The HCG EQA Conundrum

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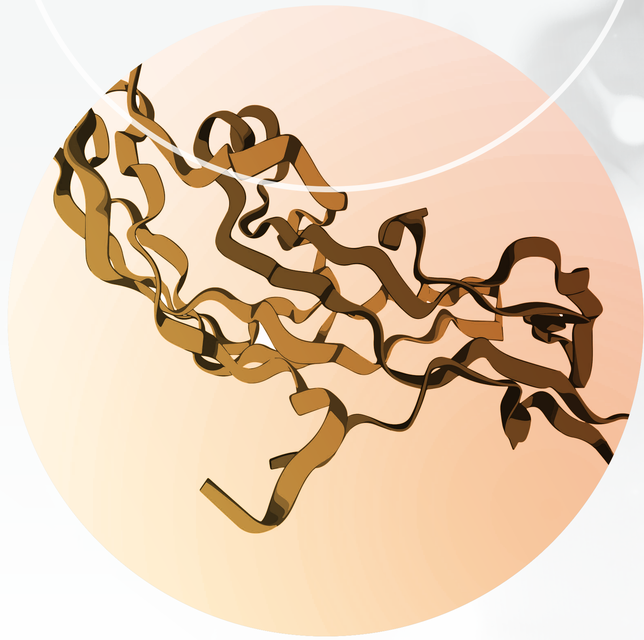

Introduction

The RCPAQAP offers serum Human Chorionic Gonadotrophin (HCG) as a measurand in our Endocrine, Tumour Marker and Serum Chemistry programs. We sought to investigate significant (unexpected) method differences for HCG in the 2024 Endocrine program samples compared to the 2023 material.

Method

Returned results for the 2024 Endocrine HCG Survey 1, from 218 participating laboratories were reviewed using RCPAQAP in-house software. The method variation in Endocrine results was then compared to the same methods in the 2024 Tumour Marker and Serum Chemistry programs as well as the analytical performance in the 2023 Endocrine samples. In addition, the survey material manufacturer was contacted to advise on any changes in production or spiking; they subsequently provided a SDS-PAGE electrophoresis comparison of the raw spikes used in the 2023 and 2024 samples.

Results

The method medians for the 2024 high level ranged from 10,176 IU/L for Ortho instruments to 77 IU/L for Siemens platforms. Intermediate levels varied from 2,703 IU/L for Roche to 311 IU/L for Abbott (Figure 1).

The between method median differences for the 2023 compared to 2024 samples in the Tumour Marker and General Serum Chemistry programs did not significantly change.

Initially, the manufacturer noted they required more than usual amount of spike to obtain the required recoveries using the Siemens Centaur, so they changed to an Abbott Alinity. The manufacturer subsequently identified a change in spike material for the 2024 Endocrine material compared to previous productions. They confirmed there was no change in spike for the Tumour Marker and Serum Chemistry programs. As part of their investigation, the manufacturer provided an SDS-PAGE of the 2023 and 2024 spikes (Figure 2). The 2024 spike showed evidence of alpha HCG as well as hCG Beta core fragment (hCG βcf), which was not present in the 2023 spike. The manufacturer also indicated that both spikes were sourced from human urine.

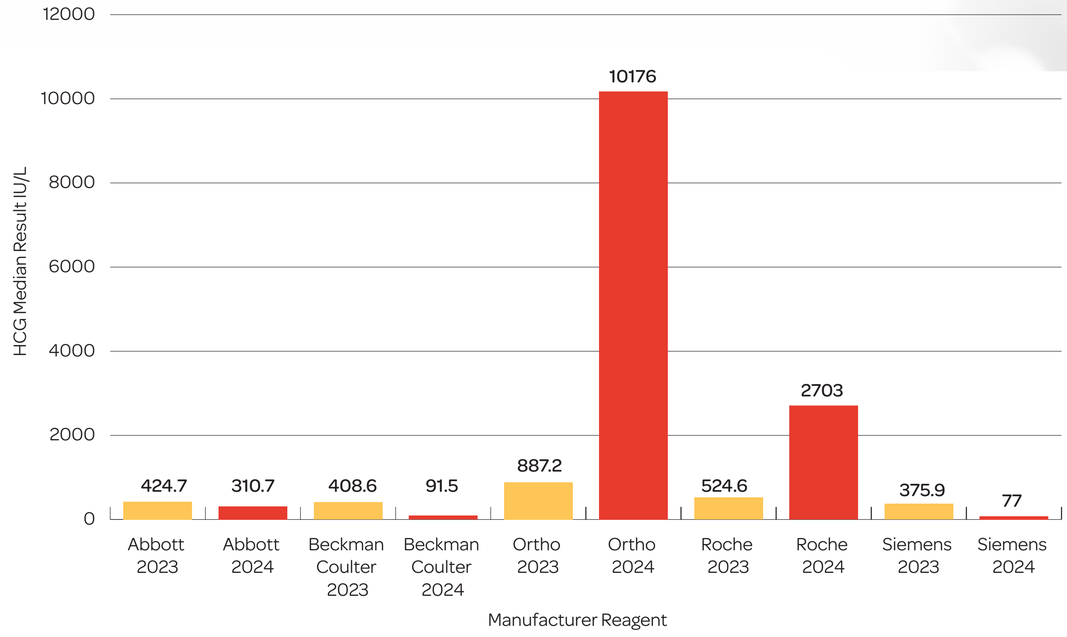

Figure 1 Comparison between recovery of samples between 2023 and 2024

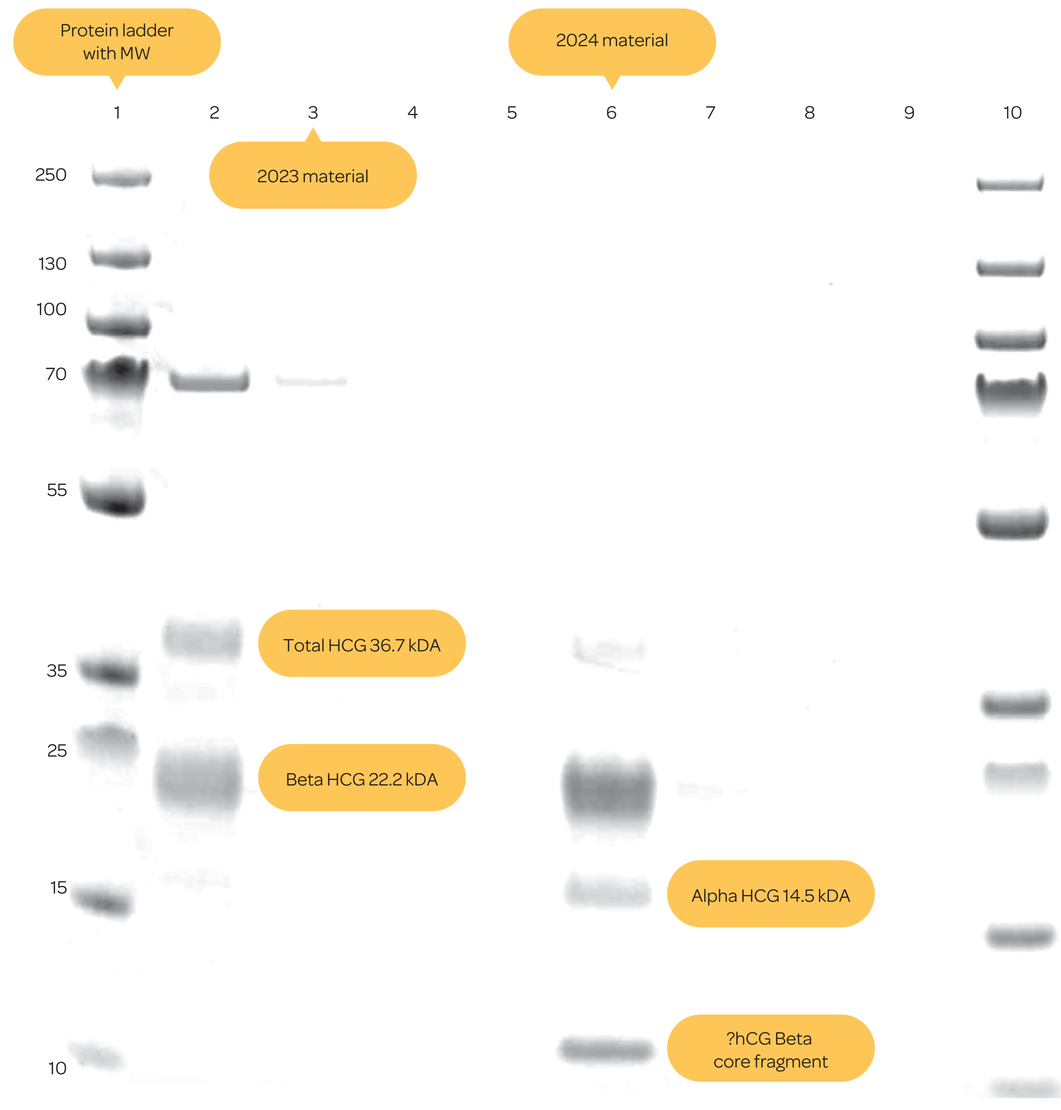

Figure 2 SDS-PAGE Electrophoresis of HCG 'spikes' used in the 2023 and 2024 Endocrine QAP

Discussion

The significant over-recoveries demonstrated by the Ortho and Roche assays may be due to additional immunoreactivity with the alpha hCG and hCG βcf variants. Likewise, interference from the variants could account for the low recoveries for Beckman and Siemens. Similar assay variations have previously been reported in the presence of excess hCG βcf in urine.[1]

Conclusion

While the change in the source of the HCG spike was eventually identified as the cause of the significant variation in HCG results, and recognising this would not be seen in a patient sample, it does still provide some insight on the different target epitopes used for HCG immunoassays and potential interference which should be considered when evaluating HCG immunoassays.

References:

1. Grenache DG, Greene DN, Dighe AS et al. Falsely Decreased Human Chorionic Gonadotropin (hCG) Results Due to Increased Concentrations of the Free β Subunit and the β Core Fragment in Quantitative hCG Assays. Clinical Chemistry 56:12. 2010.

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