Performance Qualification of the robotic system APOTECAunit for non-toxic parenteral preparations

David Ackermann[1], Helen Linxweiler[1], Judith Thiesen[1], Irene Krämer[1]

[1]Department of Pharmacy, University Medical Center of the Johannes Gutenberg University, Mainz, Germany

David.Ackermann@unimedizin-mainz.de

2-4th October 2024, Hyère (France)
COM24-54746

Background and Importance

The fully automated robotic system APOTECAunit is designed for the preparation of ready-to-administer (RTA) non-toxic parenteral products in prefilled bags and syringes. Medicinal products used as starting material are dosed volumetrically by 5 mL, 20 mL, and 50 mL syringes, supported by gravimetric in-process control (IPC) of the dosing accuracy.

Aim and Objectives

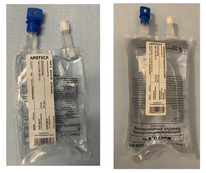
The objective of the study was the performance qualification (PQ) of the APOTECAunit for RTA bag preparation in series by assessing the dosing accuracy for each available dosing syringe.

Materials and Methods

Fully automated preparation of bupivacaine-HCl test bags with APOTECAunit

- Starting material: bupivacaine-HCl 20 mg/mL injection, 100 mL vial (Pharmacy Department UMM); prefilled 0.9% NaCl freeflex® infusion bag 50 mL, 500 mL (Fresenius, Germany)
- Dosing syringe: 5 mL, 20 mL syringe (dosing device, Loccioni, Italy), 50 mL Perfusor® Syringe (B.Braun, Germany)
- Table 1: Characteristics of RTA bupivacaine-HCl test bags

Dosing device syringe size [ml]	Injected volume bupivacaine-HCl 20 mg/ml [ml]	Bag size [ml]	Bupivacaine-HCl concentration in test bags [mg/ml]	Number of test bags [n]
5	1	50	0.36	3x20
5	2	50	0.71	3x20
20	6	50	2.00	3x20
50	35	500	1.25	3x20



Quantitative analysis - bupivacaine-HCl concentration by HPLC

- HPLC system: Alliance Waters 2695 with PDA detector
- Column: Symmetry C18; 5µm, 3.9 x 150mm (RP-HPLC, Waters)
- Mobile phase: 65% acetonitrile + 35% 32 mM phosphate buffer pH 7.7
- Flow rate: 1.1 mL/min; Runtime: 6 min
- Injection volume: 10 µL in triplicate
- Detection wavelength: 254 nm
- Validation based on ICH Q2 (R1)

  → Average bupivacaine-HCl concentration ± standard deviation (SD) per test bag

Assessment of dosing accuracy

- Calculation of dosing accuracy according to the bupivacaine-HCl concentrations measured by HPLC for each injected volume (n=60 per volume)
- Calculation of dosing accuracy according to the gravimetric IPC of the APOTECAunit for each injected volume (n=60 per volume)

Results

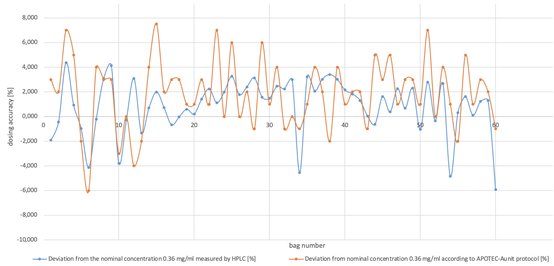


Figure 1: Dosing accuracy for 5 mL dosing syringe, 1 mL injected volume.
Blue: concentration measured by HPLC; Orange: gravimetric IPC

- Dosing accuracy according to HPLC: 1.66 %
- Dosing accuracy according to gravimetric IPC of the APOTECAunit: 2.22 %

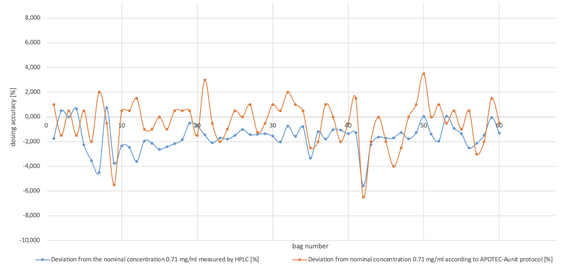
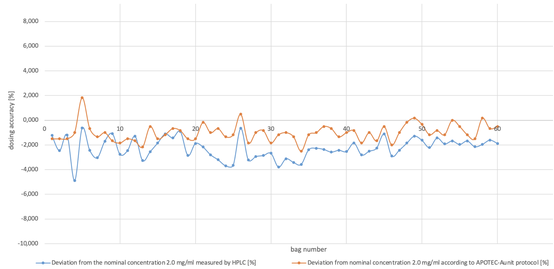


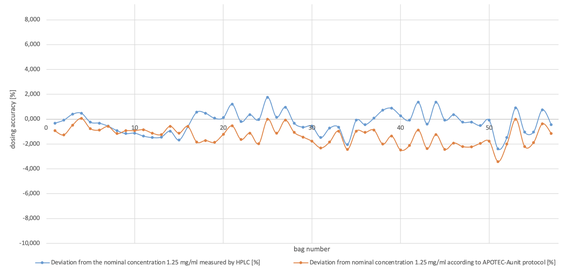
Figure 2: Dosing accuracy for 5 mL dosing syringe, 2 mL injected volume.
Blue: concentration measured by HPLC; Orange: gravimetric IPC

- Dosing accuracy according to HPLC: 0.79 %
- Dosing accuracy according to gravimetric IPC of the APOTECAunit: 1.36 %



Dosing accuracy for 20 mL dosing syringe, 6 mL injected volume.
Blue: concentration measured by HPLC; Orange: gravimetric IPC

- Dosing accuracy according to HPLC: 0.68 %
- Dosing accuracy according to gravimetric IPC of the APOTECAunit: 0.51 %



Dosing accuracy for 50 mL dosing syringe, 35 mL injected volume.
Blue: concentration measured by HPLC; Orange: gravimetric IPC

- Dosing accuracy according to HPLC: 0.68 %
- Dosing accuracy according to gravimetric IPC of the APOTECAunit: 0.61 %

The dosing accuracy proved to be acceptable for all dosing syringes and injected volumes. The 5 mL dosing syringe is suitable for injection volumes ≥ 1 mL, the 20 mL dosing syringe ≥ 6 mL, the 50 mL syringe ≥ 35 mL. The gravimetric IPC is reliable and suitable for end product control.

Conclusion

The APOTECAunit passed the PQ tests for bupivacaine-HCl RTA bags. The available dosing syringes are suitable. The dosing accuracy improves with increasing injection volumen.