are no ethical considerations to consider in this abstract.

TISSUE DISINFECTION PROCESS CHARACTERIZATION AND VALIDATION

PRIMARY QUESTIONS

- How many log reductions does the process achieve?
- Which steps of the process provide those log reductions?
- How many log reductions does each step provide?
- How much do the variables (e.g., concentration, temperature, time) influence the log reductions?
- Are all of the antibiotics in my cocktail necessary?
- Are there acceptance criteria for a specific claim for the tissue?

This validation will support years of tissue processing – make it right and fully understand it from the beginning!

PROCESS VALIDATION

Now the process is characterized, when it is all put together, does everything add up correctly? All log reductions from characterization might not be additive for the overall process; this is verified in validation. Thorough characterization means fewer variables to assess in validation.

PROCESS CHARACTERIZATION

Understand what each step of the process is intended to accomplish and to what level. Gather data to support that each step meets the expected criteria. This is where potential variables in each step are assessed (e.g., time, temperature, concentration). Characterization should be completed prior to validation.

If process characterization is not performed

- When process validation does not meet expected criteria, the company has no data to explain what has likely caused the failure.
- In routine processing, if one aspect of the process is out of specification with a batch of tissue (e.g., temperature is off by 2°C), there are no data to support that the tissue can be released.
- When a change to an ingredient or a new supplier is necessary, there are no data to compare to for assessing change control.

Don't fall into these problems!

WHICH MICROORGANISMS TO INCLUDE

Generally

- One from each general category (e.g., Gram + cocci, Gram – rod, etc.), typically from USP <71>
- Common tissue or environmental microorganisms
- Can include microorganisms of concern (e.g., group A strep)
- Not required to test every microorganism of concern or from tissue; make a rational selection to cover most types

IMPORTANCE OF NEUTRALIZATION STUDIES

Is a high log reduction due to microbial kill or due to inhibition? Neutralization studies are critical for process characterization and validation.

- Perform step or process
- Remove same aliquot to be used for routine testing
- Filter aliquot and rinse filter (if needed)
- Inoculate final rinse with ≤100 CFU of each microorganism
- Determine titer of inoculum at the same time
- Typical acceptance is ≥50%

STANDARDS AND GUIDANCE DOCUMENTS

- AATB Standards for Tissue Banking, largely Section K
- AATB Microbiological Process Validation & Surveillance Program, Sections II and III

CASE STUDY

Target inoculum titer for all was 10^6 CFU. Exposure was to an antibiotic cocktail. Only some results are provided.

MICROBE	EXPOSURE	AVG LOG REDUCTION
A brasiliensis	18-hour	0.9
	24-hour	1.0
	36-hour	1.0
C albicans	18-hour	2.0
	24-hour	3.7
	36-hour	5.1
B subtilis	18-hour	2.1
	24-hour	1.9
	36-hour	2.1
C sporogenes	18-hour	3.9
	24-hour	3.9
	36-hour	4.0

What timepoint should be used?
What should be considered to select the timepoint?

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