



The promise of microsampling, delivered



Allergan

microsampling

Introducing Quantitative, Drop-of-blood Testing

microsampling devices

DBS card



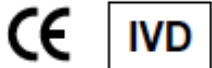
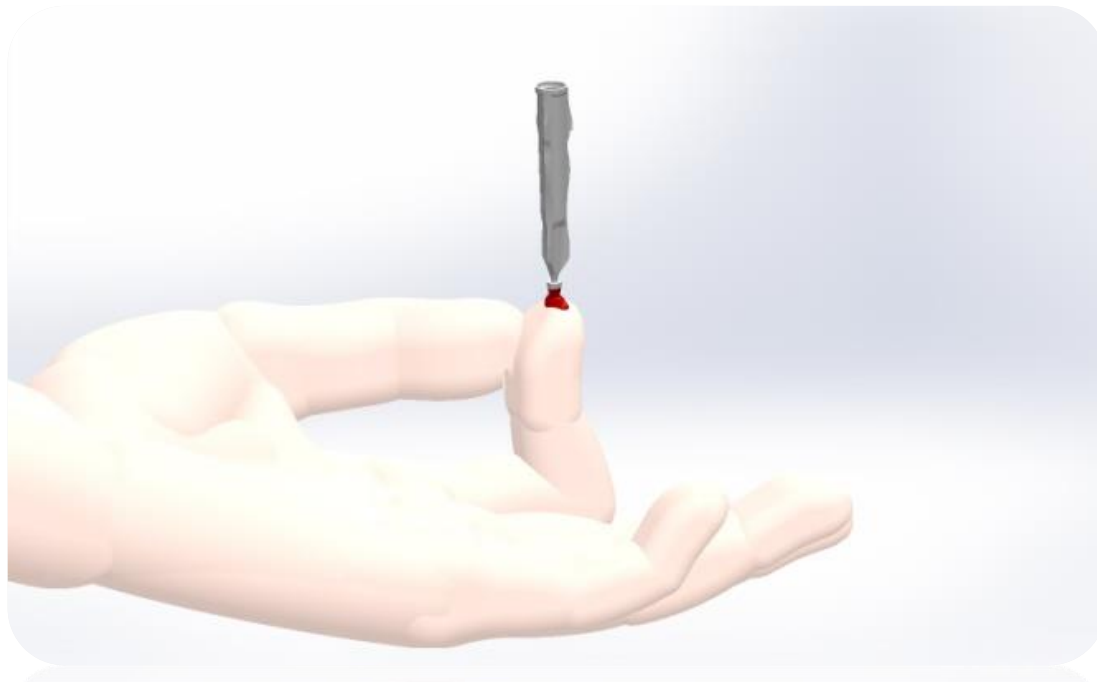
Capillary tube



No hematocrit (HCT) bias		X
Automatable extractions		
Quantitative volume collection		X
User-friendly sampling		
No freeze/thaw cycle	X	
No cold chain/biohazard shipping	X	
No sub-punching required		X

the Mitra™ microsampler

- Based on Volumetric Absorptive Microsampling (VAMS) technology
- Accurate 10 or 20 µL collection



The Mitra Microsampling Device is a FDA listed Class 1 device (D254956). Neoteryx complies with FDA good manufacturing practices, CFR 820 regulations, and ISO 13485.



the Mitra™ microsampler

- Fixed, highly reproducible internal volume
- Hydrophilic porous material
- Rapid wicking (< 6 sec)
- Accurate (10 or 20 µL volume)
- Precise (< 4% RSD)
- Automation-friendly



The Mitra Microsampling Device is a FDA listed Class 1 device (D254956). Neoteryx complies with FDA good manufacturing practices, CFR 820 regulations, and ISO 13485.

The Mitra Microsampler class I medical device is for direct specimen collection of blood and other biological fluids. It is not specific to any clinical test, and is not for use in diagnostic procedures. Use of the Mitra Microsampler in Laboratory Developed Tests (LDTs) requires further processing including the establishment of performance characteristics and successful validation by the laboratory in a manner consistent with CLIA requirements. The Mitra microsampler is patent pending.



video of rapid, simple sample collection



effect of HCT on dried blood spot (DBS) area

Hematocrit (HCT) % inversely related to blood spot area

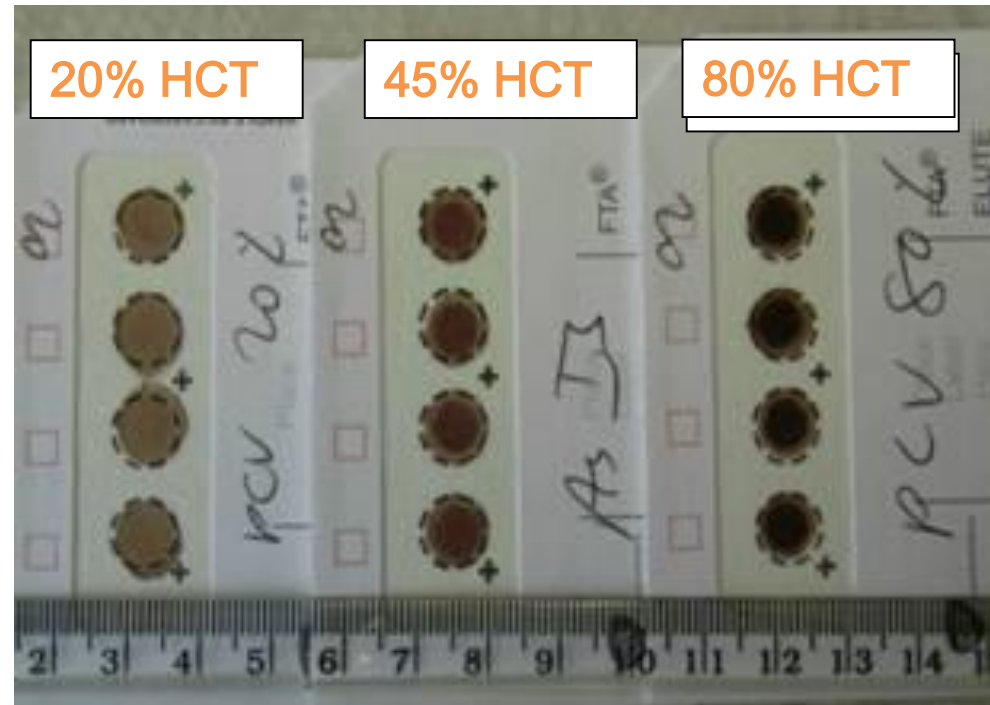
Low HCT

- Larger, light spots

High HCT

- Smaller, dark spots

Whatman™ FTA™ Elute Card



Area change = 41%



DBS spot uniformity



1. Specimen quantity insufficient for testing.



2. Specimen appears scratched or abraded.



3. Specimen not dry before mailing.



4. Specimen appears supersaturated.



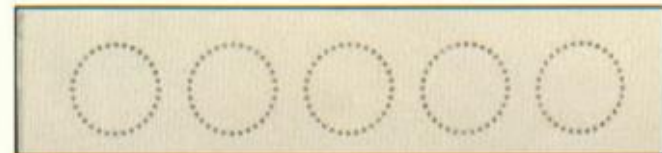
5. Specimen appears diluted, discolored or contaminated.



6. Specimen exhibits serum rings.

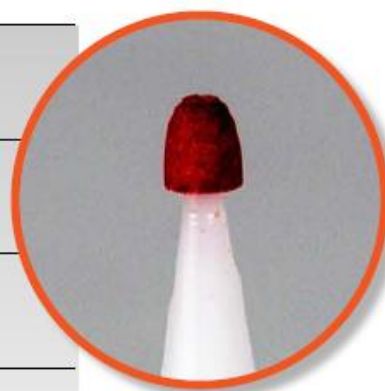
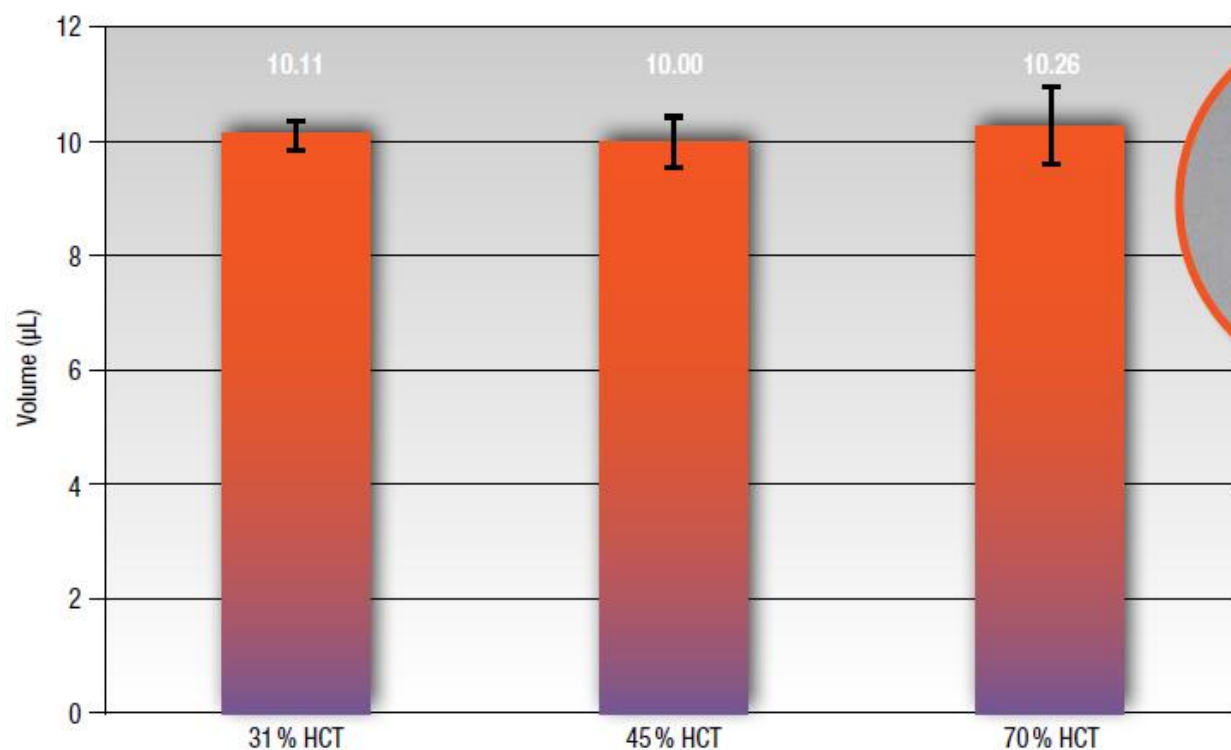


7. Specimen appears clotted or layered.



8. No blood.

HCT independent collections (10 μ L)

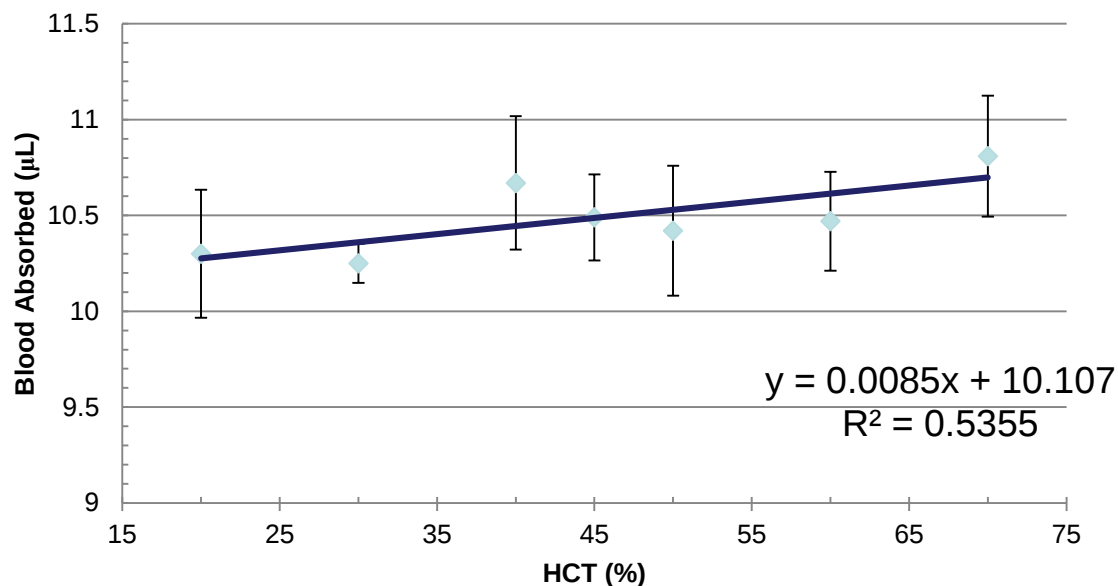


Overall average = 10.1 μ L
Overall RSD = 3.5 %

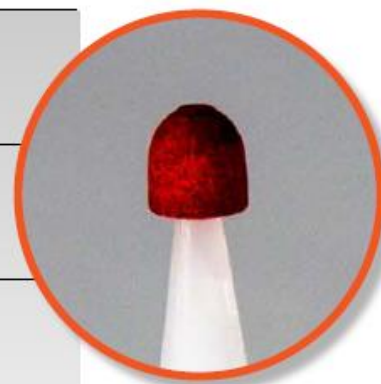
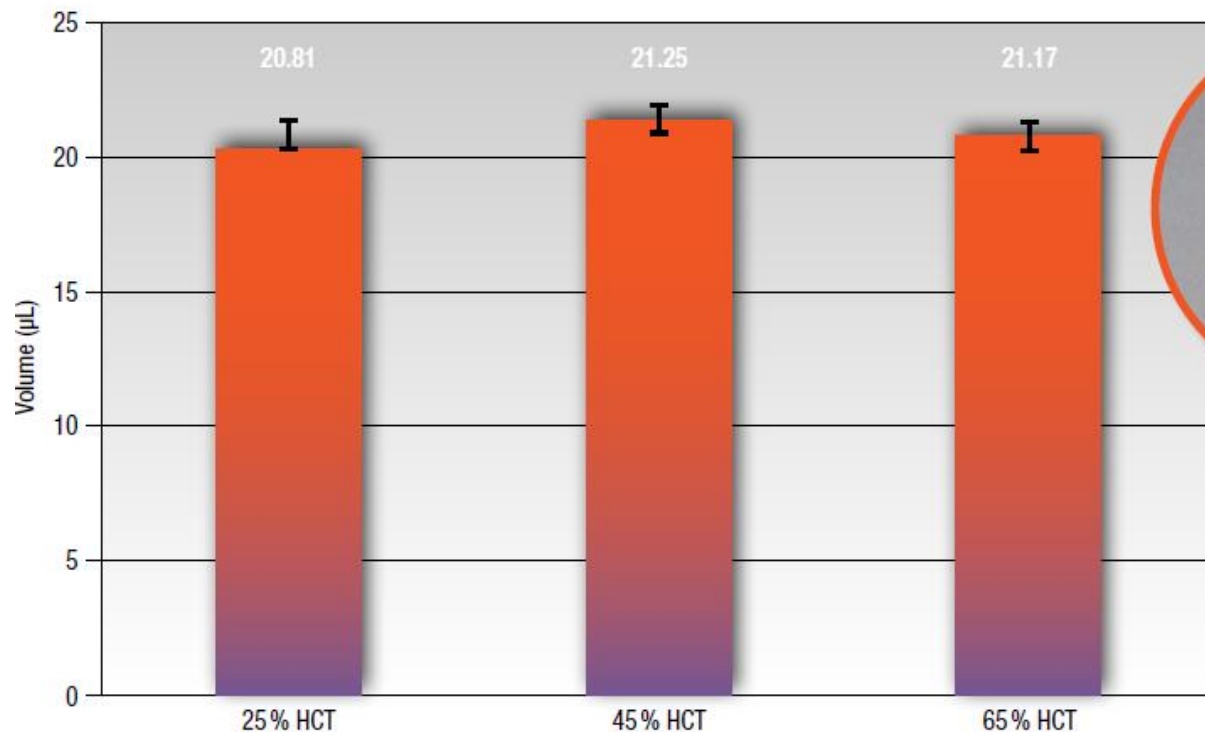
HCT effect on blood volume absorbed

- Max volume bias from 45% HCT is 3%
- 5% max volume deviation over HCT ranges 20% to 70%

Volume blood absorbed by tip (μL)



HCT independent collections (20 μ L)



Overall average = 21.08 μ L
Overall RSD = 2.5 %

accuracy and precision

Penicillins have a linear ($R^2 > 0.995$) range from 0.15 µg/mL-200 µg/mL in plasma using Mitra devices. Accuracy and precision were tested ($n=5$) in low (0.15 µg/mL), medium (20 µg/mL) and high (80 µg/mL) concentrations.

Compound	Within-day accuracy		Within-day precision (CV%)	
	Mitra sampling	10 µL blood plasma pipetting	Mitra sampling	10 µL blood plasma pipetting
Amoxicillin	2-5%	4-9%	2-4%	5-12%
Ampicillin	3-6%	4-8%	1-3%	4-7%
PenicillinG	1-5%	6-11%	2-6%	5-10%
Piperacillin	2-6%	4-10%	2-5%	5-11%
Flucloxacillin	2-7%	5-9%	3-6%	5-9%



Evaluation of the Mitra microsampling device for dry sample processing in a pharmacokinetic/pharmacodynamic study of beta-lactams

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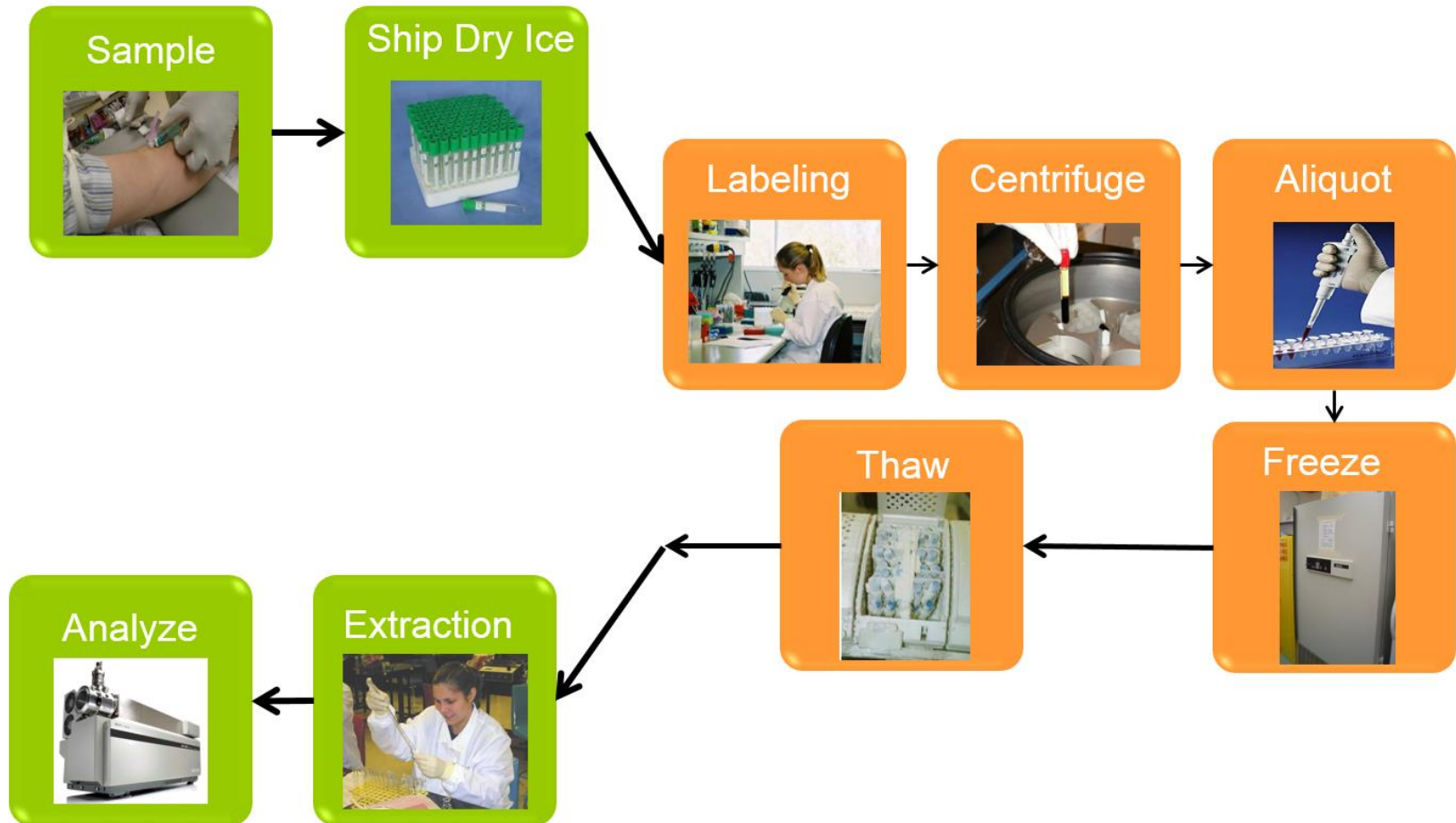
²Institute of Chemistry, University of Tartu, Ravila 14A, Tartu, Estonia, 50411

³Analytical Services International, St George's University of London Cranmer Terrace, London, SW17 0RE, United Kingdom

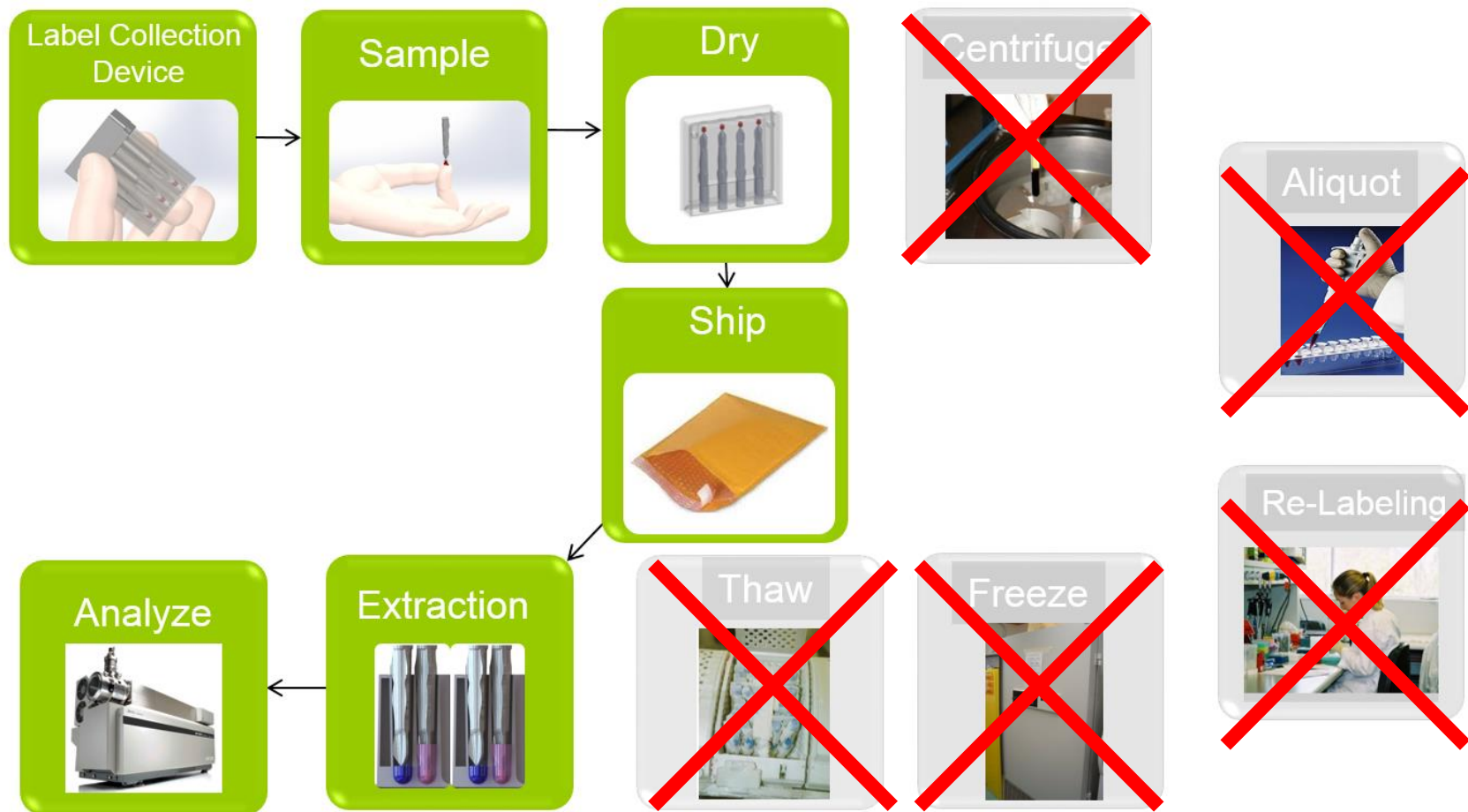
*kipper@sgul.ac.uk

 **neoteryx**[™]
The promise of microsampling, delivered

traditional blood-plasma workflow

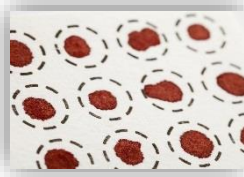


streamlined Mitra workflow



microsampling devices

DBS card



Capillary tube



Mitra® device



No hematocrit (HCT) bias by spot migration

x

x

Automatable extractions

x

Quantitative volume collection

x

x

User-friendly sampling

x

No freeze/thaw cycle

x

x

No cold chain/biohazard shipping

x

x

No sub-punching required

x

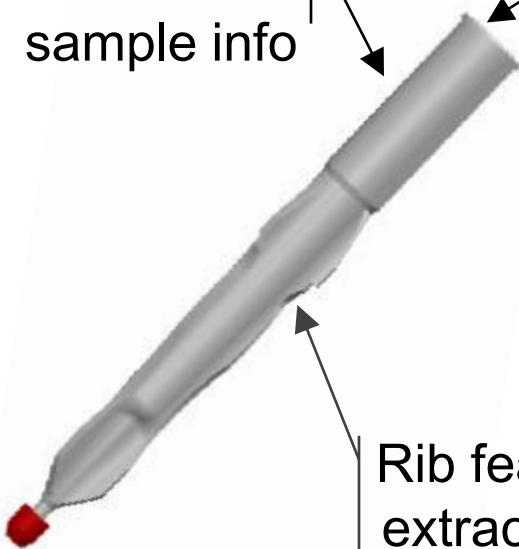
x

the sampler & sampling tool

Barrel easily
labeled or
written on for
sample info

Distal end fits to 20-200 μ L pipette head and
fits a **custom tool** for moving individual
samplers

Rib features aids alignment in
extraction well/plate, provides
slight friction and easy finger grip



Mitra[®] device formats

- Direct sampling cartridges and clamshells
- Automatable 96-racks



semi-automation of Mitra[®] device



secure sample packaging

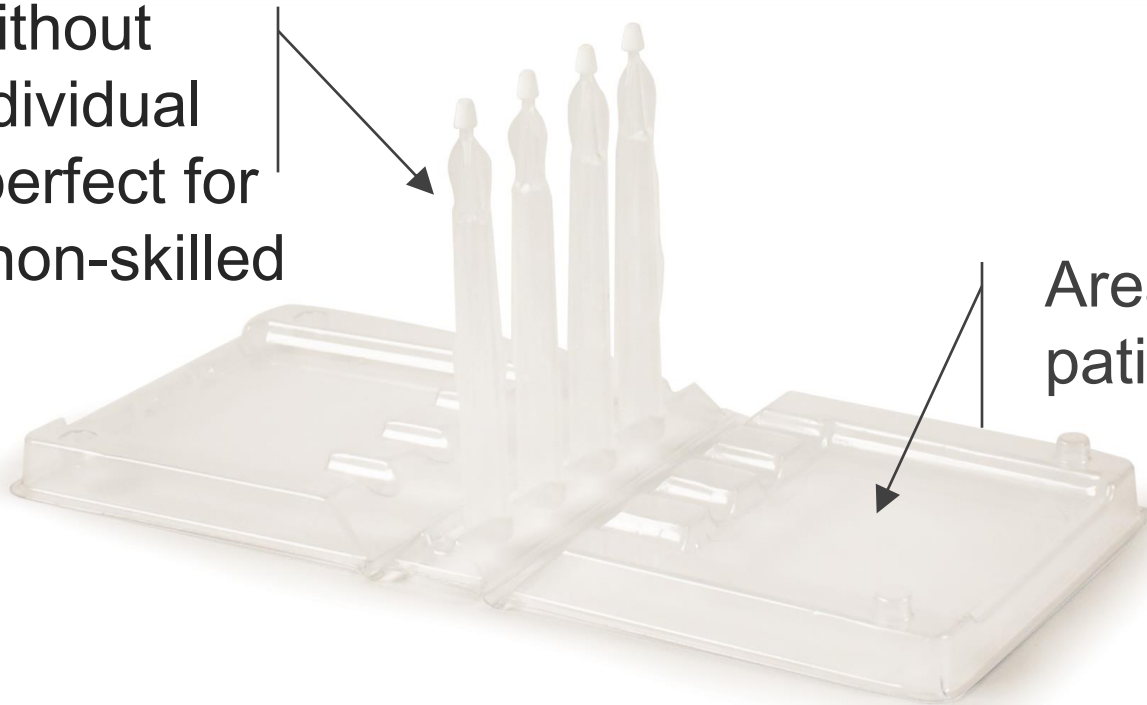
Ventilated enclosure allows immediate bagging for drying and shipment



Secure fitting of each sampler within the clamshell prevents cross-contamination during drying and shipment

clamshell format for patient use

Easy replicate
sampling without
handling individual
samplers, perfect for
at-home / non-skilled
collection



96-rack format for lab use

Storage Box

- Storing and transporting deck of samples



Removable Deck

- Holds 96 indexed samplers
- Rapid, open air drying
- Easy handling



Deck Adapter Plate

- Mounting 96-rack on deck of liquid handlers



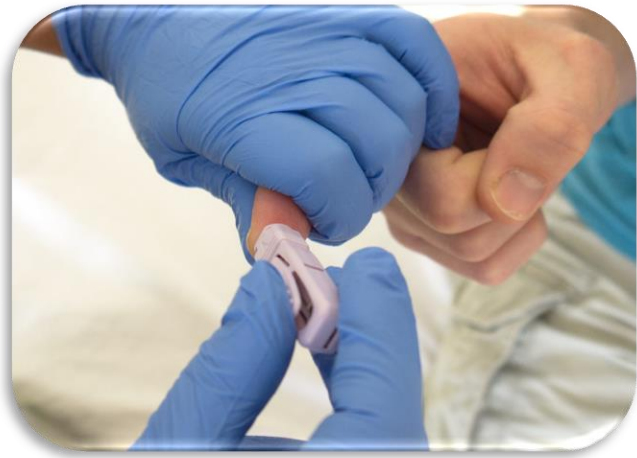
suitable applications

- Therapeutic drug monitoring (TDM)
 - Immunosuppressants, antiretrovirals
- Clinical trials
 - Pediatric studies
 - Remote location sampling
- At-home sampling
- Genetics
 - DNA testing
 - Pharmacogenomics

The Mitra Microsampler class I medical device is for direct specimen collection of blood and other biological fluids. It is not specific to any clinical test nor does it provide a clinical diagnostic outcome of any nature. Clinical diagnostic laboratories, using the Mitra device for specimen collection, must validate tests according to their organizational needs.

Mitra benefits for the patient

- Improved patient experience
 - Less painful than venipuncture
 - Easier and better compliance
 - Minimizes patient needle and blood anxiety
 - Convenience of at-home testing



Mitra benefits for the lab

- Happy patients
- Streamlined lab operations
 - No freezing/thaw cycle or centrifugation
 - Elimination of cold chain and
 - Minimal training required



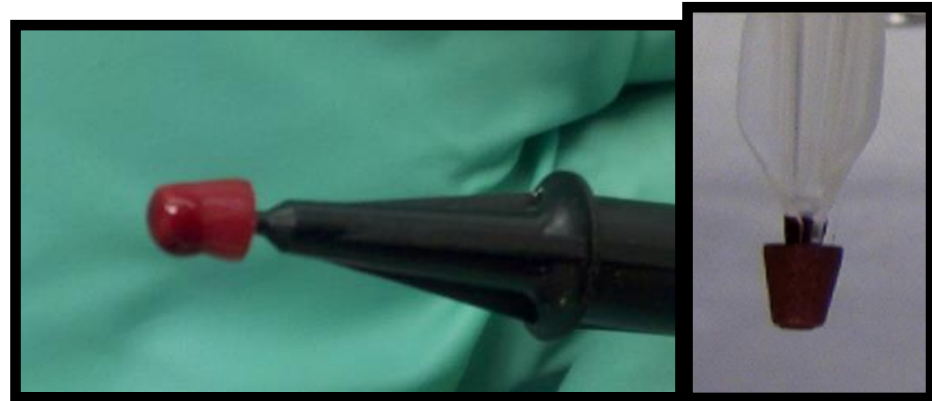
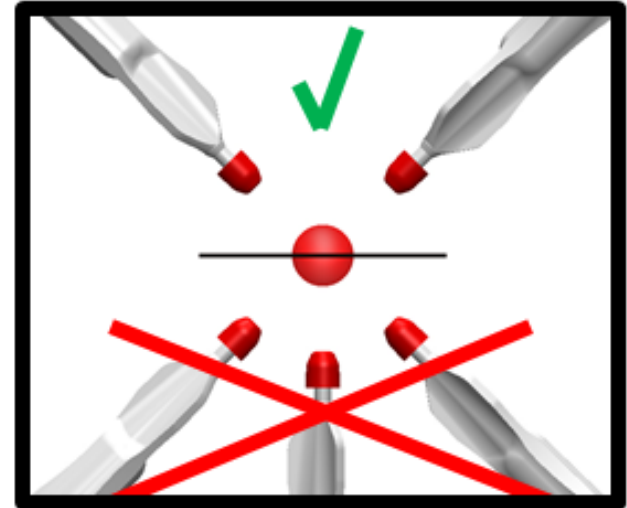
Mitra benefits for the lab

- Happy patients
- Streamlined lab operations
- Broad range assay & patient compatibility
 - Clinical chemistry, immunoassay, pharmacology, LC-MS/MS
 - Easier access to patients with low blood flow (e.g neonatal, pediatrics, geriatrics)

properties & techniques

sampling environment does not affect Mitra

- Excess contact time with samples
- Limited blood sample
- Temperature variation
- Humidity
- High or Low hematocrit*
- Minimal training required to ensure sampling from a positive angle
- Oversampling can occur if:
 - Full submersion of tip
 - Sample from negative angle



* With optimized extraction

sampling technique examples

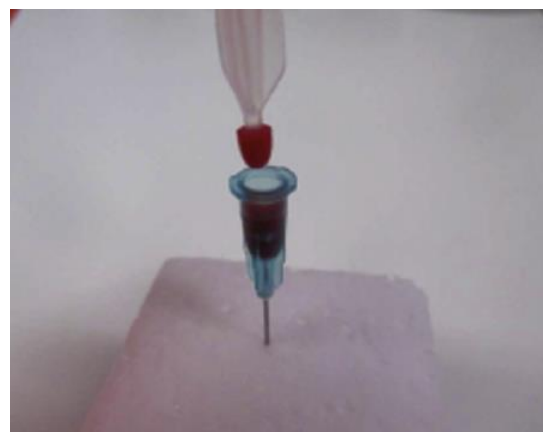
Modified Butterfly Canula



Need Hub Approach



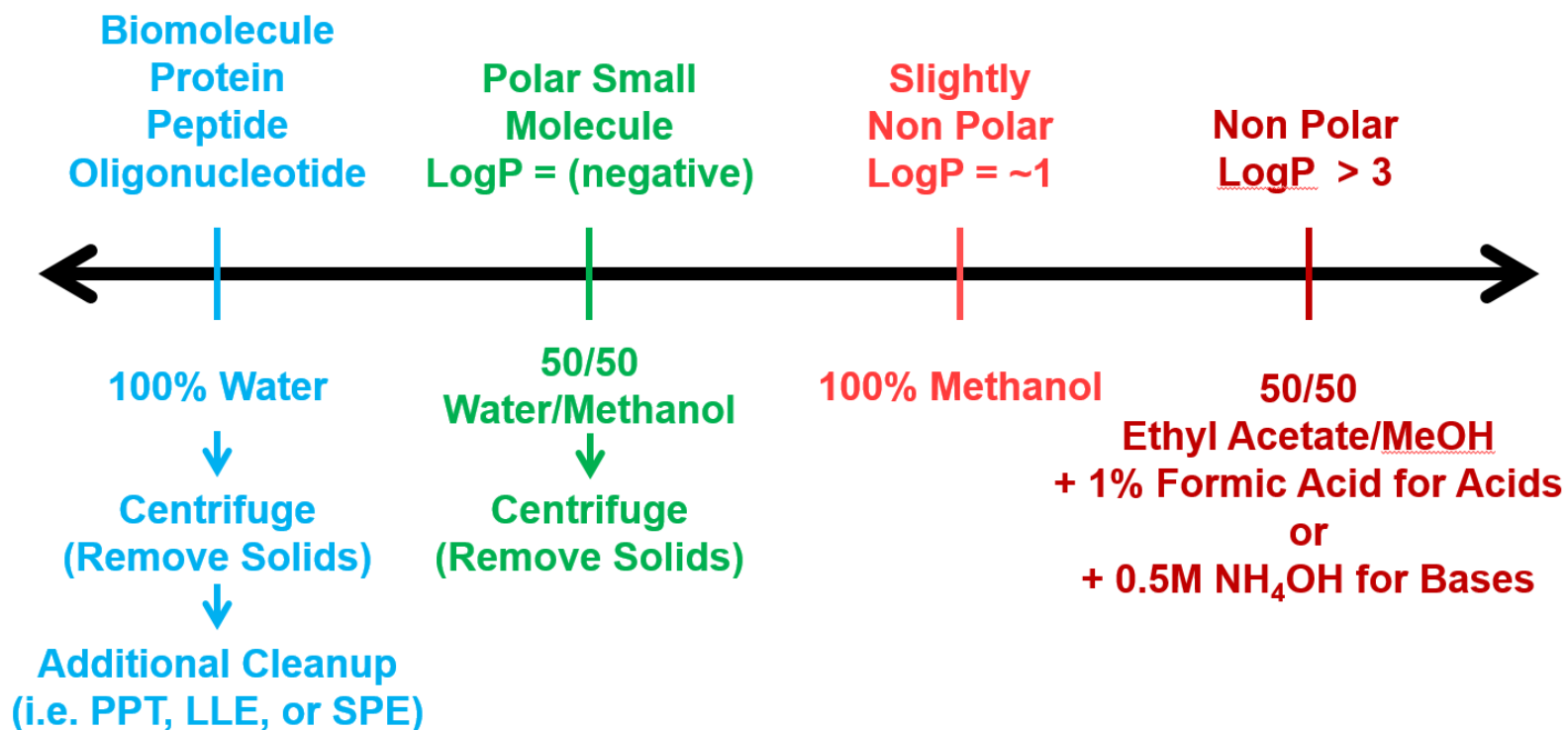
Fill



Collect

P. Denniff, S. Parry, W. Dopson, N. Spooner; Quantitative bioanalysis of paracetamol in rats using volumetric absorptive microsampling (VAMS); J Pharma Biomed Analysis Bioanalysis 108 (2015) 61–69.

extractions by analyte chemotype



mouse PK study

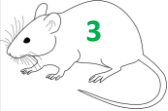
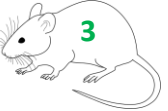
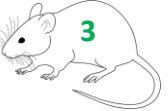
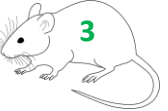
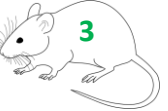
original PK protocol: 3 mice

Time Points

1 st	2 nd	3 rd	4 th	5 th	6 th	7 th	8 th	9 th
 1	 4	 7	 10	 13	 16	 19	 22	 25
 2	 5	 8	 11	 14	 17	 20	 23	 26
 3	 6	 9	 12	 15	 18	 21	 24	 27

microsampling goal: reduce pk protocol to 3 mice

Time Points

1 st	2 nd	3 rd	4 th	5 th	6 th	7 th	8 th	9 th
								
								
								

mouse PK study design

- IV Dosing Route
 - (acetaminophen 2 mg/kg into tail vein)
- 6 Time points (0.08, 0.25, 0.5, 1, 2, and 4 hours) + predose
- Cardiac Puncture collected into tubes
 - 21 Mice Sacrificed
 - Compared:
 - Whole Blood → Plasma
 - Mitra Microsampling → Dried Whole Blood

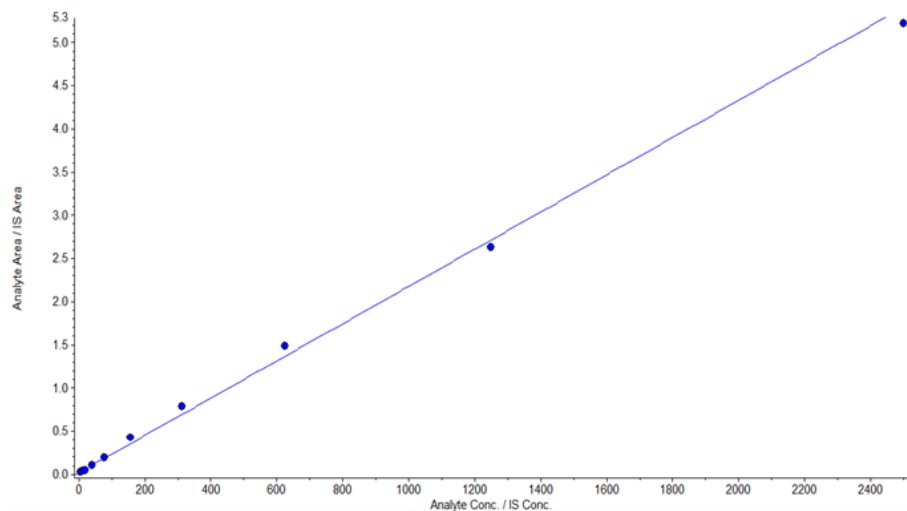
mouse PK extractions

- Whole Blood → Plasma Approach
 - 9:1 Protein Precipitation with MeOH
- Mitra → Dried Blood Approach
 - Add Tips to 100μL of Water + 1% Formic Acid; Vortex 30 mins
 - Add to Tips 100μL of MeOH; Vortex 30 mins
 - Remove Tips, and add 600μL Cold Acetonitrile; Vortex 10 mins
- The For both approaches.
 - Centrifuge, Remove Supernate
 - Evaporate, and reconstitute for injection.

mouse PK standard curves

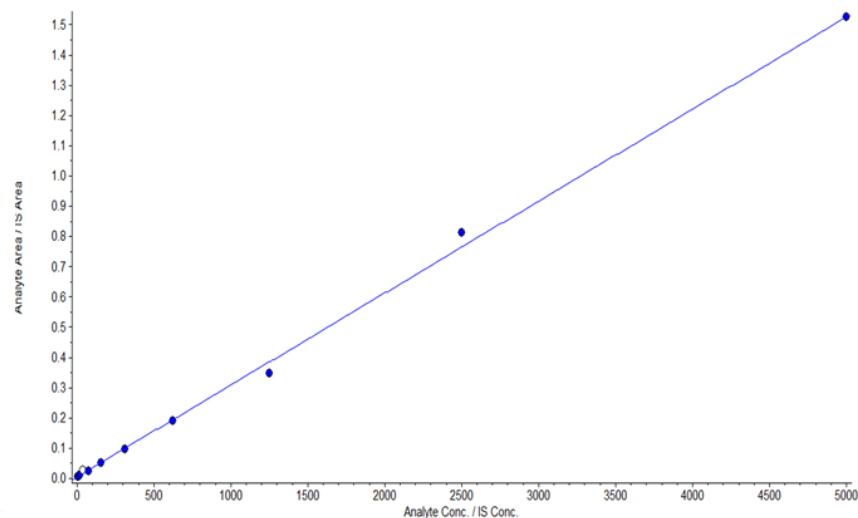
Standard curve for acetaminophen (mouse plasma)

Mouse plasma results – linear regression, $1/x$ weighting, $y=0.00216x + 0.0183$ ($r=0.9975$)

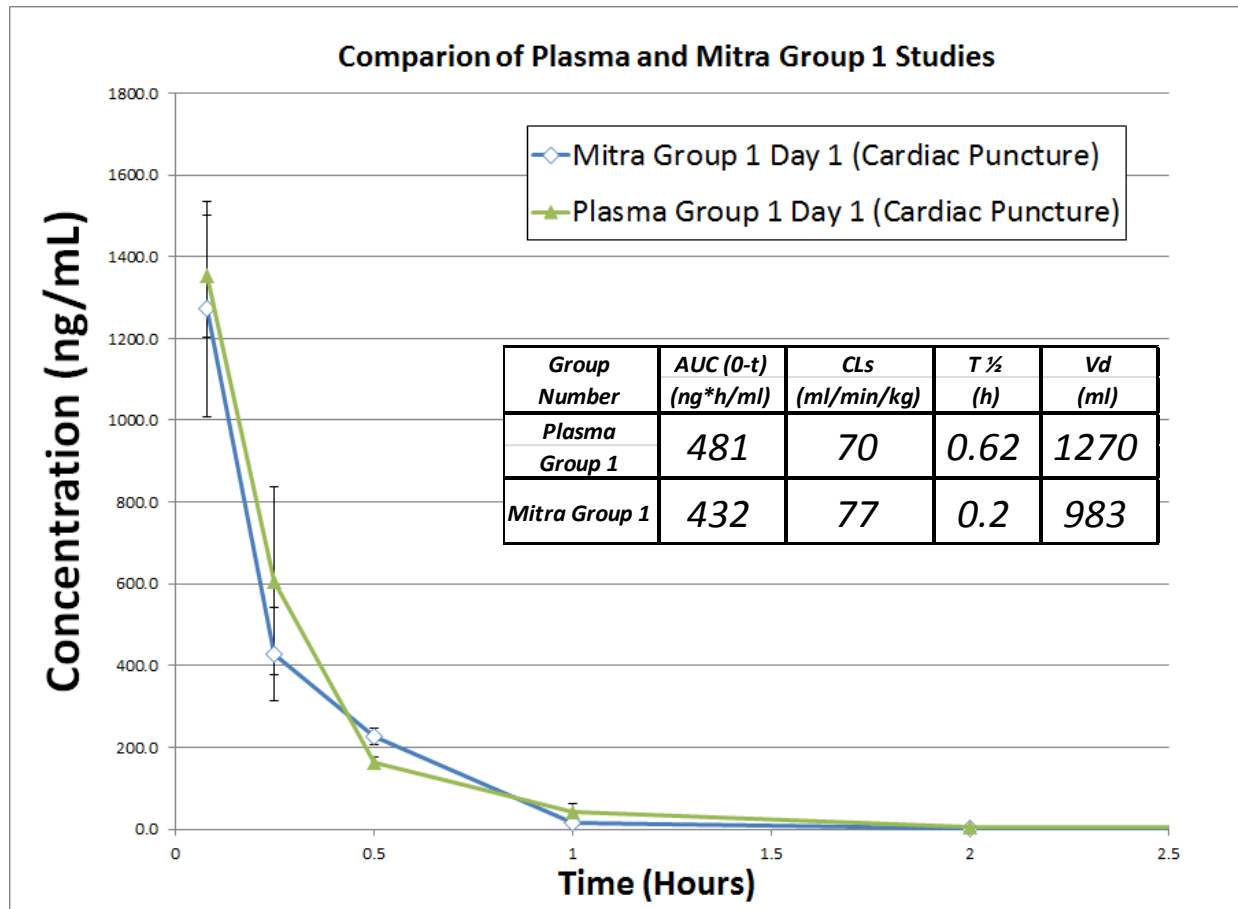


Standard curve for acetaminophen (mouse whole blood)

■ Mouse whole blood results, linear regression, $1/x$ weighting, $y=0.00216x + 0.0183$ ($r=0.9986$)

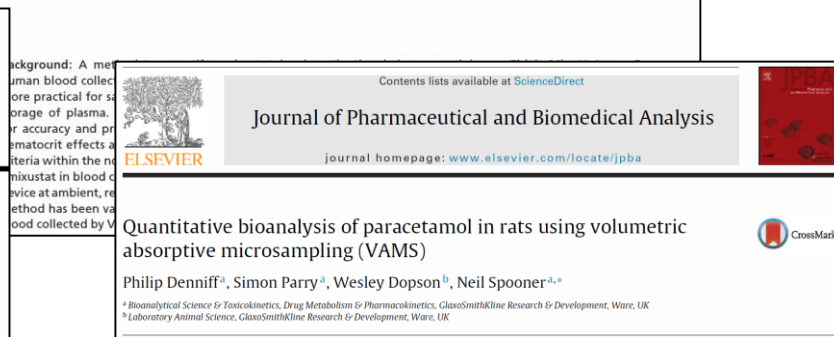
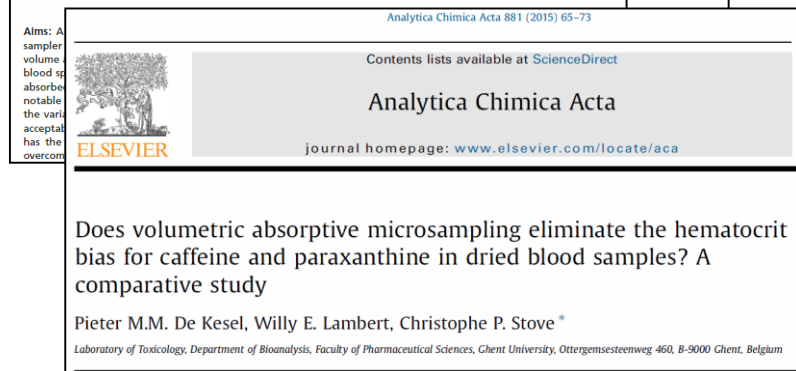
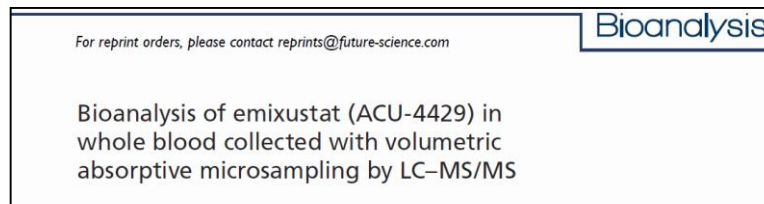
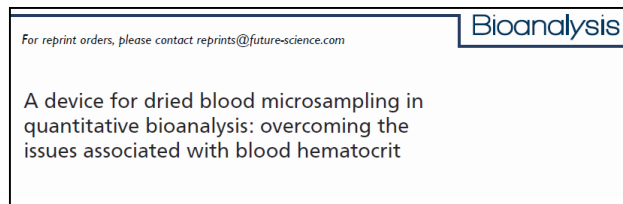


acetaminophen PK parameters



from July 2014 to now

- Over 10 Posters and ~10 publications.



resources

VAMS™ publications

general

De Kesel, P.M.M., Lambert, W. E., Stove, C. P. (2015). Does volumetric absorptive microsampling eliminate the hematocrit bias for caffeine and paraxanthine in dried blood samples? A comparative study. *Anal. Chim. Acta*, 881, 65–75.

Mano, Y.; Kita, K.; Kusano, K. (2015). Hematocrit-independent recovery is a key for bioanalysis using volumetric absorptive microsampling devices, Mitra. *Bioanalysis*, 7(15), 1821–1829.

Kushon, S., Bischofberger, A., Carpenter, A., Denniff, P., & Guo, Y. (2014). A Novel Dried Matrix Microsampling Device that Eliminates the Volume Based Hematocrit Bias Associated with DBS Sub-Punch Workflows, 62nd ASMS Conference on Mass Spectrometry and Allied Topics.

Houbart, V., Cibraiva, G., Servais, A.-C., Napp, A., Merville, M.-P., & Fillet, M. (2015). Hepcidin determination in dried blood by microfluidic LC-MS/MS: comparison of DBS and volumetric absorptive microsampling for matrix effect and recovery. *Bioanalysis*, 7(21), 2789–2799.

pharmaceutical

Spooner, N., Denniff, P., Michielsen, L., De Vries, R., Ji, Q. C., Arnold, M. E., ... Rudge, J. B. (2015). A device for dried blood microsampling in quantitative bioanalysis: overcoming the issues associated blood hematocrit. *Bioanalysis*, 7(6), 653–659.

Denniff, P., Parry, S., Dopson, W., & Spooner, N. (2015). Quantitative bioanalysis of paracetamol in rats using volumetric absorptive microsampling (VAMS). *Journal of Pharmaceutical and Biomedical Analysis*, 108, 61–69.

Miao, Z., Farnham, J. G., Hanson, G., Podoll, T., Reid, M. J. (2015). Bioanalysis of emixustat (ACU-4429) in whole blood collected with volumetric absorptive microsampling by LC-MS/MS. *Bioanalysis*, 7(16), 2071–2083.

Wachtel, D., Tobin, J., Virasingh, B., Sheldon, A., Dearborn, S., Guo, Y., ... Ribadeneira, M. (2016). A 10-Point Time Course Pharmacokinetic Study Collected from a Single Mouse by use of the Mitra Microsampling Devices. 64th ASMS Conference Poster.

Parker, S., Roberts, J., Lipman, J., & Wallis, S. C. (2015). Quantitative bioanalytical validation of fosfomycin in human whole blood with volumetric absorptive microsampling. *Bioanalysis*, 7(19), 2585–2595.

Luo, Y., Korfmacher, W., Ho, S., Shen, L., Wang, J., Wu, Z., Guo, Y., Snow, G., O'Shea, T. (2015). Evaluation of two blood microsampling approaches for drug discovery PK studies in rats. *Bioanalysis*, 7(18), 2345–2359.

continued on other side

The Mitra Microsampler class I medical device is for direct specimen collection of blood and other biological fluids. It is not specific to any clinical test, and is not for use in diagnostic procedures. Use of the Mitra Microsampler in Laboratory Developed Tests (LDTs) requires further processing including the establishment of performance characteristics and successful validation by the laboratory in a manner consistent with CLIA requirements.



VAMS™ publications

clinical research & diagnostics

Mercolini, L., Protti, M., Catapano, M. C., Rudge, J., & Sberna, A. E. (2016). LC-MS/MS and volumetric absorptive microsampling for quantitative bioanalysis of cathinone analogues in dried urine, plasma and oral fluid samples. *Journal of Pharmaceutical and Biomedical Analysis*, 123(10 May), 186–194.

Kipper, K., Barker, C., Lonsdale, D., Sharland, M., & Johnston, A. (2015). Evaluation of the Mitra microsampling device for dry sample processing in a pharmacokinetic/pharmacodynamic study of beta-lactams. 42nd Symposium of HPLC.

Mercolini, L., Protti, M., Albers, L. J., & Reist, C. (2016). Therapeutic Drug Monitoring (TDM) By Means Of Novel Sampling AND Extraction Procedures: A Comparative Study. *European Bioanalysis Forum (EBF) Symposium*.

Protti, M., Capatano, M., Somaini, L., Gerra, G., & Mercolini, L. (2016). Enhanced Stability of Dried Haematic Samples for New Psychotropic Synthetic Compound Monitoring. *European Bioanalysis Forum (EBF) Symposium*.

Neupane, B., Mulla, H., Spooner, N., Abu-Rabee, P., Rudge, J., & Pandya, H. (2016). Midazolam Measurement and Modelling using Matrix Samplers (The 4M's Study). *American Pediatrics Association (AAP) Conference*.

Stephenson, S., Dutton, J., Davison, A., Kushon, K., Rudge, J. (2016). Evaluation of the Mitra Microsampling Device for Immunosuppressants Monitoring. *Neoteryx Application Note*.

Gordon, C., Sadilkova, K., Jack, R. M., & Dickerson, J. A. (2016). Improved Sensitivity for Immunosuppressant Monitoring in Two Dried Matrices: A Proof of Concept. *MSACL Conference - Mass Spectrometry: Applications to the Clinical Lab*.

Mbughuni, M. (2016). Immunosuppressant (Tacrolimus/Cyclosporin A) Monitoring by LC-MS/MS Using Mitra Microsampling Devices. *MSACL Conference - Mass Spectrometry: Applications to the Clinical Lab*.

molecular diagnostics & proteomics

van den Broek, I., Fu, Q., Millis, K., Ekersley, T., Wood, W. W., Kowalski, M. P., ... Eyk, J. E. Van. (2016). Can volumetric absorptive micro sampling in the presence of a stable-isotope labeled protein standard control pre-analytical variability in proteomics? 64th ASMS Conference on Mass Spectrometry and Allied Topics.

El-Mogy, M., Misis, V., McGowan, S., Lam, B., & Haj-Ahmad, Y. (2016). Total RNA/DNA Purification and Detection from Blood Preserved on a Mitra Microsampling Device. *Neoteryx Application Note*.



resources

Breaking News

Mitra® microsampling devices available in cartridge formats for at-home sample collection

x



Animal Research

Clinical Trials

Clinical Research

Products

Resources

Company

Order



Resources

All Topics

neoteryx application note

Figure 1. RNA/DNA detection in dried blood.

The application note describes the use of Mitra® microsampling devices for the collection of dried blood samples (DBS) for the detection of RNA and DNA. The note includes a table showing the detection limits for various analytes and a bar chart comparing the detection limits of Mitra® devices to other methods.

application note: total RNA/DNA purification & detection from dried blood microsampling device

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neoteryx

do dried blood microsamples have a place in the clinical lab

webinar: do dried blood microsamples have a place in clinical research labs?

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VAMS publications

VAMS publications

VAMS publication list

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r&d poster: evaluation of mitra for pk/pd study of beta-lactams

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Mitra microsampling device

video: quantitative, absurdly simple microsampling

video: the next generation in biological sampling

MS ACL

microsampling data presented at MSACL 2016

mitra product brochure

conclusions

- High quality biological fluid collections **with minimal training**
- Improved **patient experience**
- **High degree of convenience** for nurses, patients, and physicians
- Replaces existing sampling avenues or supplements them with **additional sample inflow**
- Standard methods and Mitra methods **strongly correlate** using simple (or identical) extraction methodology
- Enables **at-home or remote sampling** for increased compliance and adherence



thank you!

Brandon Milan

Microsampling Specialist

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Neoteryx

Email: BrandonM@Neoteryx.com

Website: www.neoteryx.com