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Guideline

Title	Recommendations for Macroprolactin harmonisation – Part 1
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AACB Recommendations for Macroprolactin Harmonisation-part 1

The Harmonisation of Macroprolactin is a project of the AACB Harmonisation Committee and recommendations are issued in 2 parts:

Part 1 Standardisation of PEG procedure.
Note: The remainder of this document relates to this procedure.
Part 2 Consensus recommendations on reporting macroprolactin, terminology and reference intervals.
These are still under discussion and will be reported when decisions are available for release.

Harmonisation of Macroprolactin Part 1 - Standardised PEG procedure

A 2021 survey of Australian and New Zealand laboratories revealed divergent and discordant use of PEG precipitation across labs with limited or no references to literature. A set of 5 recommendations was developed to standardise macroprolactin testing by PEG precipitation.

1. PEG preparation

- PEG stock solution 25%: measure 25 g PEG 6000 and add to approximately 60 mls PBS (phosphate buffered saline). Mix until PEG is dissolved, pH to 7.0 and make up to final volume 100 mls with PBS.
- PEG stock solution should be stored at 4°C. Stable for at least six months.
- Roche laboratories may follow the IFU which recommends water as diluent rather than PBS. For these labs, the committee's recommendation is to store the stock solution at 4°C for a shorter period (< 3 months). A pH-balanced buffered salt solution is preferable to water due to stabilisation of PEG hence longer storage.

2. PEG constitution (AACB Standardised)

Accurate preparation of stock 25% PEG solution.
Make up to 100 mL total volume using PBS.
ERROR - Do not add 100 mL to 25g of PEG. This results in final 21% final concentration PEG, and the error was identified in 2022 in 2/3rd laboratories from RCPAQAP. See appendix for more information.

3. PEG precipitation of patient sera

- Bring a small aliquot of PEG 25% stock solution and patient serum to room temperature.
- Add equal volumes to an appropriately sized tube (250ul of each normally sufficient). Final concentration of PEG is 12.5 %.
- Vortex for at least 10 seconds until the mixture is homogeneous.
- Incubate the serum-PEG mixture at Room Temperature for 10 minutes.
- Centrifuge at room temperature (3000g for 20 minutes or 17000 g for 5 minutes; equivalent to 60 000 – 85 000 gmins).
- Analyse concentration of prolactin in the supernatant by automated immunoassay

4. Prolactin quality control and QA

* An appropriate prolactin internal QC is required as well as enrolment in a prolactin external QAP.
* Macroprolactin internal quality controls are difficult to obtain. One option is for the lab to store pools of residual deidentified patient sera known to be negative and positive macroprolactin. These are acceptable for ensuring reliable method performance. For external QA, participation in a program specific for macroprolactin is required.

5. Document average recovery of prolactin post-PEG

Labs should document average recovery of prolactin following PEG precipitation on their analytical platform. Deidentifed patient samples known to be negative for macroprolactin (at least 50 samples) should be used to calculate the average recovery. This average recovery accounts for the impact of of PEG on the specific prolactin immunoassay and represents expected net monomeric prolactin from your lab. Examples of average recoveries:

Abbott Architect	70%
Beckman DXL	100%
Roche Cobas	75%
Siemens Atellica	78%

Note: if your lab is making up PEG *incorrectly* (ie. 25g plus 100 mL PBS), the average recovery will be higher than the recovery reported by another lab using using the same immunoassay platform. Between-lab comparison of prolactin recovery can be a quality indicator of the PEG reconstitution procedure.

Appendix

Laboratory rigor requires solutes are added to ¾ of final volume in a measuring cylinder, the solute is dissolved and pH adjusted, then bring the solution **to final volume** (here 100 mL) by topping up.

To "q.s. the solution" means to bring the solution up to the final volume. The term "q.s." is the abbreviation of the Latin term *quantum satis*, meaning as much as is enough.
https://www.labmanager.com/how-to-make-and-dilute-aqueous-solutions-28309

Adding volume of 100 mL PBS to PEG results in PEG 21% (rather than 25%).

For feedback, questions, or requests for more information/ data, please email AACB office – Harmonisation Committee.