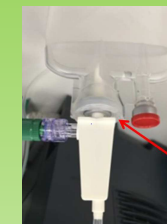


Introduction

As part of the implementation of standardized doses of anti-cancer drugs, the pharmacy wants to manufacture bags of chemotherapy in batches and in advance. The current manufacturing process involves purging the tubing with the reconstitution solvent connected to the bag. The connection of the tubing to the bag represents a critical point of microbial contamination.

Objective: Validation of the **microbiological stability** and **physical integrity** of the bags connected to the purged tubing during the entire storage period.



Methods

Microbiological stability

Mediafill test (n=550 bags)

3 arms :

- Standard (n=150, 30 bags per time)
- Worst-case → Voluntary contamination of critical point of microbial contamination (n=375, 15 bags per germ and per time)
- Positive control → Germ inoculation inside the bag (n=25, 1 bag per germ)

Bag challenge was carried out at day 0,10,30,60,90 :

- ✓ *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *E.coli*, *Candida albicans* & *Aspergillus brasiliensis*
- ✓ 10³ CFU/ septum bag (worst-case) et 10 CFU/bag (positive control)

Incubation at 20°C for 15 days and visual observation

Fertility test of the culture medium (casein trypticase soya casein) at all study times

Physical integrity

- Bubble point test at the critical point connection (5 bags tested after 0,10,30,60 and 90 days of storage)
- Evaluation of solvent evaporation (bags and infusion lines)

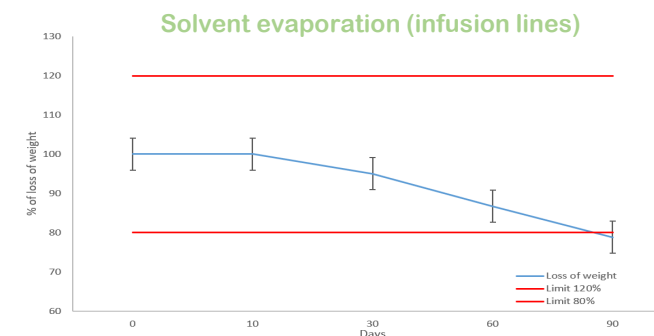
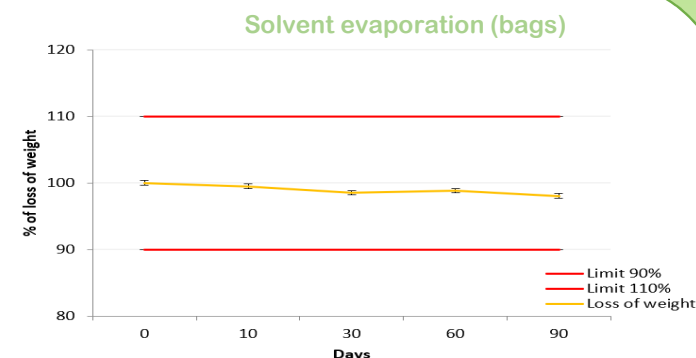
Results

Microbiological stability

- No contaminated bag in the worst-case arm (from D0 to D90)
- No contaminated bag in the standard arm (from J0 to 90)
- Positive controls: Observed growth
- Fertility and sterility tests of the culture medium: in compliance

Physical integrity

The bubble point tests all conformed between day 0 and day 90.



Discussion – Conclusion

The connection of the tubing to the bag does not lead to microbiological contamination under the storage conditions studied. Due to the evaporation of the solvent (out of specification) from the tubing at day 90, bags connected to a purged tubing can be stored for **60 days**.