

Context

- Production 5000 parenteral nutrition mixtures (PNM) per year.
- Control sodium, potassium, calcium and glucose's concentration on samples taken from the PNM
- Colorimetric assay : (Biochemistry Laboratory)



Non-compliant (NC) when the difference between the target and assayed concentration is higher than 20%.



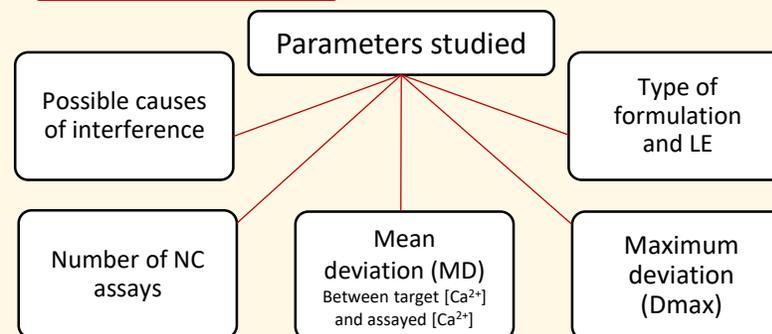
1) **NC** received : Ca determination of ternary PNM containing SMOFLIPID® (SMOF) or MEDIALIPID® (MEDIA), but not for binary PNM.

2) Hypothesis : **interferences related to lipid emulsions (LE)** ? A difference in concentration between the first NC assay and a second control assay suggests interference during the assay and not an incident during the production.

3) **Objective** : To determine the origin of the non-conformities attributable to LE.

Methods

- Retrospective** study of Ca determinations of ternary PNM :
 - From 04/04/2022 to 15/06/2022
 - Since 16/06/2022 after interference removal.
- Statistics** :
 - Student's t-test : to compare the MD comparison before and after interference removal
 - Chi-square of independence : proportion of NC dosages before and after interference removal.



Results

- **Retrospective study from 04/04/2022 to 15/06/2022**: N = 186 dosages, 26 NC (14%) 10 types of standard formulations produced over the period including :

P2T SMOF NaCl



- Diluted formulation of SMOF : 1 NC dosage

P2T MEDIA



- Concentrated formulation of MEDIA : 3 NC dosages

P4T SMOF/P2T SMOF



Concentrated formulation of SMOF :

- 52 dosages of Ca :
 - 17 P2T SMOF and 35 P4T SMOF
 - 22 NC dosages (42%) : 6 P2T SMOF and 16 P2T SMOF
- MD = 15,36 ± 10,69%
- Dmax = 38%

Automat's data sheet
(Roche Hitachi System Cobas c 701/702®)

- Causes of interference:
 - Bilirubin's concentration
 - Haemoglobin's concentration
 - Lipémique index (LI) > 1000 mg/dL**

➔ **An automatic dilution at 1/1,16** is performed by the automaton when LI>1000 mg/dL.

PNM's lipemic index :

- P2T SMOF : 3313 mg/dL
- P4T SMOF : 3248 mg/dL
- P2T MEDIA : 1600 mg/dL

- **Since 16/06/2022*** :
P4T SMOF/P2T SMOF



- A 1/5th dilution is programmed** before the "P2T SMOF" and "P4T SMOF" assays → N = 56 assays.
- Dmax = 8.9%

DM = 3,83 ± 2,38%
p=4,05x10⁻¹³

0 NC dosage
p=9,28x10⁻⁸

* Results update to 12/09/2022

Discussion

- PNM containing SMOF and MEDIA **have too high LI for the assay**.
- Automat's dilution was not enough for concentrated SMOF formulations → A higher dilution results in more accurate assays and an improvement in the deviation between the target and actual measured value.

- The automatic dilution of the MEDIA PNM is sufficient to limit the interferences but does not allow to totally eliminate the NC assays (3 on this period). The same work should be done on these PNM to verify if a 1/5 dilution reduces NC and MD in the long term,