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Despite recent advancements in microsampling, there are still associated challenges when it comes to undertaking robust and cost effective pharmacokinetic (PK) evaluation for drug development or therapeutic drug monitoring. hemaPEN[®] has been developed as an advanced precision microsampling tool that answers these challenges:

- Volumetric accuracy and precision – intra-/inter-device, inter-batch
- Sample integrity
- Fool-proof collection and storage

The following study demonstrates the key attributes of hemaPEN*:

- Volumetric accuracy and intra-/inter-device, inter-batch precision of 2.74 $\mu\text{L} \pm 5\%$
- Consistency of the sample handling independent of user and environment
- Consistent drying profile
- Four replicate samples from a single source



Figure 1: hemaPEN[®] device as an advanced precision microsampling tool to collect and store volumetrically accurate biological samples from any source, independently of user experience, blood hematocrit and device batch.

Volumetric accuracy and precision

hemaPEN leverages the accuracy and precision of capillaries to deliver fixed volumes¹ to empower any users in the collection and storage of quality blood samples.



Sample drying and storage

hemaPEN ensures a consistent drying profile of DBS samples independently of the environmental conditions. Analytical laboratory receives quality samples independent of transportation conditions since collection.

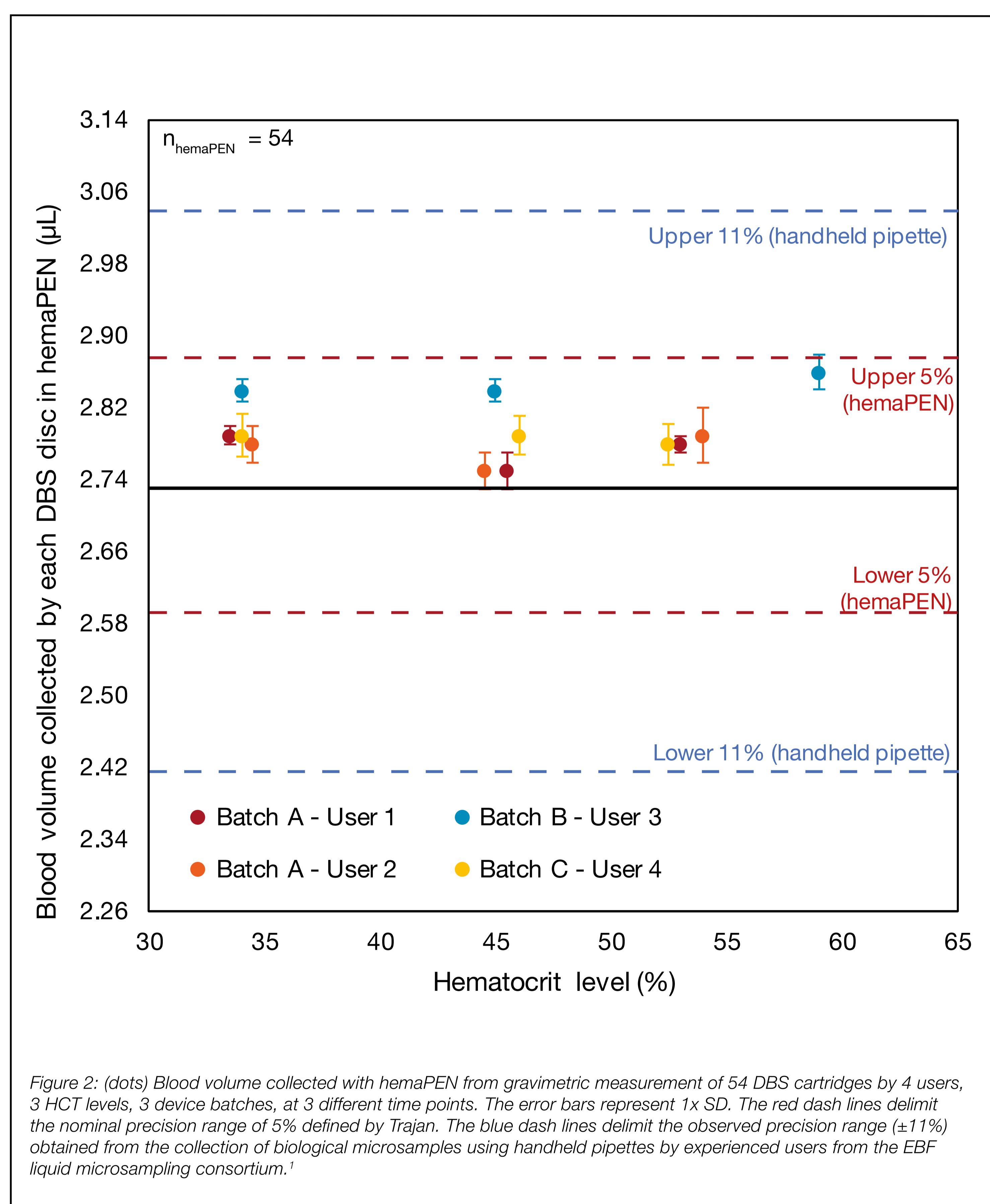
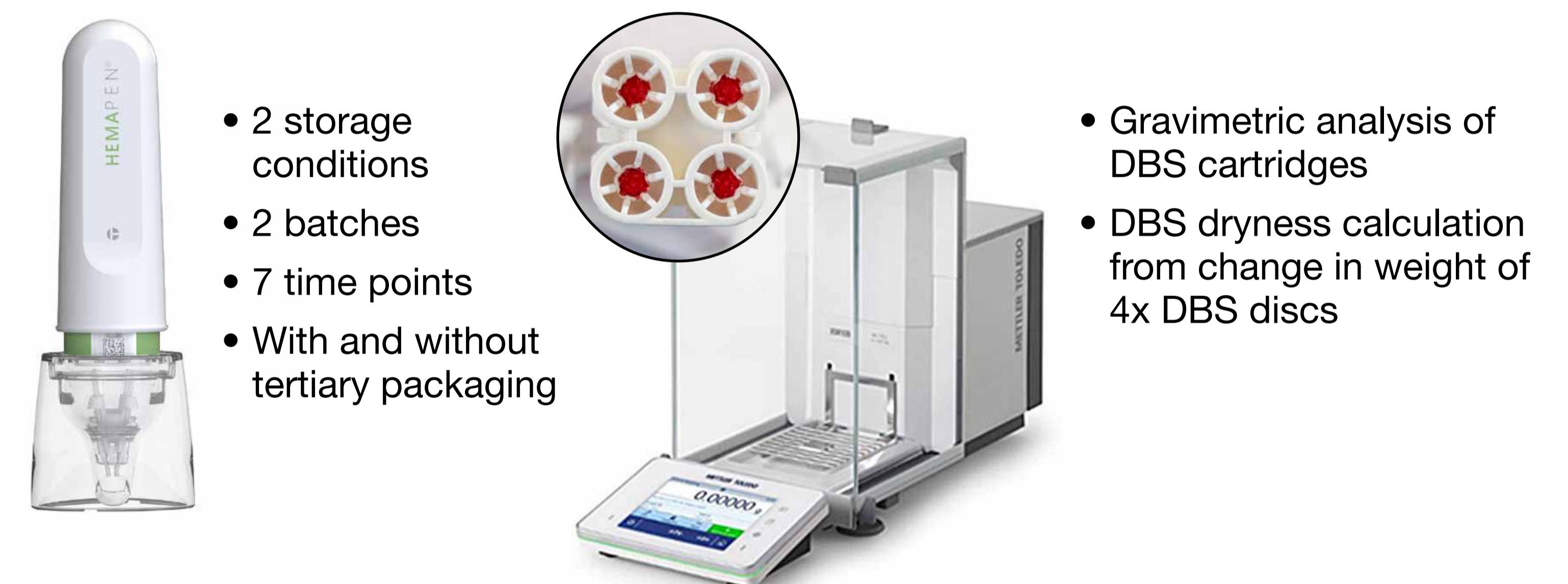


Figure 2: (dots) Blood volume collected with hemaPEN from gravimetric measurement of 54 DBS cartridges by 4 users, 3 HCT levels, 3 device batches, at 3 different time points. The error bars represent 1x SD. The red dash lines delimit the nominal precision range of 5% defined by Trajan. The blue dash lines delimit the observed precision range ($\pm 11\%$) obtained from the collection of biological microsamples using handheld pipettes by experienced users from the EBF liquid microsampling consortium.¹

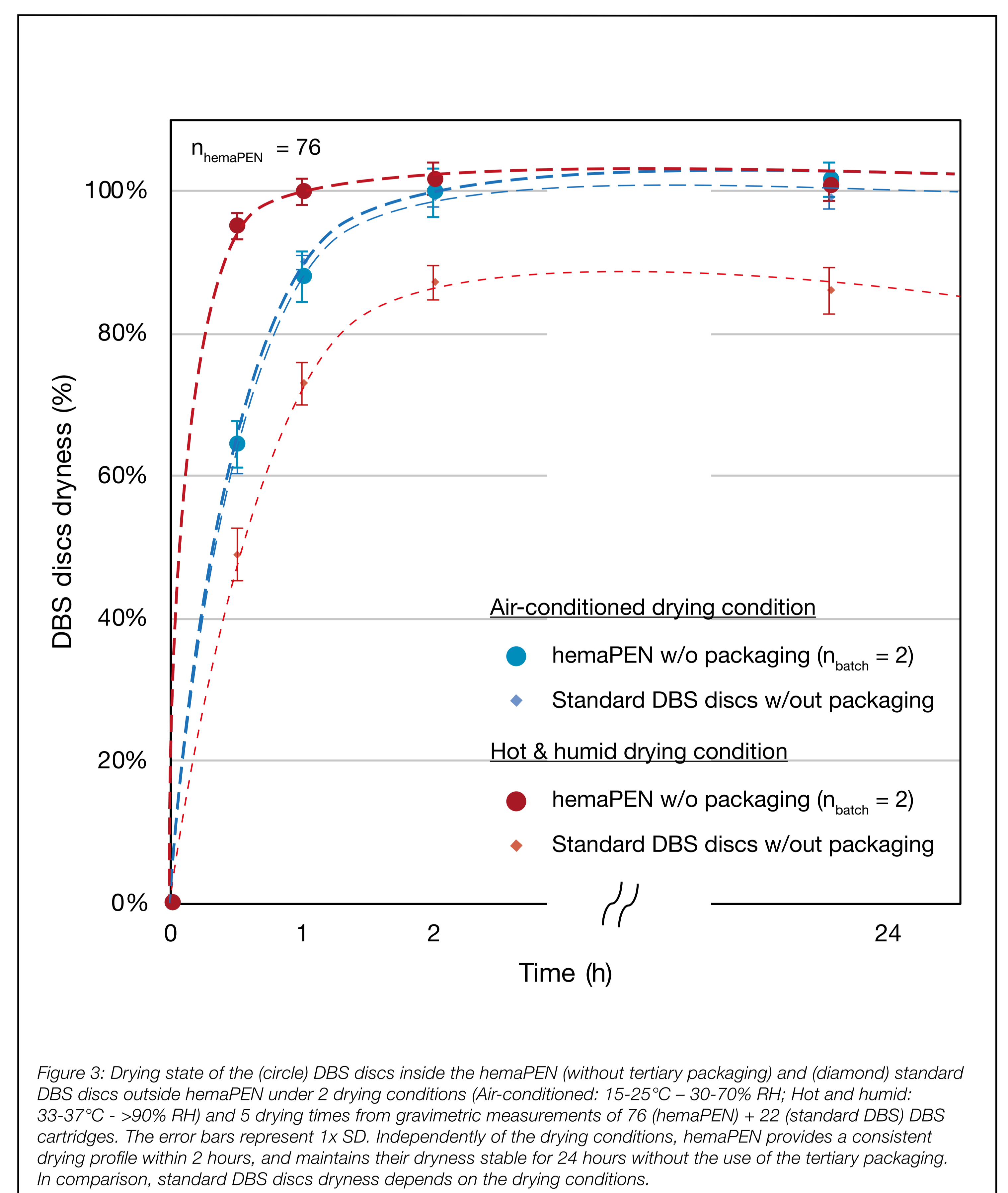


Figure 3: Drying state of the (circle) DBS discs inside the hemaPEN (without tertiary packaging) and (diamond) standard DBS discs outside hemaPEN under 2 drying conditions (Air-conditioned: 15-25°C – 30-70% RH; Hot and humid: 33-37°C – >90% RH) and 5 drying times from gravimetric measurements of 76 (hemaPEN) + 22 (standard DBS) DBS cartridges. The error bars represent 1x SD. Independently of the drying conditions, hemaPEN provides a consistent drying profile within 2 hours, and maintains their dryness stable for 24 hours without the use of the tertiary packaging. In comparison, standard DBS discs dryness depends on the drying conditions.

hemaPEN demonstrates volumetric accuracy and precision, and sample integrity in contained embodiment positioning it as an ideal device for PK studies.²

References

¹ Hawthorne, G., L. Dillen, M. Barfield, Z. Cobb, A. Kandira, K. Schroeter, S. White, et al. "Feedback from the European Bioanalysis Forum Liquid Microsampling Consortium: Microsampling: Assessing Accuracy and Precision of Handheld Pipettes and Capillaries." Bioanalysis (2019).

² Deprez, Sigrid, Lucía Paniagua González, Sofie Velghe, and Christophe P. Stove. "Evaluation of the Performance and Hematocrit Independence of the hemaPEN as a Volumetric Dried Blood Spot Collection Device." Analytical Chemistry (2019).

* Materials and methods together with detailed results overleaf under supplementary information (next page).

Objectives

1. Demonstrate collection and storage of 4 accurate and precise volumes of a blood sample irrespective of blood hematocrit (HCT), user and manufacturing batch.
2. Demonstrate hemaPEN provides a consistent drying profile and maintains the DBS discs in a dry condition independent of the environmental conditions.

Materials and method

Volumetric accuracy and precision

- Blood samples at different HCT levels (34%, 45%, 55%, 60%) were prepared from a single source of EDTA blood by adjusting plasma volume and measured with the HemoCue® HB 201+.
- Density of each hematocrit blood was calculated by gravimetric measurements of 25 µL volume using calibrated positive displacement pipette (Drummond) and was compared with two set of data from literature^{3,4} to verify the methodology employed. Later, volumes were calculated from the weight and the relevant blood densities defined by Burstain *et al.* 1994.³
- Volume collected and transferred to DBS discs was calculated from the weight of 4 x 3.5 mm discs, immediately after collection and storage of the blood sample using the hemaPEN (n = 54).
- Accuracy (Acc.%) and precision (%CV) were calculated based on the following equations:
 - Acc.% = mean actual volumes of all wet DBS across all 4 HCT levels, users, and device batch / nominal volume (2.74 µL) x 100%.
 - %CV = standard deviation / mean of all wet DBS across all 4 HCT levels, users, and device batch.

Sample drying and storage

- **Sample drying:** Disc dryness was assessed by measuring the change in weight of 4 x DBS discs stored in 76 hemaPEN under two environmental conditions (Air-conditioned: 15-25°C – 30-70% RH; Hot and humid: 33-37°C - >90% RH) without the tertiary packaging (air tight polyfoil bag) at 5 time points (0 min (control 0% dry), 30 min, 1 hour, 2 hours, 24 hours). The drying of standard DBS discs placed in 22 standalone DBS cartridges was also recorded with identical conditions for comparison.
- **Sample storage:** Dryness was assessed by measuring change in weight of 4 x DBS discs stored in the hemaPEN under same two environmental conditions with tertiary packaging (airtight polyfoil bag) and at 4 time points - 0 min (control 0% dry), 2 hours, 14 days, and 30 days.
- For each time point, drying condition and storage, DBS discs were further dried in a drying cabinet outside the hemaPEN for 4 hours and measured to establish complete dryness of samples (100% dry).

Results

Volumetric accuracy and precision

- hemaPEN collects and stores volumetrically accurate (2.74 µL) and precise (1 x SD = 0.04 µL) blood samples independently of blood hematocrit, user and device batch (Figure 2).
- The accuracy inter-hemaPEN is measured at **Acc.% = 102.3% with a %CV of 1.3%** across hematocrit, user and device batch (nominal volumetric value = 2.74 µL).
- In comparison, the EBF liquid microsampling consortium which evaluated plasma collected micro-samples (e.g. 2 µL and 4 µL) using handled pipette demonstrated precision (%CV) can be as high as 11% depending on the volume of the pipette and experience of the user.¹

Sample drying and storage

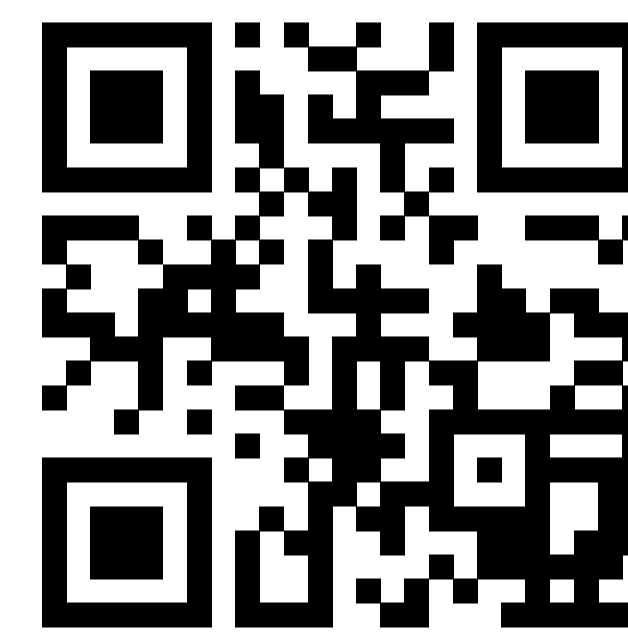
- hemaPEN provides a consistent drying profile independent of environmental conditions. DBS discs are dried within 2 hour and maintained dried for 24 hours even without the tertiary packaging (polyfoil bag) and even under hot & humid environmental conditions (Figure 3).
- In comparison, the drying state of standard DBS discs (without the use of hemaPEN) are dependent of the environmental conditions. In hot and humid conditions, the DBS discs alone cannot be dried.
- In addition, hemaPEN maintains the DBS samples in a dry condition (>85% dry) for at least 30 days when stored in the tertiary packaging independently of the environmental conditions, even if no additional desiccant was inserted inside the packaging.

References

³ Burstain, Jennifer M, Mark E Brecher, Valerie W Halling, and Alvaro A Pineda. "Blood Volume Determination as a Function of Hematocrit and Mass in Three Preservative Solutions and Saline." American journal of clinical pathology 102, no. 6 (1994): 812-15.

⁴ Kenner, T. "The Measurement of Blood Density and Its Meaning." Basic Research in Cardiology 84, no. 2 (1989): 111-24.

The hemaPEN® is a device supplied for research purposes only. This device is not for therapeutic or diagnostic use. hemaPEN® is a registered trademark owned by Trajan Scientific Australia Pty Ltd.



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