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A Review of Performance on the Weqas Quantitative Faecal Haemoglobin (FIT) EQA Programme – Are current analysers 'FIT' for purpose?

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Introduction

Faecal immunochemical tests (FIT) are designed to detect small amounts of blood in stool samples using antibodies specific to human haemoglobin (Hb).

In the UK, these tests are recommended by National Institute for Health and Care Excellence (NICE) to guide referrals for suspected colorectal cancer in symptomatic patients using a threshold of 10 µg Hb/g of faeces (guidance DG56 (formally DG30) and NG12). NICE guidance DG56 states '*Refer adults using a suspected cancer pathway referral (as outlined in NICE's guideline on suspected cancer) for colorectal cancer if they have a FIT result of at least 10 micrograms of haemoglobin per gram of faeces.*'

FIT is recommended as part of the testing strategy for the UK Bowel Cancer Screening Programmes although much higher thresholds are used.

In 2016, Weqas developed an EQA programme to assess and monitor the performance of these tests. 62 instruments were initially registered at the onset of the programme with participants within the UK and overseas. In 2024, there are 101 instruments registered.

Method

Organic material, closely mirroring the basic constituents of human faeces was spiked with a known quantity of Hb. A range of concentrations were prepared to cover the pathological range including negative samples, samples at or near the clinical cut-off used for symptomatic testing pathways and samples at the higher cut offs used in asymptomatic population screening programmes. The homogeneous material was dispensed aseptically into buffered collection devices specific to each manufacturer.

Three samples per month were distributed to all participants of the Quantitative EQA Programme (approximately 100 instruments) to assess laboratory and method performance, including linearity, bias, and within batch imprecision.

Over a period of 10 months, 3 samples were distributed at a spiked concentration of 10 µg Hb/g matrix. Two non-spiked samples were also distributed. Performance was assessed on the instruments recommended by NICE i.e. the HM-JACKarc and the OC-Sensor platforms.

Results and Discussion

For a non-spiked sample, distributed October 2022, 6 laboratories reported 0, 12 reported results between 0-1, 1 reported 2.9, 1 <1, 2 <2, 10 <7 and 3 <10 µg Hb/g for the HM-JACKarc. For the OC Sensor 18 laboratories reported a result of 0, 5 reported results between 0-1, 1 reported a results of 4, 14 reported <4, 8 <6, 1 <9.9, 4 <10 and 1<15 µg Hb/g.

For a non-spiked sample, distributed August 2023, 8 laboratories reported 0, 7 reported results between 0-1, 3 <2, 13 <7 and 5 <10 µg Hb/g for the HM-JACKarc. For the OC Sensor 18 laboratories reported a result of 0, 2 reported 0.4, 1 reported 1, 1 reported <2, 23 <4, 2 <6, 1 <9.9 and 4 <10µg Hb/g. All laboratories correctly identified the negative sample as <10µg Hb/g.

At a target concentration of 10 µg Hb/g matrix (distribution August 2022) a mean of 7.23 µg Hb/g matrix (SD 2.04, CV 27.9%, n = 23) was observed for the HM-JACKarc with a mean of 4.79 µg Hb/g matrix (SD 1.68, CV 35.1%, n=37) for the OC Sensor.

At a target concentration of 10 µg Hb/g matrix (distribution January 2023) a mean of 9.37 µg Hb/g matrix (SD 1.94, CV 20.4%, n = 29) was observed for the HM-JACKarc with a mean of 5.32 µg Hb/g matrix (SD 1.2, CV 23.5%, n=33) for the OC Sensor.

At a target concentration of 10 µg Hb/g matrix (distribution October 2023) a mean of 11.68 µg Hb/g matrix (SD 2.41, CV 20.6%, n = 35) was observed for the HM-JACKarc with a mean of 4.85 µg Hb/g matrix (SD 1.1, CV 22.7%, n=39) for the OC Sensor.

Table 1 Performance data for pools spiked to 10 µg Hb/g matrix

Pool Code	Distribution Code	HM-JACKarc Mean (ug Hb/g matrix)	HM-JACKarc SD	HM-JACKarc CV %	OC Sensor Mean (ug Hb/g matrix)	OC Sensor SD	OC Sensor CV %
310123/401	FH0123	9.37	1.94	20.7	5.32	1.25	23.5
241023/491	FH1023	11.68	2.41	20.6	4.85	1.1	22.7
300822/351	FH0822	7.32	2.04	27.9	4.79	1.68	35.1

For the spiked samples, HM-JACKarc participants reported results of <5, <7 and <10 ug Hb/g, OC Sensor participants reported results of <4, <6, <7, <9.9 and <10 ug Hb/g.

A 1.5 X difference in result was observed at the 10 µg Hb/g threshold for the two analysers in August 2022, 1.8 X difference in January 2023 and 2.4 X difference in October 2023.

Figure 1 gives a graphical representation of the method differences at lower concentrations.

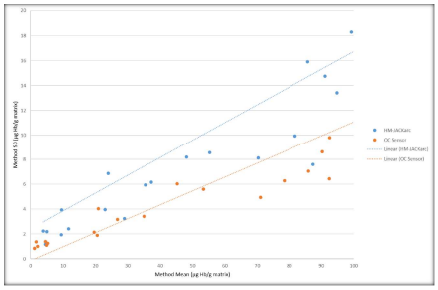
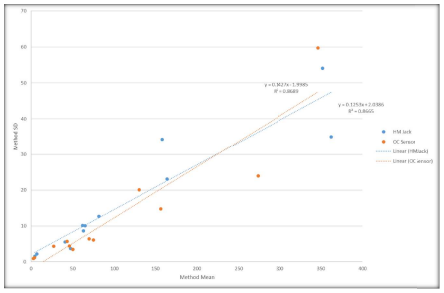


Figure 2 gives a graphical representation of the method differences across the analytical range.

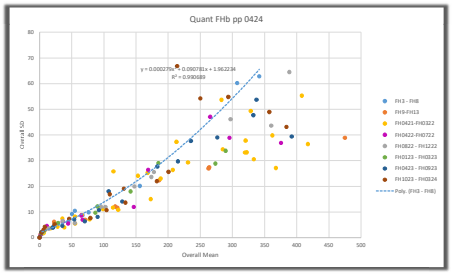
Figure 2



Analytical Performance Specifications

Analytical Performance Specifications (APS) are assigned based on Milan Model 3, 'state of the art', as there is no outcome study data or biological goals available for FIT. Performance is assessed using the same APS for all instruments.

Figure 3 shows the precision profile data used to set the APS.



Discussion and Conclusion

The stated Limit of Detection (LoD) and Limits of Quantitation (LoQ) for these instruments are stated in Table 2.

Table 2

FIT instrument	Manufacturer stated LoD (ug Hb/g faeces)	Manufacturer stated LoQ (ug Hb/g faeces)
HM-JACKarc	1.25	7
OC-Sensor	N/A	10

Data sourced from Alpha Laboratories website and reference paper 4 below. No LoD could be found for OC-Sensor

The measurement ranges for each instrument are stated as 7–400 µg Hb/g faeces for HM-JACKarc and 10–200 µg Hb/g faeces for OC-Sensor Pledia.

All except one laboratory, over the 2 distributions, correctly identified the negative sample as <10µg Hb/g.

A wide variation in lower reporting limits was observed which were not associated with test utility.

This study suggests that a universal cut-off of 10 µg Hb/g for suspected colorectal cancer in symptomatic patients may not be appropriate when such large method biases exist at low concentrations. Until such time a reference standardisation system is developed, it may be more appropriate for laboratories to use manufacturer specific cut offs.

References
1. NICE Guidance DG56 Quantitative faecal immunochemical testing to guide colorectal cancer pathway referral in primary care. **2.** NICE Guidance DG30 Quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care.
3. NICE Guidance NG12 Suspected cancer: recognition and referral. **4.** Piggott C, Carroll MRR, John C, O'Driscoll S, Benton SC. Analytical evaluation of four faecal immunochemistry tests for haemoglobin. Clin Chem Lab Med 2020;59:173–8.