

Long-term stability of a generic product of piperacilline / tazobactam in glucose 5% infusion polyolefin bags at $5^{\circ}\text{C} \pm 3^{\circ}\text{C}$ after microwave freeze-thaw treatment.

M. Godet, S.Huvelle, LM Galanti, B.Bihin B, J. Jamart, JD Hecq

¹Medical Laboratory, ²Department of Pharmacy, ³Scientific Support Unit, ⁴Drug Stability Research Group
 CHU Dinant Godinne | UCL Namur 1, avenue Therasse, 5530 Yvoir



Background

- The out of stock of the brand name of piperacilline/tazobactam require the use of a generic product.
- But little chemical stability data are available for the preparations of ready to use infusions by a centralized intravenous additive service (CIVAS)

Objective

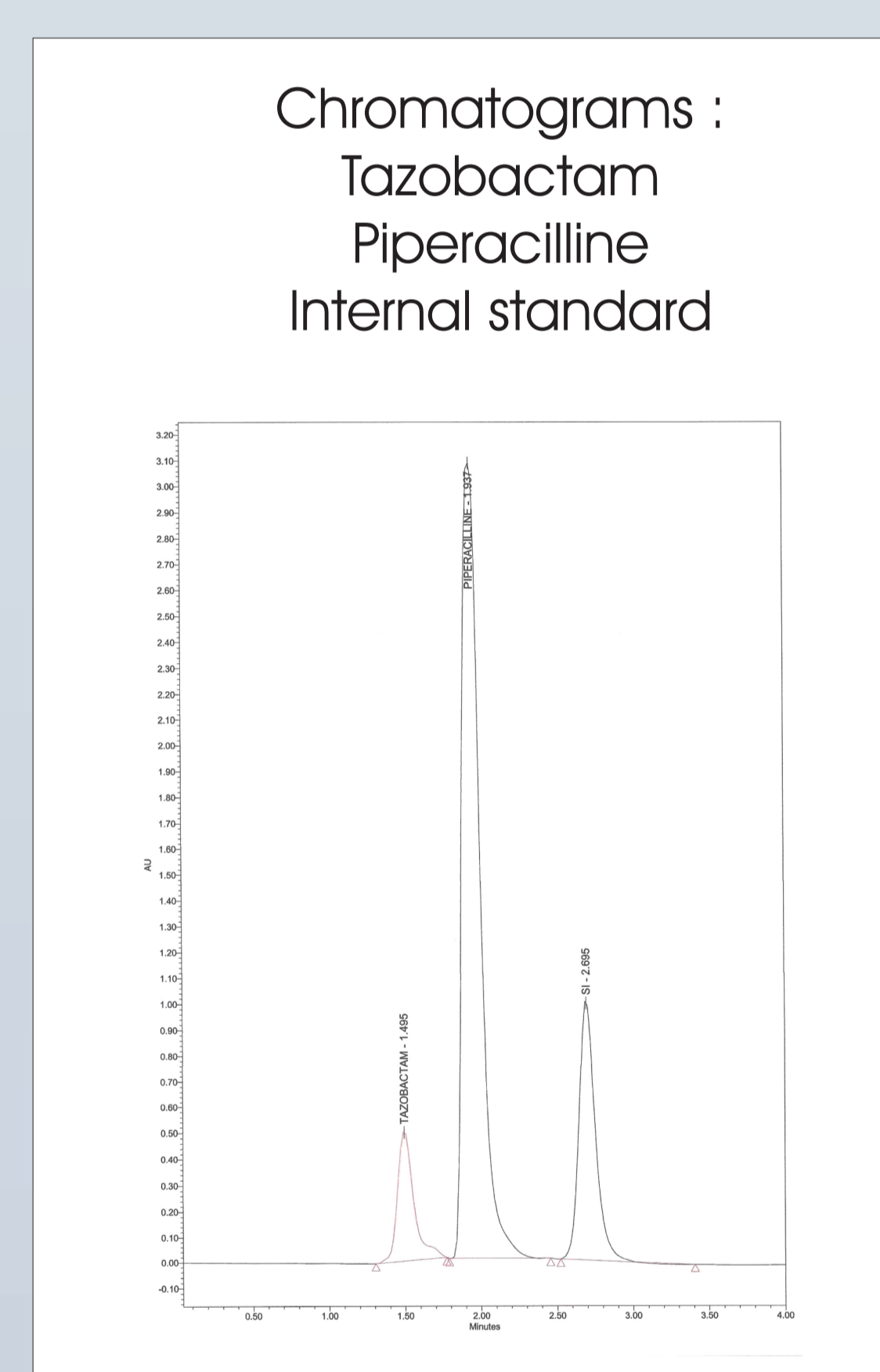
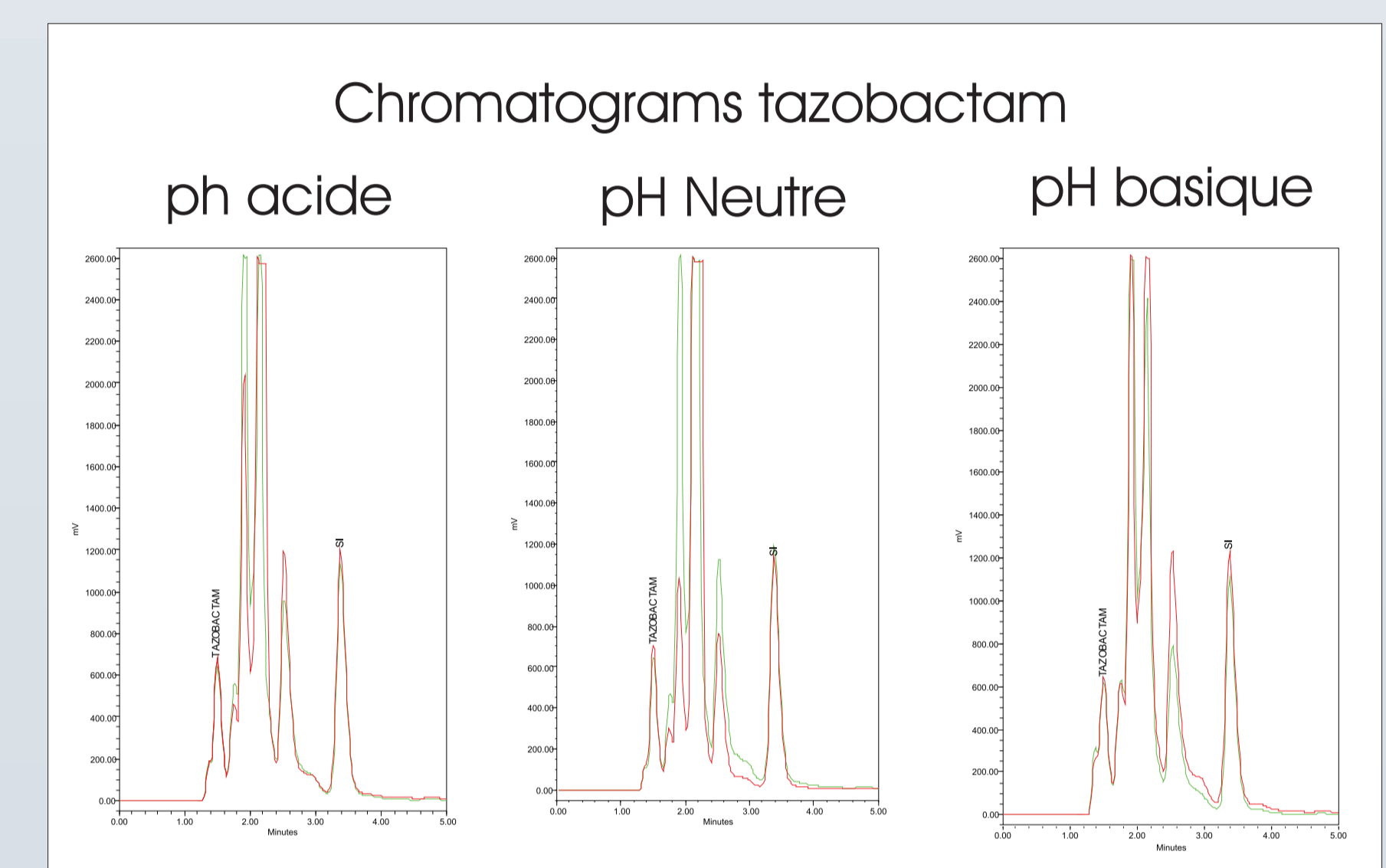
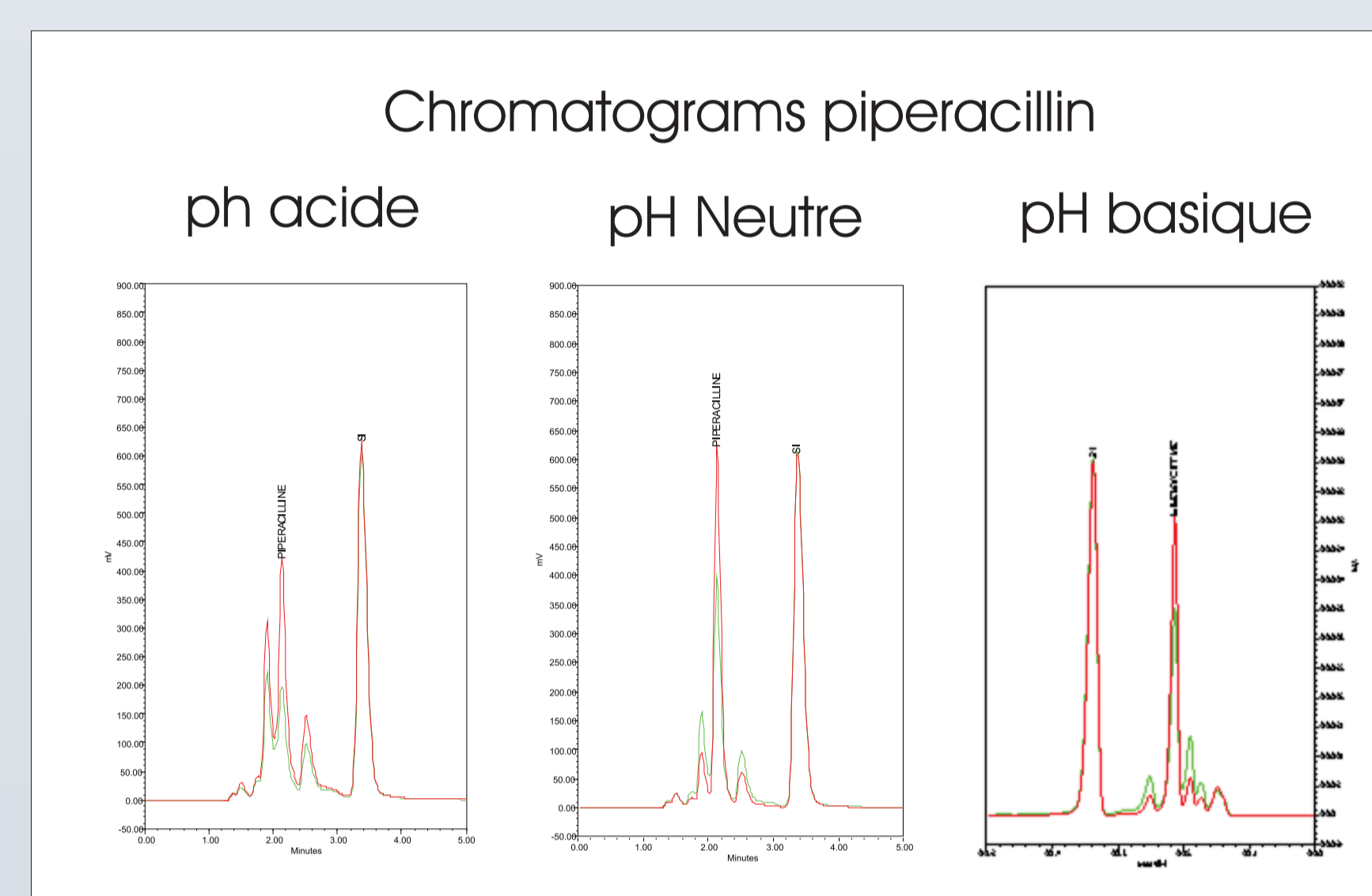
- To investigate the long term stability of a generic product of piperacilline/tazobactam in glucose 5% polyolefin bag after freezing, microwave thawing and final storage at $5 \pm 3^{\circ}\text{C}$.

Méthods

- Five bags of 4 g of Piperacilline/Tazobactam® Sandoz in 120 ml of glucose 5% were prepared under aseptic conditions and stored 3 months at -20°C then thawed and stored 58 days at $5 \pm 3^{\circ}\text{C}$.
- Optic density measurement at different wavelengths, pH measurement and optic microscope observations were performed periodically during the storage.
- A forced degradation test with HCl 12M and NaOH 5M before and after heating at 100°C was also performed.
- The concentrations were measured by high performance liquid chromatography - diode array detection, with a reversed phase column and a mobile phase (45% acetonitrile and 55% phosphate buffer pH 3).
- The detection was made at 211 nm for tazobactam and 230 nm for piperacilline.

Results

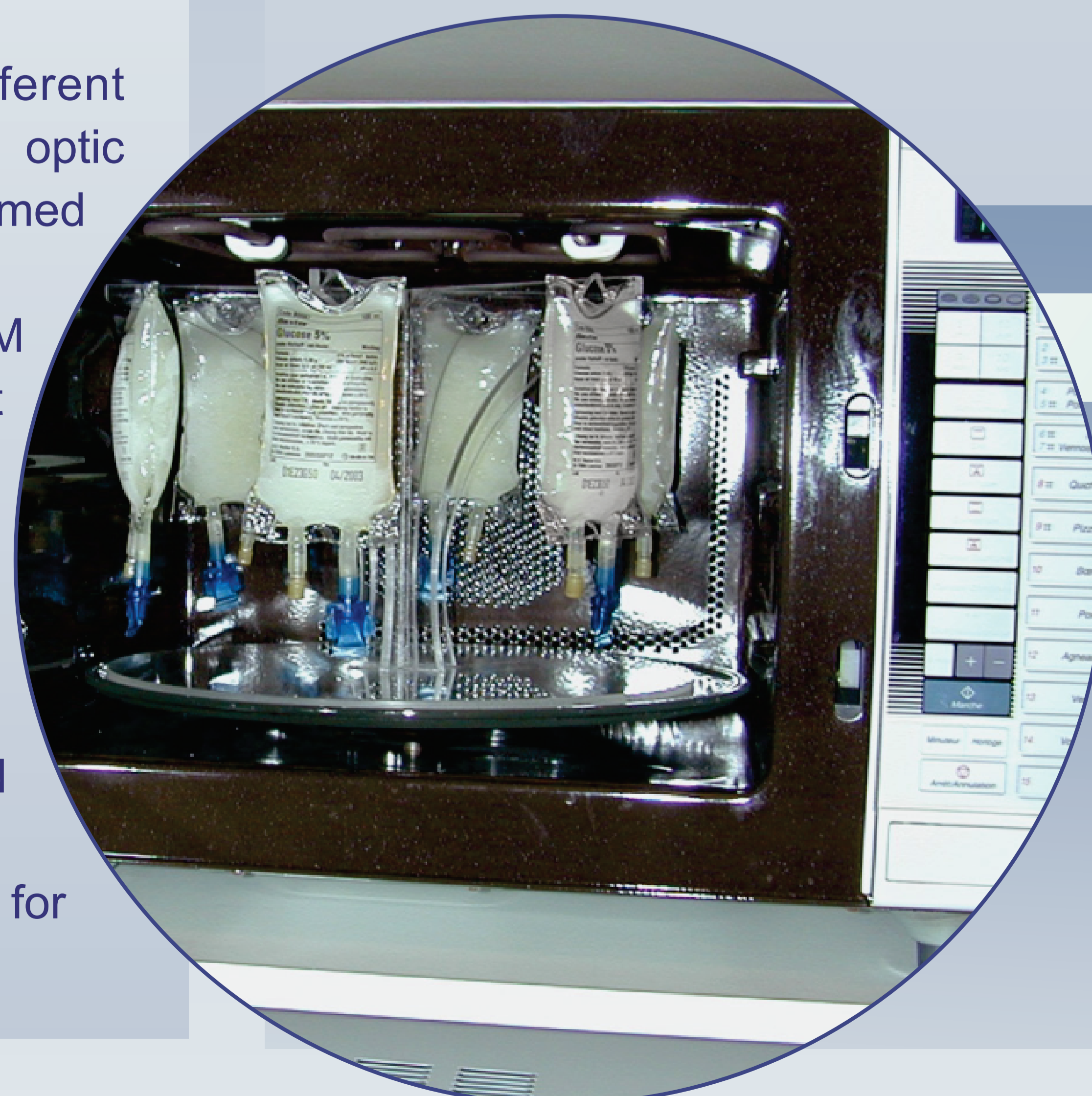
- No significant change in pH values or optic densities were seen during the study.
- No crystals were seen with the optic microscope.
- As recommended by the Food and Drug Administration (FDA), the lower confidence limit at 95% of the concentration for the solutions remains superior to 90% of the initial concentration until 44 days of storage at $5 \pm 3^{\circ}\text{C}$.



PIPERACILLINE			
%	Obs	95 % lower limit	
		Fit	Lwr
0	103.00	100.00	97.66
1	95.37	99.85	97.58
2	99.51	99.70	97.49
3	97.76	99.55	97.40
4	99.70	99.41	97.32
7	104.51	98.96	97.04
11	100.18	98.37	96.63
14	98.09	97.92	96.29
16	98.30	97.62	96.04
18	93.20	97.33	95.77
21	95.42	96.88	95.33
25	99.18	96.29	94.68
30	95.39	95.55	93.78
37	93.39	94.51	92.37
44	91.14	93.47	90.87
51	86.13	92.43	89.32
58	98.97	91.39	87.74

TAZOBACTAM			
%	Obs	95 % lower limit	
		Fit	Lwr
0	105.65	100.00	97.72
1	94.63	99.86	97.64
2	96.40	99.72	97.56
3	95.51	99.58	97.48
4	100.03	99.43	97.40
7	103.34	99.01	97.14
11	99.38	98.45	96.75
14	96.59	98.02	96.43
16	100.48	97.74	96.19
18	95.07	97.46	95.94
21	95.83	97.03	95.52
25	101.22	96.47	94.90
30	94.00	95.76	94.03
37	99.19	94.77	92.69
44	93.86	93.78	91.25
51	88.37	92.79	89.76
58	92.11	91.80	88.24

Obs : observed value / FIT : Predicted value /
 Lwr : lower confidence limit at 95 % of the concentration



Conclusion

Under the conditions of this study, Piperacilline/Tazobactam® Sandoz 4g/120ml of glucose 5% infusion in polyolefin bags remains stable at least for 44 days at $5 \pm 3^{\circ}\text{C}$ after freezing at -20°C and microwave thawing, and may be prepared in advanced by a CIVA.

References

Hecq JD & al. Effects of freezing, long-term storage, and microwave thawing on the stability of piperacillin plus tazobactam in 5% dextrose for infusion. Can J Hosp Pharm 2004;5:276