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Urine cytology - External Quality Assessment as a tool to compare laboratory measurement uncertainties

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A.G.L.A.E. provides a rich panel of test programmes to environmental and medical laboratories and cross-sectional statistical analyse to provide innovative tools for optimal control of the quality of routine analyses.

Objectives

- Specify an acceptable range around the leukocyturia decision threshold, major element in the diagnosis of urinary tract infections
- Define objective criteria for empowering staff in urine cytology

Data

Data from "Cytobacteriology of urine" proficiency tests since 2012

- About 40 PT involving on average nearly 150 participants
- 2/3 of these PT were carried out with repeated measurements
- Synthetic urine spiked with human leukocytes and red blood cells at different concentration levels (representative materials)

Three methods according to the routine procedures of the participants:

- **Microscopic Urine Analysis**: urine introduced into a counting chamber and counting of cells by an operator.
- **Sysmex UF analyzers:** flow cytometry using a blue or red semiconductor laser and classification of cells by analysing several scatter lights.
- **IQ series automated (Iris/Beckman Coulter)**: Digital Flow Morphology technology using Auto-Particle Recognition (APR) Software.

Methods

Suspended particulate aspect of the analyte:

- Expected variability described as being related to the counting of entities (*ISO/TS 20914:2019*)
- Statistical models relating to counts - Log-Normal model is likely to best describe the data dispersions (*ISO 22117:2019*).

Estimation of the means m (assigned values) and standard deviations of repeatability s_r and reproducibility s_R for each PT (*ISO 13528:2022*, *ISO 5725-1:1994*, *ISO 5725-2:2019*).

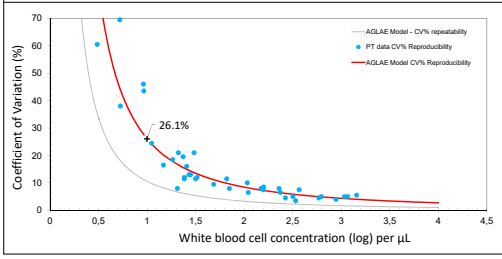
Selection of the best mathematical model of s_r and s_R (log scale) as a function of the means m (log scale) according to 7.5 of *ISO 5725-2*.

Final representation using coefficient of variation CV% , e.g. for reproducibility: $CV_R\% = s_R / m \times 100$

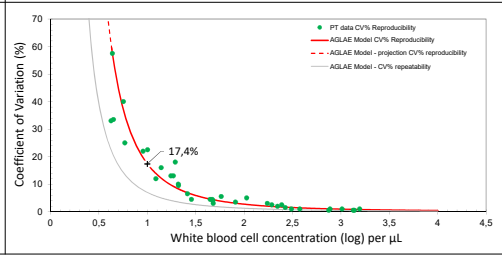
Extended intervals calculated with k = 2 (*ISO/TS 20914*)

Results - White blood cells

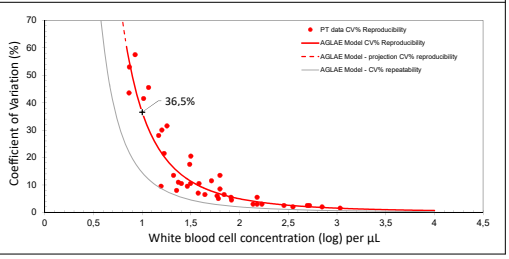
Manual microscopic analysis



Sysmex UF analysers



IRIS/Beckman IQ instruments



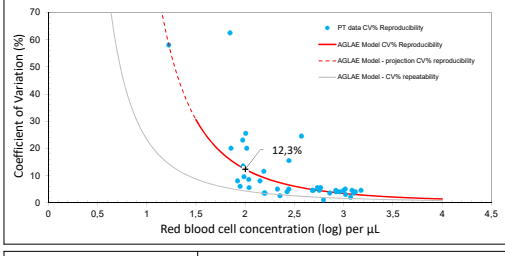
Parameters	Analytical methods	Concentration level	CVr %	CVR%	Extended intervals of repeatability [1] (Cells/µL)	Extended intervals of interlaboratory reproducibility [2] (Cells/µL)
White Blood cells (leukocytes)	Manual microscopic analysis	10 /µL	10,5	26,1	6 to 16	**3 to 33**
	Sysmex UF analysers	10 /µL	7,0	17,4	7 to 14	**4 to 22**
	IRIS/Beckman IQ instruments	10 /µL	14,5	36,5	5 to 19	**2 to 54**

[1] At the decision point, observable uncertainty within the laboratory

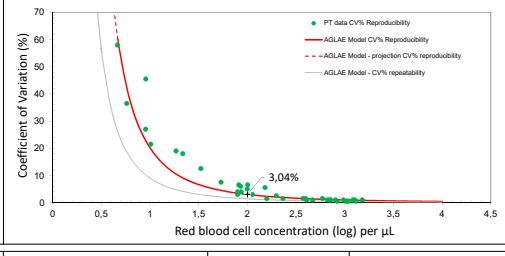
[2] At the decision point, observable uncertainty between several laboratories

Results - Red blood cells

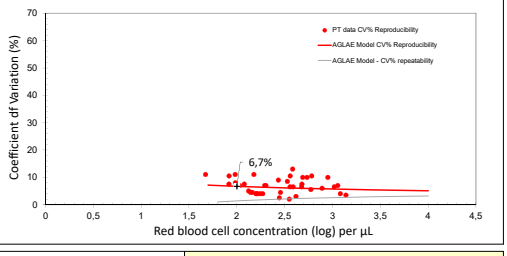
Manual microscopic analysis



Sysmex UF analysers



IRIS/Beckman IQ instruments



Parameters	Analytical methods	Concentration level [3]	CVr %	CVR%	Extended intervals of repeatability (Cells/µL)	Extended intervals of interlaboratory reproducibility [3] (Cells/µL)
Red Blood cells	Manual microscopic analysis	100 /µL	4,3	12,3	67 to 149	**32 to 311**
	Sysmex UF analysers	100 /µL	1,4	3,0	88 to 114	**76 to 132**
	IRIS/Beckman IQ instruments	100 /µL	1,4	6,7	88 to 114	**54 to 186**

[3] For red blood cells, the observable intervals around 100 cells per microlitre are shown.

Conclusion

At the pathological threshold (10 leukocytes per µl), depending on the technique used, a variation in results between 7% and 15% (log scale) is observed between two measurements performed by the same laboratory. The variation observed between two different laboratories is between 17% and 37% (log scale) depending on the method used. These variations are consistent with the literature references on repeatability and reproducibility under intra-laboratory conditions ([1], [2], [3]). It could be interesting to consider these variations in the diagnostic process. These models of variation in results according to analytical techniques could be used as an aid to decision-making within the laboratory quality system. For example, knowledge of the uncertainty observed at any point in the working range can provide objective criteria to be used for staff qualification.

[1] G. Previtali et al. Performance evaluation of the new fully automated urine particle analyser UF-5000 compared to the reference method of the Fuchs-Rosenthal chamber. Clin Chim Acta. 2017 Sep;472:123-130.
[2] E. Bakan et al. Evaluation of the analytical performances of Cobas 6500 and Sysmex UN series automated urinalysis systems with manual microscopic particle counting. Biochem Med (Zagreb). 2018 Jun 15;28(2).
[3] M. Siatkowski et al. Performance evaluation of UF-4000 body fluid mode for automated body fluid cell counting. Clin Chim Acta. 2023 Jan;538:9-14.