

# THE STABILITY OF READY-TO-USE (RTU) INSULIN IN POLYPROPYLENE SYRINGES FOR USE IN INTENSIVE CARE UNITS

S. Fleury-Souverain, [H.Ing](#), W. Griffiths, F. Sadeghipour, P. Bonnabry  
Pharmacy, University Hospitals of Geneva (HUG), Switzerland

## I. Introduction

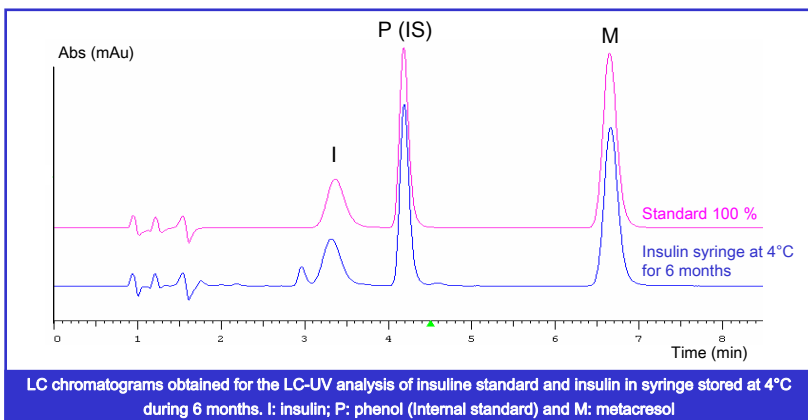
A continuous infusion of insulin is administered to a large proportion of patients hospitalised in intensive care units. Several incidents occurred in our hospital over the last few years, some of them being related to dilution errors or confusion with another drug (i.e. heparin). To improve the safety of insulin administration, we decided, in collaboration with the medical and nursing staff, to develop a ready-to-use syringe.

## II. Method

An insulin solution (1 UI/mL) was prepared by the pharmacy and filled under aseptic conditions (horizontal laminar airflow hood in a GMP class B room) into polypropylene syringes stored at  $4\pm 2^\circ\text{C}$ ,  $25\pm 2^\circ\text{C}$  and  $40\pm 2^\circ\text{C}$ . The samples were analysed using a validated stability indicating HPLC method at 0, 7, 30, 60, 90 and 180 days. The pH was measured and sterility testing was performed during the study. The potential presence of non-visible particles was also controlled (Hyac-Royco®).

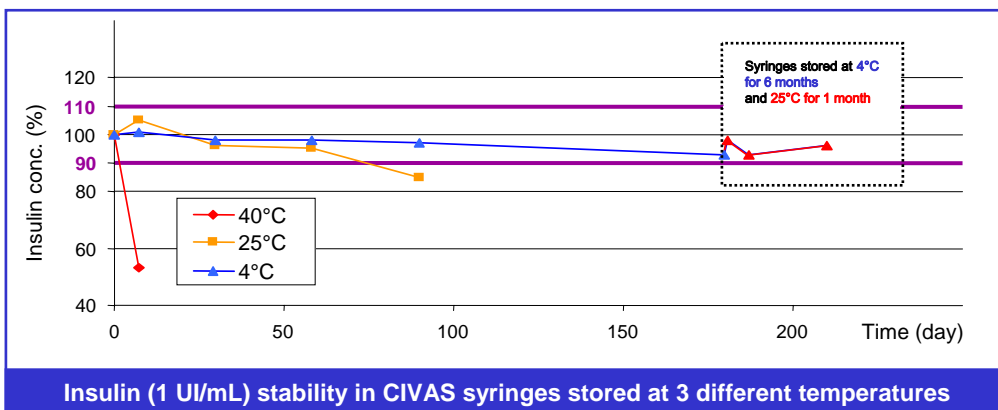
### HPLC parameters

Instrument: Merck Hitachi LaChrom with high pressure pump 7100 and UV-DAD detector L-7455  
Column: Lichrosorb® RP-8 125 x 4 mm d.i.,  $5\ \mu\text{m}\ d_p$   
Mobile phase: A.  $\text{Na}_2\text{SO}_4$  anhydre at 28.4 g/L in 1L of  $\text{H}_2\text{O}$  with pH adjusted to 2.3  
B. Acetonitrile  
C. 2-methoxyethanol (770:274:6, A:B:C)  
Injection volume: 20  $\mu\text{L}$   
Flow rate: 1.0 mL/min  
UV detection: 212 nm



## III. Results

After 1 month, insulin levels (stable if 90-110%) were under 60% for syringes stored at  $40^\circ\text{C}$  and above 95% for syringes stored at 4 and  $25^\circ\text{C}$ . After 2 months, drug levels were above 95% for syringes stored at 4 and  $25^\circ\text{C}$ . After 3 months, only syringes at  $4^\circ\text{C}$  showed an insulin level  $> 90\%$ . In these conditions, after 6 months, drug levels were still superior to 90% for syringes stored at  $4^\circ\text{C}$ . A supplementary test was achieved to simulate the possible storage and use conditions. It consists in the quantification of insulin compound in syringes stored at  $4^\circ\text{C}$  during 6 months and stored at  $25^\circ\text{C}$  during the next month. Drug levels  $> 90\%$  were also obtained. The pH did not change appreciably throughout the entire study and the sterility test results were found to be negative. Finally, syringes fulfilled all European Pharmacopoeia criteria in terms of non-visible particles in all cases.



## IV. Conclusion

Syringes of RTU insulin can be stored for **2 months at room temperature** and **at least 6 months at  $4^\circ\text{C}$**  with no significant loss in potency. Moreover, no insulin degradation was observed for syringes stored at  $4^\circ\text{C}$  during 6 months and at  $25^\circ\text{C}$  during the next month **The stability tests are continuing for syringes stored at  $4^\circ\text{C}$** . This ready-to-use preparation should contribute to an **improved safety** of insulin therapy in intensive care units.