Physicochemical stability of ready-to-administer epinephrine injection solutions 20 µg/ml, 50 ml

**Background and Purpose**
In the University Medical Center Mainz standard concentrations are defined for medicinal products to be administered by continuous injection with syringe pumps in adult intensive care patients. Patient individual doses are provided by adjusting the injection rate. Various medications are aseptically prepared in the pharmacy department as ready-to-administer products. Batch wise preparation of the products and keeping them in stock is only possible if stability of the products is tested using a validated stability indicating method.

The aim of the study was to test the stability of ready-to-administer epinephrine injections solutions 20 µg/ml in 50 ml plastic syringes.

**Materials and Methods**
Epinephrine bulk solution 20 µg/ml was prepared aseptically by diluting Suprarenin® 25 mg/25 ml Sanofi-Aventis with 5% glucose infusion solution in empty infusion bags (PP/PE). The solution was filled with the NeoCare Compounder into 50 ml opaque BD Perfusion Syringes Luer Lock Tip. The products were stored refrigerated at 2-8 °C for 6 months. Another batch of epinephrine syringes was stored for two days at 2-8 °C and then at room temperature for 14 days.

Epinephrine concentration was determined by using a validated HPLC method with UV detection at 280 nm and an innovative HPLC column Nucleodur which contains sulfonyl groups.

**Results**
The concentration of epinephrine in the 50 ml syringes and stored under refrigeration remained unchanged over a period of 6 months. After 28 days, 3 months, and 6 months of storage the concentration amounted to 100.0%, 100.1% and 97.6% of the nominal concentration, respectively. After 7 months of storage the concentration of epinephrine declined to 92.2% of the nominal concentration (s. Fig.5)

The ready-to-administer epinephrine injection solution 20 µg/ml, aseptically prepared by diluting the marketed injection concentrate with 5% glucose infusion solution in 50 ml light protected plastic syringes, is stable under refrigerated conditions for at least 6 months. At room temperature, the epinephrine injection solution is stable for a maximum of 14 days.

Neither adrenochrome nor any other degradation product was detected during the storage periods.

Conclusions
The ready-to-administer epinephrine injection solution 20 µg/ml, aseptically prepared by diluting the marketed injection concentrate with 5% glucose infusion solution in 50 ml light protected plastic syringes, is stable under refrigerated conditions for at least 6 months. At room temperature, the epinephrine injection solution is stable for a maximum of 14 days.

The Nucleodur column revealed a simple and more precise HPLC method for the quantification of epinephrine than common methods using SDS in the mobile phase.

**Literature**