Considerations for Designing a Microbial Challenge Study

Test Solutions:

Microbial challenge studies should be performed on one representative batch using test solution(s) relevant to clinical dose preparation intended for storage. A bracketing approach for dose solution concentrations is recommended where applicable.

Organism Selection:

The organisms listed in USP Chapter <51> and Ph. Eur. 5.1.3 are recommended to be used in the study. As these organisms represent a broad range of organisms, it is not required to include additional skin or nosocomial organisms.

Organism	Media Type	Incubation
Aspergillus brasiliensis	SDA	20-25°C
Candida albicans	SDA	20-25°C
Escherichia coli	TSA	30-35°C
Pseudomonas aeruginosa	TSA	30-35°C
Staphylococcus aureus	TSA	30-35°C

Method Suitability:

Verification of the method for microbial recovery from the sample preparation is needed to establish valid testing parameters. Acceptable percent recovery is 50-200%.

Time Points:

Studies should have a minimum of four time points, including Time 0. If growth is expected, inclusion of additional time points is recommended. The selection of the final time point should be at least double the intended in-use hold time.

Temperature Conditions:

The selection of temperature conditions to test should be based on the desired hold conditions of the product. Performing separate studies at each intended temperature condition is recommended, even if the product is stored at temperature cycling conditions (e.g., 2-8°C then 20-25°C).

Testing Container:

If possible, the study should be conducted using a container representative of the container used in the clinic for administration.

If an infusion solution is prepared in IV bags for administration, the study should be conducted in IV bags, if possible.

Study Controls:

At minimum, inoculum controls should be performed at Time 0 to confirm the inoculum level for each microorganism. The inoculum level should be between 10-100 CFU/mL.

For products that require dilution in the clinic prior to administration, positive controls for each organism should be performed at the initial time point in the diluents tested to demonstrate recovery in the diluent. The positive controls can also be used as the inoculum control.

Negative product controls should be included in the study design. The negative product control acts as a manipulation control.

Data Evaluation and Interpretation:

Acceptable criteria for support of storage/in-use conditions is not more than 0.5 $\log_{10}$ increase from the inoculum control concentration. Results should be evaluated for each time point.

Data should also be evaluated for any observable upward growth trends (defined as >0.3 $\log_{10}$ increase).