Development of a challenged Media Fill Test for aseptic process qualification of a pediatric parenteral nutrition compounder

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Objective :
A physico-chemical and microbiological plan is established to qualify a new pediatric parenteral nutrition (PPN) compounder: the BAXA® ExactaMix 2400.
For aseptic process validation, we decided to implement a **challenged *Media Fill Test*** to improve the sensitivity.

Material & Method :

MICROBIOLOGICAL QUALIFICATION

PPN production : ISO grade 5 horizontal Laminar Airflow Cabinet

MEDIA FILL TEST

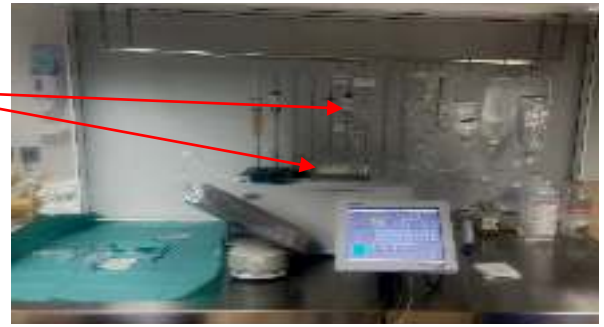
- substitution of all drugs by culture media (tryptone soja broth)
- according to simulate a real production
- Limits : level of production is too low to safely reveal microbial contamination occurrence

CHALLENGED MFT (cMFT)

Classical MFT with **intentional contaminations** by microorganisms[1] according the results of a Failure Mode, Effects and Criticality Analysis (FEMEA)[2] :

- 47 failure modes with 19 regarding the preparation process
- critical steps :
  - disinfection of the upper surfaces of vials stoppers (highest score)
  - aseptic failure during the manipulation such as misuse of gloves (elevated score)

Bacterial contamination



Results :

Concept of the cMFT

Introduce bacterial contamination to critical steps :
- the upper surfaces of vials stoppers
- the valve set
- the manipulator gloves

Worst-cases conditions :
↑ sensitivity

Escherichia coli :
- 10^6 CFU/mL
- fast-growing commensal
- referenced at European Pharmacopeia

→ **point out an aseptic compounding failure**

Visual inspection : good cleaning, disinfecting procedures, hand hygiene and garbing practices use in ISO class 5 aseptic working area

"Closed system" maintained
expected results : no microbiological growth

Each final preparation is incubated for 7 days at 32°C and 7 days at ambient temperature.

Conclusion :
Qualifications of pediatric PN compounder are essential to **guaranty sterility and quality of production** correspond to good manufacturing practices.

MFTc enhances sensibility of MFT and can *highlight possible deviations of the aseptic process.*
This practice could be applied to improve the safety of other sterile productions.

1 Sigward, E., Fourgeaud, M., Vazquez, R., Guerrault-Moro, M.-N., Brossard, D., Crauste-Manciet, S. Aseptic simulation test challenged with microorganisms for validation of pharmacy operators(2012) American Journal of Health-System Pharmacy, 69 (14), pp. 1218-1224.
2 Gratelle M.-A., Evaluation des Pratiques Professionnelles liées au processus de production des nutritions parentérales pédiatriques au Centre Hospitalier Universitaire de Bordeaux, thèse d'exercice, Limoges, 2016