

OBJECTIVE

Evaluate physico-chemical stability of 0.54 mg/mL busulfan injections in polypropylene (PP) syringes and infusion bags at $25 \pm 2^\circ\text{C}$ and $5 \pm 3^\circ\text{C}$

CONCLUSIONS

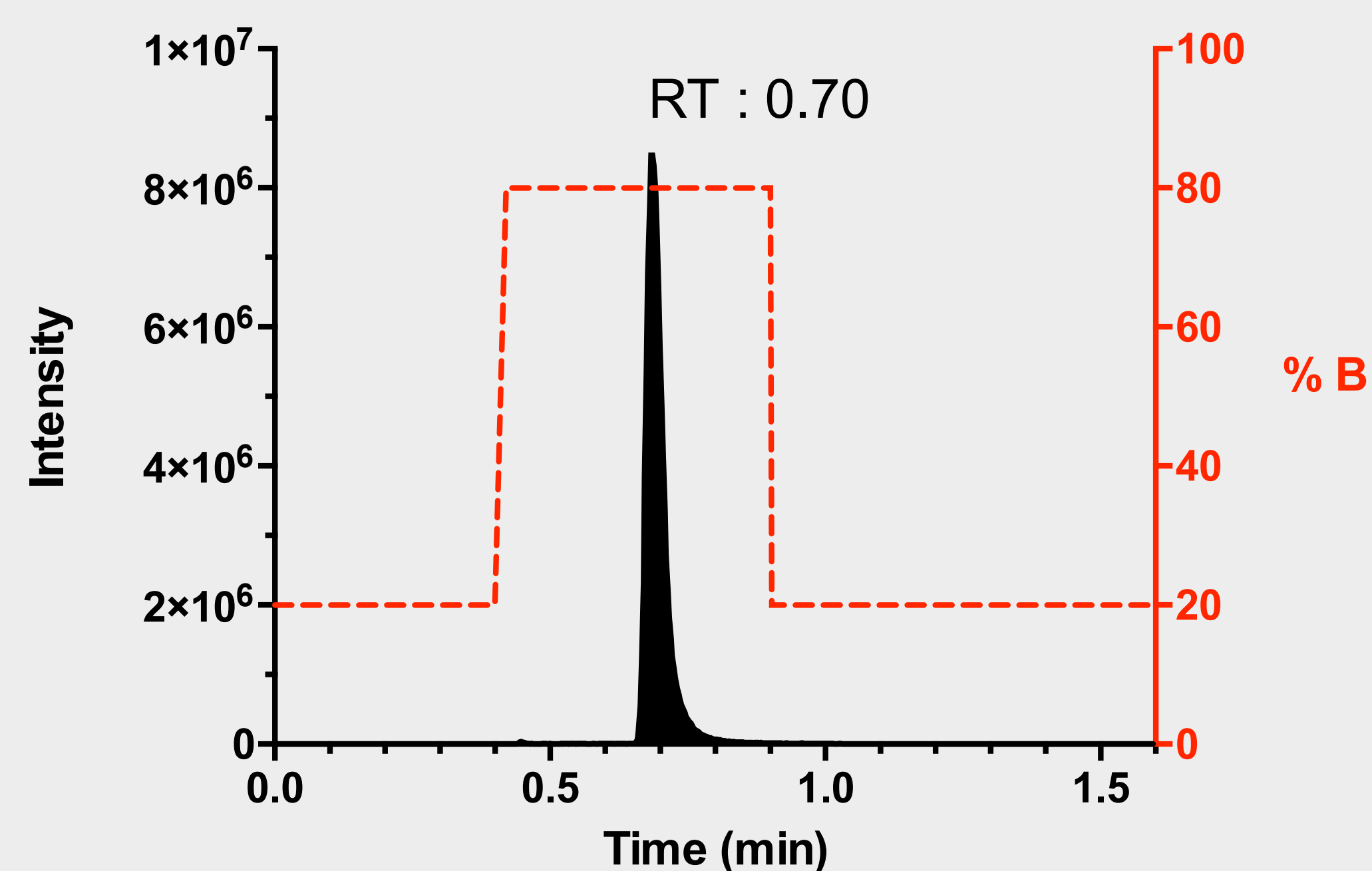
- ✓ Storage at $5 \pm 3^\circ\text{C}$ offered best stability
- ✓ 30 hours in PP-syringes
- ✓ 12 hours in 100 mL PP-infusion bags
- ✓ 9 hours in 500 mL PP-infusion bags

BACKGROUND

Busulfan is extensively used in myeloablative regimen prior to hematopoietic stem cell transplantation. Administration every six hours for four consecutive days and low stability induces organizational problems for hospital pharmacies. A few studies have already been conducted to investigate the stability of diluted busulfan solutions however published results showed an important variability.

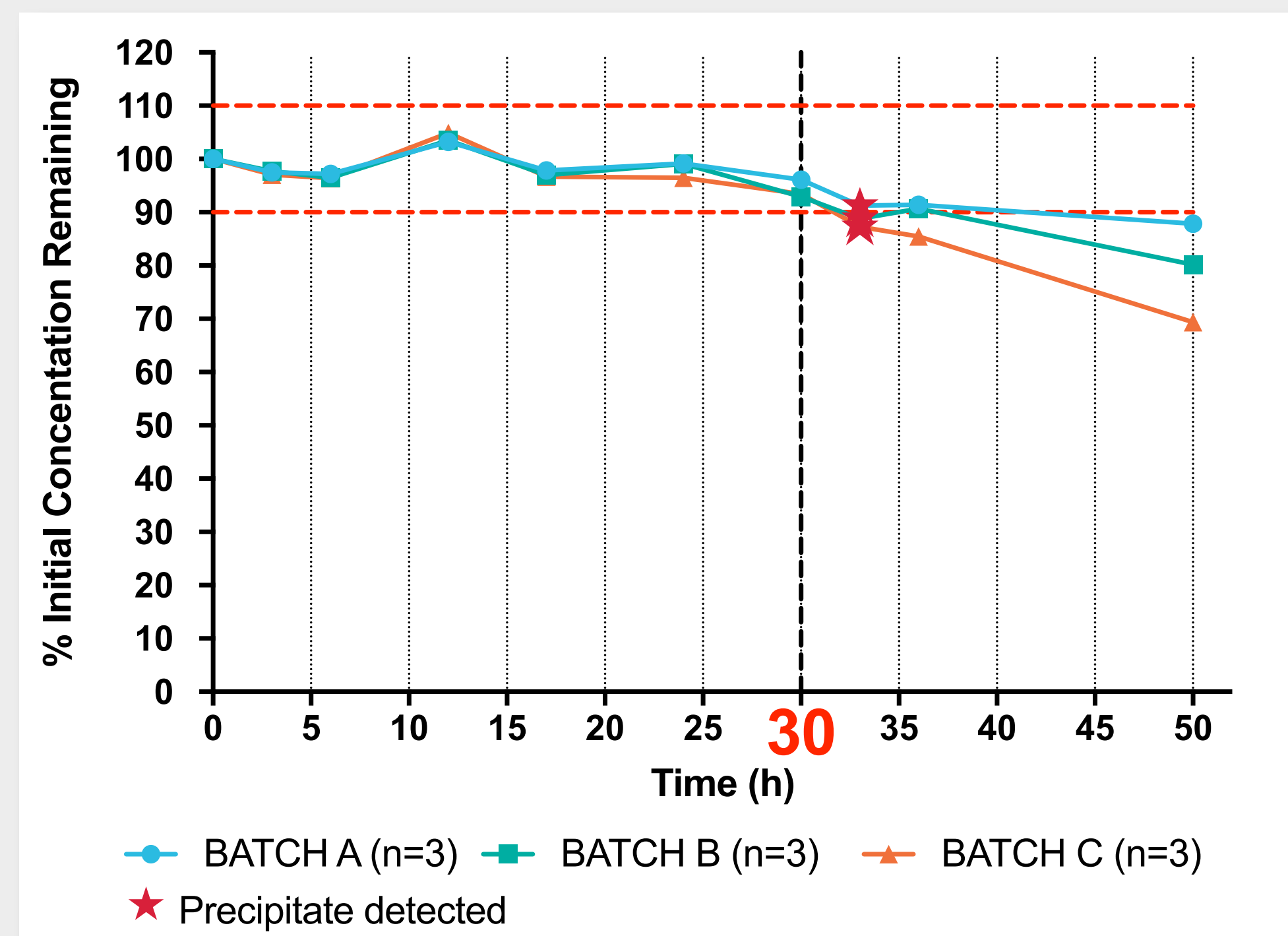
MATERIAL & METHODS

Number of batches: 3 Busilvex[®] batches
Concentration: 0.54 mg/mL in NaCl 0.9%
Containers: PP syringes (50 mL)
 PP bags (100 & 500 mL)
Storage Temp.: $25 \pm 2^\circ\text{C}$ / $5 \pm 3^\circ\text{C}$
 (protected from light)
Analysis: Visual inspection
 Quantification by LC-MS
LC-ESI/MS Stability Indicating Method:
Mobile Phase: A : 5 mM NH_4COOH / 0.1% HCOOH
 B : Acetonitrile
Column: BEH Shield RP18 2.1x50 mm 1.7 μm
Flow rate: 0.6 mL/min
Detection: Busulfan m/z: 264.1
 $[\text{2H}_8]$ -Busulfan (Int. Std.) m/z: 272.1
Analysis Time: 1.6 min



RESULTS @ 5°C

1. PP-SYRINGES



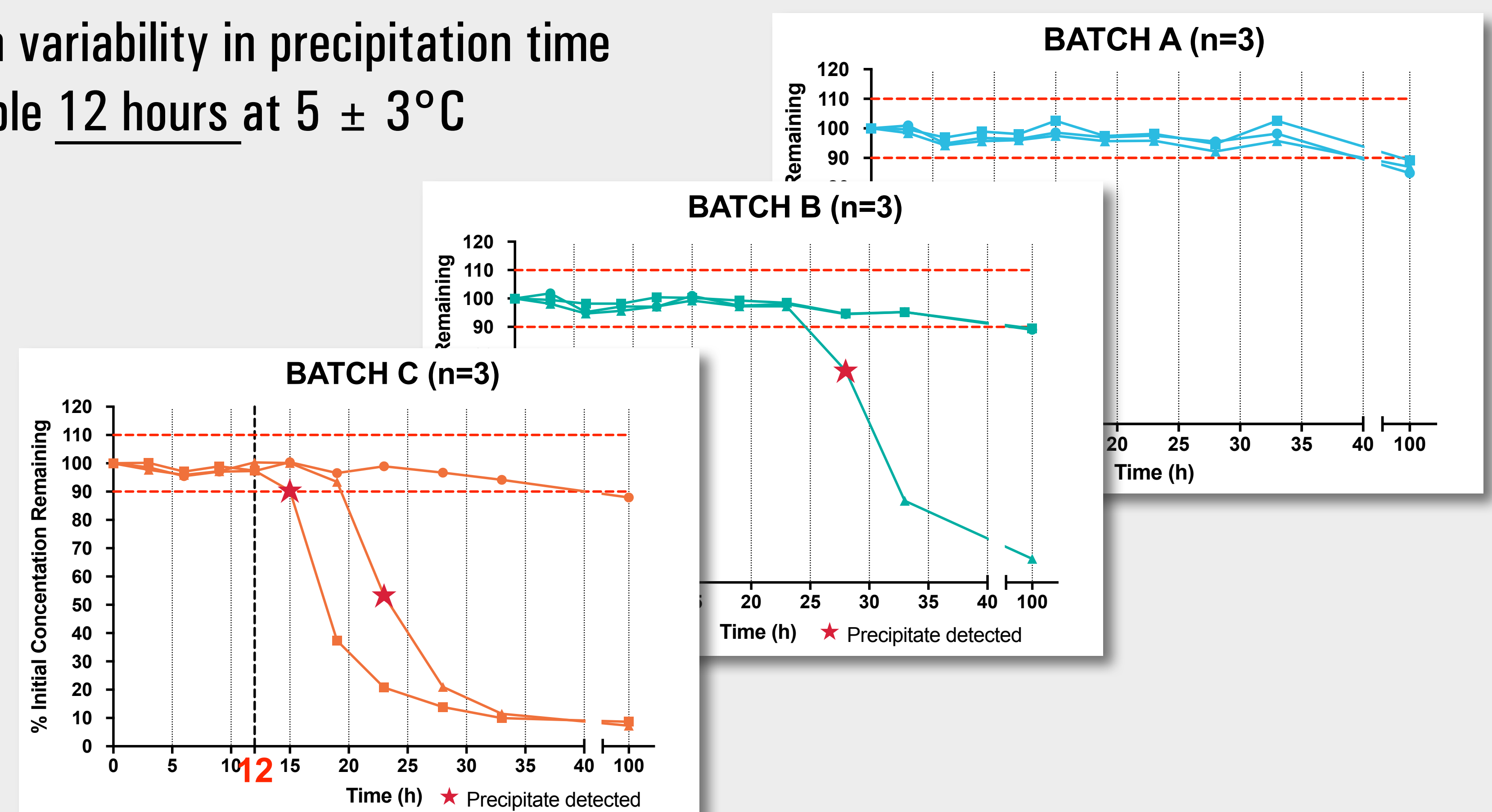
- Precipitate detected at time 33 hours for all batches
- Stable 30 hours at $5 \pm 3^\circ\text{C}$



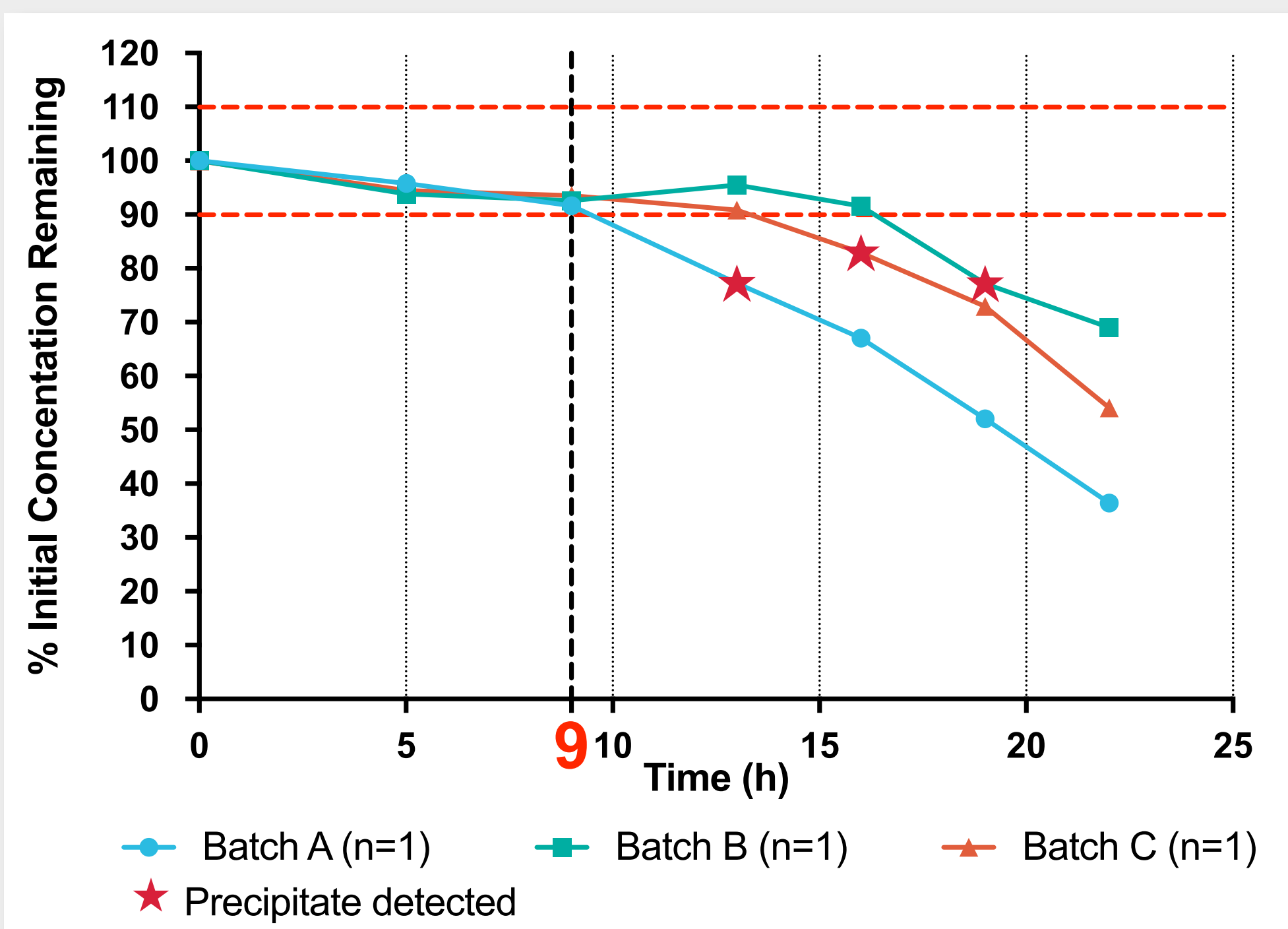
Picture of busulfan precipitates onto syringe surface

2. 100 mL PP-BAGS

- High variability in precipitation time
- Stable 12 hours at $5 \pm 3^\circ\text{C}$



3. 500 mL PP-BAGS



- High variability in precipitation time
- Stable 9 hours at $5 \pm 3^\circ\text{C}$

DISCUSSION

- Stability is strongly influenced by temperature and container type
- 2 major degradation processes:
 - Hydrolysis at $25 \pm 2^\circ\text{C}$
 - Precipitation at $5 \pm 3^\circ\text{C}$
- Extended shelf-life to 30 hours when stored in PP-syringes at $5 \pm 3^\circ\text{C}$
- Better organisation of busulfan production (one production per day)

RESULTS @ 25°C

- No precipitate detected
- Syringes : stable 12 hours
- Fast degradation (no variability)
- Bags : stable 3 hours