# INTEREST OF hemaPEN® DEVICE FOR THE THERAPEUTIC DRUG MONITORING OF IMMUNOSUPPRESSANTS

Dubois Nathalie[1,2], Charlier Corinne[1,2]

[1]*Laboratory of Clinical, Forensic, Industrial and Environmental Toxicology, University Hospital of Liege, Belgium*

[2]*CIRM, Department of Pharmacy, University of Liege, Belgium*

Objective: Immunosuppressants (IS) are used to decrease recipient immune defenses to prevent transplant rejection. Therapeutic drug monitoring (TDM) of IS is crucial because their pharmacokinetics is variable and their therapeutic range is narrow. The University Hospital of Liege is a major transplant center and some patients come from very far away to be transplanted. Because, sometimes, local clinical laboratories are not able to perform IS TDM, we were asked by nephrologists to find an alternative sample more stable than the EDTA tube classically used. For this purpose, we tested hemaPEN® devices marketed by Trajan.

Method: Blood was sampled on hemaPEN® devices which are able to collect 4 dried blood spots (DBS) simultaneously. 500µl of internal standards (ascomycine, cyclosporine D) in methanol were added to 1 DBS. After sonication, the supernatant was collected and evaporated until dryness. The residue was then reconstituted in 100µl of mobile phase and put in vial before injection. A method was developed on a UHPLC-MSMS to determine cyclosporine, everolimus, sirolimus and tacrolimus in blood collected from hemaPEN® devices. The mobile phase consisted in ammonium acetate 2mM and formic acid 0.1% in both water and methanol, it was delivered according to a gradient mode. The column was an Acquity® BEH C18, 1.7µm, 2.1x50mm (Waters) maintained at 55°C. A complete analytical validation was performed.

Results and discussion: The bias and the coefficients of variation for both repeatability and intermediate precision were lower than 15% in the dosing range and than 20% for the concentrations close to the limit of quantification (LOQ). The LOQ obtained was much lower than the therapeutic range. The stability evaluated by simulating the transfer of a sample from the Democratic Republic Congo to Liege was correct, better than for a classical EDTA Tube. The comparison of the results obtained by the two sampling methods was satisfactory.

Conclusion: The use of hemaPEN® devices to collect blood as alternative sampling method met our expectations in terms of analytical validation. The practicability of the device on real patients still needs to be evaluated.