Quantitative analysis of antiretroviral drugs by MALDI-TOF mass spectrometry
Jeroen van Kampen1,3, Peter Burgers2, Ronald de Groot1 and Theo Luider2
1 Department of Pediatrics, Erasmus MC – Sophia, Rotterdam, The Netherlands
2 Department of Neurology, Erasmus MC, Rotterdam, The Netherlands
3 j.vankampen@erasmusmc.nl

RESULTS
We aim to develop a fast, sensitive and reliable assay for quantitative analysis of antiretroviral drugs. MALDI-TOF mass spectrometry was chosen for our assay, because it is able to analyze compounds at the femtomole level in high throughput mode and is relative tolerant towards contaminants. However, reliable quantitative analysis by MALDI-TOF mass spectrometry remains a point of discussion.1 In our experience, MALDI-TOF mass spectrometry can be used for reliable quantitative analysis of HIV-1 protease inhibitors by use of an internal standard and preparation of homogeneous matrix / sample crystals.

Matrix
1 Free lithium+ is not detected.

Validation.
Sample: 500 femtomole lopinavir in 50% EtOH.
Matrix: 10 mg/mL F20TPP with 3.84 mM LiI, NaI, KI, RbI and Cal.

RESULTS
Detection of lopinavir

Cationization of lopinavir

Cationization of NFV, IDV, LPV, SQV and RTV

Lopinavir calibration curve

CONCLUSIONS
- F20TPP is a suitable matrix for analysis of HIV-1 protease inhibitors with MALDI-TOF mass spectrometry.
- Best sensitivity is obtained when F20TPP is used in combination with lithium iodide.
- The addition of water to samples has a profound effect on the SNR of lopinavir cationized by various alkali metals.
- MALDI-TOF mass spectrometry can be used for accurate, precise and sensitive quantitative analysis of lopinavir.
- The type of software used to process raw mass spectra has a profound effect on the precision and accuracy of the lopinavir calibration curve.
- The value of MALDI-TOF mass spectrometry for quantitative drug analysis in clinical studies is being investigated.

REFERENCES

ACKNOWLEDGEMENTS
- Asta Fonds, The Netherlands (project number 2004581) and VIRGO for financial support.
- Corno Bioscience for data processing with MS Integrity™.
- Abbott Laboratories for supply of lopinavir and ritonavir.
- Merck Sharp & Dohme for supply of indinavir.
- Pfizer Inc. for supply of nefilnavir.