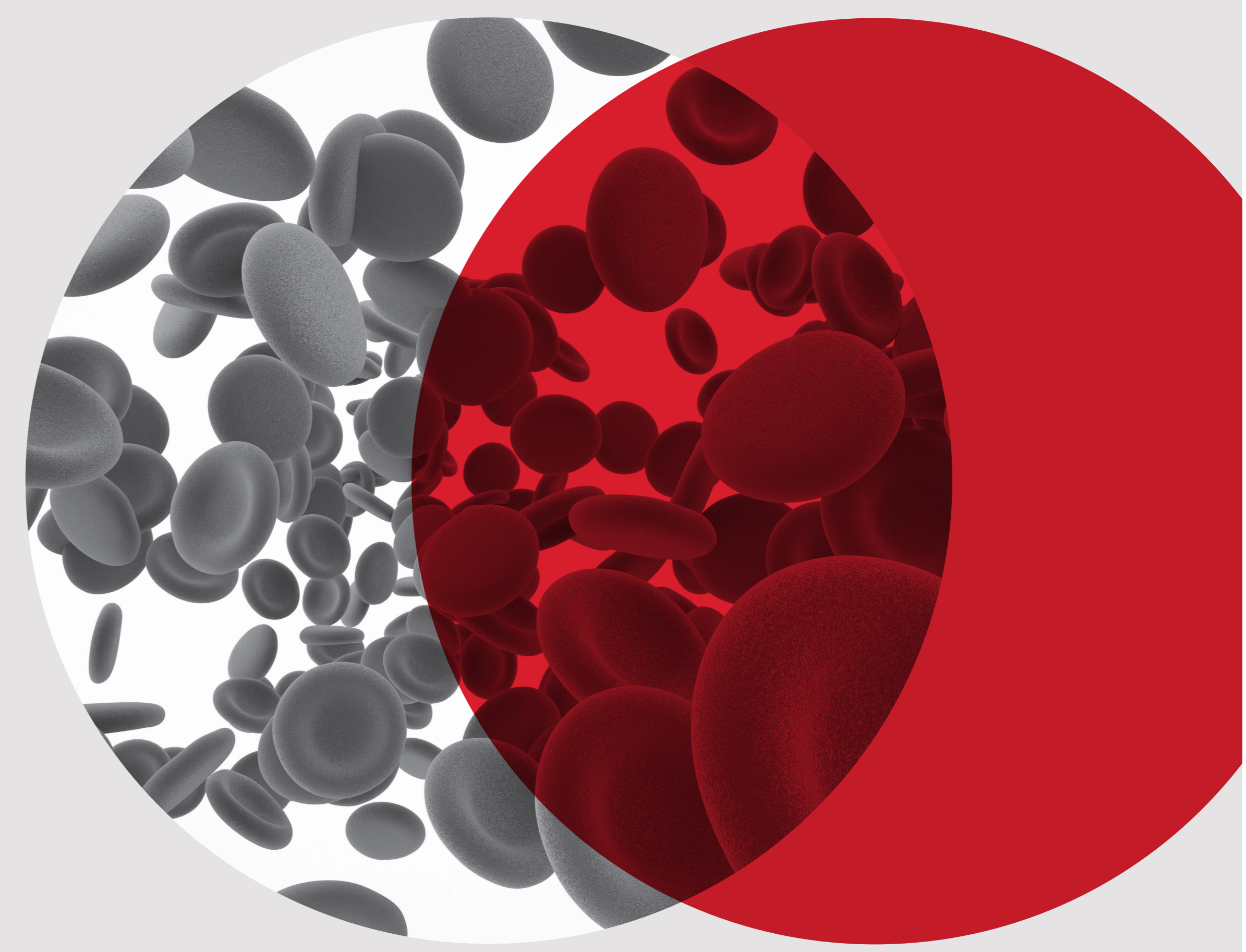


# Variation in ferritin results in commutable EQA samples



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## Introduction

Ferritin reference intervals vary between laboratories, but generally, an adult serum ferritin level  $<30 \mu\text{g/L}$  is widely recommended as one of the diagnostic markers of iron deficiency. A ferritin  $>1000 \mu\text{g/L}$  would prompt specialist referral for potential haemochromatosis. Recommended levels for long-term monitoring of haemochromatosis patients undergoing regular venesections are  $50\text{--}100 \mu\text{g/L}$ . Given clinicians are guided by recommended reference intervals for ferritin; we sought to investigate potential method differences.

## Method

The RCPAQAP have a Liquid Serum Chemistry Program that is considered commutable as it is sourced from consenting male and female haemochromatosis patients who present for therapeutic venesection. We reviewed ferritin data from 2019, 2020 and 2021 Liquid Serum Chemistry Programs. The medians of 13 different analysers submitted by up to 115 participating laboratories were compared using RCPAQAP in-house software.

## Results

The relative bias between methods was consistent for all samples from 2019–2021, as shown in Figure 1 where the medians of seven representative methods from lowest to highest are displayed. Between method differences of up to  $34 \mu\text{g/L}$  at a median of  $65 \mu\text{g/L}$  were noted; e.g. Siemens Atellica group median  $46 \mu\text{g/L}$  ( $n=18$ ) vs Roche Cobas e602 median  $80 \mu\text{g/L}$  ( $n=6$ ) (Figure 2). Similarly, Figure 3 demonstrates differences of up to  $363 \mu\text{g/L}$  at an all result median of  $734 \mu\text{g/L}$ ; e.g. Abbott reagent group median  $482 \mu\text{g/L}$  ( $n=30$ ) vs Roche  $845 \mu\text{g/L}$  ( $n=25$ ). A similar pattern was also noted in the 2022 RCPAQAP General Serum Chemistry Program (not shown here).

## Discussion

Given the Liquid Serum Chemistry samples are commutable, the variation in results may be due to calibrator and/or antibody differences e.g. the source of ferritin in the traceable International Reference (IR) standards<sup>1</sup>. We noted the Siemens Atellica assay is listed as traceable to World Health Organization (WHO) 2<sup>nd</sup> IS (80/578, source organ spleen). The Roche Elecsys Ferritin is traceable to the 1<sup>st</sup> IS (human liver) (80/602) with established traceability to the 3<sup>rd</sup> IS (94/572, sourced from human recombinant ferritin L-chain). The WHO has recently developed a 4<sup>th</sup> IS human recombinant Ferritin standard (19/118) as the stocks of the 3<sup>rd</sup> IS (in use since 1997) are almost depleted.<sup>2</sup>

## Conclusion

Where widely accepted reference intervals for ferritin are used, laboratories are advised to verify that their patient results are consistent with recommended guidelines, ideally by including confirmed iron deficiency and iron overload patients. The results from this study indicate further investigation is required.

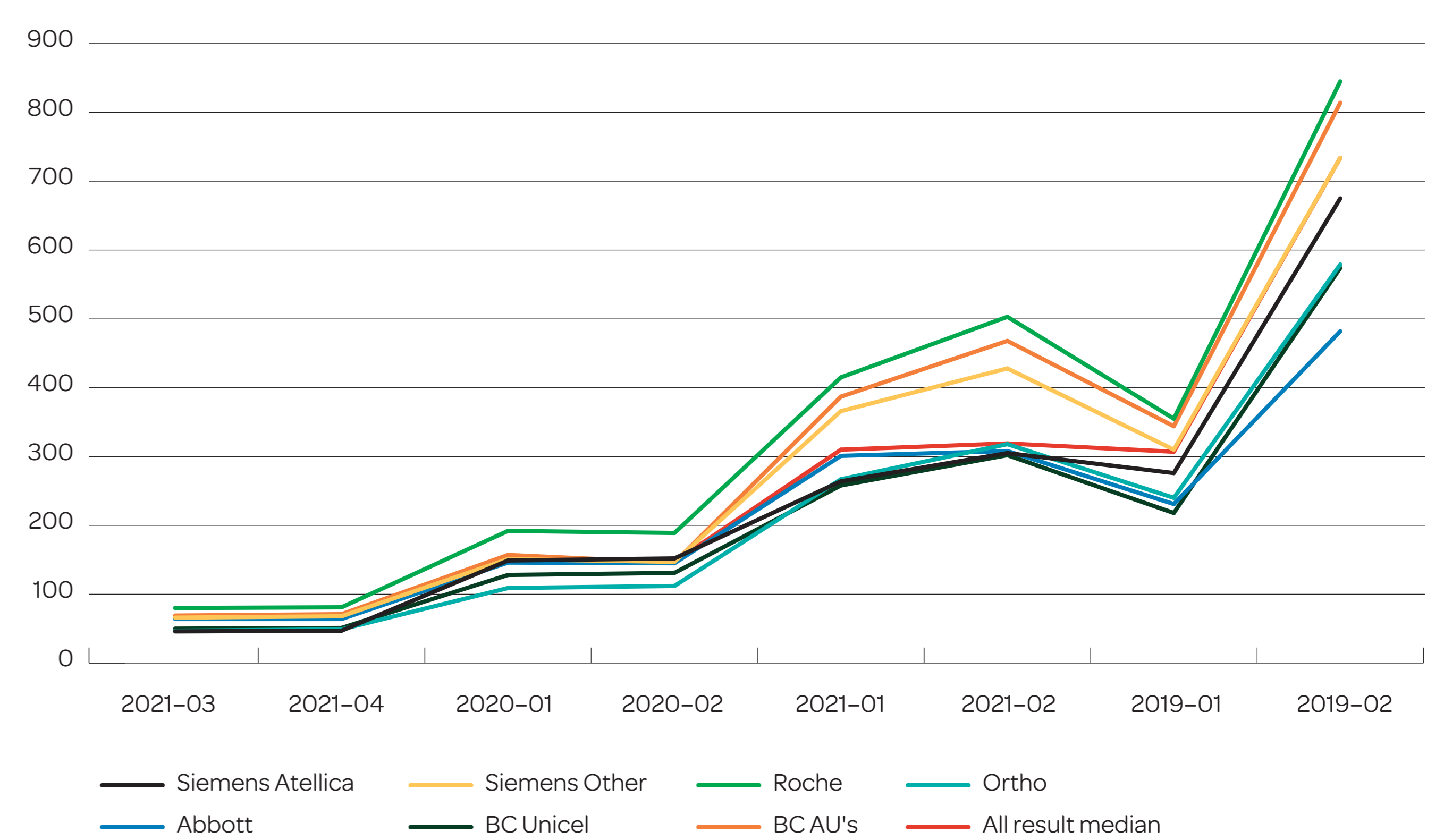


Figure 1. Liquid Serum Chemistry Ferritin medians from 2019–2021 from lowest to highest.

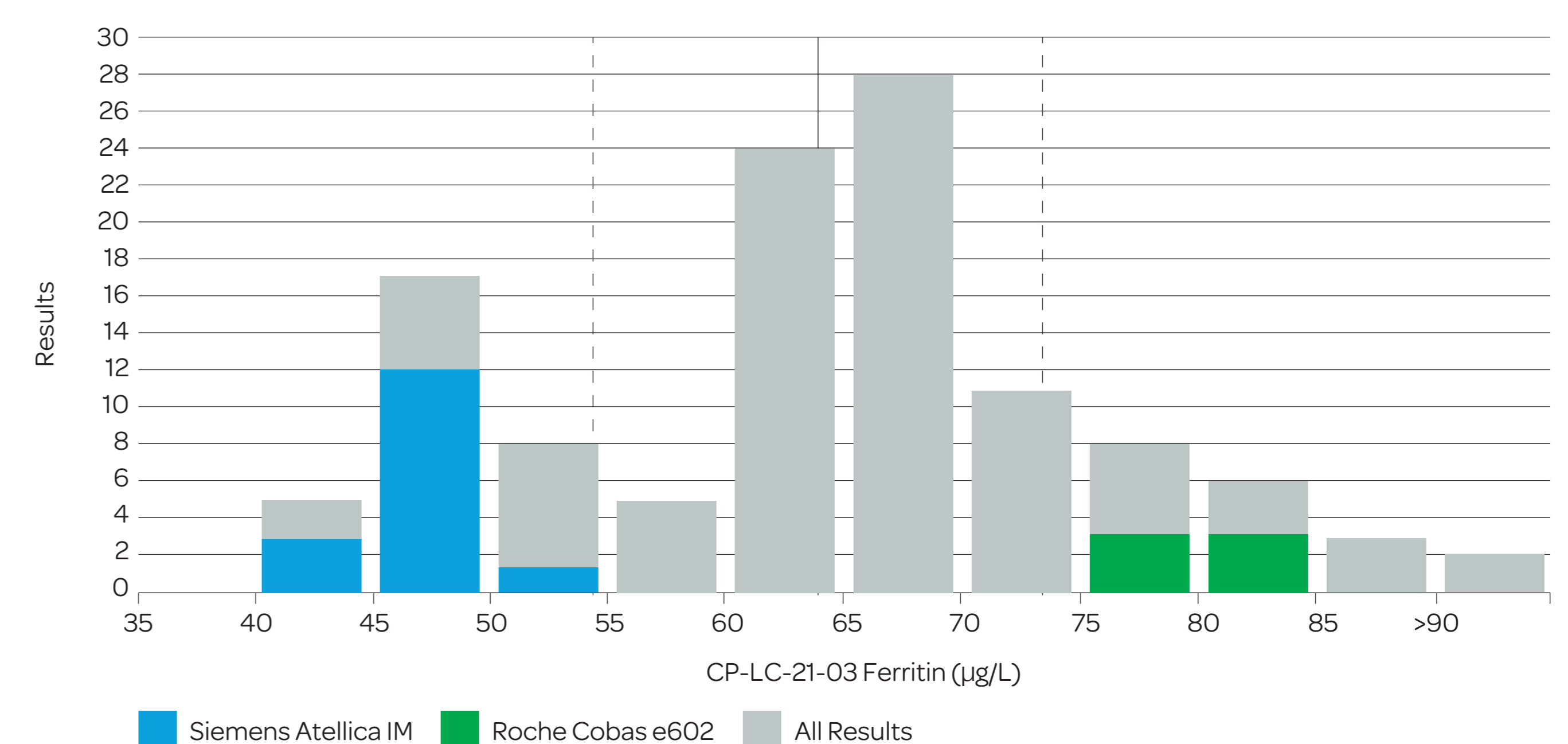


Figure 2. Histogram of 2021 Ferritin results for sample 21-03. The grey solid and dotted lines indicate the median and APS limits of all results.

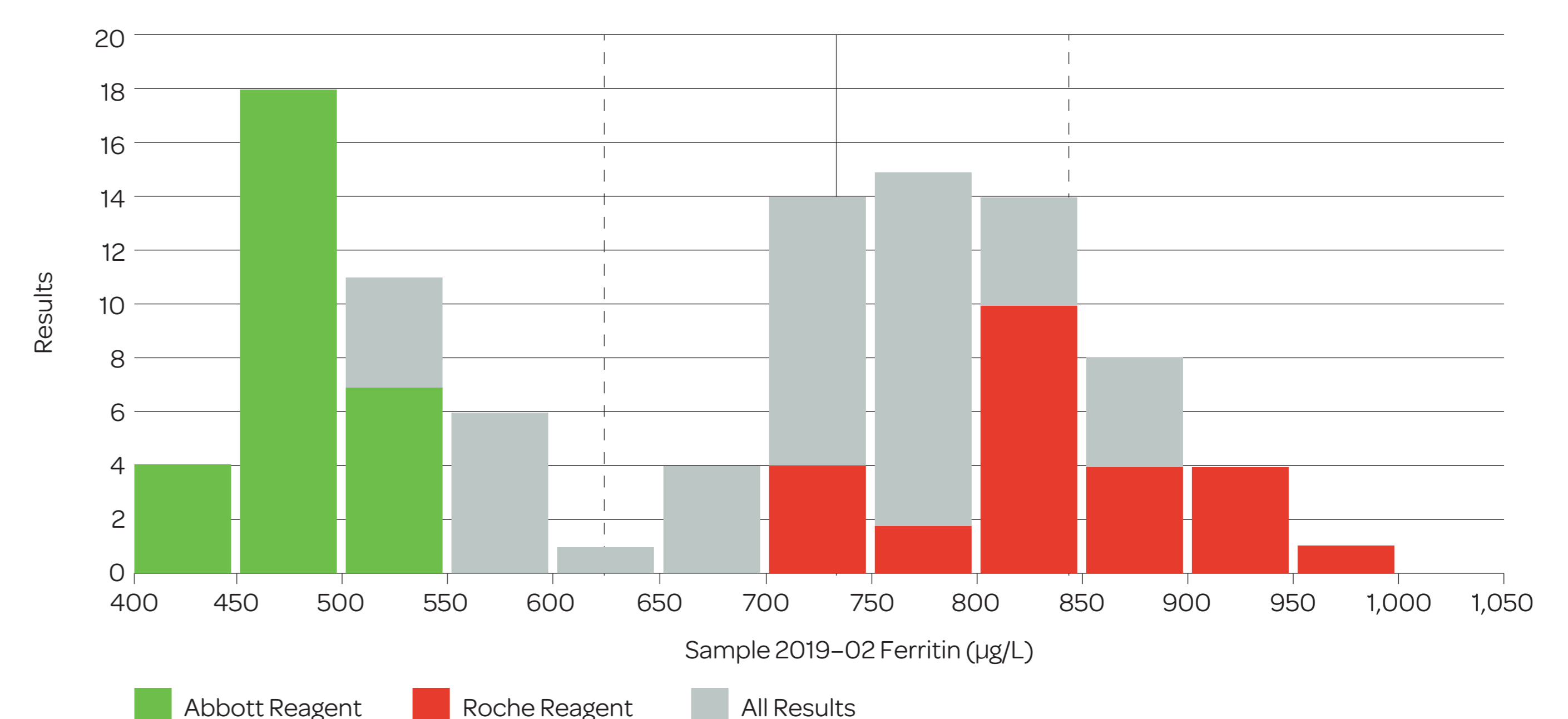


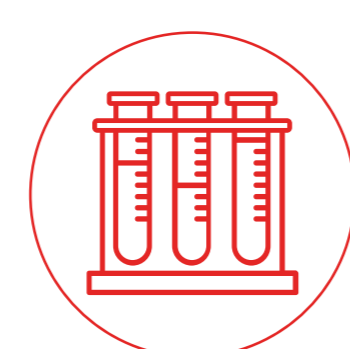
Figure 3. Histogram of 2019 Ferritin results for sample 29-02. The grey solid and dotted lines indicate the median and APS limits of all results.

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- Fox, B.; Roberts, G.; Atkinson, E.; Riggsby, P.; Ball, C. International collaborative study to evaluate and calibrate two recombinant L chain Ferritin preparations for use as a WHO International Standard. *Clin Chem Lab Med*. 2021 Dec 17; 60(3): 370–378.

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