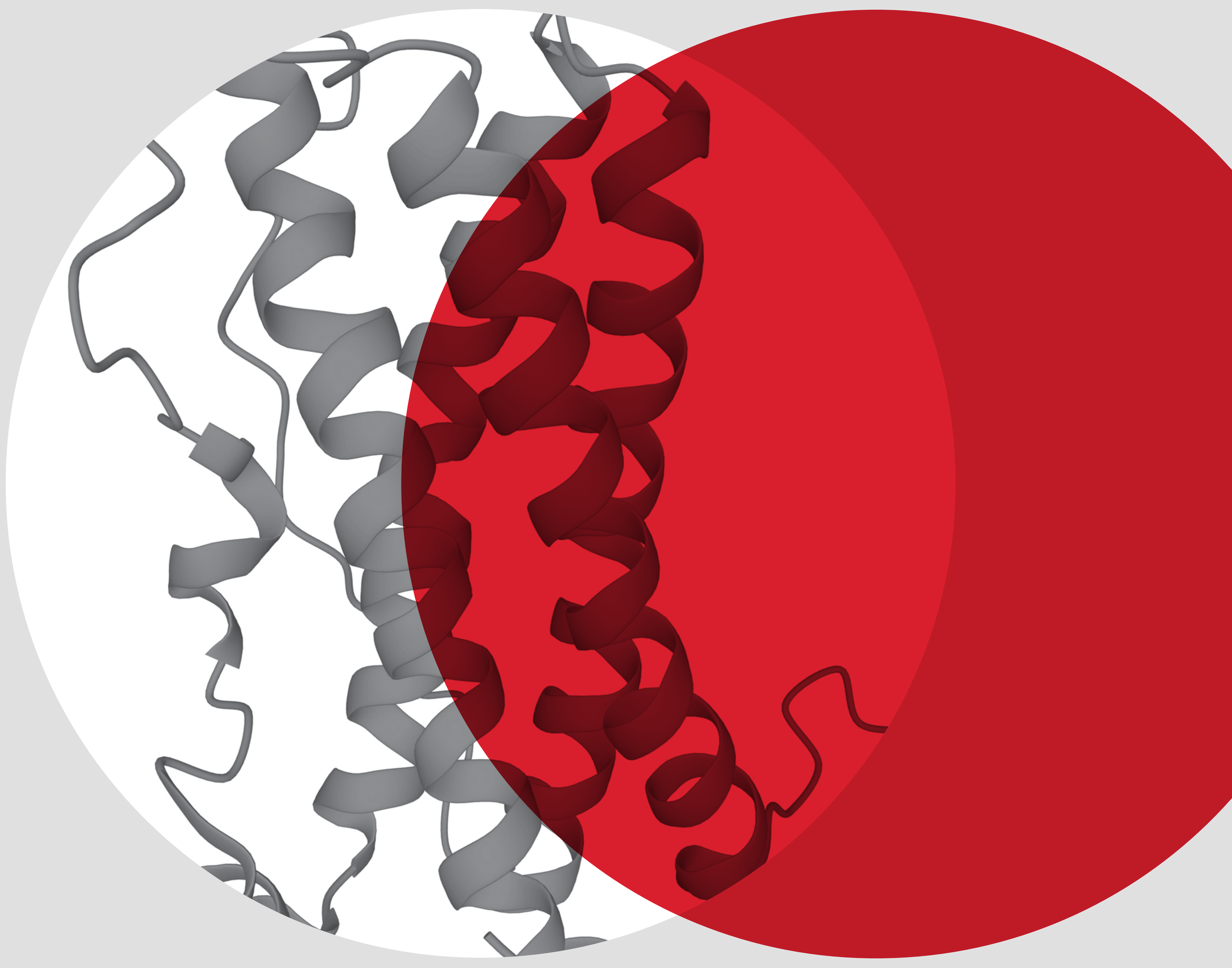
Monomeric prolactin introduction to endocrine EQA program



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Introduction

Abnormally high prolactin levels (apart from those seen in breastfeeding women) should be checked to exclude macroprolactin. Polyethylene glycol (PEG) precipitation of macroprolactin, followed by reanalysis of the bioactive monomeric prolactin, is the most common method. Recoveries of >50% post-PEG precipitation are a "rule out" for macroprolactin. It is generally recommended that all prolactin results above the upper reference interval be screened for potential macroprolactin interference.[1,2]

The RCPAQAP Endocrine program contains samples linearly related across six levels with prolactin ranging from 110 (for Level 1) to 1400mIU/L (for Level 6). The six levels each repeat four times in different combinations over a 12 month period. There is no macroprolactin in the QAP material. The option to also report Monomeric Prolactin (on the same material post-PEG precipitation) in addition to prolactin was introduced in 2022 as part of a collaboration with the Australasian Association for Clinical Biochemistry and Laboratory Medicine (AACB) Macroprolactin Harmonisation Working Group. We sought to assess the variability between PEG precipitation methods, using QAP material with prolactin levels >700mIU/L.

Method

Three method categories for the macroprolactin elimination step (PEG-water, PEG-PBS and Gel Chromatography) were provided. Participants submitting results for prolactin in the 2022 Endocrine program were also encouraged to submit their results post-PEG precipitation /Gel Chromatography of the same sample. Results for the first six 2022 surveys were analysed using in-house software, and the relative recoveries for monomeric prolactin on samples with median prolactin levels ranging in concentration from 700 to 1400mIU/L (which equated to initial and repeat results for Levels 4, 5 and 6) were assessed. Noting, comparisons between instrument platforms required a minimum of 5 results.

Results

Out of 140 laboratories submitting for prolactin, an average of 30 also provided results for monomeric prolactin. All 30 laboratories used PEG precipitation. The mean recoveries for prolactin samples > 700mIU/L were 74 and 70% for PEG- water (n=15) and PEG-PBS (n=15) respectively (Figure 1). The post PEG method CVs ranged from 6.4 – 36.8%, compared to prolactin method CVs of 3.1 – 34.5% (Table 1). The post PEG results were further divided into the type of diluent used with the PEG-water method CVs ranging from 18.9 – 25.3%, while the PEG-PBS method CVs ranged from 15 – 20.7% (Figure 2).

Discussion

Although both water and PBS are suggested diluents for the PEG precipitation protocol, it is evident that there are differences in performance for each method. Emerging research indicates that PEG dissolved in PBS leads to more reliable results.[3] This can also be inferred from the results of this study as the CVs for the PEG-PBS method group were on average 3.4% less than the PEG-water method across the six samples (Figure 2).

The noted significant increase in CVs between the prolactin results vs the post-PEG results (Table 1), suggests that the laboratory procedures in use for PEG precipitation are potentially adding variability to the overall assessment of macroprolactin. It is suspected that the primary cause may be the preparation of the 25% PEG solution itself, as recently highlighted at the 2022 AACB Harmonisation Workshop, where the addition of 100mL of deionised water to 25g of PEG (resulting in a 21% PEG solution) was directly impacting recoveries.

Conclusion

The RCPAQAP Endocrine samples are a useful monitoring tool for monomeric prolactin recoveries. The variation in recoveries between the two popular methods (PEG-water and PEG-PBS buffer) is an area for improvement. The PEG-PBS preparation has shown to exhibit less variance and may reduce the potential impact of macroprolactin interference.

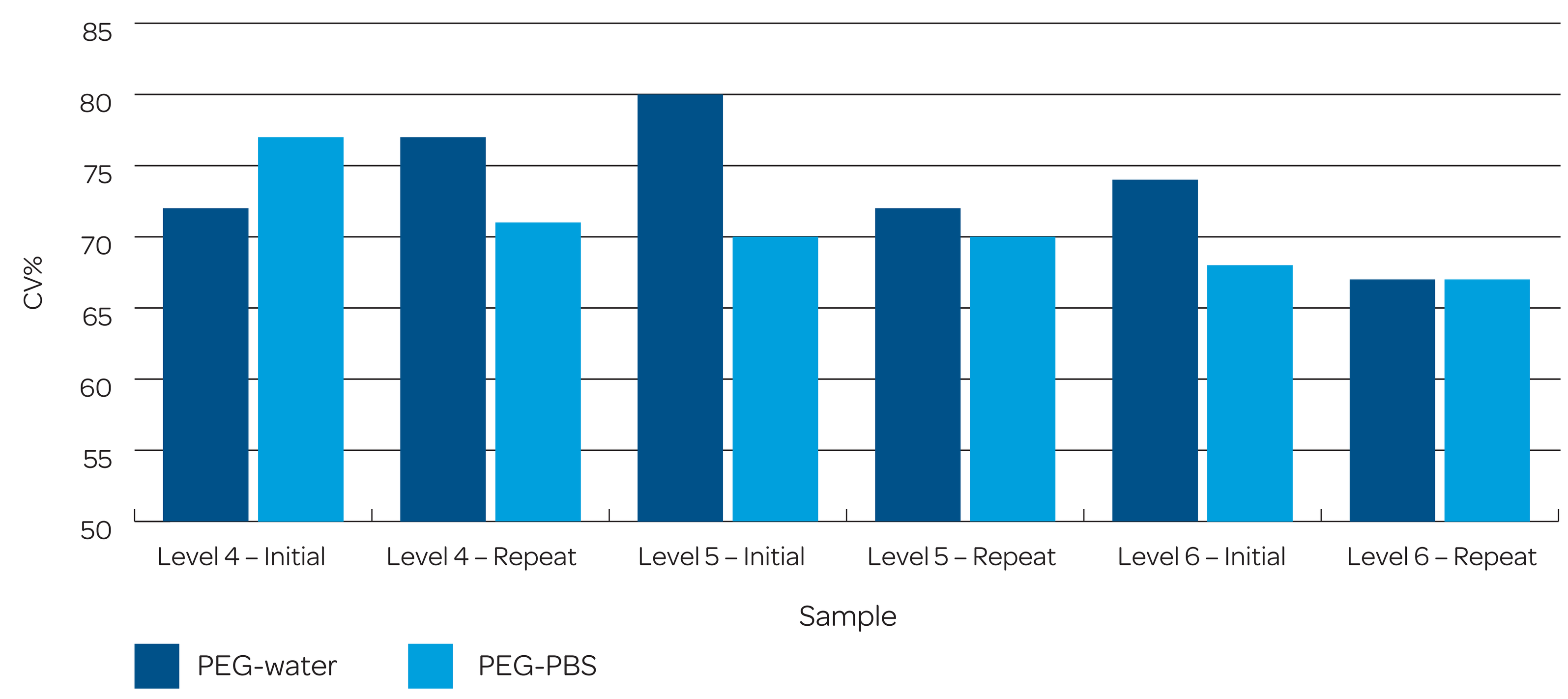

Figure 1. Mean recoveries of prolactin for 2022 Endocrine samples tested with water or PBS diluted PEG precipitation methods.

Table 1. CV comparison of 2022 Prolactin (PRL) vs Monomeric Prolactin (Post-PEG). Measurement systems without the required number of participants to calculate post-PEG CVs (n=5) were excluded from the comparison.

Measurement System	Test	Level 4 – Initial	Level 4 – Repeat	Level 5 – Initial	Level 5 – Repeat	Level 6 - Initial	Level 6 – Repeat
Abbott ARCHITECT - i2000SR	PRL	22.7	6.3	4.8	4.4	3.1	3.9
	Post-PEG	Insufficient data	6.4	Insufficient data	9.1	Insufficient data	9.4
Abbott Alinity i	PRL	4	4.6	3.8	7.5	4.3	7.5
	Post-PEG	15.6	13.2	12.9	16.9	11.2	18
Roche Diagnostics cobas e 801	PRL	3.1	20.9	3.7	3.7	4.9	3.7
	Post-PEG	13.4	9.6	17.2	8.1	8.1	9.7
Siemens Atellica IM	PRL	4.2	6.6	5.7	34.5	4	34.3
	Post-PEG	Insufficient data	36.8	Insufficient data	10.3	Insufficient data	8.5

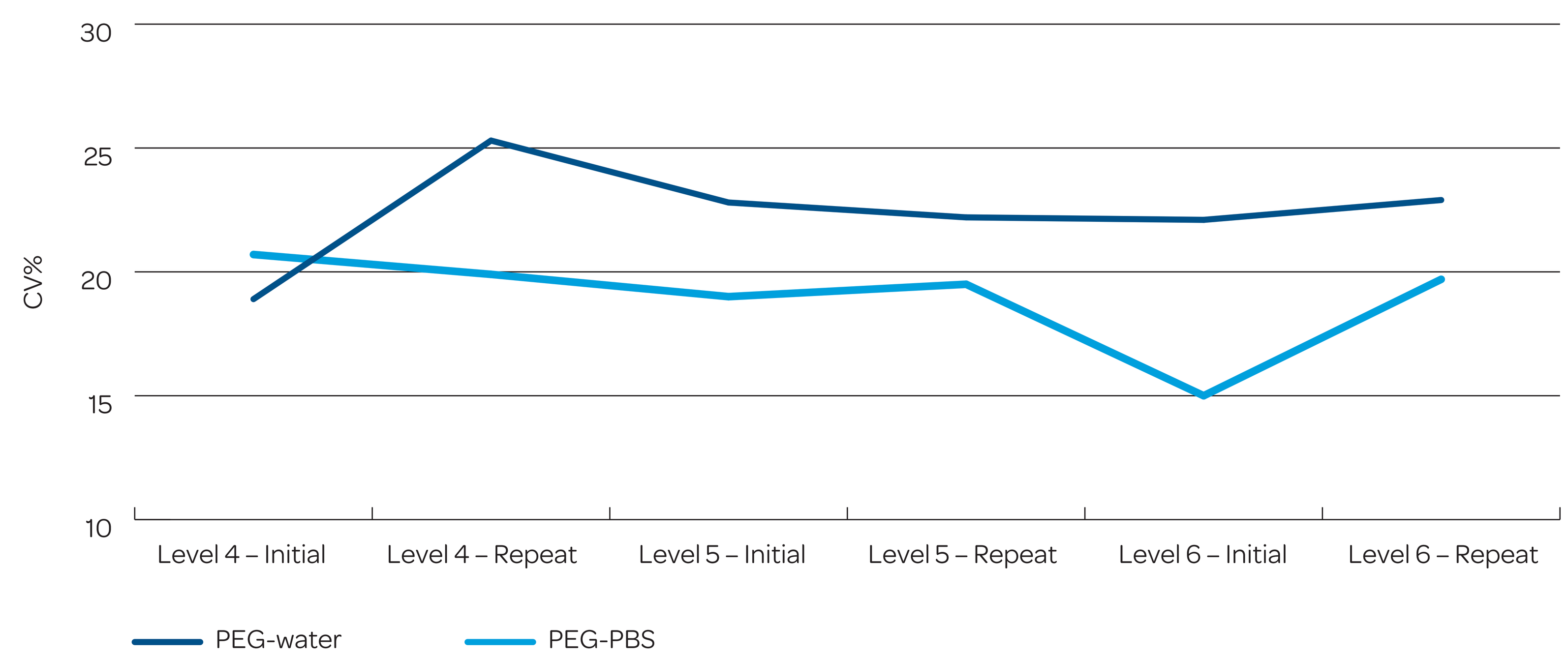

Figure 2. Line graph representing the CVs of the PEG-water and PEG-PBS methods for Monomeric prolactin in the 2022 Endocrine program.

References:

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3. NikolićS, Mijović R, Oluški D, Ostojić T, & Bajkin I. Assessment of macroprolactinemia by the polyethylene glycol precipitation method. *Medicinski pregled.* 2020;73(10):229-234. https://doi.org/10.2298/MPNS2008229N