Advances in Sample Preparation 13 (2025) 100161

Contents lists available at ScienceDirect

Advances in Sample Preparation

journal homepage: www.elsevier.com/locate/sampre

New trends in bioanalysis sampling and pretreatment: How modern microsampling is revolutionising the field

Michele Protti [a], Elisa Milandri [a], Roberta Di Lecce [b], Laura Mercolini [a,*], Roberto Mandrioli [b]

[a] Research Group of Pharmaco-Toxicological Analysis (PTA Lab), Department of Pharmacy and Biotechnology (FaBiT), Alma Mater Studiorum–University of Bologna, Via Belmeloro 6, 40126 Bologna, Italy
[b] Department for Life Quality Studies (QuVi), Alma Mater Studiorum–University of Bologna, Corso d'Augusto 237, Rimini, Italy

ARTICLE INFO

Keywords:
Microsampling
Volumetric dried blood spots
Volumetric absorptive microsampling (VAMS)
Therapeutic drug monitoring (TDM)
Patient-centric approaches
Analytical green chemistry (AGC)

ABSTRACT

Microsampling technologies are revolutionising bioanalysis by enabling minimally invasive, decentralized sample collection, offering significant advantages over traditional methods in terms of patient compliance, cost-effectiveness, and analytical efficiency. This review explores the latest advancements in microsampling devices, including microfluidic and quantitative dried blood spot systems (mfDBS and qDBS, respectively), calibrated capillary-based devices, volumetric absorptive microsampling (VAMS) technologies, microneedle-based microsampling, radial-based DBS devices, membrane-based plasma separation technologies and vacuum-assisted blood collection systems. By addressing pre-analytical variability, enhancing analyte stability, and supporting decentralized workflows, these technologies align with modern and green analytical chemistry principles. The unique capabilities of these emerging microsampling technologies and devices further demonstrate their transformative potential. However, challenges remain, including haematocrit dependency for some parameters, user variability, and standardisation across devices. This review highlights ongoing innovations and their implications for expanding to high-quality bioanalytical testing.

1. Introduction

The field of bioanalysis is experiencing a paradigm shift driven by the advent of microsampling technologies. Traditional sample collection methods, such as venipuncture, present challenges including patient discomfort, logistical complexity, and high costs, particularly in decentralized or resource-limited settings. In contrast, microsampling techniques offer innovative solutions that address these limitations while enabling precise and efficient analysis of small-volume biological samples [1,2].

It must be stressed that the advantages of microsampling over traditional venipuncture are many and varied and easily justify the need to change established protocols and the increased incurred expenses due to device costs [3]. Dried microsampling in particular removes most water content from biological fluids, thus making the resulting specimen much more easily handled, shipped and stored, and reducing the time, equipment and expenses associated with all these steps. For many analytes, stability is also greatly increased, even at room temperature (RT) [4]. The minimal invasiveness of this sampling technique greatly improves patient adherence and makes it much more widely and safely applicable than traditional sampling approaches, also opening the way to self- and home-sampling [5]. Whether dried or wet, microsamples are also much less hazardous for all people involved, and contamination or infection concerns are much less impacting than with classical biosamples [6]. Obviously, dried microsamples are even safer than wet ones in this respect.

Another interesting feature of all microsampling techniques using solid supports is that the support itself acts as an extraction means of sorts, selectively retaining or freeing specific compounds from the biological matrix [7]. This makes the subsequent sample preparation step much faster, easier and inexpensive, up to the point of making direct instrument injection or direct introduction into the separative/analytical flow possible [8,9]. This point is hardly overestimated, since high-throughput, robust sample preparation methods that produce efficient and reproducible data are of paramount importance to any omics application [10], indeed making them viable for widespread application to the general population.

Microsampling devices have evolved significantly since the introduction of dried blood spots (DBS) in the 1960s for neonatal screening. Modern innovations include volumetric absorptive microsampling

* Corresponding author.
E-mail address: laura.mercolini@unibo.it (L. Mercolini).

https://doi.org/10.1016/j.sampre.2025.100161
Received 30 January 2025; Received in revised form 17 February 2025; Accepted 19 February 2025
Available online 21 February 2025

(VAMS), advanced DBS platforms (e.g. based on microfluidics and capillary systems), membrane-based plasma separation and minimally invasive fluid capillary blood collection technologies, each tailored to specific applications and analytical needs. These devices are designed to enhance user adherence, minimize pre-analytical variability, and support high-throughput and automated workflows [11], making them invaluable, among the others, in therapeutic drug monitoring (TDM) [12–14], epidemiological studies [6,15], drug discovery and development [16], forensics [17] and anti-doping programs [18]. Most current microsampling techniques have been designed from the start to be useable by relatively inexperienced, untrained personnel, with the goal of making self- and home-sampling viable alternatives to classical venipuncture by medical staff at centralised healthcare facilities. This in turn would make precision medicine one step closer to become reality. Microsampling has the potential of allowing patients to undergo frequent monitoring and diagnostic tests with reduced costs and increased convenience, resulting in much higher adherence to treatments [19].

The original DBS techniques suffered from intrinsic problems, such as lack of volume repeatability, haematocrit effect, spot inhomogeneity and high ratios of unsuccessful sampling, which for a long time hindered their widespread adoption by laboratories, and confined them to use by trained, professional personnel and in centralised healthcare locations [20]. Sensitivity reduction in comparison to macroscopic biological fluid samples was also a factor. Starting from the 2010s, together with huge increases in analytical equipment performance leading to amazingly increased sensitivity and selectivity, innovative approaches to microsampling started to appear, which at first mostly tackled the main problem of classical DBS, i.e., lack of volume repeatability [21]. This was accomplished in several ways: for example, some novel techniques retained the finger- or heel-prick mechanism along with the “classical” cellulose card (either in full or as pre-cut fragments) but modified the sampling mechanism to obtain volume accuracy and repeatability in what is known as volumetric DBS (vDBS) approach. vDBS can be obtained by interposing between the blood drop and the card a microfluidic section (mfDBS: Hemaxis), sometimes in the form of metered channels and dissolvable valves (qDBS: Capitainer B, B50, B Vanadate), or else, calibrated capillaries (HemaPEN); or using calibrated radial wedges (HemaSpot HF). VAMS went a step further, maintaining only the prick mechanism but completely changing the sampling support from a cellulose card to a calibrated polymeric tip [21]. Other approaches dispense with a separated skin-prick moment and directly integrate microneedles into the device for better patient comfort, obtaining either fluid microsamples or dried blood samples on polymer (Tasso-M20). Larger microsample volumes can be sampled from an upper arm lancet prick by light vacuum (Tasso+) or from a finger-prick by vacuum-assisted, powered devices (HAIIM).

Finally, direct plasma separation on the support brings the game to another level altogether, since it tackles another known issue of blood microsampling: i.e., the difficulty in comparing and using results obtained from whole blood with those obtained from plasma [22]. Microsample plasma separation is usually achieved using a filtering membrane incorporated into the sampling device (Capitainer SEP10, Telimmune, Hemaspot SE).

As can be easily understood, such a wealth of options in microsampling provides a wide range of choices that can be implemented, accommodating different needs and according to diverse practical and scientific reasons, to make sampling, sample preparation and analysis ever more affordable, reliable, easier and greener [23].

This review examines these latest trends and developments in microsampling technologies, focusing on their practical applications and analytical performance, with some notes on their contributions to analytical green chemistry (AGC), sometimes also referred to as green analytical chemistry (GAC). By highlighting the strengths and limitations of these approaches, we aim to provide a comprehensive overview of their transformative role in modern bioanalysis.

2. Microsampling techniques and applications

2.1. Microfluidic-generated dried blood spot (mfDBS) sampling

Microfluidic-generated dried blood spot (mfDBS) technology represents a significant innovation in the evolution of blood microsampling. Introduced in 2016, mfDBS systems combine traditional DBS methodologies with microfluidic technology to overcome longstanding challenges such as volume inconsistency, spot inhomogeneity, and pre-analytical variability. These systems employ calibrated microfluidic channels to achieve precise volumetric sampling, enhancing the reliability and reproducibility of DBS-based analyses [24–34] (Fig. 1).

The distinctive advantage of mfDBS devices lies in their ability to produce uniformly sized and accurately measured blood spots, typically around 10 μL per spot (e.g., for the Hemaxis device). This precision is achieved through the integration of calibrated microchannels, which ensure volumetric accuracy.

The applications of mfDBS are diverse, with therapeutic drug monitoring (TDM) being a notable focus. Studies have demonstrated the effectiveness of mfDBS in quantifying blood concentrations of drugs such as aromatase inhibitors, cyclin-dependent kinase inhibitors, and psychotropic agents. Despite the minute sample volume, these applications show robust analytical performance and maintain the sensitivity needed for clinical relevance [25,26]. mfDBS has proven suitable for measuring poly(ADP-ribose) polymerase (PARP) inhibitors used in cancer treatments and trace elements such as copper and mercury. These studies highlight its versatility across analyte types and concentration ranges, particularly when coupled with high-performance techniques like LC-MS/MS and graphite furnace atomic absorption spectrometry (GFAAS) [28–30].

In epidemiological contexts, mfDBS technology has facilitated decentralized blood collection and analysis. Its utility in detecting biomarkers for diseases, such as SARS-CoV-2 antibodies, exemplifies its role in pandemic management and other large-scale public health initiatives. Integration with microfluidic nano-immunoassays has further enhanced its analytical potential, ensuring high specificity and sensitivity even in complex matrices [33,34]. mfDBS systems align closely with the principles of AGC. By enabling low-volume sampling and minimizing waste, these devices reduce the environmental impact of bioanalysis. Their compact design eliminates the need for cold chain logistics and extensive sample preparation, supporting sustainable practices in clinical and research settings. High-throughput workflows are also supported, allowing for efficient analysis of large sample cohorts without compromising data quality [34].

Despite its advantages, mfDBS technology faces challenges that require attention for broader adoption. The dependency on user training to ensure proper sample application can lead to increased result variability, particularly in decentralized or home-based sampling scenarios [24]. Additionally, non-volumetric haematocrit effects, which influence analyte recovery and quantification, remain an area of active research. Overcoming these limitations through device optimisation and standardisation is critical for achieving widespread clinical integration [27,28,32]. Future developments in mfDBS technology will likely focus on expanding analytical compatibility and improving automation to reduce operator intervention and variability. Enhancing the robustness of these devices for diverse applications, such as point-of-care testing and personalized medicine, will further solidify their role in bioanalysis [29].

By addressing the limitations of traditional DBS methods, mfDBS has established itself as a transformative tool in modern bioanalysis. Its versatility, sustainability, and analytical precision underscore its pivotal role in advancing microsampling practices across various fields.

Table 1 summarises a selection of representative studies involving microfluidic-generated dried blood spot (mfDBS) sampling.

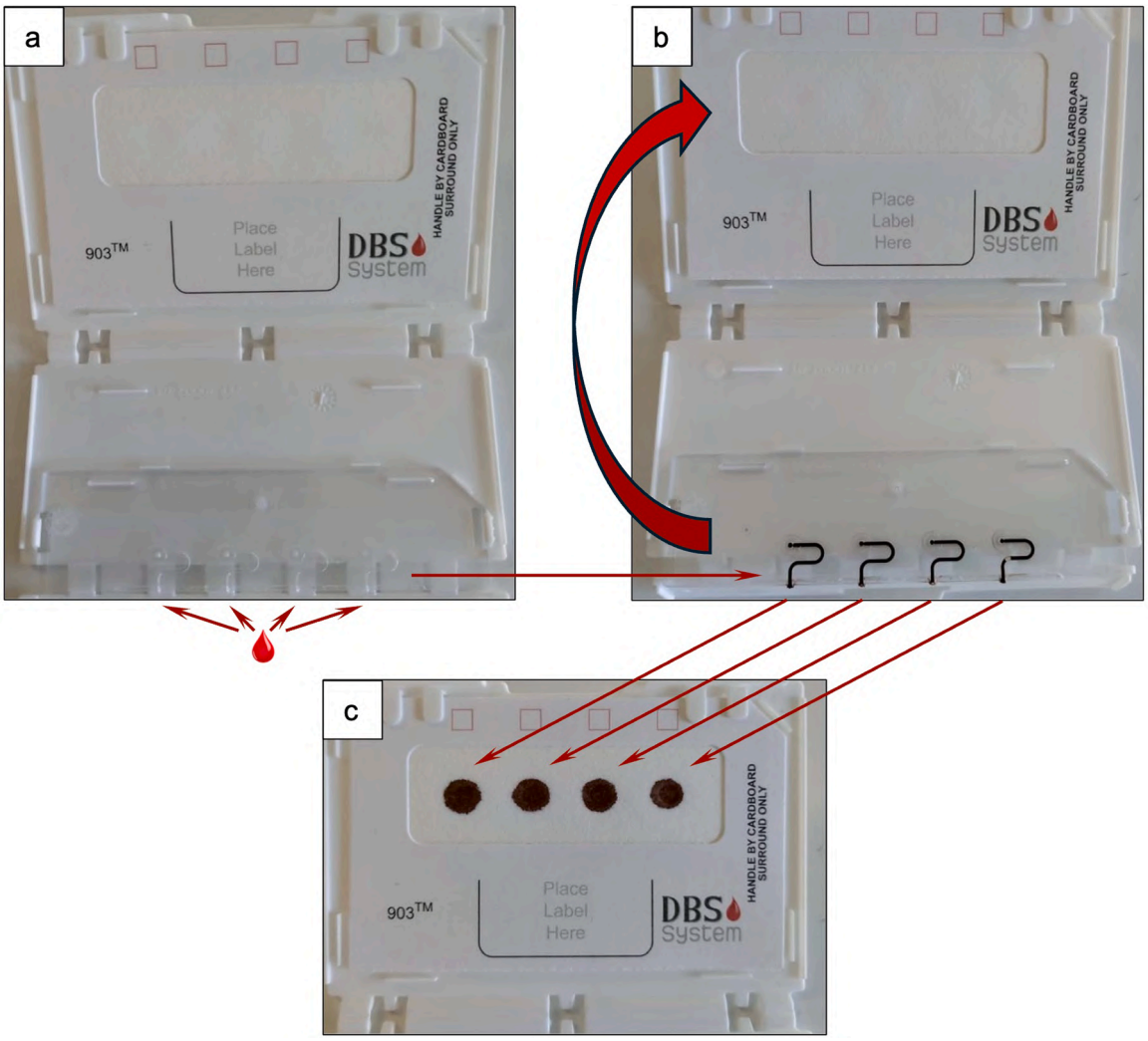

Fig. 1. Example of device for the production of volumetric dried blood spots by microfluidics (mfDBS): the HemaXis DB10. Appearance of the device (a) before use; (b) after application of one blood drop to each of the four device inlets; (c) after the formation of four 10-µL DBS. Adapted from [31]. Used with permission.

Table 1
Summary of selected studies involving microfluidic-generated dried blood spot (mfDBS) sampling.

Target analyte(s)	Microsampling technology	Sample type	Sample volume	Sample treatment	Instrumental setup	Sensitivity	Precision	Accuracy	Reference
Letrozole, palbociclib, ribociclib, abemaciclib	HemaXis DB10	Volumetric DBS	10 µL	Rehydration, P/P, centrifugation, dilution	LC-MS/MS	LOQ: 6–120 ng/mL	% CV≤12.2	93–104 %	[25]
Clozapine and metabolites	HemaXis DB10	Volumetric DBS	10 µL	UAE	HPLC-ED	LOQ: 3 ng/mL	% RSD≤5.6	89–109 %	[27]
Hg	HemaXis DB10	Volumetric DBS	10 µL	None	AAS	8.7 ng/mL	%RSD: 2.4	NR	[31]
SARS-CoV-2 Spike IgG	HemaXis DB10	Volumetric DBS	10 µL	Manual and automated extraction, incubation	Nano-immunoassay	Clinical sensitivity: 83 % (manual), 97 % (automated)	NR	94% (manual), 98 % (automated)	[33]
Phenylalanine, tyrosine	HemaXis DB10	Volumetric DBS	10 µL	Extraction, dilution	FIA-MS/MS	NR	% RSD≤4.1	-5.1 % bias with respect to fluid blood	[34]

NR: not reported.

2.2. Quantitative dried blood spot (qDBS) sampling

Quantitative dried blood spot (qDBS) technology, particularly the Capitainer® cards, has redefined the possibilities of microsampling by addressing key challenges in traditional blood sample collection. Designed for accuracy, precision, and ease of use, qDBS devices enable the consistent collection of small, defined volumes of blood, making them indispensable tools in modern bioanalysis. Among the leading models are Capitainer B, B Vanadate and B 50 (Fig. 2), each tailored to meet specific analytical and clinical needs [2,4,7,24,34–55]. The same

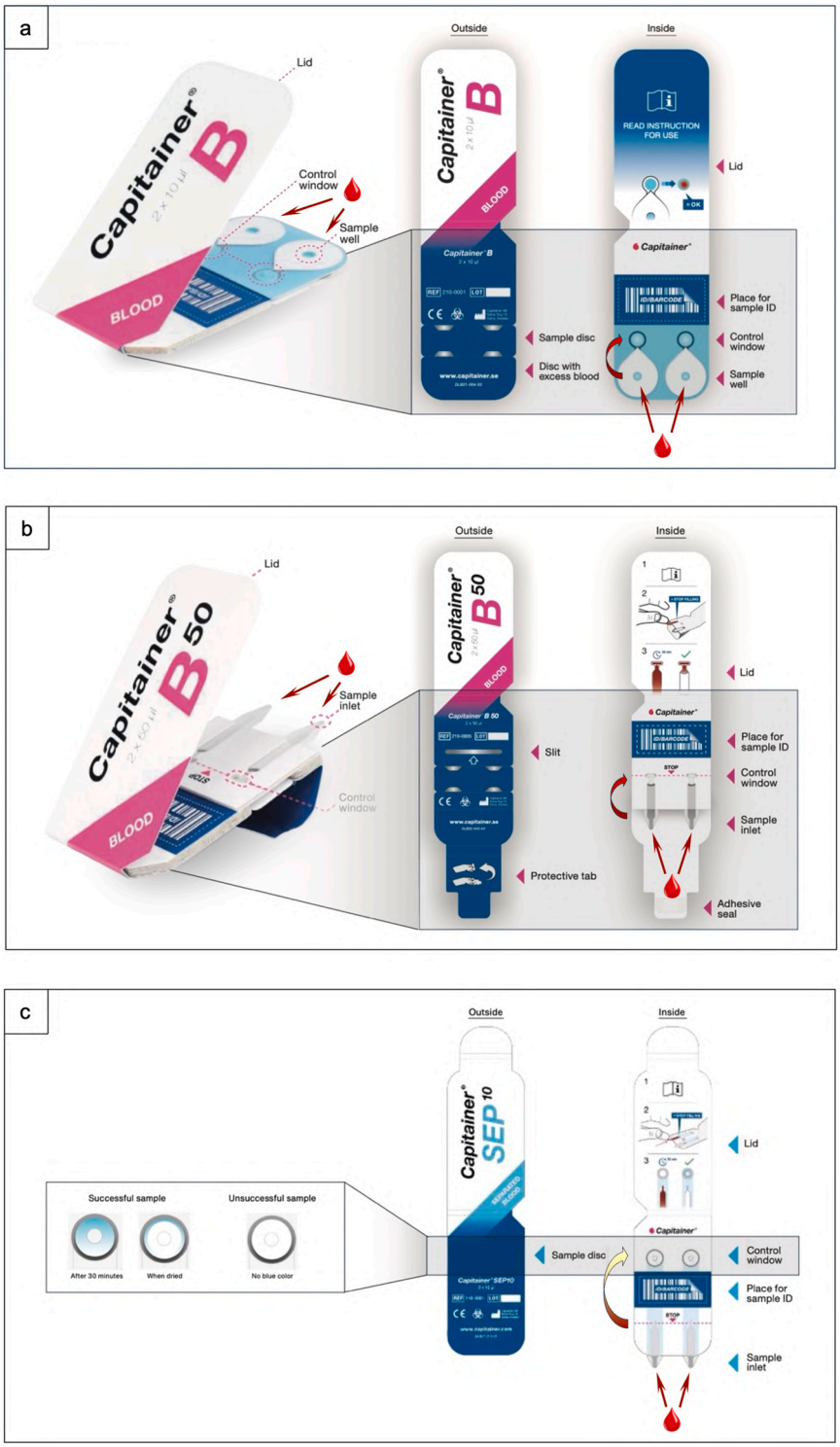

Fig. 2. Appearance and legend of the main functions of (a) Capitainer B, (b) Capitainer B 50 and (c) Capitainer SEP10 devices. Appearance of the Capitainer B Vanadate is identical to that of Capitainer B, except the cover label text. Adapted from https://capitainer.com/instructions-downloads/.

manufacturer also produces a device for volumetric plasma collection, the Capitainer SEP10 (Fig. 2c); although this latter device could be appropriately included within Section "2.7. Membrane-based volumetric plasma generation technologies", it is described here for simplicity and due to the common source and (outward) similarity with other Capitainer devices.

Capitainer B is the foundational model and represents the core of qDBS innovation. It uses an advanced microfluidic channel system to accurately collect 10 µL of blood from a single drop. A two-step valve mechanism ensures the prevention of overfilling while providing visual feedback to confirm proper usage. This feature simplifies the process for both professional and non-professional users, making it one of the most attractive choices in decentralized settings [34–36]. The B Vanadate variant modifies this model by integrating into the card a phospholipase D inhibitor to stabilize phosphatidylethanol (PEth), a key biomarker in ethanol consumption studies. This modification ensures sample integrity

during storage and handling, addressing a critical gap in biomarker analysis [38,39].

The Capitainer B 50 model expands the scope of qDBS by offering a larger sampling volume of 50 µL, suitable for workflows requiring higher amounts of analyte. This design is particularly advantageous for applications demanding increased sensitivity or broader analyte detection ranges. The SEP10 model further extends the utility of qDBS by incorporating a plasma separation mechanism by membrane filtration, enabling workflows focused on plasma-based assays while maintaining the benefits of volumetric accuracy (producing accurate 10-µL dried plasma spots, DPS) [40].

The qDBS technology has many applications. In therapeutic drug monitoring (TDM), qDBS facilitates the precise analysis of immunosuppressants, ceftazidime, and various antibiotics, ensuring that drug levels are maintained within therapeutic ranges [45–49]. Biomarker studies, including those determining glycated haemoglobin (HbA1c), ceramides, and isoprostanoids, have demonstrated the utility of qDBS in monitoring metabolic health and disease progression [36,42–44]. Toxicological applications further highlight the flexibility of qDBS, with studies detecting recreational drugs such as cocaine and nitazenes, providing critical insights into substance use and abuse [51–53].

Beyond traditional blood analysis, the qDBS technology has been adapted for alternative sample types. Capitainer B has been repurposed for dried urine and faecal spot sampling, enabling measurements of albumin/creatinine ratios and bile acid profiling [31,54,55]. These adaptations showcase the potential of qDBS to address non-invasive diagnostic needs, expanding its role in personalized medicine and public health research.

While Capitainer B remains the most extensively studied model, the newer variants—Capitainer B 50 and SEP10 in particular—are rapidly gaining recognition. Preliminary studies have highlighted their effectiveness in anti-doping programs, where precise and reliable sampling is paramount, and in advanced biomarker monitoring, where their enhanced capabilities provide critical advantages [41]. These developments position qDBS as a cornerstone of modern microsampling, aligning seamlessly with the principles of AGC and the growing need for decentralized healthcare solutions.

By combining user-friendly design, technological precision, and wide-ranging adaptability, qDBS technology continues to drive innovation in bioanalysis.

Table 2 summarises a selection of representative studies involving qDBSsampling.

2.3. Calibrated capillary-based dried blood spot sampling

HemaPEN is a pen-shaped device allowing the accurate and precise collection of samples from a single drop of blood with little or no influence from haematocrit compared to classical DBS. Blood is collected through four calibrated capillaries (2.74 µL each) and transferred onto four DBS paper discs, where it can be safely stored for relatively long times thanks to the presence of a desiccant within the device itself. The latter can then be opened with a specially designed tool and the four replicate samples removed (Fig. 3). Thus, HemaPEN has the big advantage of producing four identical DBS from a single fingerprick, but with the specular disadvantage of obtaining lower-volume DBS than other vDBS devices. The sampling procedure is generally considered quite simple (hold the device like a pen and touch a blood drop from a fingerprick), easily doable by patients at home.

The practical applications of HemaPEN are extensive and diverse [56–67]. TDM of several drug classes has emerged as a fruitful field of application. For instance, HemaPEN has been utilized for TDM of osimertinib and its metabolites (AZ5104 and AZ7550), where sample preparation involved protein precipitation (PPP) with acetonitrile and centrifugation, followed by dilution. Similarly, it has been applied to tacrolimus TDM, comparing manual and automated extraction protocols. HemaPEN was also evaluated alongside VAMS for the radiocontrast agent iohexol, showcasing comparable reliability. Preparation protocols included solvent extraction, phospholipid removal, and redissolution [61–63].

Forensic and toxicological applications have also expanded with HemaPEN's integration into workflows. For instance, the determination of cocaine and its metabolites demonstrated satisfactory haematocrit independence for both volume and final results [64]. Advanced studies included analysing 75 different per- and poly-fluoroalkyl substances (PFAS) using LC-MS/MS after sample preparation by a combination of PPP with filtration [65]. Additionally, the potential for drug detection and metabolomics in remote or challenging settings highlights the applicability of this method in forensic and clinical toxicology.

In targeted lipidomics, HemaPEN has facilitated in-field sampling scenarios, such as collecting blood from athletes on a track. Using UHPLC-MS/MS, the analysis of arachidonic acid, lactic acid, and other lipids proved unaffected by low sample volumes. Sample preparation steps included solvent extraction and ultrasound-assisted extraction (UAE). Additional studies on exercise-related metabolite changes (including amino acids and creatinine) further validated HemaPEN's practicality and reliability in dynamic environments. Targeted lipidomics approaches have also been used to monitor dietary or physiological interventions, showcasing the device's flexibility across different analytical contexts [59,60].

Clinical applications of HemaPEN have also advanced, including its use for creatinine analysis via capillary electrophoresis (CE) coupled with capacitively coupled contactless conductivity detection (C4D).

Table 2
Summary of selected studies involving quantitative dried blood spot (qDBS) sampling.

Target analyte(s)	Microsampling technology	Sample type	Sample volume	Sample treatment	Instrumental setup	Sensitivity	Precision	Accuracy	Reference
rhEPO	Capitainer B50	Volumetric DBS	50 µL	Immunoaffinity purification	SAR-PAGE, Western blot	NR	NR	NR	[41]
Isoprostanoids, prostanoids	Capitainer B	Volumetric DBS	13.5 µL	Extraction, filtration, evaporation, reconstitution, microextraction by packed sorbent (MEPS)	UHPLC-MS/MS	LOD: 15–20 ng/mL	%RSD up to 20–25 %	Bias<15 %	[44]
Immunosuppressants, creatinine	Capitainer qDBS	Volumetric DBS	10 µL	UAE, LLE, evaporation, reconstitution, P/P, centrifugation	LC-MS/MS	LOQ: 1–20 ng/mL, 15 µmol/L (creatinine)	% CV<15.9	Bias<10 %	[46]
Cocaine and metabolites	Capitainer qDBS	Volumetric DBS	10 µL	UAE, evaporation, reconstitution	UHPLC-MS	LOQ: 2.5–7.5 ng/mL	% RSD<7.5	Bias<15 %	[52]
Nitazene analogs, brorphine	Capitainer B	Volumetric DBS	10 µL	UAE, evaporation, reconstitution, centrifugation	UHPLC-MS/MS	LOQ: 1 ng/mL	% CV<15.9	Bias<14.9 %	[53]

NR: not reported

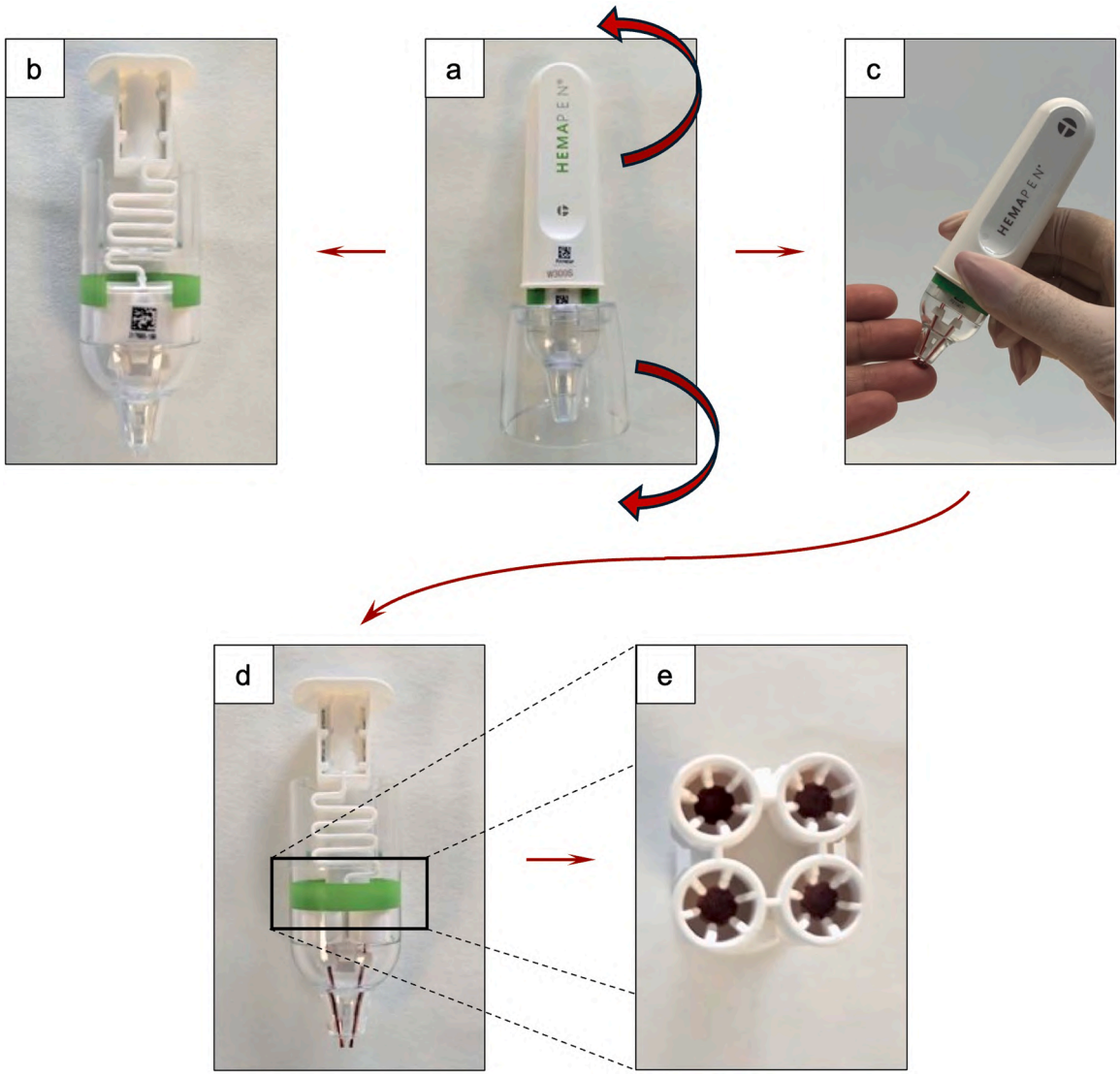

Fig. 3. Details of a HemaPEN device, including its capillaries and DBS generation process.: (a) intact, closed; (b) opened and disassembled; (c) in use, touching a blood drop with the device tip; (d) capillaries filled with blood afterward; (e) the four DBS formed after transfer of blood from the capillaries, still in their dedicated compartment. Adapted from [29] and [64]. Used with permission.

Researchers developed an automated workflow using unmodified CE instrumentation for DBS preparation and extraction. Results highlighted the method's precision and potential for high-throughput settings. Screening for lysosomal storage diseases using HemaPEN DBS also yielded results comparable to classical DBS techniques, emphasizing the feasibility of the method's introduction into tried and tested diagnostic workflows with minimal disruptions [66]. Furthermore, its integration with enzymatic assays and ligand binding platforms has enabled semi-quantitative analysis for various biomarkers, expanding its utility in early diagnostics and routine monitoring [67].

Despite its advantages, challenges persist. Haematocrit effects, although mitigated for sampling volume, can influence analyte recovery in specific scenarios. User training is crucial to ensure proper sampling and avoid undersampling. Reduced DBS volume can be challenging for applications requiring high sensitivity. These limitations highlight areas for further optimisation in device design and methodology. Future advancements may include the development of automated platforms to streamline extraction and analysis, reducing user variability and increasing throughput.

HemaPEN integration into workflows emphasizes precision and user-friendliness, underscoring its pivotal role in advancing capillary-based microsampling technologies.

Table 3 summarises a selection of representative studies involving calibrated capillary-based dried blood spot sampling.

2.4. *Volumetric absorptive microsampling*

Volumetric absorptive microsampling (VAMS), introduced in 2014 through the Mitra device by Neoteryx (now Trajan), has become a cornerstone in the field of microsampling. This technology employs a calibrated porous polymeric tip, available in 10, 20, or 30 µL sizes, to ensure precise and reproducible sample collection across biological matrices (Fig. 4). Its simplicity and versatility have made it suitable for diverse applications, including TDM, biomarker studies, and toxicological analysis [4,27,31,46,53,54,68–122].

The design of VAMS integrates seamlessly with standard laboratory workflows, resembling a pipette tip to facilitate high-throughput analysis using automated liquid handling platforms. Sampling is as simple as touching the device to a liquid, allowing rapid absorption without oversampling. This feature makes VAMS particularly appealing for decentralized diagnostics, home-based sampling, and clinical trials where accessibility and reliability are critical.

Table 3
Summary of selected studies involving calibrated capillary-based dried blood spot sampling.

Target analyte(s)	Microsampling technology	Sample type	Sample volume	Sample treatment	Instrumental setup	Sensitivity	Precision	Accuracy	Reference
Fluoxetine, sertraline, and metabolites	HemaPEN	Volumetric DBS	2.74 µL	UAE, centrifugation	LC-MS/MS	LOQ: 5–7 ng/mL	%RSD<12 %	91–106%	[57]
Acetaminophen	HemaPEN	Volumetric DBS	2.74 µL	Extraction, P/P	LC-MS/MS	LOQ: 2 µg/mL	%CV≤6.83	83.7–106.5 %	[58]
Lipids	HemaPEN	Volumetric DBS	2.74 µL	Extraction	UHPLC-MS/MS	NR	Good repeatability based on Westgard's rules	NR	[59]
PFAS	HemaPEN	Volumetric DBS	2.74 µL	Filtered P/P	LC-MS/MS	MRL: 0.05–0.34 ng/mL	%RSD<15	NR	[65]
Creatinine	HemaPEN	Volumetric DBS	2.74 µL	Manual and automated extraction and P/P	CE-C^4D	LOQ: 16.7 µmol/L	%RSD<7.2	NR	[66]

NR: not reported.

Table 4
Summarises a selection of representative studies involving VAMS. Table 4. Summary of selected studies involving volumetric absorptive microsampling (VAMS).

Target analyte(s)	Microsampling technology	Sample type	Sample volume	Sample treatment	Instrumental setup	Sensitivity	Precision	Accuracy	Reference
Cardiovascular Drugs	Mitra	Blood VAMS	10 µL	UAE, evaporation, reconstitution	LC-HRAM MS	LOQ: 0.1–50 ng/mL	%CV<9.2	Bias<5.2 %	[74]
Antidepressant drugs and metabolites	Mitra	Blood and oral fluid VAMS	20 µL	UAE, evaporation, reconstitution, MEPS	HPLC-UV-FL	LOQ: 1–10 ng/mL	% RSD<8.9	86–94 %	[75]
Trace elements	Mitra	Blood VAMS	30 µL	Digestion, dilution	ICP-MS/MS	LOQ: 5 nmol/L–8.6 µmol/L	%CV<34	Negligible bias for Cu, Pb, Se and Zn; up to 146 % bias for Hg and As	[103]
Protein biomarkers	Mitra	Blood VAMS	10 µL	Automated extraction, incubation, digestion, dilution	LC-MS/MS	NR	%CV: 3.4–12.6	Acceptable correlation with plasma (average peptide abundance, R: 0.8383)	[110]
Tryptophan related biomarkers	Mitra	Blood VAMS	10 µL	UAE, centrifugation	LC-MS/MS	LOQ: 0.1–25 ng/mL	% RSD<9.6	90–107 %	[111]
rEPO	Mitra	Blood VAMS	20 µL	Immunoaffinity purification	SAR-PAGE, Western blot	Compliant with WADA MRPL	NR	NR	[114]
Drugs of abuse	Mitra	Blood VAMS	20 µL	PALME, dilution	UHPLC-MS/MS	LOQ: 1.0–5.0 ng/mL	%CV<26	Bias<11 %	[116]
Cocaine and metabolites	Mitra	Blood and plasma VAMS	20 µL	UAE, DPX	LC-MS/MS	LOQ: 1.0–2.5 ng/mL	% RSD<6.0	93–104 %	[117]
Novel psychoactive substances (NPS)	Mitra	Blood VAMS	10 µL	UAE, evaporation, reconstitution	UHPLC-MS	LOQ: 10–50 ng/mL	% RSD<10.8	NR	[118]
Anabolic androgenic steroids	Mitra	Urine VAMS	30 µL	Extraction, evaporation, reconstitution	LC-MS/MS	LOQ: 1.0–1.5 ng/mL	%RSD: 5.3–7.0	89–97 %	[122]

NR: not reported.

Applications of VAMS span multiple domains. In TDM, it has been used to monitor CNS drugs, antidepressants, anticancer agents, cardiovascular drugs, and immunosuppressants, offering reliable data to optimise patient treatment plans, including for drugs such as baricitinib, mycophenolic acid, mitotane, sirolimus, voriconazole (plus metabolite), giredestrant, paracetamol, meropenem, fosfomycin, emixustat, midazolam, clozapine (plus metabolites), cariprazine and (Val)ganciclovir [46,70,71–102]. In biomarker studies, VAMS has enabled the measurement of inflammation markers, vitamin D levels, IGF-1, lipid profiles, circulating protein biomarkers, and tryptophan-related biomarkers [106–112]. These capabilities contribute to a deeper understanding of health and disease states. The technology has also been integral to toxicological applications, supporting the detection of anabolic steroids, recreational drugs, and trace elements such as lead and iron. Applications in this field also include monitoring novel psychoactive substances (NPS) and conducting toxicological screenings [53,103–105,113–119].

Beyond blood sampling, VAMS has been adapted to alternative biological matrices, including urine and saliva, demonstrating its utility in non-invasive diagnostics. For example, urine has been analysed for biomarkers and drug residues, including clenbuterol, endogenous urinary metabolites, anabolic androgenic steroids, and peptide hormones and growth factors, while oral fluid has facilitated antidepressant drug monitoring [27,31,54,75,120–122]. These applications are particularly beneficial in paediatric and geriatric populations, where traditional sampling methods may be less feasible.

Despite its strengths, VAMS is not without challenges. Haematocrit

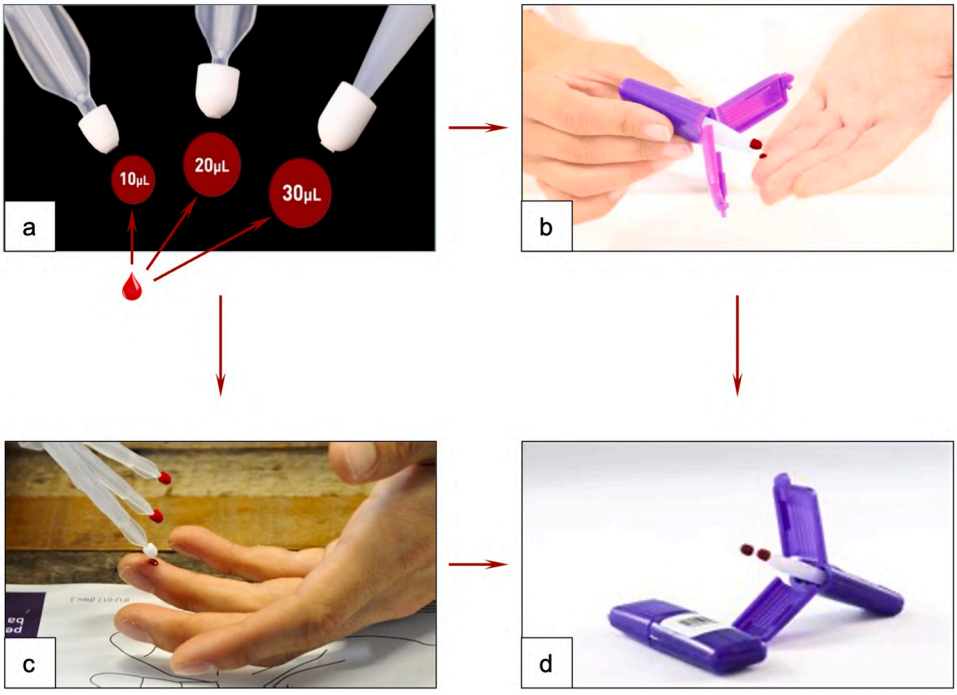

Fig. 4. Characteristics of VAMS microsampling devices and operation: (a) different sizes of the device tip; (b) sampling with free-standing devices and (c) with devices within a handheld storage clamshell; (d) sampled blood VAMS within an open and a closed clamshell. Adapted from https://www.neoteryx.com/.

bias, where variations in red blood cell concentrations impact analyte recovery, has been noted in certain applications. Studies continue to address this limitation, aiming to refine methodologies for consistent performance across different sample types [27,29,34,71]. Nonetheless, VAMS remains a benchmark technology in microsampling due to its balance of technical robustness and user-friendly design. Its reliability, adaptability, and alignment with sustainable practices ensure its relevance in clinical diagnostics, research, and public health initiatives.

2.5. Microneedle-based blood microsampling

Microneedle-based blood microsampling is a pivotal advancement in decentralized diagnostics, combining patient-centric designs with robust analytical capabilities. The TASSO series, including the TASSO-M20, TASSO+, and TASSO-SST, exemplifies this innovation by offering devices optimised for diverse diagnostic needs (Fig. 5). For the lower volume versions, the Tasso technology uses multiple microneedles arranged in a circular shape, and this seems to make blood sampling even less discomforting than for other microsampling techniques [1,71,95,114,123–164]; the larger volume microsamplers use a normal lancet. In any case, the device is applied to the upper arm instead of the fingertip.

A similar microneedle approach has been applied with the development of TAP (Touch-Activated Phlebotomy) devices from yourbio™ (YourBio Health, Inc.) [165] and RedDrop ONE devices from RedDrop Dx [166].

The TASSO-M20 is optimised for dried blood workflows, collecting 80 µL of capillary blood and dividing them into four 17.5 µL aliquots on polymeric tips (rather similar in appearance to VAMS tips). Its high adherence rates (95 % in longitudinal studies) have been demonstrated in haematocrit and reticulocyte monitoring over six weeks, with participants praising its minimal invasiveness and intuitive operation [123–125]. Similarly, in anti-doping programs, athletes achieved weekly sampling without schedule disruptions, highlighting the device's ease of use compared to traditional venipuncture [124,126,127].

The TASSO+ extends usability to broader contexts, including at-home blood collection for pharmacokinetics, by collecting variable amounts of fluid blood in standard collection tubes, without drying it on a support. In a study involving 120 participants, it achieved a 98 % success rate for decentralized sampling [1]. Feedback emphasized its straightforward instructions and painless operation, making it suitable for decentralized clinical trials and population health studies. In rural health surveys involving 300 participants, the device maintained over 90 % adherence, demonstrating its adaptability to low-resource environments [128,129].

The TASSO-SST (not yet available on the market), with its integrated plasma separation feature, will further support workflows requiring comparability/compatibility with standard plasma analyses. This device reduces pre-analytical variability by enabling high-quality plasma sample collection without the need for centrifugation. It has proven effective in biomarker studies for inflammation (e.g., CRP, IL-6, ferritin), achieving reproducibility (CV < 5 %) and strong correlation with venous samples ($R^2 > 0.9$) [130,131]. The device also simplifies pharmacokinetic studies, maintaining sample stability for drugs such as gefapixant and abrocitinib during ambient storage [132,133].

The analytical performance of TASSO devices has been rigorously validated across applications. The TASSO-M20 demonstrates excellent correlation ($R^2 > 0.95$) with venous samples for haematological biomarkers like haematocrit and reticulocyte percentages [71,124]. In anti-doping, it has shown suitability for detecting human growth hormone (hGH) isoforms, aligning with WADA-approved methodologies [124,134]. The TASSO-SST consistently achieves recovery rates exceeding 95 % for testosterone, cortisol, and other biomarkers, meeting FDA bioanalytical standards [132,133]. In infectious disease diagnostics, the TASSO-M20 preserves RNA stability for four weeks under ambient conditions, enabling decentralized HIV monitoring [135–137]. It also supports antibody detection in SARS-CoV-2 serological studies, achieving concordance coefficients above 0.95 with venous samples [128,138].

Sustainability is an intrinsic feature of the TASSO series, just like for the other microsampling techniques described herein. By eliminating cold chain logistics and minimizing consumable waste, these devices align with AGC principles, and a few studies are now starting to appear, where this aspect has been carefully evaluated. In one field study, TASSO-M20 reduced transport costs and emissions by 40 % compared to

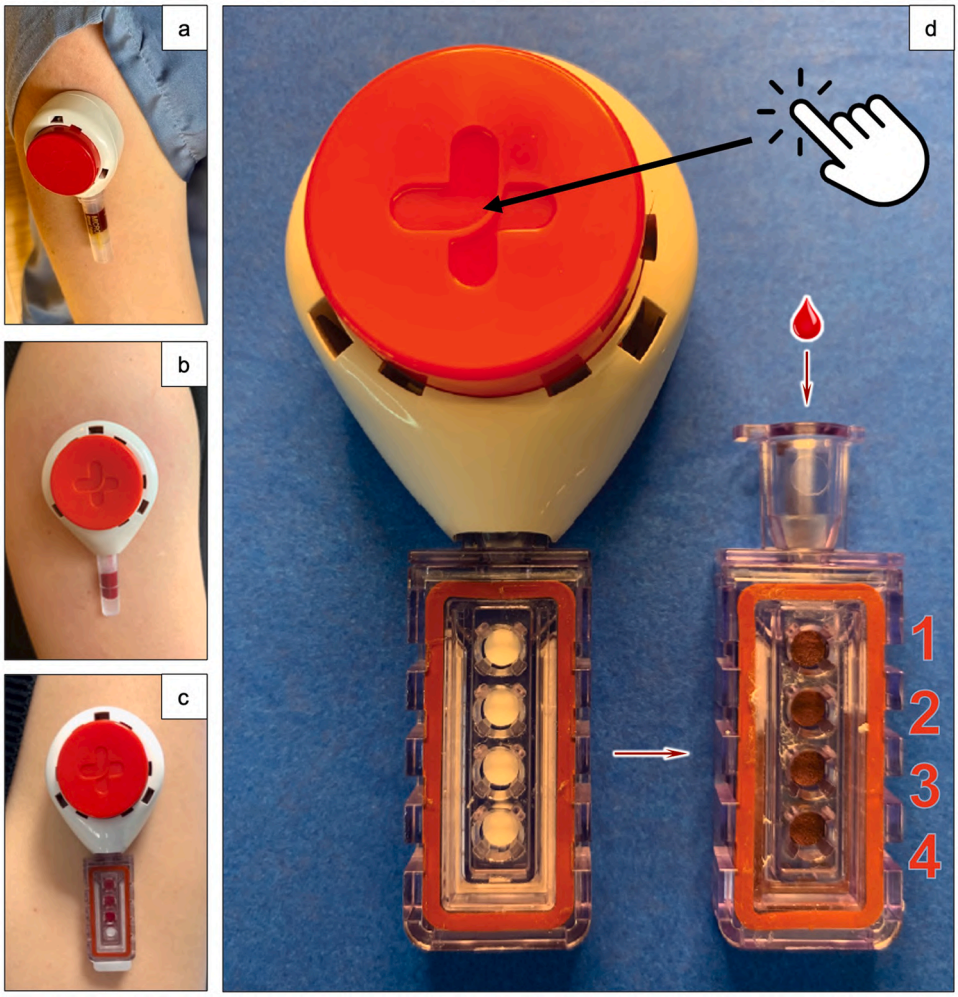

Fig. 5. Design of the Tasso microsampling devices: (a) Tasso+, (b) Tasso-SST and (c) Tasso-M20. Panel (d) reports details on Tasso-M20: button-activated lancet and sample cartridge (left) and sample cartridge after filling with whole blood (right). Adapted from [133,137] and [156] . Used with permission.

traditional venous sampling [126,139]. The TASSO-M20 has demonstrated to retain analyte integrity for six weeks at RT in a few long-term storage and large-scale epidemiological initiatives [129,140]. The TASSO-SST similarly maintains sample stability for plasma biomarkers during transport, addressing logistical challenges in remote settings [130–133].

TASSO devices have demonstrated adaptability across diverse applications. In anti-doping programs, the TASSO-M20 enabled longitudinal haematological monitoring with compliance rates exceeding 95 %, providing strong correlation with venous samples ($R^2 > 0.95$) [124,126,141]. The TASSO-SST has been validated for multi-biomarker pharmacokinetic studies, enabling the simultaneous analysis of inflammatory, steroidal, and metabolic markers with high precision [139,142]. For infectious disease diagnostics, the TASSO+ preserves HIV RNA and SARS-CoV-2 antibodies for decentralized monitoring [135,136,143]. The devices' performance in chronic disease management, environmental sustainability, and field-based applications reinforces their transformative role in modern diagnostics.

The TAP device has been applied to blood analysis in different fields, ranging from toxicological (heavy metals [167]), omics (proteomics [168,169], metabolomics and lipidomics [170,171]) and biomarker assays (carcinoembryonic antigen [172], autoantibodies [156]) to anti-doping testing (low molecular mass peptide and non-peptide doping agents [173]).

On the other hand, to the best of our knowledge, only one scientific paper has been published until now on the use of the RedDrop ONE device, regarding the determination of the Athlete's Biological Passport (ABP) haematological module parameters [152]. The authors compared the performance of RedDRop ONE with that of Tasso+ and found both suitable for the purpose.

Table 5 summarises a selection of representative studies involving microneedle-based blood microsampling.

2.6. *Radial-based multisampling DBS technologies*

Radial-based multisampling DBS technologies, exemplified by Hemaspot devices, provide innovative solutions for DBS sampling. Distinguished by their unique radial design, these devices feature segmented, petal-like wedges that allow each segment to serve as an independent replicate for analytical workflows (Fig. 6). This design mitigates issues such as uneven spot distribution and intra-sample variability, common in traditional DBS cards. With a collection volume of 20–50 μL per petal, Hemaspot devices enable precise and efficient use of limited blood samples. Certain models are equipped for plasma separation, catering to applications requiring analyte-specific assays. These features make Hemaspot ideal for use in remote diagnostics, TDM and epidemiological studies [174–190].

Hemaspot devices are tailored for simplicity and user comfort, promoting decentralized blood sampling. Blood from a fingerprick is applied to the device's central collection point and then diffuses evenly across radial segments. This self-contained system ensures even sample distribution across the wedges, reducing spot variability and enhancing

Table 5
Summary of selected studies involving microneedle-based blood microsampling.

Target analyte(s)	Microsampling technology	Sample type	Sample volume	Sample treatment	Instrumental setup	Sensitivity	Precision	Accuracy	Reference
Athlete Biological Passport parameters	Tasso+	Capillary blood	500 μL	None	Automated hematology analyser	NR	NR	Good correlation with venous samples (R^2 > 0.94)	[140]
Autoantibodies, C-reactive protein	Tasso+	Serum from capillary blood	Mean serum volume: 287 μL	Serum separation	Immunoassay	NR	NR	94.7 % concordance with classic venous samples	[156]
Tacrolimus, mycophenolic acid	Tasso-M20	Pooled whole blood	20 μL	Bead-based impact-assisted extraction	LC-MS/MS	LOQ: 1 ng/mL	%CV <9.7	%RE<11.5	[157]
Cytomegalovirus DNAemia	Tasso+	Plasma from capillary blood	~500 μL whole blood	Plasma separation	qPCR	50 IU/mL	NR	High correlation with venous samples (R^2 = 0.99)	[161]
Endogenous steroids, luteinizing hormone	Tasso SST	Serum from capillary blood	100/200 μL serum (steroid/LH analysis)	Serum separation, LC-MS analysis	LC-MS/MS (steroid analysis), immunoassay (LH analysis)	LOQ: 0.1 ng/mL (steroids)	NR	Good correlation with venous samples (R^2>0.96)	[164]

NR: not reported.

replicability. Notably, Hemaspot systems have been effectively deployed in low-resource settings, such as rural epidemiological studies, where conventional sampling methods would be logistically prohibitive. In these trials, participants consistently reported ease of use, with over 95 % of individuals indicating satisfaction with the process. The devices required minimal training, enabling self-collection or low-supervision sampling [175,177,178].

In TDM studies of antiretroviral drugs such as dolutegravir, Hemaspot achieved recovery rates of 91–98 %, with inter-replicate variability remaining below 5 %. Additionally, cytokine profiling demonstrated intra-assay coefficients of variation (CVs) under 8 %, illustrating robust performance in protein-based assays. Hemaspot's compatibility with molecular diagnostics has also been demonstrated; RNA extraction studies showed preserved integrity for up to 72 h at RT, with detection rates of viral RNA comparable to venous plasma samples ($R^2 > 0.95$). Such results confirm Hemaspot's adaptability across a range of analytes, from small molecules to nucleic acids [179–182].

Like for most other dried microsampling approaches, one of Hemaspot's critical strengths is its ability to maintain sample integrity under diverse storage and transport conditions. Studies demonstrate that analytes remain stable for up to four weeks at ambient temperatures, with plasma-separated samples preserving stability for 14 days without refrigeration. This robustness significantly reduces logistical burdens in field studies and decentralized workflows by obviating the need for cold-chain transport. For instance, HIV-1 viral load quantification showed consistent results when samples were stored for three weeks at fluctuating environmental conditions (25–40 °C). This feature has been pivotal for epidemiological studies [175,183,184].

In TDM applications, over 90 % of antiretroviral drug measurements correlated strongly with venous blood results ($R^2 > 0.98$), demonstrating suitability for monitoring medication adherence in HIV patients. In SARS-CoV-2 studies, Hemaspot achieved sensitivity and specificity rates of 96 % and 98 %, respectively, across multiple immunoassays, making it a reliable option for seroprevalence and antibody detection studies. Furthermore, hepatitis B and C diagnostics benefited from Hemaspot's capacity for high-throughput workflows, with an 89 % diagnostic accuracy achieved across 200 samples. Cytokine profiling studies revealed consistent and reproducible results for biomarkers of immune response, such as IL-6 and TNF-α, making Hemaspot a versatile tool for research into infectious and inflammatory diseases [178,179,185,186].

Despite its many advantages, Hemaspot faces some limitations. Sample volume constraints can limit the number of analytes tested per petal, particularly in plasma-separated configurations. Improper blood application during self-collection may also lead to uneven distribution across wedges, potentially compromising assay reliability. These challenges, however, are mitigated by clear user instructions and robust training protocols. Anyway, the need for carefully optimised and tailored workflows in high-throughput laboratory settings remains a consideration for broader adoption [178,183,187].

Table 6 summarises a selection of representative studies involving radial-based multisampling DBS.

2.7. *Membrane-based volumetric plasma generation technologies*

In addition to the already described Capitainer SEP10 (see Section "2.2. Quantitative dried blood spot (qDBS) sampling") and TASSO-SST (see Section "2.5. Microneedle-based blood microsampling") devices, the most widespread technology in this space, representing a transformative advancement in haematic matrix microsampling, is Telimmune plasma separation cards (formerly Noviplex). Designed to simplify the process of plasma extraction from whole blood, these devices use a specialized, proprietary hydrophilic membrane to isolate plasma through capillary action and deposit it on pre-cut cards to form volumetrically accurate DPS (Fig. 7). This approach enables rapid and reliable separation of plasma without requiring centrifugation. However, it should be noted that, in general, the exact composition of plasma/serum obtained by any filtration membrane is not necessarily identical to that of plasma/serum obtained by centrifugation/coagulation. For this reason, concordance studies between "classical" plasma/serum results and "membrane-based" plasma/serum results should always be carried out before trying to achieve widespread application of this kind of microsampling approaches (just like volume accuracy/precision studies should always be carried out before extensively applying a specific volumetric microsampling technique to a new biological matrix).

The compact and easy-to-use design minimizes sample handling errors, ensuring consistent and high-quality plasma generation suitable for a range of analytical workflows.

The technology requires at least 25 μL (Telimmune Uno) or 60 μL (Telimmune Duo) of blood, achieving plasma separation in about 3 min and producing one or two 3-μL vDPS per device [191,192]. This design feature is particularly advantageous in applications requiring stringent quality control, such as pharmacokinetic and biomarker studies.

The utility of Telimmune cards has been validated across various

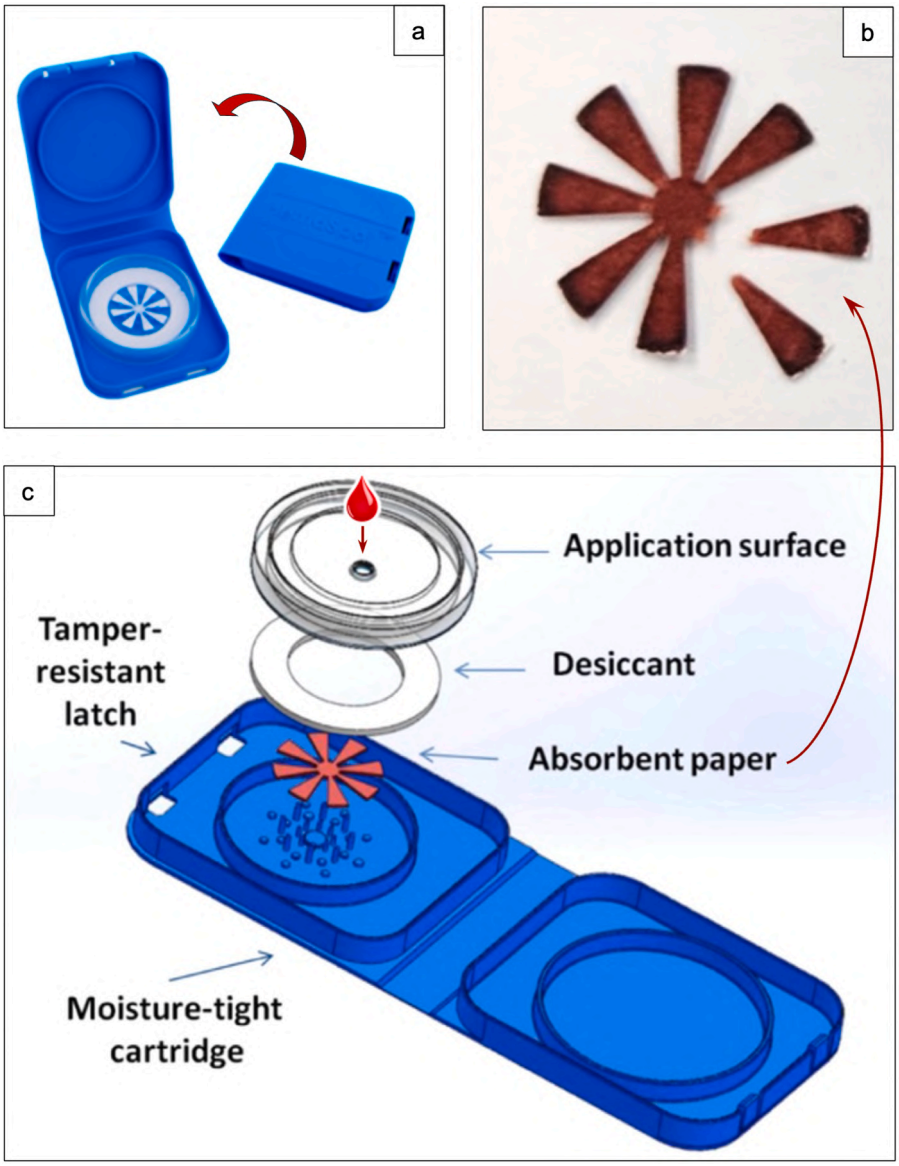

Fig. 6. Design of the HemaSpot microsampling device: (a) Self-contained device with wedge-shaped filter paper, built-in desiccant, and a plastic cover, (b) Sampled HemaSpot with two wedges (sample replicates) torn off and (c) exploded view of the blood collection device showing fan-shaped collection support (in red). Once blood has been applied through the hole in the application surface, the device is folded over and closed. Adapted from [182,184] and [185]. Used with permission.

Table 6
Summary of selected studies involving radial-based multisampling DBS sampling.

Target analyte(s)	Microsampling technology	Sample type	Sample volume	Sample treatment	Instrumental setup	Sensitivity	Precision	Accuracy	Reference
Measles and Rubella IgG	HemaSpot-HF	DBS	~150 µL	Incubation, extraction	ELISA kit	>98 % correct identification	NR	NR	[180]
CYP3A4 and CYP1A2 activity (caffeine, paraxanthine, midazolam OH-midazolam)	HemaSpot	Venous DBS	50 µL	Hydrolysis, incubation, extraction	LC-MS/MS	LOQ: 0.1–25 ng/mL	CV<15%	±20 %	[181]
HbA1c	HemaSpot	DBS	65–105 µL	Hemolysis, extraction	HPLC	NR	NR	Good correlation with venous samples (R^2>0.97)	[182]
HIV-1 RNA	HemaSpot-HF	DBS	NR	Incubation, extraction	RT-PCR	832 copies/mL	NR	NR	[183]
HIV-1 Viral Load	HemaSpot-HF	Venous DBS	~140 µL	Incubation, extraction	RT-PCR	1000 copies/mL (91.3 % accuracy)	NR	91.3 % correct identification (VL<1000 copies/mL)	[164, 190]

NR: not reported.

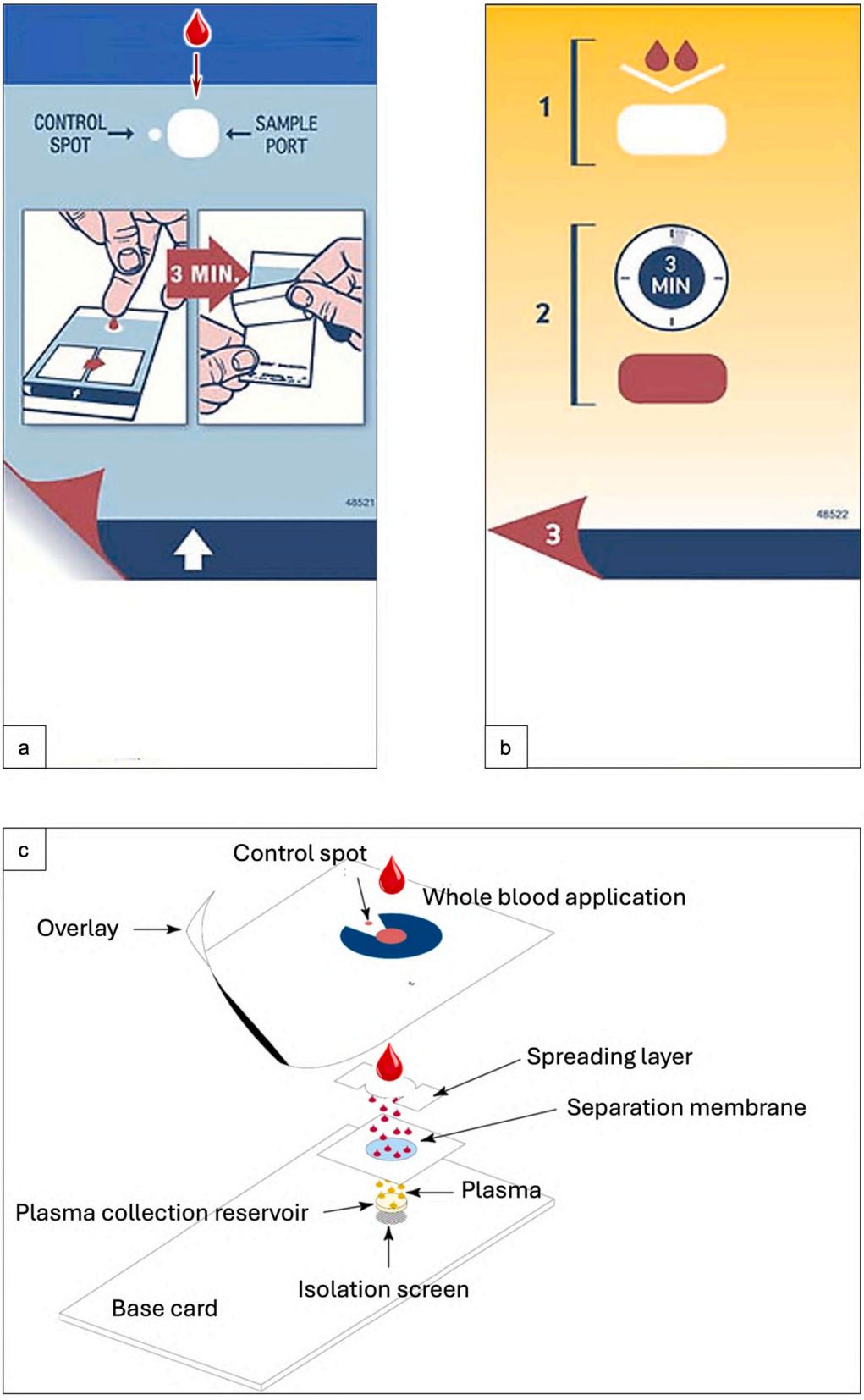

Fig. 7. Design of the Telimmune (formerly Noviplex) card microsampling technology for in-situ, membrane-based plasma separation and volumetric dried plasma spot collection, (a) front, (b) back and (c) and exploded view. Adapted from [191] and [193]. Used with permission.

analytes, including small molecules, proteins, and other biomarkers. Studies consistently demonstrate high concordance between plasma generated via Telimmune cards and traditional venous plasma methods. For instance, plasma extracted using Telimmune cards showed correlation coefficients above 0.95 when compared with venous plasma for a wide range of analytes, including therapeutic drugs and diagnostic biomarkers [193]. The cards also exhibited strong agreement in toxicokinetic studies [194].

One study highlighted the utility of Telimmune cards in the analysis of immunosuppressant drugs, where the cards facilitated reliable measurement of tacrolimus and mycophenolic acid with inter-assay precision below 7 % and accuracy exceeding 95 % [192]. Additionally, in infectious disease diagnostics, plasma generated via Telimmune cards enabled sensitive and specific detection of viral antigens and antibodies using ELISA platforms, with no significant differences observed between microsampled plasma and venous plasma [194,195].

Telimmune plasma separation cards have gained recognition for their robustness in field and decentralized settings. Their small size and self-contained design allow them to be used at the point of care, eliminating the need for bulky centrifugation equipment. Plasma generated on-site can either be analysed immediately or stored for later analysis, with studies confirming the stability of plasma and analytes under diverse conditions. For example, plasma samples stored at RT for up to 48 h retained over 95 % of analyte stability, aligning with international bioanalytical standards [191].

In resource-limited settings, the use of Telimmune cards has streamlined sample collection and transportation. Plasma collected on the cards demonstrated minimal degradation during transport, even under non-ideal conditions. This capability is especially beneficial in large-scale epidemiological studies and clinical trials, where logistical simplicity is critical [195].

Despite their numerous advantages, Telimmune cards are not without limitations. Relatively large volumes of blood are needed, and inadequate filling can lead to inconsistent plasma yields or incomplete separation. Additionally, while the cards are highly effective for most applications, specific high-sensitivity assays or those requiring extremely pure plasma may face limitations when using this technology.

Moreover, the cost-effectiveness of Telimmune cards relative to traditional methods remains an area for further exploration. While they reduce logistical costs by simplifying collection and transport, the per-unit expense may impact their widespread adoption in low-resource settings [196].

Table 7 summarises a selection of representative studies involving membrane-based volumetric plasma generation.

2.8. Vacuum-assisted fingertip fluid blood collection

Vacuum-assisted blood collection technologies represent a novel advancement in microsampling, designed to streamline and improve the collection of fluid whole blood samples for laboratory and point-of-care testing. The HAIIM device, developed by Winnoz, exemplifies this approach by employing vacuum assistance to draw blood in a controlled and minimally invasive manner (Fig. 8). This technology has gained recognition for its potential applications in different settings, especially in underserved communities where traditional phlebotomy methods pose logistical and practical challenges and other common forms of microsampling do not provide adequate sample volumes [197–199].

The HAIIM device operates on the principle of creating a controlled vacuum to extract capillary blood from a small puncture site, typically on the fingertip. By applying gentle suction, it ensures the collection of a variable volume of blood into a sealed collection chamber. This controlled approach minimizes haemolysis and reduces contamination risks, resulting in high-quality samples suitable for a wide range of diagnostic applications. The device supports the collection of up to 200 µL of blood in a single use, addressing the needs of various diagnostic and analytical assays [197–199].

One of the most notable features of the HAIIM device is its ease of use, allowing healthcare providers or patients to perform blood collection with minimal training. Its compact and portable nature makes it ideal for use in home-based sampling and remote healthcare settings. The minimally invasive nature of the device reduces pain and discomfort during blood collection, thereby enhancing patient adherence [197–199].

Winnoz has now established partnerships in different countries for expanding and improving pharmacy services. For example, it collaborates in Germany with Healyzer® to integrate Haiim into pharmacy IT services and provide timely, convenient onsite testing as well as subscription-based diagnostics; in Italy with diagnosti.care® to expand the diagnostic capabilities of pharmacies; in Brazil with Labpoc® to extend testing services to remote and rural areas; and in Slovakia for liver cirrhosis prevention [200].

While specific clinical studies involving the HAIIM device as the sampling approach are not yet detailed, the principles underlying its operation suggest strong alignment with the growing demand for patient-centric blood sampling technologies [197,199].

However, further validation studies are needed to establish its performance across a broader range of diagnostic applications and to compare its efficacy with other microsampling technologies. Such research would provide valuable insights into its reliability, accuracy, and overall utility in real-world healthcare settings [198,199].

The HAIIM device exemplifies the promise of vacuum-assisted blood

Table 7
Summary of selected studies involving membrane-based volumetric plasma generation.

Target analyte (s)	Microsampling technology	Sample type	Sample volume	Sample treatment	Instrumental setup	Sensitivity	Precision	Accuracy	Reference
Vitamin D metabolites	Telimmune/ Noviplex	DPS	2.5 µL (from 25 µL whole blood)	Extraction, derivatisation	LC-MS/MS	~400 pg/ mL	%RSD<10	NRn	[191]
Small molecule drugs	Telimmune/ Noviplex	DPS	1.5 mg (from 30 µL whole blood)	Extraction, centrifugation	Paper spray MS	NR	NR	-9–10 % deviation from fluid plasma	[192]
Giredestrant	Telimmune/ Noviplex DUO	DPS	3.8 µL (from ~70 µL whole blood)	Extraction, SLE, evaporation, reconstitution	LC-MS/MS	LOQ: 1 ng/ mL	%RSD: 0.4–38.6	60.6–159.5 %	[193]
Sulfur mustard-albumin adduct	Telimmune/ Noviplex DUO	DPS	2 × 3.8 µL (from 100 µL whole blood)	Extraction, proteolysis, P/P, evaporation, reconstitution	LC-MS/MS	LOD: 0.05 µmol/L	%RSD: 1.7–5.0	NR	[194]
Meropenem	Telimmune/ Noviplex DUO	DPS (from venous blood)	2x ~3 µL (from 40 µL whole blood)	Extraction	LC-MS/MS	LOQ: 0.5 µg/mL	%CV<8.7	91.5–103.9 %	[195]

NR: not reported.

Fig. 8. Setup and use of the Winnoz Haiim Vacuum-assisted fingertip fluid blood collection: (a) insertion of the disposable cassette into an anticoagulant-treated microtube, (b) connection of the cassette to the main device and (c) process of fingertip fluid blood collection. Adapted from www.winnoz.com.

collection technologies in modern healthcare. As interest in decentralized healthcare continues to grow, technologies like the HAIIM device are likely to play a critical role in reshaping diagnostic practices and expanding access to quality healthcare.

3. Conclusion

Microsampling technologies are reshaping the landscape of bioanalysis, offering unprecedented opportunities for decentralized and patient-centric testing. Device usability by patients has been a cornerstone of modern microsampling design; although arguably these efforts have achieved variable degrees of success, the final aim of making precision, personalised medicine a concrete perspective is closer than ever. Microsampling is inherently far easier and more feasible than venipuncture, and regardless of the method, it is now clear that many patients will soon be able to use the former to become independent from healthcare facilities for the purposes of TDM or diagnostic testing.

Devices such as VAMS, advanced and volumetric DBS platforms, membrane-based plasma separation and minimally invasive fluid capillary blood collection technologies have demonstrated their utility across diverse applications, from TDM to infectious disease diagnostics and anti-doping programs. Their alignment with AGC principles further underscores their relevance in sustainable bioanalysis. However, despite this common feature, only generic AGC compliance is currently assured, since only a handful of specifically tailored, quantitative studies have been carried out for this purpose. Thus, AGC score comparison among microsampling techniques and applications is currently impossible and this represents a possible critical area, open to significant advances and refinements.

The availability of such a wide range of microsampling techniques provides unprecedented flexibility and opportunities, enabling patients and clinicians alike to choose the best approach based on personal and community preferences, needs, perspectives and targets. Through these technologies, the goal of generally applicable precision/personalised medicine is becoming ever closer, year by year.

Despite these advancements, challenges such as haematocrit dependency, user variability and standardisation persist, necessitating ongoing research and development. As these technologies continue to evolve, they hold the potential to democratize access to high-quality analytical testing, particularly in remote and underserved settings. However, for the very same reasons, to obtain a transformative effect on a wide range of analytical applications for both clinical and non-clinical purposes, these innovative microsampling techniques must first achieve wide acknowledgement and adoption, which in turn can only be obtained through consistently effected commercial availability, as well as regulatory approval for the intended use, in most countries and regions.

Future efforts should focus on enhancing device reliability, expanding analytical capabilities and achieving better integration of

these tools into routine clinical and research workflows, as well as rigorously evaluating and quantifying adherence to AGC principles. By doing so, microsampling technologies will cement their position as cornerstones of modern bioanalysis.

CRediT authorship contribution statement

Michele Protti: Writing – review & editing, Writing – original draft, Visualization, Methodology, Conceptualization. **Elisa Milandri:** Writing – review & editing, Visualization, Methodology. **Roberta Di Lecce:** Writing – review & editing, Visualization, Methodology. **Laura Mercolini:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis, Conceptualization. **Roberto Mandrioli:** Writing – review & editing, Writing – original draft, Validation, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding sources

The Authors acknowledge the financial contribution from Alma Mater Studiorum–University of Bologna through Fundamental Oriented Research (RFO) funds.

Data availability

No data was used for the research described in the article.

References

[1] X. Yang, K. Williams, R. Elliott, M. Hokom, J. Allen, S.K. Fischer, Validation of low-volume sampling devices for pharmacokinetic analysis: technical and logistical challenges and solutions, Bioanalysis 15 (2023) 1407–1419, https://doi.org/10.4155/bio-2023-0156.

[2] Z. Chen, C.C. Goudarzi, T.W. Sikorski, N. Weng, Enhancing drug development and clinical studies with patient-centric sampling using microsampling techniques: opportunities, challenges, and insights into liquid chromatography-mass spectrometry strategies, J. Mass Spectrom. 59 (2024) e5023, https://doi.org/10.1002/jms.5023.

[3] K.R. Baillargeon, C.R. Mace, Microsampling tools for collecting, processing, and storing blood at the point-of-care, Bioeng. Transl. Med. 8 (2023) e10476, https://doi.org/10.1002/btm2.10476.

[4] M. Protti, P.M. Sberna, A.E. Sberna, R. Ferrante, R. Mandrioli, L. Mercolini, Enhanced urinary stability of peptide hormones and growth factors by dried urine microsampling, J. Pharm. Biomed. Anal. 204 (2021) 114234, https://doi.org/10.1016/j.jpba.2021.114234.

[5] M.I. Francke, L.E.J. Peeters, D.A. Hesselink, S.M. Kloosterboer, B.C.P. Koch, H. Veenhof, B.C.M. De Winter, Best practices to implement dried blood spot sampling for therapeutic drug monitoring in clinical practice, Ther. Drug Monit. 44 (2022) 696–700, https://doi.org/10.1097/FTD.0000000000000994.

[6] L. Mercolini, R. Mandrioli, M. Protti, Quantitative microsampling for bioanalytical applications related to the SARS-CoV-2 pandemic: usefulness, benefits and pitfalls, J. Pharm. Biomed. Anal. 191 (2020) 113597, https://doi.org/10.1016/j.jpba.2020.113597.

[7] R. Maršala, M. Dvořák, P. Kubáň, Automated capillary electrophoresis analyses of dried blood samples after patient-centric volumetric absorptive microsampling, Adv. Sample Prep. 13 (2025) 100142, https://doi.org/10.1016/j.sampre.2024.100142.

[8] E. Metscher, S. Meziyerh, E.J. Arends, Y.K.O. Teng, A.P.J. de Vries, J.J. Swen, D.J. A.R. Moes, Dried blood spot LC-MS/MS quantification of voclosporin in renal transplant recipients using volumetric dried blood spot sampling, J. Pharm. Biomed. Anal. 255 (2025) 116647, https://doi.org/10.1016/j.jpba.2024.116647.

[9] P. Opitz, I. Waltering, G. Hempel, Development and validation of a quantification method for direct oral anticoagulants from capillary blood using volumetric absorptive microsampling and online SPE-LC-MS, J. Chromatogr. B 1251 (2025) 124423, https://doi.org/10.1016/j.jchromb.2024.124423.

[10] L. Mercolini, M. Protti, L.B. Carvalho, P.A.D. Teigas-Campos, S. Palano, E. Milandri, C. Volpi, C. Lodeiro, H.M. Santos, J.L. Capelo, R. Mandrioli, Insights into the use of microsampling for omics studies, J. Integr. Omics 13 (2023) 1–3, https://doi.org/10.5584/jiomics.v13i1.221.

[11] M. Protti, L. Mercolini, R. Mandrioli, Review: the role of automation in improving the performance and throughput of microsample bioanalysis, Anal. Chim. Acta, in press.

[12] M. Protti, R. Mandrioli, L. Mercolini, Microsampling for therapeutic drug monitoring (TDM) in psychiatric practice, Int. Clin. Psychopharmacol. 39 (2024) 42–45, https://doi.org/10.1097/YIC.0000000000000503.

[13] I.R. Müller, G. Linden, M.F. Charão, M.V. Antunes, R. Linden, Dried blood spot sampling for therapeutic drug monitoring: challenges and opportunities, 16 (2023) 691–701. https://doi.org/10.1080/17512433.2023.2224562.

[14] H.Y. Tey, H.H. See, A review of recent advances in microsampling techniques of biological fluids for therapeutic drug monitoring, J. Chromatogr. A 1635 (2021) 461731, https://doi.org/10.1016/j.chroma.2020.461731.

[15] J. Rudge, S. Kushon, Volumetric absorptive microsampling: its use in COVID-19 research and testing, Bioanalysis 13 (2021) 1851–1863, https://doi.org/10.4155/bio-2021-0102.

[16] N. Spooner, K.D. Anderson, J. Siple, E.R. Wickremsinhe, Y. Xu, M. Lee, Microsampling: considerations for its use in pharmaceutical drug discovery and development, Bioanalysis 11 (2019) 1015–1038, https://doi.org/10.4155/bio-2019-0041.

[17] G. Nys, M.G.M. Kok, A.-C. Servais, M. Fillet, Beyond dried blood spot: current microsampling techniques in the context of biomedical applications, TrAC - Trends Anal. Chem. 97 (2017) 326–332, https://doi.org/10.1016/j.trac.2017.10.002.

[18] M. Protti, R. Mandrioli, L. Mercolini, Perspectives and strategies for anti-doping analysis, Bioanalysis 11 (2019) 149–152, https://doi.org/10.4155/bio-2018-0290.

[19] D. Bernieh, G. Lawson, S. Tanna, Quantitative LC–HRMS determination of selected cardiovascular drugs, in dried blood spots, as an indicator of adherence to medication, J. Pharm. Biomed. Anal. 142 (2017) 232–243, https://doi.org/10.1016/j.jpba.2017.04.045.

[20] J.C. McElnay, DBS sampling: a journey, Bioanalysis 7 (2015) 1967–1970, https://doi.org/10.4155/bio.15.140.

[21] P. Denniff, N. Spooner, Volumetric absorptive microsampling: a dried sample collection technique for quantitative bioanalysis, Anal. Chem. 86 (2014) 8489–8495, https://doi.org/10.1021/ac5022562.

[22] V. Iacuzzi, B. Posocco, M. Zanchetta, S. Gagno, A.S. Poetto, M. Guardascione, G. Toffoli, Dried blood spot technique applied in therapeutic drug monitoring of anticancer drugs: a review on conversion methods to correlate plasma and dried blood spot concentrations, Pharm. Res. 38 (2021) 759–778, https://doi.org/10.1007/s11095-021-03036-6.

[23] F. Li, S. Ploch, Will green aspects of dried blood spot sampling accelerate its implementation and acceptance in the pharmaceutical industry? Bioanalysis 4 (2012) 1259–1261, https://doi.org/10.4155/bio.12.106.

[24] L. Heughebaert, A. Williams, A. Roberts, C. Jacobs, C. Szuster, C. Walker, E. V. Nuffel, E. Atkin, F. Minelli, K. Groves, K. Sime, K. Zeiser, M. Protti, L. Wagmann, O. Knight, R. Stewart, R. Penford, S. Calogero, P. Timmerman, Feedback from the 8th European bioanalysis forum young scientist symposium, Bioanalysis 14 (2022) 1471–1477, https://doi.org/10.4155/bio-2022-0232.

[25] E. Cecchin, M. Orleni, S. Gagno, M. Montico, E. Peruzzi, R. Roncato, L. Gerratana, S. Corsetti, F. Puglisi, G. Toffoli, B. Posocco, Quantification of letrozole, palbociclib, ribociclib, abemaciclib, and metabolites in volumetric dried blood spots: development and validation of an LC-MS/MS method for therapeutic drug monitoring, Int. J. Mol. Sci. 25 (2024) 10453, https://doi.org/10.3390/ijms251910453.

[26] E. Carniel, K.A. dos Santos, L. de Andrade de Lima, R. Kohlrausch, R. Linden, M. V. Antunes, Determination of clozapine and norclozapine in dried plasma spot and dried blood spot by liquid chromatography-tandem mass spectrometry, J. Pharm. Biomed. Anal. 210 (2022) 114591, https://doi.org/10.1016/j.jpba.2022.114591.

[27] C. Marasca, R. Mandrioli, R. Sardella, T. Vovk, A. Armirotti, A. Cavalli, A. Serretti, M. Protti, L. Mercolini, Dried volumetric microsampling approaches for the therapeutic drug monitoring of psychiatric patients undergoing clozapine treatment, Front. Psychiatry 13 (2022) 794609, https://doi.org/10.3389/fpsyt.2022.794609.

[28] G. Canil, M. Orleni, B. Posocco, S. Gagno, A. Bignucolo, M. Montico, R. Roncato, S. Corsetti, M. Bartoletti, G. Toffoli, LC-MS/MS method for the quantification of PARP inhibitors olaparib, rucaparib, and niraparib in human plasma and dried blood spots: development, validation, and clinical validation for therapeutic drug monitoring, Pharmaceutics 15 (2023) 1524, https://doi.org/10.3390/pharmaceutics15051524.

[29] M.C. García-Poyo, C. Pécheyran, L. Rello, E. García-González, S. Alonso Rodríguez, F.V. Nakadi, M. Aramendía, M. Resano, Determination of Cu in blood: via direct analysis of dried blood spots using high-resolution continuum source graphite furnace atomic absorption spectrometry, J. Anal. At. Spectrom. 36 (2021) 1666–1677, https://doi.org/10.1039/d1ja00155h.

[30] A.B. Volynsky, R. Wennrich, Mechanisms of the action of platinum metal modifiers in electrothermal atomic absorption spectrometry: aims and existing approaches, Spectrochim. Acta B 57 (2002) 1301–1316, https://doi.org/10.1016/S0584-8547(02)00063-0.

[31] F.V. Nakadi, R. Garde, M.A.M.S. Da Veiga, J. Cruces, M. Resano, A simple and direct atomic absorption spectrometry method for the direct determination of Hg in dried blood spots and dried urine spots prepared using various microsampling devices, J. Anal. At. Spectrom. 35 (2020) 136–144, https://doi.org/10.1039/c9ja00348g.

[32] Z. Swank, G. Michielin, H.M. Yip, P. Cohen, D.O. Andrey, N. Vuilleumier, L. Kaiser, I. Eckerle, B. Meyer, S.J. Maerkl, A high-throughput microfluidic

nanoimmunoassay for detecting anti–SARS-CoV-2 antibodies in serum or ultralow-volume blood samples, Proc. Natl. Acad. Sci. U.S.A. 118 (2021) e2025289118, https://doi.org/10.1073/pnas.2025289118.
[33] G. Michielin, F. Arefi, O. Puhach, M. Bellon, P. Sattonnet-Roche, A.G. L'Huillier, I. Eckerle, B. Meyer, S.J. Maerkl, Clinical sensitivity and specificity of a high-throughput microfluidic nano-immunoassay combined with capillary blood microsampling for the identification of anti-SARS-CoV-2 spike IgG serostatus, PLoS One 18 (2023) e0283149, https://doi.org/10.1371/journal.pone.0283149.
[34] R.S. Carling, E.C. Emmett, S.J. Moat, Evaluation of volumetric blood collection devices for the measurement of phenylalanine and tyrosine to monitor patients with phenylketonuria, Clin. Chim. Acta 535 (2022) 157–166, https://doi.org/10.1016/j.cca.2022.08.005.
[35] O. Beck, N.K. Modén, S. Seferaj, G. Lenk, A. Helander, Study of measurement of the alcohol biomarker phosphatidylethanol (PEth) in dried blood spot (DBS) samples and application of a volumetric DBS device, Clin. Chim. Acta 479 (2018) 38–42, https://doi.org/10.1016/j.cca.2018.01.008.
[36] A. Marchand, I. Roulland, F. Semence, O. Beck, M. Ericsson, Use of quantitative dried blood spots to evaluate the post-vaccination level of neutralising antibodies against SARS-CoV-2, Life 11 (2021) 1125, https://doi.org/10.3390/life11111125.
[37] E.J. Berm, J. Paardekooper, E. Brummel-Mulder, E. Hak, B. Wilffert, J.G. Maring, A simple dried blood spot method for therapeutic drug monitoring of tricyclic antidepressants amitriptyline, nortriptyline, imipramine, clomipramine, and their active metabolites using LC–MS/MS, Talanta 134 (2015) 165–172, https://doi.org/10.1016/j.talanta.2014.10.041.
[38] O. Beck, M. Mellring, C. Löwbeer, S. Seferaj, A. Helander, Measurement of the alcohol biomarker phosphatidylethanol (PEth) in dried blood spots and venous blood—Importance of inhibition of post-sampling formation from ethanol, Anal. Bioanal. Chem. 413 (2021) 5601–5606, https://doi.org/10.1007/s00216-021-03211-z.
[39] A. Schröck, A. Henzi, P. Bütikofer, S. König, W. Weinmann, Determination of the formation rate of phosphatidylethanol by phospholipase D (PLD) in blood and test of two selective PLD inhibitors, Alcohol 73 (2018) 1–7, https://doi.org/10.1016/j.alcohol.2018.03.003.
[40] Capitainer A.B., Capitainer SEP10 instructions for use. Available from https://capitainer.com/wp-content/uploads/2024/11/IFU-SEP10-v2.pdf (accessed on January 3, 2025).
[41] C.E. Heiland, M. Lehtihet, A. Börjesson, L. Ekström, Evaluation of a single Eporatio® micro-dose in urine and dried blood spots, Drug Test. Anal. 16 (2024) 1319–1322, https://doi.org/10.1002/dta.3651.
[42] M. Boutin, P. Lavoie, M. Beaudon, G. Kabala Ntumba, D.G. Bichet, B. Maranda, C. Auray-Blais, Mass spectrometry analysis of globotriaosylsphingosine and its analogues in dried blood spots, Int. J. Mol. Sci. 24 (2023) 3223, https://doi.org/10.3390/ijms24043223.
[43] T. Meikopoulos, O. Begou, G. Theodoridis, H. Gika, Ceramides biomarkers determination in quantitative dried blood spots by UHPLC-MS/MS, Anal. Chim. Acta 1255 (2023) 341131, https://doi.org/10.1016/j.aca.2023.341131.
[44] D. Biagini, S. Antoni, S. Ghimenti, A. Bonini, F. Vivaldi, C. Angelucci, C. Riparbelli, A. Cuttano, R. Fuoco, F. Di Francesco, T. Lomonaco, Methodological aspects of dried blood spot sampling for the determination of isoprostanoids and prostanoids, Microchem. J. 175 (2022) 107212, https://doi.org/10.1016/j.microc.2022.107212.
[45] N. Rollborn, A. Larsson, K. Kultima, Analysis of HbA1c using microfluidic card (Capitainer qDBS card) as a pre-step before determination of the HbA1c value with an immunological method, Scand. J. Clin. Lab. Invest. 84 (2024) 11–15, https://doi.org/10.1080/00365513.2024.2303720.
[46] S. Deprez, K. Van Uytfanghe, C.P. Stove, Liquid chromatography-tandem mass spectrometry for therapeutic drug monitoring of immunosuppressants and creatinine from a single dried blood spot using the Capitainer® qDBS device, Anal. Chim. Acta 1242 (2023) 340797, https://doi.org/10.1016/j.aca.2023.340797.
[47] N.T. Vethe, A. Åsberg, A.M. Andersen, R. Heier Skauby, S. Bergan, K. Midtvedt, Clinical performance of volumetric finger-prick sampling for the monitoring of tacrolimus, creatinine and haemoglobin in kidney transplant recipients, Br. J. Clin. Pharmacol. 89 (2023) 3690–3701, https://doi.org/10.1111/bcp.15870.
[48] H. Veenhof, R.A. Koster, L.A.T. Junier, P. Zweipfenning, D.J. Touw, Results from a proficiency testing pilot for immunosuppressant microsampling assays, Ther. Drug Monit. 45 (2023) 61–68, https://doi.org/10.1097/FTD.0000000000001019.
[49] J. Lv, Q. Wu, S. Li, H. Yi, F. Xie, Development and validation of a UPLC-PDA method for quantifying ceftazidime in dried blood spots, J. Pharm. Biomed. Anal. 239 (2024) 115928, https://doi.org/10.1016/j.jpba.2023.115928.
[50] Q. Liu, L. Liu, Y. Yuan, F. Xie, A validated UHPLC–MS/MS method to quantify eight antibiotics in quantitative dried blood spots in support of pharmacokinetic studies in neonates, Antibiotics 12 (2023) 199, https://doi.org/10.3390/antibiotics12020199.
[51] C. Ververi, C. Gentile, M. Massano, A. Salomone, M. Vincenti, Quantitative determination by UHPLC-MS/MS of 18 common drugs of abuse and metabolites, including THC and OH-THC, in volumetric dried blood spots: a sustainable method with minimally invasive sampling, J. Chromatogr. B 1247 (2024) 124337, https://doi.org/10.1016/j.jchromb.2024.124337.
[52] S. Palano, D. Turoňova, M. Protti, L. Kujovská Krčmová, R. Sardella, P. Mladěnka, R. Mandrioli, S. Girotti, L. Mercolini, Next generation microsampling towards sustainable forensic analysis: volumetric DBS for cocaine and metabolites, Microchem. J. 203 (2024) 110937, https://doi.org/10.1016/j.microc.2024.110937.
[53] C. Ververi, M. Galletto, M. Massano, E. Alladio, M. Vincenti, A. Salomone, Method development for the quantification of nine nitazene analogs and brorphine in dried blood spots utilizing liquid chromatography–tandem mass spectrometry, J. Pharm. Biomed. Anal. 241 (2024) 115975, https://doi.org/10.1016/j.jpba.2024.115975.
[54] L. Löfgren, M. von Euler Chelpin, M. Bhat, M. Althage, A. Hober, F. Edfors, T. Ruckh, B. Challis, P. Davidsson, T. Miliotis, Patient-centric quantitative microsampling for accurate determination of urine albumin to creatinine ratio (UACR) in a clinical setting, J. Appl. Lab. Med. 9 (2024) 329–341, https://doi.org/10.1093/jalm/jfad111.
[55] M.A. Engevik, S. Thapa, I.M. Lillie, M.B. Yacyshyn, B. Yacyshyn, A.J. Percy, D. Chace, T.D. Horvath, Repurposing dried blood spot device technology to examine bile acid profiles in human dried fecal spot samples, Am. J. Physiol. Gastrointest. Liver Physiol. 326 (2024) 95–106, https://doi.org/10.1152/ajpgi.00188.2023.
[56] S. Deprez, L. Paniagua-González, S. Velghe, C.P. Stove, Evaluation of the performance and hematocrit independence of the HemaPEN as a volumetric dried blood spot collection device, Anal. Chem. 91 (2019) 14467–14475, https://doi.org/10.1021/acs.analchem.9b03179.
[57] M. Protti, C. Marasca, M. Cirrincione, A. Cavalli, R. Mandrioli, L. Mercolini, Assessment of capillary volumetric blood microsampling for the analysis of central nervous system drugs and metabolites, Analyst 145 (2020) 5744–5753, https://doi.org/10.1039/d0an01039a.
[58] A. Sen, M. Gillett, L. Weaver, M. Barfield, P. Singh, F. Lapierre, N. Spooner, In vitro testing of the hemaPEN microsampling device for the quantification of acetaminophen in human blood, Bioanalysis 12 (2020) 1725–1737, https://doi.org/10.4155/bio-2020-0271.
[59] A. Laurent, C. Nix, G. Cobraiville, J. Crommen, M. Fillet, A targeted UHPLC-MS/MS method to monitor lipidomic changes during a physical effort: optimization and application to blood microsamples from athletes, J. Pharm. Biomed. Anal. 229 (2023) 115373, https://doi.org/10.1016/j.jpba.2023.115373.
[60] C. Nix, M. Hemmati, G. Cobraiville, A.-C. Servais, M. Fillet, Blood microsampling to monitor metabolic profiles during physical exercise, Front. Mol. Biosci. 8 (2021) 681400, https://doi.org/10.3389/fmolb.2021.681400.
[61] L. Maritz, N.J. Woudberg, A.C. Bennett, A. Soares, F. Lapierre, J. Devine, M. Kimberg, P.J. Bouic, Validation of high-throughput, semiquantitative solid-phase SARS coronavirus-2 serology assays in serum and dried blood spot matrices, Bioanalysis 13 (2021) 1183–1194, https://doi.org/10.4155/bio-2021-0065.
[62] G. Rosé, N. Tafzi, S. El Balkhi, J.-P. Rerolle, M. Debette-Gratien, P. Marquet, F. Saint-Marcoux, C. Monchaud, New perspectives for the therapeutic drug monitoring of tacrolimus: quantification in volumetric DBS based on an automated extraction and LC-MS/MS analysis, J. Chromatogr. B 1223 (2023) 123721, https://doi.org/10.1016/j.jchromb.2023.123721.
[63] V. Ion, C. Legoff, E. Cavalier, P. Delanaye, A.-C. Servais, D.-L. Muntean, M. Fillet, Determination of iohexol by capillary blood microsampling and UHPLC-MS/MS, J. Pharm. Anal. 9 (2019) 259–265, https://doi.org/10.1016/j.jpha.2019.06.003.
[64] M. Smidt, M.F. Bastiani, R.Z. Hahn, L.D. Lima Feltraco Lizot, M.S. Perassolo, R. Linden, Evaluation of hemaPEN® sampling device for measurement of cocaine and metabolites in capillary blood by LC-MS/MS, Bioanalysis 14 (2022) 1295–1303, https://doi.org/10.4155/bio-2022-0192.
[65] J.M. Partington, J. Marchiandi, D. Szabo, A. Gooley, K. Kouremenos, F. Smith, B. O. Clarke, 2024. Validating blood microsampling for per- and polyfluoroalkyl substances quantification in whole blood, J. Chromatogr. A 464522 (1713), https://doi.org/10.1016/j.chroma.2023.464522.
[66] M. Dvořák, P. Kubáň, Automated analyses of dried blood spots collected by volumetric microsampling devices, Anal. Chim. Acta 1310 (2024) 342718, https://doi.org/10.1016/j.aca.2024.342718.
[67] F. Ducatez, C. Pilon, J. Ferey, S. Marret, S. Bekri, A. Tebani, Evaluation of dried-blood spots and a hematocrit-independent procedure in lysosomal diseases screening using multiplexed tandem mass spectrometry assays, Clin. Chim. Acta 542 (2023) 117278, https://doi.org/10.1016/j.cca.2023.117278.
[68] S.R. Patel, J. Barricklow, P. Bryan, C. Rospo, N. Spooner, M. Wang, J.T. White, A. Wilson, Case studies on the use of microsampling for nonclinical studies in pharmaceutical drug discovery and development, AAPS J. 26 (2024) 110, https://doi.org/10.1208/s12248-024-00975-x.
[69] Neoteryx, Mitra press factsheet & frequently asked questions. Available from https://www.neoteryx.com/hubfs/Page%20Graphics/archive%20old%20web%20pages/Press%20Page/press-factsheet-may-2020-v2.pdf (Accessed on January 3, 2025).
[70] A. Kocur, T. Pawiński, Volumetric absorptive microsampling in therapeutic drug monitoring of immunosuppressive drugs—from sampling and analytical issues to clinical application, Int. J. Mol. Sci. 24 (2023) 681, https://doi.org/10.3390/ijms24010681.
[71] A.D. Leino, J. Takyi-Williams, J.M. Park, S.P. Norman, D. Sun, K.B. Farris, M. P. Pai, Clinical validation of two volumetric absorptive microsampling devices to support home-based therapeutic drug monitoring of immunosuppression, Br. J. Clin. Pharmacol. 90 (2024) 2897–2909, https://doi.org/10.1111/bcp.16182.
[72] L. Paniagua-González, C. Díaz-Louzao, E. Lendoiro, E. Otero-Antón, C. Cadarso-Suárez, M. López-Rivadulla, A. Cruz, A. de-Castro-Ríos, Volumetric absorptive microsampling (VAMS) for assaying immunosuppressants from venous whole blood by LC–MS/MS using a novel atmospheric pressure ionization probe (UniSpray™), J. Pharm. Biomed. Anal. 189 (2020) 113422, https://doi.org/10.1016/j.jpba.2020.113422.
[73] R.A. Koster, P. Niemeijer, H. Veenhof, K.V. Hateren, J.-W.C. Alffenaar, D.J. Touw, A volumetric absorptive microsampling LC-MS/MS method for five

immunosuppressants and their hematocrit effects, Bioanalysis 11 (2019) 495–508, https://doi.org/10.4155/bio-2018-0312.
[74] S. Tanna, A. Alalaqi, D. Bernieh, G. Lawson, Volumetric absorptive microsampling (VAMS) coupled with high-resolution, accurate-mass (HRAM) mass spectrometry as a simplified alternative to dried blood spot (DBS) analysis for therapeutic drug monitoring of cardiovascular drugs, Clin. Mass Spectrom. 10 (2018) 1–8, https://doi.org/10.1016/j.clinms.2018.08.002.
[75] C. Marasca, M. Protti, R. Mandrioli, A.R. Atti, A. Armirotti, A. Cavalli, D. De Ronchi, L. Mercolini, Whole blood and oral fluid microsampling for the monitoring of patients under treatment with antidepressant drugs, J. Pharm. Biomed. Anal. 188 (2020) 113384, https://doi.org/10.1016/j.jpba.2020.113384.
[76] R. Simeoli, S. Cairoli, F. Galaverna, M. Becilli, E. Boccieri, G. Antonetti, A. Vitale, A. Mancini, C. Rossi, C.D. Vici, B.M. Goffredo, Utilization of volumetric absorptive microsampling and dried plasma spot for quantification of anti-fungal triazole agents in pediatric patients by using liquid chromatography-tandem mass spectrometry, J. Pharm. Biomed. Anal. 236 (2023) 115688, https://doi.org/10.1016/j.jpba.2023.115688.
[77] S. Zimmermann, F. Aghai-Trommeschlaeger, S. Kraus, G.U. Grigoleit, A. Gesierich, B. Schilling, C. Kalogirou, M.-E. Goebeler, M. Kurlbaum, H. Klinker, N. Isberner, O. Scherf-Clavel, Clinical validation and assessment of feasibility of volumetric absorptive microsampling (VAMS) for monitoring of nilotinib, cabozantinib, dabrafenib, trametinib, and ruxolitinib, J. Pharm. Biomed. Anal. 228 (2023) 115311, https://doi.org/10.1016/j.jpba.2023.115311.
[78] M. Radovanovic, J.J. Schneider, M. Shafiei, J.H. Martin, P. Galettis, Measurement of 5-fluorouracil, capecitabine and its metabolite concentrations in blood using volumetric absorptive microsampling technology and LC-MS/MS, J. Chromatogr. B 1188 (2022) 123075, https://doi.org/10.1016/j.jchromb.2021.123075.
[79] A. Hagemann, D. Klimpel, E. Schmitter, C.G. Bien, B. Dufaux, T.W. May, C. Brandt, Validation of conversion factors for therapeutic drug monitoring of lacosamide, lamotrigine, and levetiracetam in dried capillary blood, Ther. Drug Monit. 45 (2023) 546–553, https://doi.org/10.1097/FTD.0000000000001056.
[80] A. D'Urso, M. Locatelli, A. Tartaglia, L. Molteni, C. D'Ovidio, F. Savini, J. Rudge, U. De Grazia, Therapeutic drug monitoring of antiseizure medications using volumetric absorptive microsampling: Where are we? Pharmaceuticals 14 (2021) 627, https://doi.org/10.3390/ph14070627.
[81] M. Stern, M. Giebels, T. Fey, M. Lübking, J. Alferink, G. Hempel, Validation and clinical application of a volumetric absorptive microsampling method for 14 psychiatric drugs, Bioanalysis 12 (2020) 1129–1147, https://doi.org/10.4155/bio-2020-0136.
[82] H. Kramer, C. Bicer, C. Otoul, C. Rospo, M. Macpherson, M. Watling, M. Bani, D. Sciberras, H. Chanteux, Clinical bridging studies and modeling approach for implementation of a patient centric sampling technique in Padsevonil clinical development, AAPS J. 26 (2024) 1, https://doi.org/10.1208/s12248-023-00866-7.
[83] X.-Y. Li, C. Hu, X.-H. Zhu, Y. Wang, S.-Q. Shu, Z. Luo, Pharmacokinetics and safety of Padsevonil in healthy Chinese subjects and comparison of two sampling methods for Padsevonil quantification, Eur. Rev. Med. Pharmacol. Sci. 27 (2023) 4698–4707, https://doi.org/10.26355/eurrev_202305_32482.
[84] M.T. Gustavsen, K. Midtvedt, N.T. Vethe, I. Robertsen, S. Bergan, A. Åsberg, Tacrolimus area under the concentration versus time curve monitoring, using home-based volumetric absorptive capillary microsampling, Ther. Drug Monit. 42 (2020) 407–414, https://doi.org/10.1097/FTD.0000000000000697.
[85] A. Kocur, D. Marszałek, J. Rubik, A. Czajkowska, T. Pawiński, Therapeutic drug monitoring of Tacrolimus based on volumetric absorptive microsampling technique (VAMS) in renal transplant pediatric recipients—LC-MS/MS method development, hematocrit effect evaluation, and clinical application, Pharmaceutics 15 (2023) 299, https://doi.org/10.3390/pharmaceutics15010299.
[86] H. Veenhof, R.A. Koster, L.A.T. Junier, S.P. Berger, S.J.L. Bakker, D.J. Touw, Volumetric absorptive microsampling and dried blood spot microsampling vs. Conventional venous sampling for tacrolimus trough concentration monitoring, Clin. Chem. Lab. Med. 58 (2020) 1687–1695, https://doi.org/10.1515/cclm-2019-1260.
[87] L. Paniagua-González, E. Lendoiro, E. Otero-Antón, M. López-Rivadulla, A. de-Castro-Ríos, A. Cruz, Comparison of conventional dried blood spots and volumetric absorptive microsampling for tacrolimus and mycophenolic acid determination, J. Pharm. Biomed. Anal. 208 (2022) 114443, https://doi.org/10.1016/j.jpba.2021.114443.
[88] C.E. Scuderi, S.L. Parker, M. Jacks, G.T. John, B. McWhinney, J. Ungerer, A. J. Mallett, H.G. Healy, J.A. Roberts, C.E. Staatz, Serum creatinine and tacrolimus assessment with VAMS finger-prick microsampling: a diagnostic test study, Kidney Med. 5 (2023) 100610, https://doi.org/10.1016/j.xkme.2023.100610.
[89] X. Wang, X. Dai, S. Wan, Y. Fan, L. Wu, H. Xu, L. Yan, X. Gong, Y. Li, Y. Luo, Y. Bai, Y. Li, A volumetric absorptive microsampling UPLC-MS/MS method for simultaneous quantification of tacrolimus, mycophenolic acid and creatinine in whole blood of renal transplant recipients, Pharmaceutics 14 (2022) 2547, https://doi.org/10.3390/pharmaceutics14122547.
[90] A. Kocur, A. Czajkowska, K. Rębis, J. Rubik, M. Moczulski, B. Kot, M. Sierakowski, T. Pawiński, Personalization of pharmacotherapy with sirolimus based on volumetric absorptive microsampling (VAMS) in pediatric renal transplant recipients—from LC-MS/MS method validation to clinical application, Pharmacol. Rep. 75 (2024) 1026–1042, https://doi.org/10.1007/s43440-024-00663-9.
[91] A. Kocur, J. Rubik, P. Czarnowski, A. Czajkowska, D. Marszałek, M. Sierakowski, M. Górska, T. Pawiński, Therapeutic drug monitoring of mycophenolic acid (MPA) using volumetric absorptive microsampling (VAMS) in pediatric renal transplant recipients: ultra-high-performance liquid chromatography-tandem mass spectrometry analytical method development, cross-validation, and clinical application, Pharmacol. Rep. 75 (2023) 1026–1042, https://doi.org/10.1007/s43440-023-00509-w.
[92] E.R. Wickremsinhe, R.L. Decker, L.B. Lee, E. Lelle, L.A. Carlton, S.Y. Keller, A. Prakash, Microsampling in pediatric studies: pharmacokinetic sampling for baricitinib (Olumiant™) in global pediatric studies, Bioanalysis 15 (2023) 621–636, https://doi.org/10.4155/bio-2023-0044.
[93] B. Friedl, M. Kurlbaum, M. Kroiss, M. Fassnacht, O. Scherf-Clavel, A method for the minimally invasive drug monitoring of mitotane by means of volumetric absorptive microsampling for a home-based therapeutic drug monitoring, Anal. Bioanal. Chem. 411 (2019) 3951–3962, https://doi.org/10.1007/s00216-019-01868-1.
[94] G.S. Moorthy, C. Vedar, N. Zane, J.L. Prodell, A.F. Zuppa, Development and validation of a volumetric absorptive microsampling assay for analysis of voriconazole and voriconazole N-oxide in human whole blood, J. Chromatogr. B 1105 (2019) 67–75, https://doi.org/10.1016/j.jchromb.2018.12.007.
[95] R. Johnson, I. Rehmani, M. Leahy, A. Walker, X. Liang, B. Dean, J. Wang, Volumetric absorptive microsampling-LC-MS/MS assays for quantitation of giredestrant in dried human whole blood, Bioanalysis 14 (2022) 1377–1389, https://doi.org/10.4155/bio-2022-0189.
[96] J. Kujala, N. Wester, T.J. Lohela, M. Kurkela, J.T. Backman, B. Mikladal, T. Laurila, J. Koskinen, T.O. Lilius, E.A. Kalso, Introduction of an electrochemical point-of-care assay for quantitative determination of paracetamol in finger-prick capillary whole blood samples, Br. J. Clin. Pharmacol. 89 (2023) 2933–2938, https://doi.org/10.1111/bcp.15794.
[97] O. Ramadan, L.M. Schatz, I. Van Den Heuvel, K. Masjosthusmann, A.H. Groll, G. Hempel, Developing a method for quantifying meropenem in children - volumetric adsorptive microsampling versus plasma sampling, Ther. Drug Monit. 45 (2023) 623–630, https://doi.org/10.1097/FTD.0000000000001105.
[98] S.L. Parker, J.A. Roberts, J. Lipman, S.C. Wallis, Quantitative bioanalytical validation of fosfomycin in human whole blood with volumetric absorptive microsampling, Bioanalysis 7 (2015) 2585–2595, https://doi.org/10.4155/bio.15.173.
[99] Z. Miao, J.G. Farnham, G. Hanson, T. Podoll, M.J. Reid, Bioanalysis of emixustat (ACU-4429) in whole blood collected with volumetric absorptive microsampling by LC-MS/MS, Bioanalysis 7 (2015) 2071–2083, https://doi.org/10.4155/bio.15.125.
[100] J. Millán-Santiago, R. Vitagliano, F. Mondella, R. Mandrioli, R. Sardella, T. Vovk, R. Lucena, S. Cárdenas, F. Boaron, A. Serretti, C. Petio, M. Protti, L. Mercolini, Volumetric absorptive microsampling for the therapeutic drug monitoring of psychiatric patients treated with cariprazine, J. Pharm. Biomed. Anal. 236 (2023) 115740, https://doi.org/10.1016/j.jpba.2023.115740.
[101] P. Abu-Rabie, B. Neupane, N. Spooner, J. Rudge, P. Denniff, H. Mulla, H. Pandya, Validation of methods for determining pediatric midazolam using wet whole blood and volumetric absorptive microsampling, Bioanalysis 11 (2019) 1737–1754, https://doi.org/10.4155/bio-2019-0190.
[102] A. Kocur, A. Czajkowska, M. Moczulski, B. Kot, J. Rubik, T. Pawiński, Assessment of dried serum spots (DSS) and volumetric-absorptive microsampling (VAMS) techniques in therapeutic drug monitoring of (Val)Ganciclovir—Comparative study in analytical and clinical practice, Int. J. Mol. Sci. 25 (2024) 8760, https://doi.org/10.3390/ijms25168760.
[103] A. Breton, C.M. Cirtiu, C. Muehlethaler, J. Rudge, N. Fleury, Validation of Mitra™ VAMS™ as a blood collection technique for trace elements analysis using ICP-MS/MS, Bioanalysis 16 (2024) 203–217, https://doi.org/10.4155/bio-2023-0180.
[104] Y. Anoshkina, M. Costas-Rodríguez, F. Vanhaecke, Iron isotopic analysis of finger-prick and venous blood by multi-collector inductively coupled plasma-mass spectrometry after volumetric absorptive microsampling, J. Anal. At. Spectrom. 32 (2017) 314–321, https://doi.org/10.1039/c6ja00394j.
[105] A. Breton, C.M. Cirtiu, N. Fleury, A. Lajeunesse, J. Rudge, Method development for the quantification of lead levels in whole blood sampled on Mitra® with VAMS® tips by inductively coupled plasma-MS/MS, Bioanalysis 15 (2023) 71–81, https://doi.org/10.4155/bio-2022-0242.
[106] C. Jones, G.J. Dunseath, J. Lemon, S.D. Luzio, Microsampling collection methods for measurement of C-peptide in whole blood, J. Diab. Sci. Technol. 12 (2018) 1024–1028, https://doi.org/10.1177/1932296818763464.
[107] R. McMahon, C. Hill, J. Rudge, B. Herbert, E. Karsten, Stability of inflammation markers in human blood collected using volumetric absorptive microsampling (VAMS) under typical laboratory storage temperatures, Cytokine 171 (2023) 156355, https://doi.org/10.1016/j.cyto.2023.156355.
[108] C. Tuma, A. Thomas, H. Braun, M. Thevis, Quantification of 25-hydroxyvitamin D2 and D3 in Mitra® devices with volumetric absorptive microsampling technology (VAMS®) by UHPLC-HRMS for regular vitamin D status monitoring, J. Pharm. Biomed. Anal. 228 (2023) 115314, https://doi.org/10.1016/j.jpba.2023.115314.
[109] A. Marchand, I. Roulland, F. Semence, M. Audran, Volumetric absorptive microsampling (VAMS) technology for IGF-1 quantification by automated chemiluminescent immunoassay in dried blood, Growth Horm. IGF Res. 50 (2020) 27–34, https://doi.org/10.1016/j.ghir.2019.12.001.
[110] I. van den Broek, Q. Fu, S. Kushon, M.P. Kowalski, K. Millis, A. Percy, R. J. Holewinski, V. Venkatraman, J.E. Van Eyk, Application of volumetric absorptive microsampling for robust, high-throughput mass spectrometric quantification of circulating protein biomarkers, Clin. Mass Spectrom. 4-5 (2017) 25–33, https://doi.org/10.1016/j.clinms.2017.08.004.
[111] M. Protti, M. Cirrincione, R. Mandrioli, J. Rudge, L. Regazzoni, V. Valsecchi, C. Volpi, L. Mercolini, Volumetric absorptive microsampling (VAMS) for targeted

LC-MS/MS determination of tryptophan-related biomarkers, Molecules 27 (2022) 5652, https://doi.org/10.3390/molecules27175652.
[112] C. Marasca, M.E.B. Arana, M. Protti, A. Cavalli, L. Mercolini, A. Armirotti, Volumetric absorptive microsampling of blood for untargeted lipidomics, Molecules 26 (2021) 262, https://doi.org/10.3390/molecules26020262.
[113] A. Marchand, I. Roulland, F. Semence, M. Ericsson, EPO transgene detection in dried blood spots for antidoping application, Drug Test. Anal. 13 (2021) 1888–1896, https://doi.org/10.1002/dta.3059.
[114] C.E. Heiland, L. Martin, X. Zhou, L. Zhang, M. Ericsson, A. Marchand, Dried blood spots for erythropoietin analysis: detection of micro-doses, EPO c.577del variant and comparison with in-competition matching urine samples, Drug Test. Anal. 16 (2024) 650–654, https://doi.org/10.1002/dta.3596.
[115] C. Tuma, A. Thomas, H. Braun, M. Thevis, Development of an LC-HRMS/MS method for quantifying steroids and thyroid hormones in capillary blood: a potential tool for assessing relative energy deficiency in sport (RED-S), Metabolites 14 (2024) 328, https://doi.org/10.3390/metabo14060328.
[116] I.O. Mestad, A. Gjelstad, S. Pedersen-Bjergaard, E.L. Øiestad, Green and sustainable drug analysis–combining microsampling and microextraction of drugs of abuse, Sustain. Chem. Pharm. 24 (2021) 100517, https://doi.org/10.1016/j.scp.2021.100517.
[117] R. Mandrioli, L. Mercolini, M. Protti, Blood and plasma volumetric absorptive microsampling (VAMS) coupled to LC-MS/MS for the forensic assessment of cocaine consumption, Molecules 25 (2020) 1046, https://doi.org/10.3390/molecules25051046.
[118] M. Protti, I. Varfaj, A. Carotti, D. Tedesco, M. Bartolini, A. Favilli, S. Gerli, L. Mercolini, R. Sardella, Microsampling and enantioselective liquid chromatography coupled to mass spectrometry for chiral bioanalysis of novel psychoactive substances, Talanta 257 (2023) 124332, https://doi.org/10.1016/j.talanta.2023.124332.
[119] P. Houzé, I. Borowski, E. Bito, R. Magny, A. Morcos, S. Voicu, B. Mégarbane, L. Labat, New trend in toxicological screening using volumetric absorptive microsampling (VAMS) and high-resolution mass spectrometry (HR/MS) combination, Molecules 28 (2023) 3466, https://doi.org/10.3390/molecules28083466.
[120] M. Protti, P.M. Sberna, R. Sardella, T. Vovk, L. Mercolini, R. Mandrioli, VAMS and StAGE as innovative tools for the enantioselective determination of clenbuterol in urine by LC-MS/MS, J. Pharm. Biomed. Anal. 195 (2021) 113873, https://doi.org/10.1016/j.jpba.2020.113873.
[121] J.M. Taylor, A.T. Hughes, A.M. Milan, J. Rudge, A.S. Davison, L.R. Ranganath, Evaluation of the Mitra microsampling device for use with key urinary metabolites in patients with alkaptonuria, Bioanalysis 10 (2018) 1919–1932, https://doi.org/10.4155/bio-2018-0193.
[122] M. Protti, C. Marasca, M. Cirrincione, A.E. Sberna, R. Mandrioli, L. Mercolini, Dried urine microsampling coupled to liquid chromatography-tandem mass spectrometry (LC-MS/MS) for the analysis of unconjugated anabolic androgenic steroids, Molecules 25 (2020) 3210, https://doi.org/10.3390/molecules25143210.
[123] S. Tripathy, K.X. Wan, M.H. Shahin, J.A. Winton, B.K. Malhotra, O. Kavetska, Patient-centric microsampling for abrocitinib pharmacokinetics: multiple-analytes assay bridging using Tasso device, Bioanalysis 16 (2024) 825–834, https://doi.org/10.1080/17576180.2024.2388939.
[124] G.D. Miller, J. Husk, A.K. Crouch, D. Eichner, Growth hormone isoform testing in capillary dried blood spots: results from single and multiple dose administration studies and large-scale field collections, Drug Test. Anal. 14 (2022) 1255–1263, https://doi.org/10.1002/dta.3248.
[125] E.R. King, H.E. Garrett, H. Abernathy, C.A. Cassidy, C.R. Cabell, B.E. Shook-Sa, J. J. Juliano, R.M. Boyce, A.E. Aiello, E.J. Ciccone, Comparison of capillary blood self-collection using the Tasso-SST device with venous phlebotomy for anti-SARS-CoV-2 antibody measurement, J. Immunol. Methods 520 (2023) 113523, https://doi.org/10.1016/j.jim.2023.113523.
[126] J.D. Jett, R. Beck, D. Tyutyunnyk, J. Sanchez, D.L. Weeks, M.A. Javors, N. Hill-Kapturczak, M. Lopez-Cruzan, L. Kriegel, B.C. Ginsburg, L. Cabassa, M. G. McDonell, Feasibility of a telehealth-based contingency management intervention for alcohol use disorders using the phosphatidylethanol (PEth) 16:0/18:1 alcohol biomarker: a pilot randomized trial, Am. J. Drug Alcohol Abuse 50 (2024) 162–172, https://doi.org/10.1080/00952990.2023.2283691.
[127] T. Hendelman, A. Chaudhary, A.C. LeClair, K. Van Leuven, J. Chee, S.L. Fink, E. J. Welch, E. Berthier, B.A. Quist, A. Wald, M.H. Wener, A.N. Hoofnagle, C. Morishima, Self-collection of capillary blood using Tasso- SST devices for Anti-SARS-CoV-2 IgG antibody testing, PLoS One 16 (2021) e0255841, https://doi.org/10.1371/journal.pone.0255841.
[128] R.A. Binder, A.M. Matta, C.S. Forconi, C.I. Oduor, P. Bedekar, P.N. Patrone, A. J. Kearsley, B. Odwar, J. Batista, S.N. Forrester, H.K. Leftwich, L.A. Cavacini, A. M. Moormann, Minding the margins: evaluating the impact of COVID-19 among Latinx and black communities with optimal qualitative serological assessment tools, PLoS One 19 (2024) e0307568, https://doi.org/10.1371/journal.pone.0307568.
[129] S.A. Solheim, T.K. Ringsted, N.B. Nordsborg, Y. Dehnes, M.C.S. Levernæs, J. Mørkeberg, No pain, just gain: painless, easy, and fast dried blood spot collection from fingertip and upper arm in doping control, Drug Test. Anal. 13 (2021) 1783–1790, https://doi.org/10.1002/dta.3135.
[130] J. Brandsma, J.G. Chenoweth, M.K. Gregory, S. Krishnan, P.W. Blair, D. A. Striegel, R. Mehta, K.L. Schully, J.S. Dumler, C.S. Sikorski, K. O'Connor, S. A. Reichert-Scrivner, C.M. Paguirigan, C.F.T. Uyehara, V. Ngauy, C.A. Myers, D. V. Clark, Assessing the use of a micro-sampling device for measuring blood protein levels in healthy subjects and COVID-19 patients, PLoS One 17 (2022) e0272572, https://doi.org/10.1371/journal.pone.0272572.
[131] L. Boffel, A. Van Mensel, J. Pauwels, E. Den Hond, J. Bessems, K. Van Uytfanghe, Self-sampling by adolescents at home: assessment of the feasibility to successfully collect blood microsamples by inexperienced individuals, AAPS J. 26 (2024) 75, https://doi.org/10.1208/s12248-024-00947-1.
[132] T. Mohammed, J.V.V. Brewer, M. Pyatt, S.B. Whitbourne, J.M. Gaziano, C. Edson, M. Holodniy, Evaluation of independent self-collected blood specimens for COVID-19 antibody detection among the US veteran population, Diagn. Microbiol. Infect. Dis. 104 (2022) 115770, https://doi.org/10.1016/j.diagmicrobio.2022.115770.
[133] A.J. Haack, F.Y. Lim, D.S. Kennedy, J.H. Day, K.N. Adams, J.J. Lee, E. Berthier, A. B. Theberge, homeRNA: a self-sampling kit for the collection of peripheral blood and stabilization of RNA, Anal. Chem. 93 (2021) 13196–13203, https://doi.org/10.1021/acs.analchem.1c02008.
[134] M.C.S. Levernæs, S.A. Solheim, L. Broderstad, E. Zandy, J. Mørkeberg, Y. Dehnes, Detection of doping substances in paired dried blood spots and urine samples collected during doping controls in Danish fitness centers, Drug Test. Anal. 16 (2024) 1510–1527, https://doi.org/10.1002/dta.3660.
[135] R.C. Fyffe-Freil, P.J. Jannetto, P.M. Vanderboom, To boldly go where no device has gone before: specimen self-collection for the clinical laboratory, Clin. Microbiol. Newsl. 45 (2023) 29–37, https://doi.org/10.1016/j.clinmicnews.2023.02.001.
[136] E. Wickremsinhe, A. Fantana, B.A. Quist, D. Lopez de Castilla, C. Fix, K. Chan, J. Shi, M.G. Walker, J.F. Kherani, H. Knoderer, A. Regev, J.J. Harding, Standard venipuncture vs a capillary blood collection device for the prospective determination of abnormal liver chemistry, J. Appl. Lab. Med. 8 (2023) 535–550, https://doi.org/10.1093/jalm/jfac127.
[137] K. Wan, O. Kavetska, B. Damle, H. Shi, D.S. Cox, O. Oladoyinbo, P. Chan, R.S. P. Singh, S. Craft, E. Berthier, B. Corrigan, Patient centric microsampling to support Paxlovid clinical development: bridging and implementation, Clin. Pharmacol. Ther. 115 (2024) 42–51, https://doi.org/10.1002/cpt.3025.
[138] D. Wixted, C.E. Neighbors, C.F. Pieper, A. Wu, C. Kingsbury, H. Register, E. Petzold, L.K. Newby, C.W. Woods, Comparison of a blood self-collection system with routine phlebotomy for SARS-CoV-2 antibody testing, Diagnostics 12 (2022) 1857, https://doi.org/10.3390/diagnostics12081857.
[139] C. Cannon, K. Holzhauer, M. Golden, Implementation and evaluation of a home-based pre-exposure prophylaxis monitoring option: protocol for a randomized controlled trial, JMIR Res. Protoc. 13 (2024) e56587, https://doi.org/10.2196/56587.
[140] J.M. Goodrum, L.A. Lewis, M.N. Fedoruk, D. Eichner, G.D. Miller, Feasibility of microvolumetric capillary whole blood collections for usage in athlete biological passport analysis, Drug Test. Anal. 14 (2022) 1291–1299, https://doi.org/10.1002/dta.3254.
[141] H. Dasari, A. Smyrnova, J. Leng, F.M. Ducharme, Feasibility, acceptability, and safety of a novel device for self-collecting capillary blood samples in clinical trials in the context of the pandemic and beyond, PLoS One 19 (2024) e0304155, https://doi.org/10.1371/journal.pone.0304155.
[142] A. Marchand, G. Miller, L. Martin, C. Gobbo, A.K. Crouch, D. Eichner, M. Ericsson, Detection of erythropoiesis stimulating agent Luspatercept after administration to healthy volunteers for antidoping purposes, Drug Test. Anal. 14 (2022) 1952–1961, https://doi.org/10.1002/dta.3341.
[143] S. Mandlekar, D.S. Sutaria, X. Yang, R. Johnson, Y. Zou, B. Dean, L. Chen, R. Sane, K. Williams, A. Cardenas, M. Simon, S. Fischer, Evaluation of patient-centric sample collection technologies for pharmacokinetic assessment of large and small molecules, Clin. Pharmacol. Ther. 116 (2024) 782–794, https://doi.org/10.1002/cpt.3272.
[144] G.D. Miller, J.M. Goodrum, A.K. Crouch, D. Eichner, Assessing EPO stability in urine and comparing recombinant EPO detectability in matched urine, venous serum, and capillary serum following a controlled epoetin alfa administration, Drug Test. Anal. (2024), https://doi.org/10.1002/dta.3736.
[145] M.M. Dewes, L. Cé da Silva, Y. Fazenda Meireles, M. Viana de Freitas, M.F. Frank Bastiani, L.F. Feltraco Lizot, R.Z. Hahn, M.V. Antunes, R. Linden, Evaluation of the Tasso-SST® capillary blood microsampling device for the measurement of endogenous uracil levels, Clin. Biochem. 107 (2022) 1–6, https://doi.org/10.1016/j.clinbiochem.2022.06.003.
[146] K.J. Williams, J. Lutman, C. McCaughey, S.K. Fischer, Assessment of low volume sampling technologies: utility in nonclinical and clinical studies, Bioanalysis 13 (2021) 679–691, https://doi.org/10.4155/bio-2021-0027.
[147] K.X. Wan, D. Potts, P. Gonzalez, I. Smith, H. Shi, O. Kavetska, Bioanalytical method validation and sample analysis for nirmatrelvir in dried blood collected using the Tasso-M20 device, Bioanalysis 14 (2022) 1305–1315, https://doi.org/10.4155/bio-2022-0167.
[148] O. Sala-Torra, L. Beppu, Q. Wu, E. Welch, E. Berthier, J.P. Radich, V.G. Oehler, Point-of-care BCR::ABL1 transcript monitoring using capillary dried blood in chronic myeloid leukemia patients, Leukemia 38 (2024) 1822–1824, https://doi.org/10.1038/s41375-024-02285-9.
[149] C. Schmetzer, E. Vogt, L. Stellar, E.-T. Godonou, A.-M. Liphardt, F. Muehlensiepen, N. Vuillerme, A.J. Hueber, A. Kleyer, G. Krönke, G. Schett, D. Simon, J. Knitza, Self-collection of capillary blood and saliva to determine COVID-19 vaccine immunogenicity in patients with immune-mediated inflammatory diseases and health professionals, Front. Public Health 10 (2022) 994770, https://doi.org/10.3389/fpubh.2022.994770.
[150] L. Lewis, J. Goodrum, C. Cai, T. Muir, K. Boutard, T. Capdevielle, S. Longo, M. Fedoruk, G. Miller, Application of micro capillary blood sampling in an anti-

doping setting, Drug Test. Anal. 16 (2024) 835–840, https://doi.org/10.1002/dta.3603.
[151] J.D. Jett, R. Beck, D. Tyutyunnyk, J. Sanchez, M. Lopez-Cruzan, B.C. Ginsburg, S. M. McPherson, M.A. Javors, M.G. McDonell, N. Hill-Kapturczak, Validation of the quantification of phosphatidylethanol 16:0/18:1 concentrations in TASSO-M20 devices, Alcohol Clin. Exp. Res. 47 (2023) 748–755, https://doi.org/10.1111/acer.15024.
[152] L. Lewis, M. Smith, K. Boutard, M. Fedoruk, G. Miller, Comparison of microcapillary blood sampling devices for use in anti-doping, Drug Test. Anal. (2024), https://doi.org/10.1002/dta.3818.
[153] C.J.D. Goense, Y.J. Evers, I.H.M. Van Loo, R.J.M. Heuts, C.J.P.A. Hoebe, C. A. Cannon, N.H.T.M. Dukers-Muijrers, Using an innovative method for self-collection of capillary blood for HIV and syphilis testing among men who have sex with men who use pre-exposure prophylaxis in the Netherlands; Limburg4zero, Sex. Transm. Dis. 51 (2024) 521–526, https://doi.org/10.1097/OLQ.0000000000001969.
[154] B. Roadcap, A. Hussain, D. Dreyer, K. Carter, N. Dube, Y. Xu, M. Anderson, E. Berthier, F. Vazvaei, K. Bateman, E. Woolf, Clinical application of volumetric absorptive microsampling to the gefapixant development program, Bioanalysis 12 (2020) 893–904, https://doi.org/10.4155/bio-2020-0074.
[155] B. Hosseini, H. Dasari, A. Smyrnova, C. Bourassa, J. Leng, C. Renaud, F. M. Ducharme, Concordance in COVID-19 serology, bone mineralization, and inflammatory analytes between venous and self-collected capillary blood samples exposed to various pre-analytical conditions, Ann. Clin. Biochem. 60 (2023) 259–269, https://doi.org/10.1177/00045632231159279.
[156] J. Zarbl, E. Eimer, C. Gigg, G. Bendzuck, M. Korinth, C. Elling-Audersch, A. Kleyer, D. Simon, S. Boeltz, M. Krusche, J. Muehlensiepen, N. Vuillerme, G. Krönke, G. Schett, J. Knitza, Remote self-collection of capillary blood using upper arm devices for autoantibody analysis in patients with immune-mediated inflammatory rheumatic diseases, RMD Open 8 (2022) e002641, https://doi.org/10.1136/rmdopen-2022-002641.
[157] A.D. Leino, J. Takyi-Williams, B. Wen, D. Sun, M.P. Pai, Application of a new volumetric microsampling device for quantitative bioanalysis of immunosuppression, Bioanalysis 14 (2022) 1141–1152, https://doi.org/10.4155/bio-2022-0155.
[158] J. Knitza, K. Tascilar, N. Vuillerme, E. Eimer, P. Matusewicz, G. Corte, L. Schuster, T. Aubourg, G. Bendzuck, M. Korinth, C. Elling-Audersch, A. Kleyer, S. Boeltz, A. J. Hueber, G. Krönke, G. Schett, D. Simon, Accuracy and tolerability of self-sampling of capillary blood for analysis of inflammation and autoantibodies in rheumatoid arthritis patients—results from a randomized controlled trial, Arthritis Res. Ther. 24 (2022) 125, https://doi.org/10.1186/s13075-022-02809-7.
[159] X. Yang, E. Logis, K. Williams, X.R. Sheng, S.K. Fischer, Evaluation of low volume sampling devices for a pharmacodynamic biomarker analysis: challenges and solutions, J. Pharm. Biomed. Anal. 251 (2024) 116454, https://doi.org/10.1016/j.jpba.2024.116454.
[160] C.A. Cannon, M.S. Ramchandani, M.R. Golden, Feasibility of a novel self-collection method for blood samples and its acceptability for future home-based PrEP monitoring, BMC Infect. Dis. 22 (2022) 459, https://doi.org/10.1186/s12879-022-07432-0.
[161] T. Phan, L. Kumar, M. Woo, A. Sadowska-Klasa, J. Castor, G. Pepper, C.E. Fisher, A.P. Limaye, Evaluation of the Tasso+ blood self-collection device for quantitation of plasma cytomegalovirus (CMV) DNAemia in adult solid organ transplant recipients (SOTr), Microbiol. Spectr. 12 (2024) e0003024, https://doi.org/10.1128/spectrum.00030-24.
[162] H.-H. Huynh, L. Barahona-Carrillo, D. Moncrieffe, D. Cowan, K. Forrest, J. Becker, M. Emrick, A. Thomas, M. Thevis, D. Eichner, P. Byers, G. Miller, A. Hoofnagle, A novel high-throughput immunoaffinity LC–MS/MS assay for P-III-NP and other fragments of type III procollagen in human serum, Drug Test. Anal. (2024), https://doi.org/10.1002/dta.3814.
[163] B. El-Sabawi, S. Huang, K. Tanriverdi, A.S. Perry, K. Amancherla, N. Jackson, J. Hulsey, J.E. Freedman, R. Shah, B.R. Lindman, Capillary blood self-collection for high-throughput proteomics, Proteomics 24 (2024) 2300607, https://doi.org/10.1002/pmic.202300607.
[164] J.M. Goodrum, K. Peek, C. Moore, D. Eichner, G.D. Miller, Is blood blood? Comparing quantitation of endogenous steroids and luteinizing hormone in concurrently collected venous serum and Tasso+ SST capillary serum samples, Drug Test. Anal. (2024), https://doi.org/10.1002/dta.3738.
[165] YourBio Health, Inc., Revolutionizing blood collection. Available from https://yourbiohealth.com/(accessed on February 10, 2025).
[166] RedDrop Dx, General. Available from https://www.reddropdx.com/device (accessed on February 10, 2025).
[167] B.K. Yılmaz, Ö. Evliyaoğlu, A. Yorgancı, Ş. Özyer, Y.E. Üstün, Serum concentrations of heavy metals in women with endometrial polyps, J. Obstet. Gynaecol. 40 (2020) 541–545, https://doi.org/10.1080/01443615.2019.1634022.
[168] J. Xing, J. Loureiro, M.T. Patel, D. Mikhailov, A.I. Gusev, Evaluation of a novel blood microsampling device for clinical trial sample collection and protein biomarker analysis, Bioanalysis 12 (2020) 919–935, https://doi.org/10.4155/bio-2020-0063.
[169] D. Lee, C.G. Rapp, J. Loureiro, M.T. Patel, D. Mikhailov, A.I. Gusev, Decentralized clinical trial design using blood microsampling technology for serum bioanalysis, Bioanalysis 15 (2023) 1287–1303, https://doi.org/10.4155/bio-2023-0136.
[170] B.B. Collier, W.C. Brandon, M.R. Chappell, P.M. Kovach, R.P. Grant, Maximizing microsampling: measurement of comprehensive metabolic and lipid panels using a novel capillary blood collection device, J. Appl. Lab. Med. 8 (2023) 1115–1126, https://doi.org/10.1093/jalm/jfad066.
[171] A. Catala, R. Culp-Hill, T. Nemkov, A. D'Alessandro, Quantitative metabolomics comparison of traditional blood draws and TAP capillary blood collection, Metabolomics 14 (2018) 100, https://doi.org/10.1007/s11306-018-1395-z.
[172] K.R. Voigt, L. Wullaert, P.D. Gobardhan, P.G. Doornebosch, C. Verhoef, O. Husson, C. Ramakers, D.J. Grünhagen, Feasibility, reliability and satisfaction of (automated) capillary carcinoembryonic antigen measurements for future home-based blood sampling: the prospective CASA-I study, Colorec. Dis. 26 (2024) 1560–1568, https://doi.org/10.1111/codi.17085.
[173] T. Lange, A. Thomas, K. Walpurgis, M. Thevis, Fully automated dried blood spot sample preparation enables the detection of lower molecular mass peptide and non-peptide doping agents by means of LC-HRMS, Anal. Bioanal. Chem. 412 (2020) 3765–3777, https://doi.org/10.1007/s00216-020-02634-4.
[174] H. Setoyama, N. Nishida, S. Nagashima, K. Ko, T. Yamazoe, Y. Tanaka, M. Mizokami, J. Tanaka, T. Kanto, Dried blood spot-based host genome analysis technique targeting pathological associations with hepatitis B: development and clinical application in the Cambodian population, Hepatol. Res. 53 (2023) 1147–1155, https://doi.org/10.1111/hepr.13949.
[175] J.E. Diaz, D. Ghanooni, L. Atkins, S.S. Sam, R. Kantor, M. Miller-Perusse, C. C. Chuku, O. Valentin, R.R. Balise, L. Davis-Ewart, A. Tisler, K.J. Horvath, A. W. Carrico, S. Hirshfield, Challenges and opportunities with at-home blood collection for HIV-1 viral load monitoring among sexual minoritized men who use stimulants, AIDS Behav. 28 (2024) 3809–3818, https://doi.org/10.1007/s10461-024-04453-5.
[176] K. Izuora, A. Alver, A. Basu, K. Batra, S.J. Williams, J.L. Ebersole, The association of dietary micronutrient intake and systemic inflammation among patients with type 2 diabetes: a cross-sectional study, Healthcare (Switzerland) 12 (2024) 1804, https://doi.org/10.3390/healthcare12181804.
[177] P.A. Kothare, P.R. Jadhav, P. Gupta, J.C. Harrelson, L. Dickmann, Harnessing the potential of emerging digital health and biological sampling technologies for clinical drug development: promise to reality, Clin. Pharmacol. Ther. 104 (2018) 1125–1135, https://doi.org/10.1002/cpt.1100.
[178] K. Brooks, A. De Long, M. Balamane, L. Schreier, M. Orido, M. Chepkenja, E. Kemboi, M. D'Antuono, P.A. Chan, W. Emonyi, L. Diero, M. Coetzer, R. Kantor, HemaSpot, a novel blood storage device for HIV-1 drug resistance testing, J. Clin. Microbiol. 54 (2016) 223–225, https://doi.org/10.1128/JCM.02853-15.
[179] J.M. Hall, C.F. Fowler, M.A. Pollock, S.M. MacRury, Haemoglobin A1c determination from dried blood spots prepared with HemaSpot™ blood collection devices: comparison with fresh capillary blood, Clin. Chem. Lab. Med. 59 (2021) 79–82, https://doi.org/10.1515/cclm-2020-0675.
[180] C. Prosperi, O. Kaduskar, V. Bhatt, A.Z. Hasan, J.W.V. Thangaraj, M.S. Kumar, R. Sabarinathan, S. Kumar, A. Duraiswamy, G.R. Deshpande, U.P. Thankappan, S. L. Chauhan, R.N. Kulkarni, A.K. Bansal, I.K. Chaaithanya, N.R. Salvi, S. Sharma, W.J. Moss, L. Sangal, N. Gupta, M.V. Murherkar, S.M. Mehendale, G.N. Sapkal, K. Hayford, Diagnostic accuracy of dried blood spots collected on HemaSpot HF devices compared to venous blood specimens to estimate measles and Rubella seroprevalence, mSphere 6 (2021) 1–10, https://doi.org/10.1128/mSphere.01330-20.
[181] C.A. Sobsey, N. Mady, V.R. Richard, A. LeBlanc, T. Zakharov, C.H. Borchers, R. T. Jagoe, Measurement of CYP1A2 and CYP3A4 activity by a simplified Geneva cocktail approach in a cohort of free-living individuals: a pilot study, Front. Pharmacol. 15 (2024) 1232595, https://doi.org/10.3389/fphar.2024.1232595.
[182] J.M. Hall, C.F. Fowler, F. Barrett, R.W. Humphry, M. Van Drimmelen, S. M. MacRury, HbA1c determination from HemaSpot™ blood collection devices: comparison of home prepared dried blood spots with standard venous blood analysis, Diabet. Med. 37 (2020) 1463–1470, https://doi.org/10.1111/dme.14110.
[183] S. Hirshfield, R.A. Teran, M.J. Downing Jr., M.A. Chiasson, H.-V. Tieu, L. Dize, C. A. Gaydos, Quantification of HIV-1 RNA among men who have sex with men using an at-home self-collected dried blood spot specimen: feasibility study, JMIR Public Health Surveill. 4 (2018) e10847, https://doi.org/10.2196/10847.
[184] M.M. Manak, H.R. Hack, A.L. Shutt, B.A. Danboise, L.L. Jagodzinski, S.A. Peel, Stability of human immunodeficiency virus serological markers in samples collected as Hemaspot and Whatman 903 dried blood spots, J. Clin. Microbiol. 56 (2018) e00933, https://doi.org/10.1128/JCM.00933-18.
[185] O.P. Trifonova, D.L. Maslov, E.E. Balashova, P.G. Lokhov, Evaluation of dried blood spot sampling for clinical metabolomics: effects of different papers and sample storage stability, Metabolites 9 (2019) 277, https://doi.org/10.3390/metabo9110277.
[186] A. Manne, A. DeLong, W. Nyandiko, A.K. DeLong, R. Vreeman, V. Novitsky, A. Ngeresa, E. Sang, A. Chory, J. Aluoch, E. Jepkemboi, M. Orido, C. Ashimosi, F. Sang, J.W. Hogan, R. Kantor, Real-life feasibility of HIV drug resistance testing using dried filter analytes in Kenyan children and adolescents living with HIV, microbiol, Spectrum 10 (2022) e0267521, https://doi.org/10.1128/spectrum.02675-21.
[187] A.C. Rosypal, L.D. Pick, J.O.E. Hernandez, D.S. Lindsay, Evaluation of a novel dried blood spot collection device (HemaSpot™) to test blood samples collected from dogs for antibodies to Leishmania infantum, Vet. Parasitol. 205 (2014) 338–342, https://doi.org/10.1016/j.vetpar.2014.07.031.
[188] C. Yamamoto, S. Nagashima, M. Isomura, K. Ko, C. Chuon, T. Akita, K. Katayama, J. Woodring, M.S. Hossain, K. Takahashi, J. Tanaka, Evaluation of the efficiency of dried blood spot-based measurement of hepatitis B and hepatitis C virus seromarkers, Sci. Rep. 10 (2020) 3857. https://doiorg/10.1038/s41598-020-60703-1.

[189] O. Kaduskar, V. Bhatt, C. Prosperi, K. Hayford, A.Z. Hasan, G.R. Deshpande, B. Tilekar, J.W.V. Thangaraj, M.S. Kumar, N. Gupta, M.V. Murhekar, W.J. Moss, S. M. Mehendale, L. Sangal, G. Sapkal, Optimization and stability testing of four commercially available dried blood spot devices for estimating measles and rubella IgG antibodies, mSphere 6 (2021) 1–12, https://doi.org/10.1128/mSphere.00490-21.

[190] A. Vubil, A.F. Zicai, N. Sitoe, C. Nhachigule, P. da Costa, C. Magul, B. Meggi, S. Viegas, N. Mabunda, I. Jani, Performance of two plasma separation devices for HIV-1 viral load measurement in primary healthcare settings, Microbiol. Spectr. 11 (2023), https://doi.org/10.1128/spectrum.00546-23.

[191] J.H. Kim, T. Woenker, J. Adamec, F.E. Regnier, Simple, miniaturized blood plasma extraction method, Anal. Chem. 85 (2013) 11501–11508, https://doi.org/10.1021/ac402735y.

[192] B.J. Bills, N.E. Manicke, Development of a prototype blood fractionation cartridge for plasma analysis by paper spray mass spectrometry, Clin. Mass Spectrom. 2 (2016) 18–24, https://doi.org/10.1016/j.clinms.2016.12.002.

[193] Y. Tang, L. Chen, X. Liang, B. Dean, J. Wang, Exploring the potential of dried plasma collection cards for liquid chromatography coupled with tandem mass spectrometry quantitation of giredestrant in human plasma, Biomed. Chromatogr. 37 (2023) e5554, https://doi.org/10.1002/bmc.5554.

[194] H. John, S. Willoh, P. Hörmann, M. Siegert, A. Vondran, H. Thiermann, Procedures for analysis of dried plasma using microsampling devices to detect sulfur mustard-albumin adducts for verification of poisoning, Anal. Chem. 88 (2016) 8787–8794, https://doi.org/10.1021/acs.analchem.6b02199.

[195] H. Cao, Y. Jiang, S. Wang, H. Cao, Y. Li, J. Huang, Dried plasma spot based LC-MS/MS method for monitoring of meropenem in the blood of treated patients, Molecules 27 (2022) 1991, https://doi.org/10.3390/molecules27061991.

[196] A. Cvetko, M. Tijardović, I. Bilandžija-Kuš, O. Gornik, Comparison of self-sampling blood collection for *N*-glycosylation analysis, BMC Res. Notes 15 (2022) 61, https://doi.org/10.1186/s13104-022-05958-9.

[197] L.D. Noble, C. Dixon, A. Moran, C. Trottet, M. Majam, S. Ismail, V.T. Msolomba, K. Mathobela, A. Queval, J. George, L.E. Scott, W.S. Stevens, Painless capillary blood collection: a rapid evaluation of the onflow device, Diagnostics (Basel) 13 (2023) 1754, https://doi.org/10.3390/diagnostics13101754.

[198] N. Zoratto, D. Klein-Cerrejon, D. Gao, T. Inchiparambil, D. Sachs, Z. Luo, J. C. Leroux, A bioinspired and cost-effective device for minimally invasive blood sampling, Adv. Sci. (Weinh) 11 (2024) e2308809, https://doi.org/10.1002/advs.202308809.

[199] K.F. Maass, M.D. Barfield, M. Ito, C.A. James, O. Kavetska, M. Kozinn, P. Kumar, M. Lepak, L.A. Leuthold, W. Li, D. Mikhailov, S. Patel, N.L. Perez, D.J. Rudd, B. Vakkalagadda, T.M. Williams, J. Zha, X. Zhang, M.D. Anderson, Leveraging patient-centric sampling for clinical drug development and decentralized clinical trials: promise to reality, Clin. Transl. Sci. 15 (2022) 2785–2795, https://doi.org/10.1111/cts.13411.

[200] Winnoz Technology Inc., HAIIM blood collection. Available from https://winnoz.com/haiim/(accessed on February 10, 2025).