EVALUATION OF QUANTITATIVE FAECAL IMMUNOCHEMICAL TESTS FOR HAEMOGLOBIN

GMEC
Guildford Medical Device Evaluation Centre

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NHS BOWEL CANCER SCREENING SOUTHERN PROGRAMME HUB

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PLEASE NOTE:
This is a revised version of the report that includes revised summary text and a new Summary Table (pages *i-iii*) to assist direct comparison of the analysers' technical performance. All revisions made to the original report are described in Appendix 12. Page and original table numbering are unchanged.

The evaluation

This evaluation was commissioned by the NHS Bowel Cancer Screening Programme (BCSP) in England.

The Faecal Immunochemical Test for haemoglobin (FIT)

The faecal immunochemical test for haemoglobin (FIT) measures the concentration of human blood in faeces using polyclonal or monoclonal antibodies raised against the globin moiety of human haemoglobin (Hb). The FIT evaluated in this study use antibodies bound to either polysaccharide carrier particles (latex) or to gold carrier particles [1]. When human Hb is added to a reaction mixture containing these antibodies, the globin protein binds to the antibodies and forms small aggregates. The aggregation of polysaccharide or gold particles changes the turbidity of the reaction mixture in proportion to the concentration of added Hb and this enables quantitation of Hb in the sample.

Scope of use

The 2010 *European guidelines for quality assurance in colorectal cancer screening and diagnosis* recommended the adoption of quantitative FIT as the primary screening modality for colorectal cancer [2,3]. The evidence presented in these guidelines demonstrated that FIT was analytically more sensitive and specific than the guaiac faecal occult blood test (gFOBT) and in population screening it showed greater clinical effectiveness in the detection of cancer and advanced adenoma. In recommending the adoption of FIT, the guidelines state that FIT have other significant practical benefits for population screening. The merits of FIT have been promoted by the World Endoscopy Organization (WEO) Colorectal Cancer Screening Committee's Expert Working Group (EWG) on 'FIT for Screening' (http://www.worldendo.org/weo-crcsc-expert-working-group-fit-for-screening.html); FIT enables objective and automated measurement, a single FIT device requiring a single faecal sample is acceptable for screening, it uses a simpler and more attractive sampling technique than that used by the gFOBT, it allows the positivity rate to be adjusted to meet local circumstances and the Hb concentration can be incorporated into a multivariate risk score to enable a higher positive predictive value for cancer or advanced adenoma.

Evaluation systems

Evaluation of quantitative FIT products commenced in November 2012, at which time four products met essential criteria identified by BCSP. The Guildford Medical Device Evaluation Centre (GMEC) team commenced evaluation of the following four products; the HM-JACKarc, the NS-PLUS C15, the OC-SENSOR DIANA and the Sentinel FOB Gold NG for Hb analysed on the BioMajesty.

The collection devices and analysers were recommended and provided by the manufacturers. The analysers were installed into the GMEC research laboratory at the University of Surrey by the suppliers and training was provided to two members of the GMEC team. Cascade training was then used to train a third member of the team. The practical evaluation work took place between December 2012 and August 2013.

SUMMARY

The evaluation used both faecal and aqueous Hb samples. Faecal samples had human blood added (spiked) at specified Hb concentrations, as did the aqueous solutions that were prepared in sample collection buffer. These two preparations were used to assess analytical sensitivity, carryover, imprecision, precision profiles, linearity and Hb stability in the sample collection devices (stability defined for this evaluation as a fall in Hb concentrations to <50% of initial concentrations). Questionnaire surveys were performed to assess user preferences for the four collection devices. Existing laboratory users of the evaluated analytical systems were contacted to gather information and pool their experience.

Evaluation outcomes: operational performance/considerations

HM-JACKARC

The HM-JACKarc collection tube has flattened sides, which make it easy to write on, although it proved the most difficult device to use. A paper tab connects the lid to the collection tube and this is a valuable feature that provides a useful check to the receiving laboratory that the device has been opened and used. The device collects only 2 mg of faeces, which is the smallest amount for the devices evaluated, and some participants in the questionnaire survey thought that they should sample the faeces multiple times to ensure that it was adequate to give a reliable result.

The HM-JACKarc analyser is a small bench-top analyser dedicated to FIT analysis. It measures the faecal Hb concentration using an integrated sphere that collects light from the latex turbidimetric reaction. The instrument and its menu systems are easy to follow and use. 'Single-use' cuvettes are used, which avoids the need to wash cuvettes between analyses but increases the consumption of plastic consumables and creates a large amount of plastic clinical waste. Only a small volume of liquid waste is produced, as the system carries out limited washes of the reagent and sampling probes.

NS-PLUS C15

The NS-PLUS collection device was very easy to use. The lid has an easy-to-grip flat surface, and there is an audible 'click' on closure. The blue coloured collection buffer disguises the addition of faecal matter, and changes to green once a sample has been added. This is a unique feature of this system and provides the laboratory with a means of checking that the sample collection device has been used.

The analyser is a small bench-top automated clinical chemistry analyser and therefore has a large capacity for a range of reagents. Unlike the other systems evaluated, the NS-PLUS C15 uses antibodies bound to colloidal gold particles.

The analyser proved very easy to use, and the software was very easy to follow. Due to the use of reusable cuvettes, more water and wash solution are required than for the HM-JACKarc, and more liquid waste is produced. The NS-PLUS C15 can be attached to mains drainage to avoid frequent manual emptying of the waste container. This reduces the amount of plastic clinical waste produced.

OC-SENSOR DIANA

The 'OC-Auto Sampling Bottle 3' collection device is well-designed with an easy-to-open top and the flat surfaces of the tube make it easy to write on. The device incorporates a small filter that removes faecal particulate matter from a sample before analysis, a feature that reduces the possibility of miss-sampling. The tube has a narrow neck that, whilst it might mitigate against collection of excessively large samples, does make replacement of the sample probe after faeces collection more difficult (an observation made by participants in the questionnaire survey). It is important to note that in December 2012 the buffer used in this collection device was changed to a buffer that increased sample stability; this significant change was not marked by a change in product designation.

The OC-SENSOR DIANA is a small bench-top analyser dedicated to FIT analysis that uses latex-coated beads in a turbidimetric assay. Whilst the analyser is easy to use, some of the menu systems are complex and some procedures proved more difficult to navigate than on the other analysers evaluated. The OC-SENSOR DIANA, as with the NS-PLUS C15, uses reusable cuvettes between each test, which reduces the consumption of plastic consumables but increases the consumption of wash solution and produces large volumes of liquid waste. The OC-SENSOR DIANA can be attached to mains drainage to avoid frequent manual emptying of the waste container.

SENTINEL/BIOMAJESTY

The FOB Gold NG collection device is produced by Sentinel and uses a conventional blood sample-sized tube, which makes FOB Gold suitable for analysis using a wide range of clinical chemistry analysers. The collection device is different from the others and the curved surface makes writing a name or date on the device label more difficult than on flat surfaces. The device has a larger probe than the other devices making it easier to see when a sample has been collected and easy to reinsert after faecal sampling. The device has a second screw cap at the base of the tube (at the opposite end to the sample probe). The cap is removed before analysis but in the tube's current design the cap could be removed mistakenly by a screening participant, resulting in total or partial loss of the sample and collection buffer and rendering the sample unsuitable for analysis.

The BioMajesty analyser was provided by Sysmex UK Ltd, Milton Keynes, for FOB Gold analysis. It is a conventional floor-standing fast-throughput automated clinical chemistry analyser. It requires a large volume of purified water and therefore is suitable for use only in a well-equipped laboratory. The Sentinel FOB Gold reagents are latex-bound polyclonal antibodies used for conventional turbidimetric analysis. The BioMajesty is a multi-analyte analyser, much larger and necessarily more complex than the other analysers evaluated. The analyser software is complex beyond what is necessary to meet the needs of just FIT analysis and more appropriate for situations when FIT is one test amongst a repertoire of 20 or 30 others; the analyser was not evaluated in that context. The throughput of the analyser with reusable cuvettes requires two cycles of washing each day (25-30 minutes each), which uses a substantial volume of deionised water.

Summary Table: Evaluation outcomes: technical performance

HM-JACKarc	NS-PLUS C15	OC-SENSOR DIANA	BIOMAJESTY
Analytical sensitivity (lower limit of detection in aqueous samples)			
Measured lower limit of detection met manufacturer's claims. Detects very low Hb concentrations.	Measured lower limit of detection met manufacturer's claims. Detects very low Hb concentrations.	Measured lower limit of detection met manufacturer's claims but does not detect Hb at concentrations as low as that seen with the other analysers.	Measured lower limit of detection met manufacturer's claims. Detects very low Hb concentrations.
Carryover (assessment of system cleaning between aqueous samples)			
Very little carryover of sample between samples with a high and low concentration.	Very little carryover of sample between samples with a high and low concentration.	Very little carryover of sample between samples with a high and low concentration.	Very little carryover of sample between samples with a high and low concentration.
Imprecision (consistency of repeat measurements of aqueous and faecal samples)			
Repeatability of aqueous results was shown to be consistent with manufacturer's claims, although there was no within-laboratory imprecision data provided by the manufacturer. Data from one faecal sample consistent with claims, whilst data from other sample not consistent.	Repeatability of results and within-laboratory imprecision of the analyser not as good as those claimed by the manufacturer for both buffer and faecal material. At lower concentrations (around possible cut-off values) imprecision was good, however at higher concentrations measurement more imprecise.	Positive bias of results prevented a simple comparison of imprecision with that claimed by the manufacturer and the Diana had the most imprecise method of the analysers evaluated.	Positive bias of results prevented a simple comparison of imprecision with that claimed by the manufacturer although it had good imprecision at lower concentrations, but imprecision of measurement increased with increasing Hb concentration.

Summary Table: Evaluation outcomes: technical performance (continued)

HM-JACKarc	NS-PLUS C15	OC-SENSOR DIANA	BIOMAJESTY
Bias (closeness results for aqueous samples to expected results)			
Slight positive bias of Hb concentration in aqueous solutions.	Results closer to the expected Hb concentrations than was seen with the other products evaluated.	Results showed a positive bias and gave results higher than expected.	Results showed a positive bias and gave results higher than expected.
Linearity/measurement range (aqueous samples)			
Good linearity (quoted measurement range 7-400 µg Hb/g faeces); it has no system for diluting samples that have a high Hb concentration.	Good linearity across the quoted measurement range (3.8-228 µg Hb/g faeces); there is a facility for automatic dilution of samples with high Hb concentrations extending the dilution range to >500 µg Hb/g faeces.	Good linearity (quoted measurement range 10-200 µg Hb/g faeces). Dilution semi-automated (manual identification of 'over-range' samples and manual replacement of the sample tube on the analyser). Dilution extends the range beyond the undiluted upper limit to 50,000 µg Hb/g faeces.	Not linear, particularly above 120 µg Hb/g faeces (quoted measurement range 2.55-153 µg Hb/g faeces). The instrument can dilute high samples automatically but, even when this facility was enabled, the assay remained markedly non-linear at high concentrations.
Precision profile (variability of results across the claimed measurement range for aqueous samples)			
Good precision through the measurement range.	Good precision through the measurement range.	Good precision through the measurement range.	Good precision but results above 100 µg Hb/g faeces were inaccurate.

Summary Table: Evaluation outcomes: technical performance (continued)

HM-JACKarc	NS-PLUS C15	OC-SENSOR DIANA	BIOMAJESTY
Hook/prozone effect (potential for erroneously low results at exceptionally high concentrations for aqueous samples)			
No evidence of hook/prozone effect.	Evidence of the hook/prozone effect (two cases of false negative results in very highly concentrated samples); whilst only at high concentrations, there is potential for misleading results.	No evidence of hook/prozone effect; all results were reported as 'Over Range'.	Evidence of a hook/prozone effect (some very high concentrations of Hb reported as 'weakly positive'); whilst only at high concentrations, there is potential for misleading results.
Stability (of faecal and aqueous samples in the collection devices at -21°C, 6°C, 20°C, 35°C)			
Consistent with manufacturer's claims (stability 120 days at 4°C and 14 days at 25°C); at a sustained temperature of 35°C the stability of faecal samples was less than 3 days.	Consistent with manufacturer's claims (stability 7 days at 2-8°C and 3 days at 18-25°C); at a sustained temperature of 35°C the stability of faecal samples was less than 3 days.	Consistent with manufacturer's claims (stability 14 days at 2-10°C and 7 days at room temp); at a sustained temperature of 35°C the stability of faecal samples was less than 2 days.	Consistent with manufacturer's claims (stability 14 days at 2-8°C and 7 days at 15-30°C); at a sustained temperature of 35°C the stability of faecal samples was less than 9 days.

FIT Units

Manufacturers have conventionally reported FIT concentrations as the amount of Hb (ng) in the collection buffer (mL). Since sampling devices collect different amounts of faecal sample into different volumes of buffer, the reported concentrations cannot be compared between devices. Following an initiative by the WEO EWG on FIT for Screening, manufacturers and the screening community are adopting reporting units of µg Hb/g faeces; this requires knowledge of each product's typical faecal sample mass and buffer volume. The comparative evaluation has used µg Hb/g faeces throughout by referring to the sample mass and buffer volume data provided by each manufacturer. Table 1 shows manufacturers' data and the conversion factor required to change from ng Hb/mL buffer to µg Hb/g faeces.

Table 1: Data supplied by the manufacturers that enable conversion from ng Hb/mL buffer to µg Hb/g faeces.

	Sample weight (mg)	*Buffer volume (mL)*	*Conversion factor*
HM-JACKarc	2	2.0	1.00
NS-PLUS C15	10	1.9	0.19
OC-SENSOR DIANA	10	2.0	0.20
FOB Gold/BioMajesty	10	1.7	0.17

INTRODUCTION

The NHS Bowel Cancer Screening Programme (BCSP) in England is preparing to replace guaiac faecal occult blood tests (gFOBT) with quantitative faecal immunochemical tests for haemoglobin (FIT), commencing with a 6-month pilot from March 2014. As well as being easier to use than gFOBT [4], quantitative FIT provide a numerical haemoglobin (Hb) concentration and an opportunity for fast objective automated analysis. FIT provide the opportunity for the faecal Hb concentration to contribute to a multivariate measure of colorectal cancer (CRC) risk with further enhancement to its positive predictive value. The NHS BCSP FIT working group has agreed a software specification with the Health and Social Care Information Centre which makes provision for the implementation of new CRC risk algorithms as they are developed by the screening research community. The working group will finalise the organisational model, develop new programme literature, monitor and evaluate the pilot and progress analytical arrangements necessary to support FIT system procurement. The Guildford Medical Device Evaluation Centre (GMEC) has undertaken three previous evaluations for the NHS BCSP and was commissioned again by the Programme to provide a detailed evaluation to support the FIT pilot, procurement and rollout. GMEC has a close association with the BCSP Southern Hub, one of the five Hubs that support the BCSP in England. The Southern Hub typically receives between 2,000 and 6,000 samples a day, and must be able to analyse up to 9,000 samples a day in exceptional circumstances.

GMEC had the remit to evaluate all FIT systems that purport to be suitable for automated, quantitative, population-based colorectal cancer screening using FIT analysis. The faecal sample collection systems need to be suitable for unaided home faecal sample collection, meet EU requirements for the mailing of human tissues by the Royal Mail (UN3373 and P650) and have adequate sample stability. The analytical instrumentation should be suitable for reliable analysis of between 2,000 and 9,000 faecal samples a day, although workloads may be split between several analysers if necessary.

This evaluation addressed important product characteristics including service support, training, ease-of-use, device design, and all pertinent aspects of analytical performance. The evaluation also investigated a range of standardisation issues highlighted by the World Endoscopy Organization (WEO) Colorectal Cancer Screening Committee's Expert Working Group (EWG) on Faecal Immunochemical Tests for Haemoglobin (FIT); these included the reported sample stability, sample mass, traceability and cross reactivity. This report will contribute valuable information to manufacturers, screening services and laboratories on procedures for FIT product standardisation.

Following a review of commercially available FIT, conducted under the auspices of the WEO EWG, four FIT products were identified by GMEC as potentially suitable for use in the NHS BCSP in England:

- HM-JACKarc, *Kyowa Medex Co Ltd, Japan*
- NS-PLUS C15 Hb, *Alfresa Pharma Corp, Japan*
- OC-SENSOR DIANA, *Eiken Chemical Co. Ltd, Japan*
- FOB Gold NG, Sentinel CH. SpA, Italy, analysed on BioMajesty, Jeol, Japan.

These were the only products that were identified in October 2012 as able to provide laboratory-based, automated, quantitative analysis and a faecal collection device suitable for home use and postal transport. All are CE-marked with respect to the In Vitro Diagnostic Medical Devices Directive (98/79/EC) [5]. Table 2 describes the analyser specifications.

Table 2: Summary of analyser descriptions (N/A: not applicable)

Measuring system	***HM-JACKarc***	***NS-PLUS C15***	***OC-SENSOR DIANA***	***FOB Gold/BioMajesty***
Analyser				
Manufacturer	Kyowa Medex (Japan)	Alfresa (Japan)	Eiken (Japan)	Jeol (Japan)
UK supplier	Alpha Laboratories Ltd	Alere Ltd	Mast Diagnostics Division	Sysmex UK Ltd
World launch	February 2010	December 2004	2007	2010
UK launch	October 2013	January 2007 (CE Mark)	2007	European distributor 2010
World launch of assay	February 2010	December 2004	2007 (updated buffer 2012)	November 2003
Analyser information				
Type of analyser	Bench top	Bench top	Bench top	Floor standing
Analyser size (mm) WxDxH	500 x 600 x 610	435 × 430 × 580	630 x 560 x 560	1220 x 850 x 1108
Space for accessories (mm)	300 x 250	450 x 350 x 350 for deionised water, drain and wash solution bottles	300 both sides of analyser deionised water, drain and wash solution bottles	740 x 730 x 1108
Weight of analyser	56 kg	43 kg	60 kg	450 kg
Power supply-sockets	1	3 (analyser, PC and display)	1	4
Water requirements	N/A	2.4 L/hr	1.1 L/hr	20 L/hr
Wash requirements	5 L /1,000 tests	0.4 L/hr	0.5 L/hr	Detergents
Waste	Solid waste: non-recyclable cuvettes and cuvette holders Liquid waste: gravity drains to 5 L collection bottle	Liquid waste: gravity drains to 10 L collection bottle. Can be fed directly into mains drains	Liquid waste: pumped into 10 L collection bottle. Can be fed directly into mains drains	Liquid waste: 20.2 L/hr, pumped directly into mains drains

Table 2: Summary of analyser descriptions (continued)

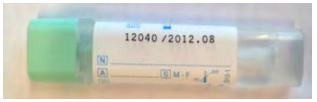
Measuring system	***HM-JACKarc***	***NS-PLUS C15***	***OC-SENSOR DIANA***	***FOB Gold/BioMajesty***
Software				
Password requirements	To change some settings	To use computer, others to change some settings	To change some settings	To change some settings
Data entry method				
Device identification	Barcode	Barcode	Barcode	Barcode, but order entry also required
Reagent identity	Handheld barcode reader on side of instrument	Automatic reagent scan as the reagent lid is shut	Barcode scanner in middle of instrument	User defined reagent scan used on bottle barcodes
Printout of results	Automatic on thermal paper	Automatic on computer	Automatic on thermal paper	User defined when required
External software connections	USB, RS232C	RS232C	USB, LAN, RS232C	Yes
Analysis information				
Method	Polyclonal antibodies. Latex immunoturbidimetry with detection by integrated sphere turbidimetry[1]	Polyclonal antibodies. Colloidal gold immunoturbidimetry	Polyclonal antibodies. Latex immunoturbidimetry	Polyclonal antibodies. Latex immunoturbidimetry
Calibration traceable to	In-house reference Hb	Not known	WHO	BCR-522
Reference material	Human Hb (commercial source)	Human Hb (commercial source)	Accuglobin	BCR-522
Reference method	Cyanmethaemoglobin	Cyanmethaemoglobin	Cyanmethaemoglobin	Cyanmethaemoglobin
Calibration range	25-400 ng/mL	0-1200 ng/mL	50-1,000 ng/mL	0-800 ng/mL
Number of QCs	Two (high and low)	Three (high, low and -ve)	Two (high and low)	Two (high and low)
Concentration range of QCs	20-30 ng/mL (low) 80-120 ng/mL (high)	80-150 ng/mL (low) 200-350 ng/mL (high)	111-160 ng/mL (low) 379-513 ng/mL (high)	64-87 ng/mL (low) 240-360 ng/mL (high)
Reported measurement range (µg Hb/g faeces)	7-400	3.8-228 (without dilution)	10-200 (without dilution)	2.55-153 (without dilution)

[1] Integrated sphere turbidimetry – see Appendix 1.

Table 2: Summary of analyser descriptions (continued)

Measuring system	***HM-JACKarc***	***NS-PLUS C15***	***OC-SENSOR DIANA***	***FOB Gold/BioMajesty***
Measurement cuvettes	40 in reaction ring at one time, 80 can be loaded onto the analyser at once	50 reaction cuvettes	55 reaction cuvettes	231 reaction cuvettes
Sample volume	12 µL	12 µL	Aspirates 45 µL, dispenses 35 µL	6 µL
Reagents	Latex and buffer	Reagents 1 and 2 and optional diluent	Latex and buffer	Latex, buffer and optional diluent
Maximum test capacity of loaded reagents	200 tests	900 tests with diluent 1200 without diluent	500 tests	1500 tests if full test capacity setup
Maximum sample capacity on analyser	80 (10 samples on 8 racks)	160 (10 samples on 16 racks)	150 (10 samples on 15 racks)	84 samples on the analyser Can use a track system
Time to first result	5.6 mins	8 mins	15 mins	12.5 mins
Time to subsequent result	18 seconds	12 seconds	13 seconds	5 seconds
Time to stop following final result	Immediate	40 seconds	10 mins	2.5 mins
Claimed throughput	200/hr	300/hr	280/hr	800/hr
GMEC-measured throughput	200/hr	300/hr	280/hr	800/hr with track 150/hr without track

Table 2: Summary of analyser descriptions (continued)

Measuring system	***HM-JACKarc***	***NS-PLUS C15***	***OC-SENSOR DIANA***	***FOB Gold/BioMajesty***
Sample collection device				
				
Sampling device design	Round stick with two dimples	Round grooved stick	Round grooved stick	Round grooved stick
Mass of faeces collected	2 mg	10 mg	10 mg	10 mg
Volume of buffer	2.0 mL	1.9 mL	2.0 mL	1.7 mL
Device closing system	Twist and click	Twist and click	Push and click	Twist
Size of label for written information (mm)	40 x 10	40 x 8	36 x 11	20 x 20
Manual cap remove prior to analysis	No	No	No	Yes
Sample filtration system within device	No	No	Yes	No
Product support				
Finance options	Subject to local distributor	Available	Available	Subject to local distributor
Warranty	12 mths for analyser, service parts from the day of purchase	Not available for NS-Plus C15	12 mths	12 mths
Maintenance contract	Subject to local distributor	Yes	Subject to agreed Terms and Conditions	Subject to local distributor

STUDIES UNDERTAKEN

The following studies were undertaken to assess both faecal sample collection devices and analysis.

Technical performance:

- Analytical sensitivity
- Carryover
- Imprecision
- Precision profile
- Linearity
- Hook/prozone effect
- Stability

Operational performance:

- Design of the collection devices
- Hb concentration conversion factors
- Participant survey
- Analytical system - user evaluations
- Ease-of-use
- Consumables
- Maintenance and servicing

Sundry operational considerations:

- Analyser requirements
- Staff requirements
- Economic considerations
- Environmental considerations.

Preparation of test samples

Faeces

Faecal samples from 10 healthy volunteers were collected and analysed on all evaluation systems to ensure that the samples were negative for occult blood. The samples were then mixed by hand in stomacher bags for five minutes to create a master pooled sample. The pool was kept at 4°C before use in the stability study; remaining pool sample was frozen at -20°C before use in other aspects of the evaluation.

Human red blood cell lysate

A human Hb lysate solution was prepared from a lithium heparin whole blood sample provided by a healthy volunteer. Before centrifugation, the volume of the total sample was recorded. The resulting cells were washed three times in physiological saline before being reconstituted to the original sample volume with deionised water. The cells were frozen overnight to complete the lysation process. Following a 1 in 2 dilution in saline, the Hb concentration was measured on an Advia®120 (Siemens AG, Germany) haematology analyser.

Faecal/Hb preparation

The required faecal/Hb preparations were produced by adding lysate to aliquots of the faecal pool followed by thorough manual mixing for 5 minutes. After mixing, the collection devices for each analytical system were used to sample the faecal/Hb preparation, adhering strictly to manufacturers' instructions for use, and stored as appropriate for each study. Any remaining faecal matter was frozen at -20°C.

Buffer/Hb preparation

The buffer/Hb preparations were prepared using the red blood cell lysate by pipetting diluted lysate directly into each system-specific collection buffer to give solutions at the desired concentrations. These samples were used for evaluation of each analyser's technical performance; precision, precision profile, linearity and hook/prozone effect.

Analytical sensitivity

The lower limit of detection for each product was determined by measuring Hb concentration in 20 unused (no sample added) collection devices. The lower limit of detection was defined as the mean of those 20 measurements plus two standard deviations.

Carryover

All of the evaluated analysers use reusable probes to transfer sample from the collection device to the reaction cuvette, and between samples these probes are cleaned automatically. To determine the thoroughness of probe cleaning, sample carryover was assessed using the protocol described by Broughton *et al.* [6].

Three aliquots of a high Hb concentration and three aliquots of a low Hb concentration were prepared in sample buffer. The concentrations were chosen to enable comparison of the four analytical systems. Three samples with high Hb concentrations (a_1, a_2, a_3) followed by three samples with low Hb concentrations (b_1, b_2, b_3) were measured. This set of six measurements was repeated 10 times. The carryover factor, k, was calculated as follows using the mean of the 10 samples:

$$k = \frac{b1 - b3}{a3 - b3}$$

Imprecision

Imprecision is a "measure of the closeness of agreement between independent measurement results obtained under stated conditions" [7]. The 2006 Clinical and Laboratory Standards Institute (CLSI) EP15-A2 protocol for user verification of performance for precision and trueness [8] was used to determine repeatability and within-laboratory precision (see below for definitions). The protocol enables users to demonstrate that the reliability and accuracy of their analyser is consistent with claims by the manufacturer. The comparison assumes that the manufacturer has assessed the instrument using either CLSI EP05-A2 [9] or a similar protocol to establish and validate the analytical performance of the method.
Three replicate samples of Hb diluted in each product collection buffer contained in their collection tubes, at selected concentrations, were analysed on a single analytical 'run' (same date and time), on each of five days.

All aliquots were prepared and stored at 4˚C on the first day of the evaluation. Each day 16 samples were removed from storage, allowed 15 minutes to come to room temperature and then analysed.

Faecal samples were prepared to compare the four analysers at the same concentrations. Samples of Hb diluted in each manufacturer-specific buffer were prepared to give expected concentrations of 15, 30, 60, and 120 µg Hb/g faeces within samples collection devices. Ten samples were prepared for analysis on day one, when each sample was measured ten times; a further ten samples were prepared for analysis in duplicate on five consecutive days.

The CLSI protocol EP15-A2 states that the estimated repeatability standard deviation can be larger than the manufacturer's claim, but not statistically significantly larger. To determine whether this was the case, a verification value was calculated using the formula specified in the protocol [8]. These values were then used to calculate a verified standard deviation value specific for each concentration against which the GMEC-determined value could be compared.

Imprecision definitions taken from the EP15-A2 protocol [8]

Imprecision (of measurement): the closeness of agreement between independent test results obtained under defined conditions. Imprecision is typically represented as standard deviation (SD) or coefficient of variation (CV).

Repeatability: closeness of agreement between results of successive measurements of the same sample carried out under the same conditions of measurement.

Within-laboratory imprecision: imprecision over a defined time and using defined operators, within the same facility and using the same equipment. Calibration and reagents may vary. Within-laboratory precision is also known as total imprecision.

Precision profile

The precision profile is a series of measurements of imprecision across a range of concentrations. The precision profile for this evaluation spanned the range of concentrations reported for each of the four products. The profile for each analyser was determined using Hb diluted in manufacturer-specific buffer, and measured in analyser cups. The profile was determined between 0 and 400 µg Hb/g faeces; each concentration was measured ten times, and the mean and standard deviation plotted for all analysers across the measurement range.

Linearity

To determine the linearity of the measurement method, duplicate serial dilutions of Hb in manufacturer-specific buffer were analysed on all instruments. The range of the concentration of the samples used in this study was determined to cover a range that is inclusive of that for each analyser. This enabled comparison between devices.

Hook/prozone effect

The prozone or high-dose hook effect produces false negative results in samples with a very high concentration of analyte. This analytical problem can occur with some immunoassay methods when the amount of antigen present (in this case Hb) is markedly greater than the amount of antibody present. This excess of antigen produces a fall in the turbidity of the solution.

Five very high concentrations of human Hb diluted in manufacturer-specific buffer, and all above the quoted measurement ranges for each analyser, were assayed to look for the presence of a hook/prozone effect, and to determine how each of the analysers responds to out-of-range results.

Stability

For the purposes of this evaluation, stability was defined as a fall in Hb concentrations to below 50% of initial concentrations. The evaluation examined both the stability of Hb diluted in manufacturer-specific buffer and the stability of Hb diluted in faeces. Both evaluations used samples collected into the manufacturer's sample collection device.

Four concentrations of Hb were prepared, both as samples of Hb in faeces and as Hb in buffer; the concentrations used ranged from the detection limit to a strong positive FIT result. All samples were incubated at room temperature for 24 hours to enable initial equilibration to occur, including potential adsorption of Hb to the sample matrix. After equilibration, all tubes were kept in thermostatically monitored conditions at a range of temperatures, averaging -21°C (range -22.8 to -19.5°C), 6°C (5.2-6.5°C), 20°C (19.6-21.4°C) and 35°C (33-41.2°C). Each sample was analysed in triplicate daily for 10 days, and then on alternate days for a maximum of 30 days.

Analytical sensitivity

The lower limit of detection for each product was determined using the method described in the Evaluation Methods section of this report. For all analysers the measured lower limit of detection was lower than that quoted by the manufacturer (Table 3), with the NS-PLUS C15 and HM-JACKarc being the most analytically sensitive.

Table 3: Measured lower limit of detection for each analyser. Quoted lower limits of detection were provided by each manufacturer in their data sheets.

	Mean concentration of 20 un-spiked collection tubes (µg Hb/g faeces)	*Standard deviation*	*Lower limit of detection (µg Hb/g faeces)*	*Quoted lower limit of detection (µg Hb/g faeces)*
HM-JACKarc	0.3	0.1	**0.6**	7
NS-PLUS C15	0.0	0.0	**0.0**	4
OC-SENSOR DIANA	2.1	0.9	**3.8**	10
FOB Gold/BioMajesty	0.5	0.4	**1.3**	2.55

Carryover

Carryover was determined using the Broughton method [6] described in the Evaluation Methods section of this report. All analysers showed very little carryover of sample between the high and low concentration samples (Table 4). A *k* value of less than 5 indicates acceptable performance [5]; all were well within this limit.

Table 4: Carryover determined using the equation described by Broughton *et al*. [6]

	HM JACKarc	*NS-PLUS C15*	*OC SENSOR DIANA*	*BioMajesty*
Carryover factor k	0.004	- 0.008	0.008	0.001
% Interaction	0.4%	- 0.8%	0.8%	0.1%

Imprecision

Imprecision measured against manufacturers' mean concentrations

The method used to determine imprecision has been described in the Evaluation Methods section of this report and is the internationally recommended 2006 Clinical and Laboratory Standards Institute (CLSI) EP15-A2 protocol [8]. GMEC targeted its imprecision assessment to the mean concentrations provided by individual manufacturers. This approach enabled comparison between published manufacturers' data and that obtained by the evaluation. A significant difference between GMEC calculated mean values and those obtained at analysis using the OC-SENSOR DIANA and BioMajesty analysers made simple comparison of imprecision impossible with these two systems.

Tables 5 a, b and c show the GMEC-measured imprecision and that quoted by the manufacturer. Where mean values are similar the table indicates whether the GMEC and quoted imprecision were consistent. For this study we present the data using the concentration units quoted by the manufacturer.

Tables 5a-c: KEY (see Evaluation Methods section for definitions)
sr – GMEC measured estimate of repeatability
sl – GMEC measured estimate of within-laboratory repeatability
σr – manufacturers' claimed repeatability
σl – manufacturers' claimed within-laboratory repeatability
NSD – Not statistically different from manufacturers' claim
*Verification value – see Evaluation Methods section for explanation

Table 5a: Imprecision in buffer samples

	GMEC data		*Manufacturer data*			*Consistent/*
	mean	*sr*	*σ mean*	*σr*	*Verification value**	*not consistent with claim*
HM-JACKarc	13.5	0.9	11.3	0.6	0.9	NSD
(µg Hb/g faeces)	58.8	1.3	56.1	2.4	3.5	Consistent
	319.4	5.4	279.5	7.9	11.6	Consistent
NS-PLUS C15	46.7	3.0	62.3	2.0	3.0	NSD
(ng Hb/mL buffer)	89.8	3.3	112.9	1.2	1.8	NSD
	193.3	9.2	215.8	2.5	3.7	Not Consistent
	384.2	52.6	406.8	7.5	11.3	Not Consistent
OC-SENSOR DIANA	197.8	12.4	132.0	2.8	4.0	-
(ng Hb/mL buffer)	646.4	30.5	450.0	7.4	10.6	-
FOB Gold/ BioMajesty	114.1	4.3	81.2	2.5	3.7	-
(ng Hb/mL buffer)	192.0	9.3	133.8	3.6	5.3	
	510.1	51.6	327.7	5.2	7.7	-

Table 5b: Within-laboratory imprecision of buffer samples (N/A: not applicable)

	GMEC data		Manufacturer data			*Consistent/ not consistent with claim*
	mean	*sl*	*σ mean*	*σl*	*Verification value**	
HM-JACKarc	13.5	1.1	N/A	N/A	N/A	-
(µg Hb/g faeces)	58.8	2.4	N/A	N/A	N/A	-
	319.4	8.5	N/A	N/A	N/A	-
NS-PLUS C15	46.7	9.0	62.3	2.0	4.2	Not Consistent
(ng Hb/mL buffer)	89.8	8.6	112.9	1.3	1.8	Not Consistent
	193.3	12.0	215.8	2.5	3.9	Not Consistent
	384.2	49.4	406.8	7.5	11.1	Not Consistent
OC-SENSOR DIANA	197.8	11.9	135.0	1.7	2.1	-
(ng Hb/mL buffer)	646.4	30.8	442.0	3.1	3.8	-
FOB Gold/ BioMajesty	114.1	3.6	81.2	2.2	3.1	-
(ng Hb/mL buffer)	192.0	6.4	133.8	3.1	4.6	-
	510.1	43.0	327.7	4.5	6.6	-

Table 5c: Imprecision in faecal samples (N/A: not applicable)

	GMEC data		Manufacturer data			*Consistent/ not consistent with claim*
	mean	*sr*	*σ mean*	*σr*	*Verification value**	
HM-JACKarc	9.0	2.1	N/A	N/A	N/A	
(µg Hb/g faeces)	43.5	18.2	50.9	9.1	13.4	Not Consistent
	124.3	7.1	163.6	26.3	38.8	Consistent
NS-PLUS C15	30.2	9.5	38.3	1.1	1.6	Not Consistent
(ng Hb/mL buffer)	196.5	18.7	265.0	3.6	5.4	Not Consistent
	554.4	59.0	N/A	N/A	N/A	-
OC-SENSOR DIANA	42.5	7.0	N/A	N/A	N/A	-
(ng Hb/mL buffer)	218.1	7.0	N/A	N/A	N/A	-
	704.5	32.3	N/A	N/A	N/A	-
FOB Gold/ BioMajesty	82.6	16.6	N/A	N/A	N/A	-
(ng Hb/mL buffer)	365.5	89.6	N/A	N/A	N/A	-
	1099.6	86.6	N/A	N/A	N/A	-

Tables 5a and 5b provide the data derived from a comparison of the imprecision and within-laboratory repeatability of the analysers using Hb diluted in buffer (also see Appendix 2).

The repeatability of the HM-JACKarc was consistent with the manufacturer's claimed repeatability. No data were provided for within-laboratory precision. Data from one faecal sample were consistent with claims, whilst the other was not. In general the HM-Jack displayed good imprecision at all concentrations studied.

The NS-PLUS C15 was inconsistent with claimed values for both repeatability and within-laboratory precision in both buffer and faecal material. At the lower concentrations studied (around possible cut-off values) the imprecision was good, however at the higher concentrations measurement was more imprecise.

The OC-SENSOR DIANA has the most imprecise method of analysis, with high sr and sl at both concentrations measured.

The BioMajesty had good imprecision at the lower concentrations studied, but imprecision of measurement decreased with increasing Hb concentration.

In all analysers studied, when faecal samples were spiked with Hb, the imprecision was much poorer (Table 5c and Appendix 3). This can be explained partly by the introduction of sampling variation when using the collection probe and faecal matter.

The OC-SENSOR DIANA and BioMajesty could not be compared with manufacturers' claimed values for Hb in buffer, because the measured concentrations were not within two standard deviations of the expected, calculated concentrations. Neither of the manufacturers provided data for the imprecision of measurements of Hb in faeces and therefore comparison with GMEC data was not possible.

Imprecision: comparison of analysers

All analysers were compared using Hb diluted in manufacturer-specific buffer at four concentrations, with 10 samples at each concentration, each of which was measured 10 times; the results can be seen in Table 6 and 7.

When Hb was directly diluted in manufacturers' buffer (to reduce sampling imprecision) the imprecision of analysis with each method could be measured and compared across analysers. The analytical imprecision of all analysers was limited, both when samples were measured within the same run, and when measured on consecutive days. The NS-PLUS C15 showed a negative bias in both investigations, whilst the other three analysers all showed a positive bias with respect to the expected concentration.

Table 6: Same-day repeatability

Expected concentration	*15 µg Hb/g Faeces*			*30 µg Hb/g Faeces*			*60 µg Hb/g Faeces*			*120 µg Hb/g Faeces*		
	Mean	*SD*	*%CV*	*Mean*	*SD*	*%CV*	*Mean*	*SD*	*%CV*	*Mean*	*SD*	*%CV*
HM-JACKarc	20.4	0.8	4.1	39.6	1.6	4.0	74.3	2.2	3.0	147.6	6.4	4.3
NS-PLUS C15	10.3	0.9	8.5	25.4	2.0	7.7	51.9	2.4	4.5	104.6	7.2	6.9
OC-SENSOR DIANA	20.4	0.9	4.5	49.1	2.3	4.6	89.4	2.9	3.3	179.7	11.6	6.4
FOB Gold/ BioMajesty	14.5	1.0	7.1	36.8	1.5	4.1	90.4	3.3	3.7	189.7	3.7	1.9

Table 7: Inter-day repeatability

Expected concentration	*15 µg Hb/g Faeces*			*30 µg Hb/g Faeces*			*60 µg Hb/g Faeces*			*120 µg Hb/g Faeces*		
	Mean	*SD*	*%CV*	*Mean*	*SD*	*%CV*	*Mean*	*SD*	*%CV*	*Mean*	*SD*	*%CV*
HM-JACKarc	18.9	1.0	5.1	38.0	1.8	4.6	71.5	3.0	4.6	139.2	10.8	7.8
NS-PLUS C15	9.7	0.8	8.8	26.5	2.2	8.2	50.8	2.2	4.3	103.1	6.8	6.6
OC-SENSOR DIANA	21.2	1.8	8.4	47.2	2.3	4.8	86.4	3.8	4.8	170.4	10.2	6.0
FOB Gold/ BioMajesty	17.7	1.0	5.7	39.0	1.8	4.5	93.3	3.8	4.1	195.8	4.3	2.2

Linearity

Figures 1-4 show the linearity of each analytical system across the expected measurement range. The figure on the left shows the whole concentration range (0-500 µg Hb/g faeces) and that on the right the range 0-120 µg Hb/g faeces.

The FOB Gold/BioMajesty was linear in the range 0-120 µg Hb/g faeces. The analyser remained non-linear for all concentrations >120 µg Hb/g faeces even after auto-dilution. The other three analysers all showed good linearity in the range 0-400 µg Hb/g faeces. All analysers displayed a positive bias; that shown by NS-PLUS C15 was very small and that by FOB Gold/BioMajesty was the largest.

Figure 1: Linearity: HM-JACKarc

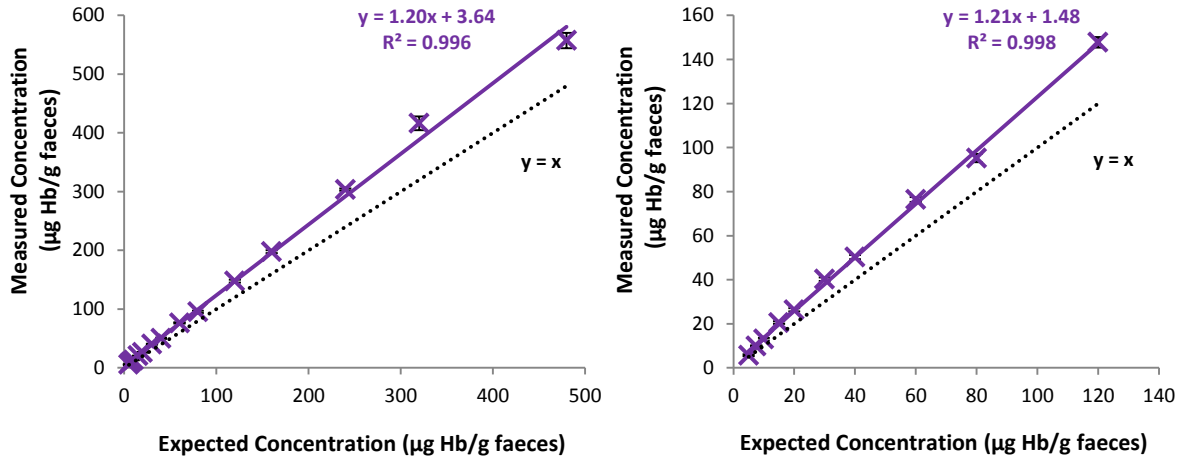


Figure 2: Linearity: NS-PLUS C15

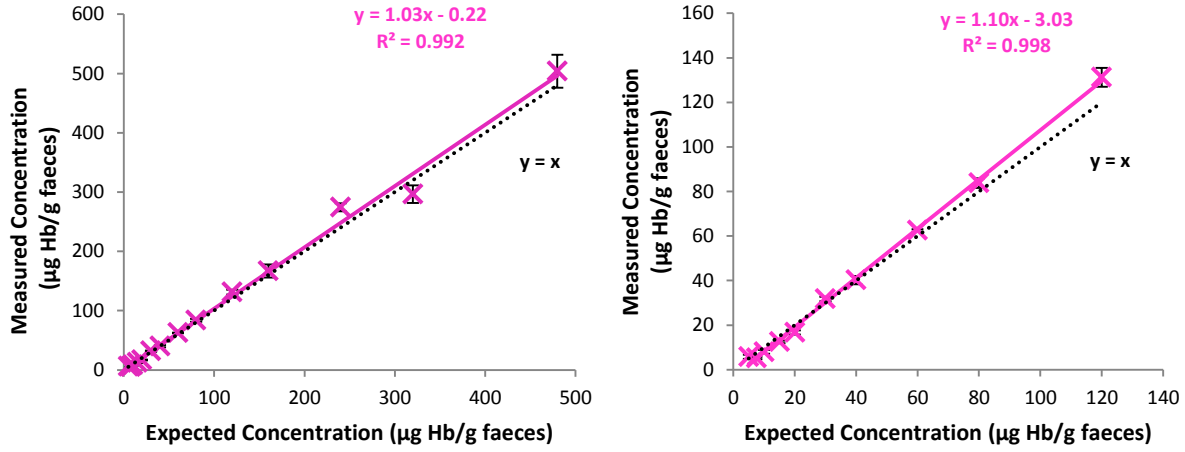


Figure 3: Linearity: OC-SENSOR DIANA

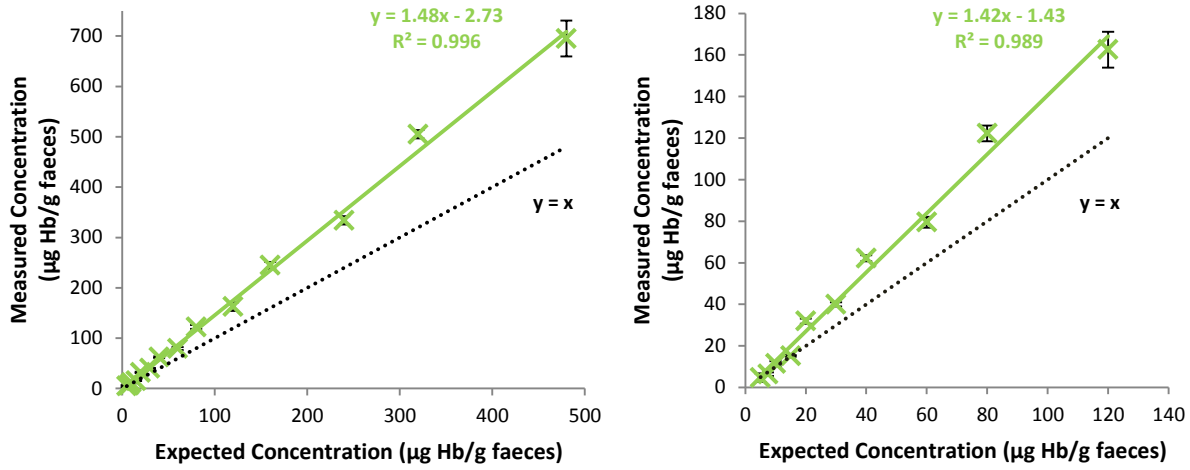
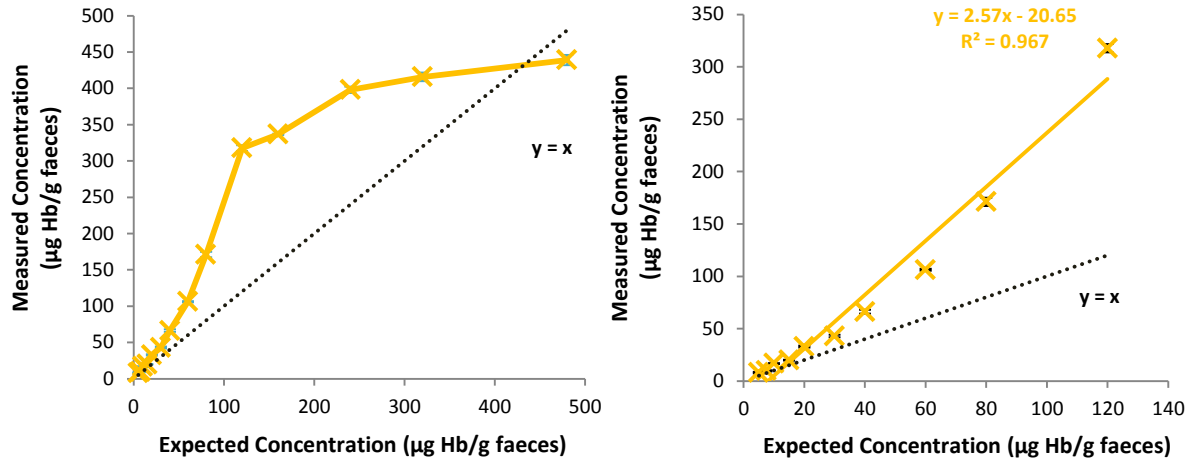


Figure 4: Linearity: FOB Gold/BioMajesty



Precision profile

Precision profiles show the likely variability (precision) of the measurement system across the reported measurement range (see Appendix 4 for data in a table).

Precision profiles were determined for each analyser. The HM-JACKarc, NS-PLUS C15 and OC-SENSOR DIANA were all linear throughout the range studied, as previously described; the FOB Gold/BioMajesty was linear up to 100 µg Hb/g faeces (Figures 5 & 6).

Below 100 µg Hb/g faeces, all analysers showed good precision.

The HM-JACKarc had the best precision with CV below 6% at all concentrations.

The NS-PLUS C15 showed good precision from 20-100 µg Hb/g faeces with a CV below 10%, although below and above this range (0-20 µg Hb/g faeces and 120-400 µg Hb/g faeces) the CV increased to between 10 and 20%.

The OC-SENSOR DIANA had very good precision above 20 µg Hb/g faeces with a CV of less than 5%. At 10 µg Hb/g faeces and 5 µg Hb/g faeces the precision was poor, (15 and 27% respectively), although the quoted lower limit of detection for the OC-SENSOR DIANA is 10 µg Hb/g faeces indicating that the system is not designed for use at these low concentrations.

The FOB Gold/BioMajesty demonstrated good precision with a CV of <10% at all concentrations. Above 100 µg Hb/g faeces, while still displaying good precision, the FOB Gold/BioMajesty system was inaccurate.

Figure 5: Precision profiles of all analysers from 0 – 400 µg Hb/g faeces. (Hollow markers indicate samples that were diluted; error bars show ± 1 standard deviation.)

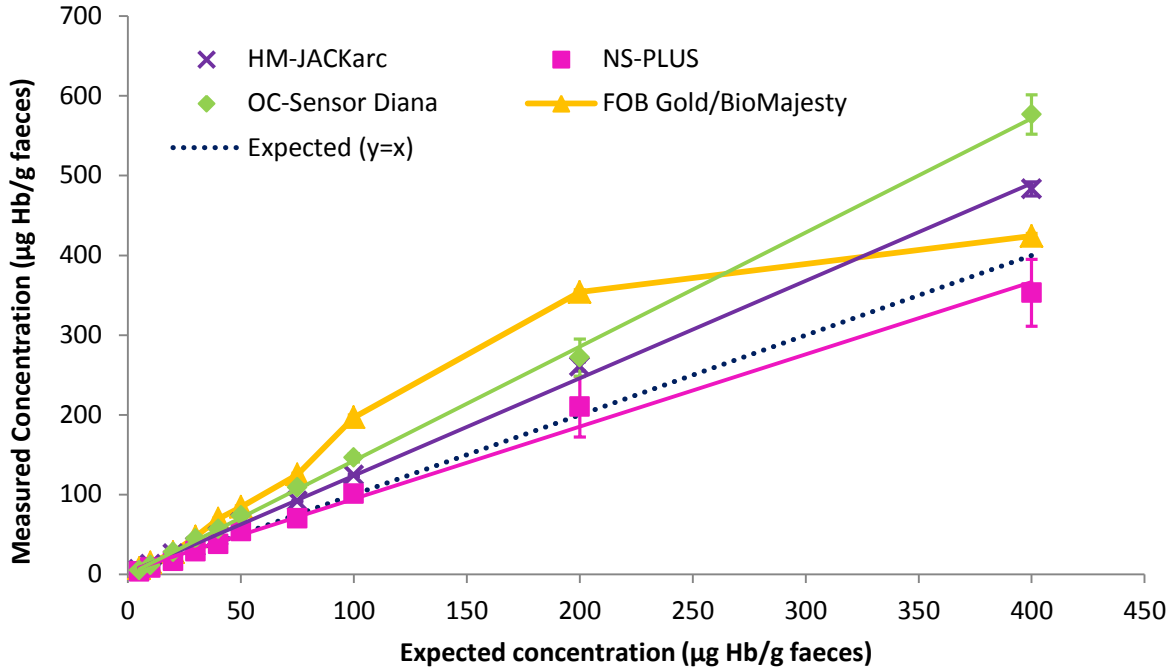
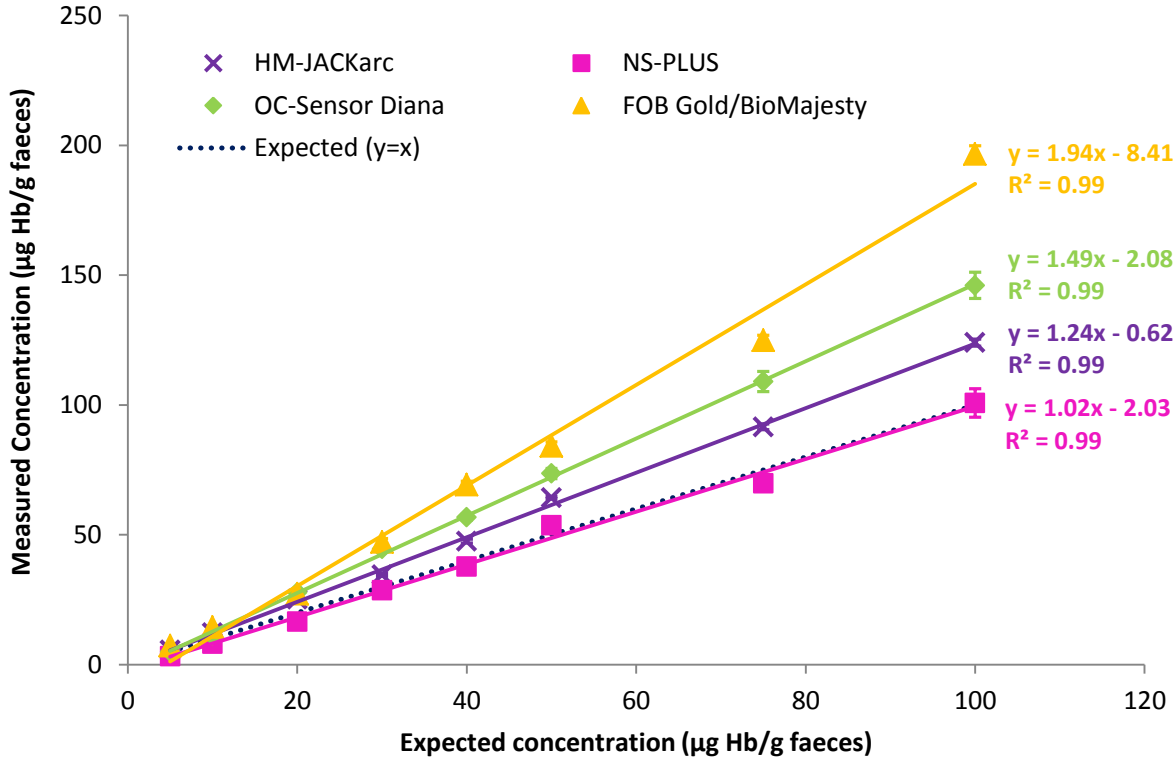


Figure 6: Precision profiles of all analysers from 0 – 100 µg Hb/g faeces. (Error bars show ± 1 standard deviation.)



Hook/prozone effect

Immunoassays may give erroneously low values at exceptionally high concentrations, an effect known as the hook or prozone effect. All analysers were assessed to determine their performance at very high Hb concentrations (Table 8).

Table 8: Analysis of the hook/prozone effect for each analyser. Analytical results are in black and error codes in red.

GMEC expected concentration *(µg Hb/g faeces)*	GMEC measured concentration *(µg Hb/g faeces)*			
	HM- JACKarc	*NS-PLUS C15*	*OC-SENSOR DIANA*	*FOB Gold/ BioMajesty*
200,000	441 P	60 P	OR	149
100,000	431 P	HR P	OR	309 HR
50,000	428 P	66950 P	OR	303 HR
25,000	432 P	28705	36150	258 HR
12,500	460 P	14690	18725	188 HR

Key: P = prozone detected; OR = over range; HR = the result was high and automatically diluted.

The HM-JACKarc is not designed to give accurate results in samples above 400 µg Hb/g faeces, and in general use the analyser will give a result of '>400 µg Hb/g faeces' rather than giving numerical values. For this study numerical values were made available by changing the analyser set-up. 'P' indicates that the analyser detected a hook/prozone effect and warns the user that the result could be falsely low.

The NS-PLUS C15 showed evidence of hook/prozone effect on two out of four samples measured at the highest concentration (200,000 µg Hb/g faeces), presenting false low results with no indication that they were inaccurate, although this is an unexpected concentration in the normal sampling procedure and the results were positive. However, the other two samples measured at that concentration and also all samples measured at 100,000 and 50,000 µg Hb/g faeces gave the error code 90, which shows these results were picked up as over range hook/prozone effect samples.

The OC-SENSOR DIANA gave the 'over range' error code 'OR' on all samples. The OR code is displayed when the result is higher than the upper limit of the analytical range. On dilution, the re-tested samples at concentrations of 12,500 and 25,000 µg Hb/g faeces gave concentrations of 18,725 and 36,150 µg Hb/g faeces respectively. All samples measured at 50,000, 100,000 and 200,000 µg Hb/g faeces gave the OR code on the re-tested diluted samples.

The BioMajesty consistently gave a result of 785 ng Hb/mL of buffer (± 14.0) (equivalent to 149 µg Hb/g faeces, ± 2.6) for all very highly concentrated samples. This result was flagged with 'h' which indicated that the concentration was above the cut-off limit, but did not require diluting; this error is typical of the hook/prozone effect. All other results were flagged with 'H' and subsequently diluted (giving the result code 'HR'), but still gave results well below the expected values, with no indication that there was the possibility of hook/prozone effect. If these results were to be incorporated into a risk score (see Introduction) this could contribute to a misleading measure of CRC risk.

Stability

Stability of measured Hb was assessed in samples with blood added directly to the collection buffer, and in samples where faecal samples had been added to the collection devices. The study examined four concentrations of Hb at four different temperatures. The results are provided in Table 9.

Hb stability in samples subjected to sustained temperatures of 20°C and below was generally good at all four concentrations and with all four analytical systems. Stability at 35°C was much poorer, particularly in faecal samples spiked with Hb (see Table 9 and Appendices 5-8 for graphical representation of the data).

Haemoglobin in the HM-JACKarc collection tubes (in the absence of faeces) is quoted by Kyowa Medex to be stable for 120 days at 4°C, and 14 days at 25°C. These claims are supported in this study, although this evaluation did not examine samples exposed to a sustained temperature of 25°C and it did show that at 35°C stability was poor, particularly in faecal samples spiked with Hb. At 35°C the concentration of Hb decreased by at least 50% within 3 days at all concentrations tested. The faeces-free solution was much more stable, particularly at high concentrations – it took more than 10 days for the concentration of Hb to decrease below 50% of the initial concentration. Samples that were initially positive became negative after 2 days (at the two middle concentrations) and after 6 days with the highest concentration, which could result in falsely negative results if sampled after this time.

Hb in the NS-PLUS C15 collection tube (in the absence of faeces) is quoted by Alfresa to be stable for 7 days at 2-8°C, and 3 days at 18-25°C. These claims were supported in this study although the evaluation did not examine samples exposed to a sustained temperature of 25°C. GMEC found that at 35°C in faecal samples spiked with Hb, samples at highest concentration dropped by 50% in less than three days. During the period tested (28 days) the samples remained positive when using the manufacturer's suggested cut-off of 20 µg Hb/g faeces.

Eiken quote stability for Hb in the OC-SENSOR OC-Auto Sampling Bottle 3 as 7 days at room temperature, and 14 days between 2 and 10°C. These claims were confirmed. At 35°C, as with the NS-PLUS C15, the faecal sample with the highest initial concentration decreased to below 50% of the initial concentration within 2 days. However, all samples positive at the start remained above a cut-off of 20 µg Hb/g faeces after 30 days. The OC-SENSOR was similar to the NS-PLUS C15 in that faecal Hb degraded faster than Hb diluted in buffer, with the level dropping below 50% within 4-18 days (at 35°C).

Sentinel state that samples are stable in the sample collection devices for 14 days at 2-8°C, or 7 days at 15-30°C. These claims were confirmed and Hb in sample buffer with no faecal material showed very little sample deterioration over 30 days. However, at 35°C in a faecal sample the Hb decreased by 50% within 9 days at all concentrations.

Table 9: Measured stability of diluted Hb and faecal samples spiked with Hb

Temperature	*- 20°C*	*4°C*	*20°C*	*35°C*			
Concentration (µg Hb/g faeces)	*All concs*	*All concs*	*All concs*	*10*	*40*	*80*	*160*
HM-JACKarc				Days for 50% fall from initial conc			
Hb in buffer	STS	STS	STS	2d	5d	10d	12d
Hb in faeces	STS	STS	STS	2d	3d	3d	3d
NS-PLUS C15				Days for 50% fall from initial conc			
Hb in buffer	STS	STS	STS	19d	25d	3d	3d
Hb in faeces	STS	STS	STS	STS	STS	STS	4d
OC-SENSOR				Days for 50% fall from initial conc			
Hb in buffer	STS	STS	STS	6d	11d	18d	4d
Hb in faeces	STS	STS	STS	STS	STS	STS	2d
FOB Gold/BioMajesty				Days for 50% fall from initial conc			
Hb in buffer	STS	STS	STS	STS	STS	STS	STS
Hb in faeces	STS	STS	STS	9d	8d	9d	8d

KEY: STS – Stable throughout study (*i.e.* the concentration of Hb did not fall below 50% of the initial concentration during the study). Conc – concentration.

Numerical values show the day on which the measured concentration fell below 50% of the initial measured concentration.

Collection devices

All collection devices consist of a vessel that contains a buffer (a solution designed to limit the degradation of Hb), and a probe to collect the faecal sample. All the probes are connected to the lid of the device.

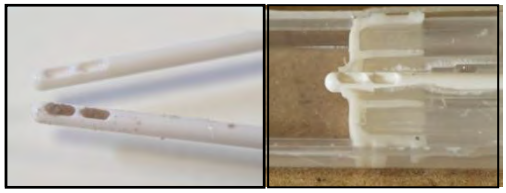


Figure 7: HM-JACKarc collection probe dimples, with and without sample, and collection device septum.

THE HM-JACKarc collection probe consists of a plastic stick (with two small dimples) at one end that is used to collect approximately 2 mg of faeces, and at the other end it has a screw-on lid. A paper label seals the lid to the collection tube and when broken for sample collection the seal provides a useful indicator that the device has been opened. The open device has three holes in the top and the sample probe is returned to the central hole after sample collection.

The neck of the collection tube has a rubber septum that scrapes off excess faecal sample to control the amount that enters the buffer. The tube is placed on the analyser rack with the lid pointing downwards; the other end is covered by a small paper and then a plastic seal. The analyser specimen probe pierces the plastic seal to reach the sample.

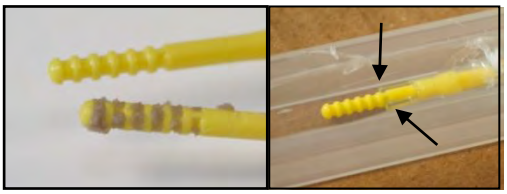


Figure 8: NS-PLUS collection probe, with and without sample and collection device cleaning teeth.

THE NS-PLUS collection device is a plastic probe with six grooves that collect approximately 10 mg of faecal sample. The probe is attached to a flat easy-to-hold lid.

The collection device contains a narrow neck to control the amount of sample transferred into the buffer. At the entrance to the buffer compartment two 'teeth' scrape the collected sample from the probe and into the collection buffer.

The blue-coloured buffer changes to green after a sample has been added, which is a useful indicator that the device has been used by the screening participant. The sample tube is placed with the lid downwards in the analyser rack and the foil seal facing upwards. The analyser specimen probe pierces the foil to collect the sample below.

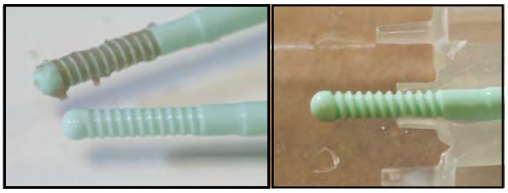


Figure 9: OC-AUTO Sampling Bottle 3 probe with and without sample; and the sampling bottle neck, narrowed to remove excess sample.

THE OC-SENSOR DIANA uses the new OC-Auto Sampling Bottle 3. The probe is plastic and attached to a twist and push lid. Eleven fine grooves at one end collect approximately 10 mg of faecal matter.

The collection device contains a plastic narrow neck to control the amount of sample entering the buffer. The collection tube is placed on the analyser rack with the lid downwards and a foil seal upwards.

The analyser pierces the foil and uses a hammer to squeeze the bottle and force the buffer through a filter into the analytical compartment. The filter removes particulate matter ensuring that the analyser sample probe does not become blocked. Once the pressure is removed any solution remaining in the analytical compartment returns to the main compartment for repeat analysis, if required.

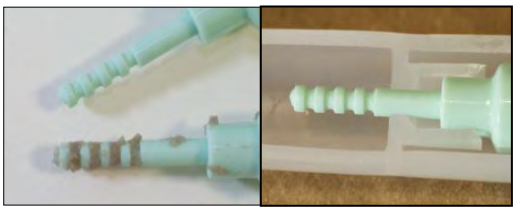


Figure 10: Sentinel FOB Gold collection probe, with and without sample; and the collection tube excess sample remover.

THE FOB GOLD collection probe (FOB Gold Tube) used on the BioMajesty analyser consists of a plastic stick attached to a screw-on lid. Four broad and deep grooves collect approximately 10 mg of sample.

The collection device contains a narrow neck and a septum to remove excess sample and control the quantity entering the buffer compartment. The device is placed on the analyser with the green lid downwards.

The other end of the device has a white plastic screw-on lid with a small seal to hold it in place. The white plastic lid must be removed before placing on the analyser, and should be replaced following analysis. If the white lid is removed by a screening participant, the collection buffer can be lost easily making the device unusable.

Unit conversion values

Manufacturers have conventionally reported FIT concentrations as the amount of Hb (ng) in the collection buffer (mL). Since sampling devices collect different amounts of faecal sample into different volumes of buffer, the reported concentrations cannot be compared between devices. Following an initiative by the WEO EWG on FIT, all manufacturers have been advised that they should adopt the use of µg Hb per g faeces [10].

The adoption of these units requires an accurate measure of the volume of buffer in the collection tube, and the mean mass of faecal sample that is likely to be added to the collection device buffer. In product descriptions, each manufacturer provides quoted values of the volume of buffer used in their device and their estimate of expected faecal sample mass. These manufacturers' values have been used throughout this report and have enabled us to convert Hb concentrations in buffer (ng Hb/mL buffer) to Hb in faeces (µg Hb/g faeces).

GMEC has performed an independent assessment of sampled faecal load and buffer volume using the same method for each device. The buffer volume was determined using 20 collection devices that were weighed, their liquid contents removed and the devices dried in an incubator for 1 week. The devices were then re-weighed and the difference in initial and final weights used to give an approximate buffer volume (assuming a specific gravity for the buffer solution of 1.0 (the same as water)).

The weight of sample collected was determined using an artificial faecal matrix (Kyokuto Pharmaceutical Industrial Co., Ltd.) prepared to a consistency similar to soft faeces. A collection device was cut in half to allow access to the tip of the probe. The matrix was sampled, the probe pushed into the device and then the tip of the probe was cut off (at the point at which it emerged from the septum) and weighed. The tips were then washed, dried and re-weighed. The difference in mass between the two measurements was thereby determined as an estimate of the weight of the sample collected. The GMEC-derived conversion factors are provided in Table 10.

The mass of faeces collected by a sample probe will be dependent upon a range of factors including the nature of the faecal sample. For the GMEC estimation, the artificial faecal matrix was a rice-based product with a specified volume of added liquid. Further work needs to be undertaken to determine the effect of different matrices on the sample probes to provide confidence in the assigned sample mass.

Table 10: Conversion factors provided by manufacturers and determined by GMEC

	Manufacturer quoted values			*GMEC measurements*		
	Sample mass (mg)	*Buffer volume (mL)*	*Conversion factor*	*Sample mass (mg (±SD))*	*Buffer volume (mL (±SD))*	*Conversion factor*
HM-JACKarc	2	2.0	1.00	4 (± 1.2)	2.0 (± 0.02)	0.50
NS-PLUS C15	10	1.9	0.19	14 (± 3.9)	1.9 (± 0.03)	0.14
OC-SENSOR DIANA	10	2.0	0.20	15 (± 2.0)	2.0 (± 0.03)	0.13
FOB Gold/BioMajesty	10	1.7	0.17	16 (± 2.8)	1.8 (± 0.05)	0.11

Application of the GMEC conversion factors (Table 10) that are different from those quoted by manufacturers (see also Table 1) will change the interpretation of some of the evaluation data. For example, compare the graphs in Figures 11a and b. Figure 11a illustrates precision calculated using the conversion factor provided by the manufacturer (as per Figure 6). Figure 11b illustrates precision calculated using the GMEC-determined conversion factor. The differences are described below.

- The BioMajesty continues to have a positive bias, but the measured concentration is much closer to the expected concentration.
- The HM-JACKarc, NS-PLUS C15 and OC-SENSOR DIANA all become negatively biased, the OC-SENSOR DIANA results becoming much closer to expected concentrations and the HM-JACKarc and NS-PLUS C15 moving further away from the expected concentrations.

Figure 11a: Precision profiles for all analysers between 0 and 100 µg Hb/g faeces using manufacturers' conversion factors. Error bars show ± 1 standard deviation.

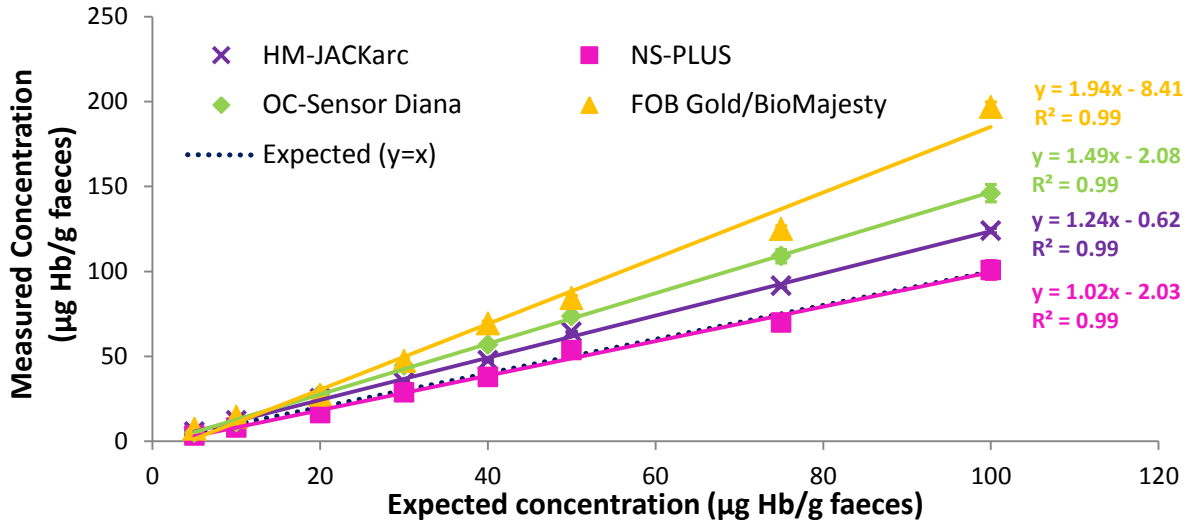
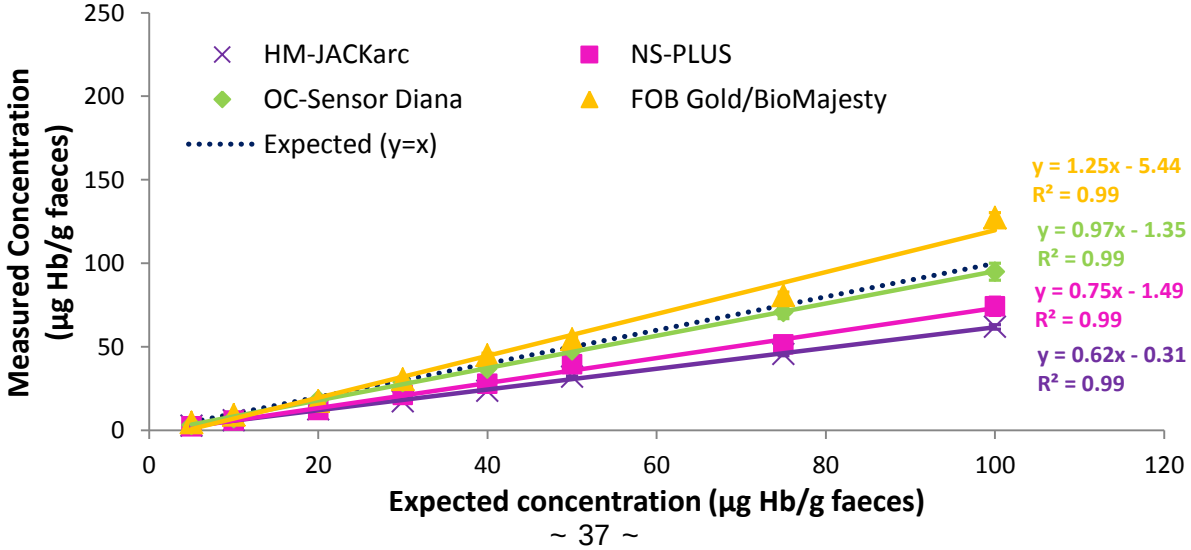


Figure 11b: Precision profiles for all analysers between 0 and 100 µg Hb/g faeces using GMEC-measured conversion factors. Error bars show ± 1 standard deviation.



Participant survey

The four FIT collection devices and a short questionnaire were sent to 25 volunteer participants aged between 25 and 85 years. Each participant was asked to collect a sample of faeces with each device and then answer the questions.

Participants were asked to record their satisfaction with the mechanism/method for:

- Opening the device
- Collecting a faecal sample
- Returning the sample and probe to the device
- Closing the device.

Participants were invited to comment on the strengths and weaknesses of each device and where they would like to see improvements. Participants were also asked which devices they would be happy to use, and which of the four devices they preferred. The results are presented in Figures 12-17.

Participants found the HM-JACK device small and awkward to use. Replacement of the probe into the device was made more difficult because it has three potential entry holes at the head of the device and poor eye sight was thought likely to accentuate this design weakness. Participants reported incidents where faeces did not appear to adhere to the dimples that are a unique feature of this device. Participants were left concerned that kits would give negative results because no faeces would be present in the test buffer.

Participants found the size and shape of the lid of the NS-PLUS C15 collection device easy to hold and open. Participants were concerned that unscrewing the lid might prove difficult for individuals with restricted dexterity, such as those with arthritis, due to stiffness of the screw thread. Overall the NS-PLUS C15 collection device performed well and was thought the easiest to use.

Most participants were happy to use the OC-SENSOR device and it was thought to be the easiest to open. The size of the entry hole at the top of the device was thought by some participants to be too small and individuals with restricted dexterity could find it difficult to return the collection probe to the tube.

Participants found the FOB GOLD device easiest to use for sample collection, returning the probe to the tube and closing the device. Participants repeated the concern reported in the earlier GMEC evaluation [11] that it was easy to open the wrong end of the device and release the sample buffer. When asked which device participants preferred, this device ranked just behind NS-PLUS C15.

Figure 12: How easy was it to open the device?

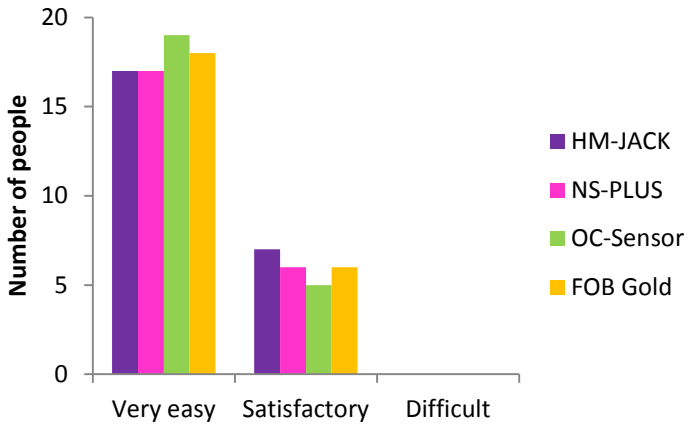


Figure 13: How easy was it to collect the sample?

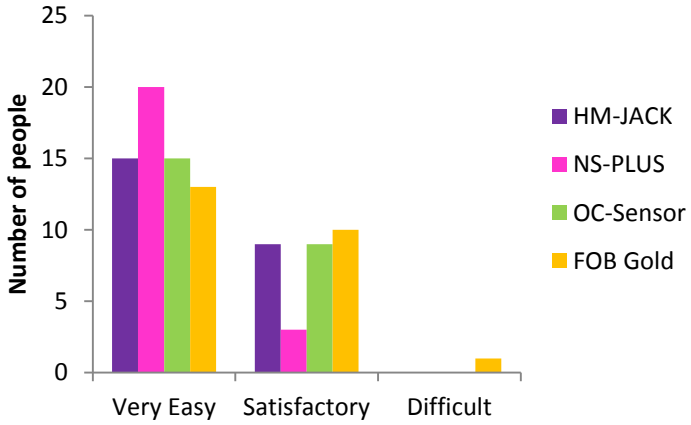


Figure 14: How easy was it to replace the sample and sample probe into the collection tube?

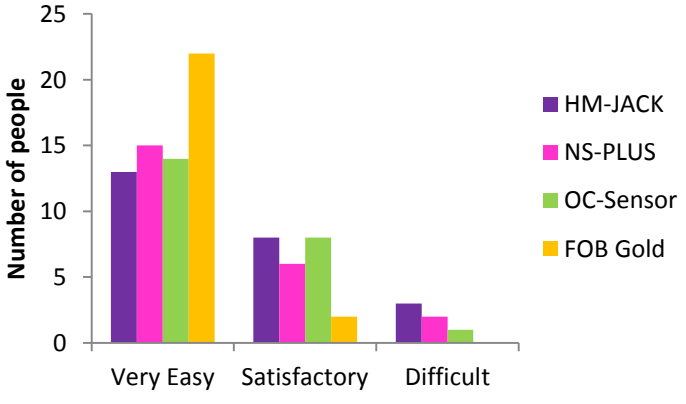


Figure 15: How easy was it to close the device?

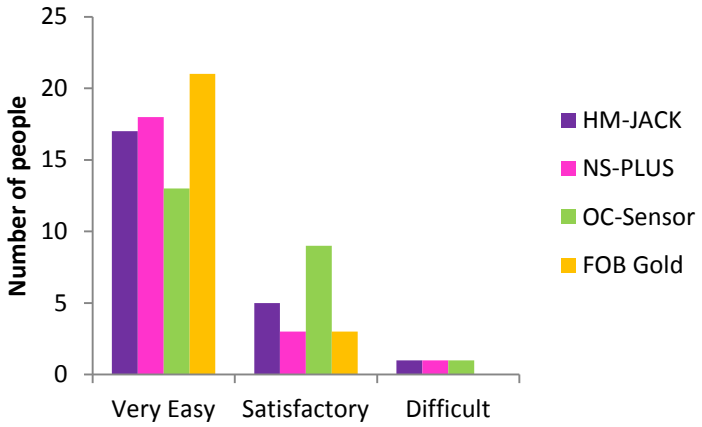


Figure 16: Which devices are you happy to use, which ones are you not happy to use?

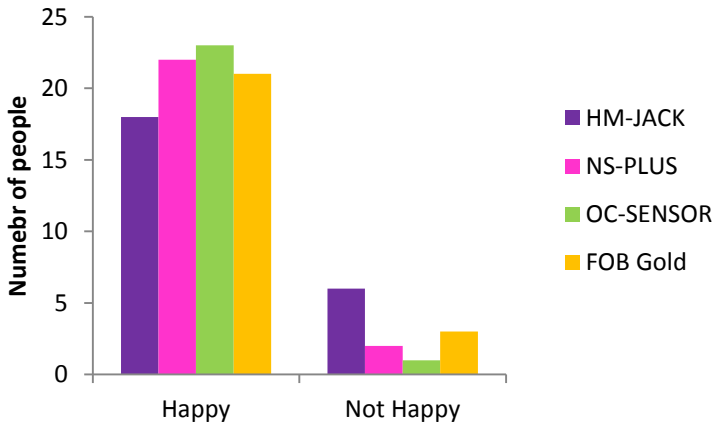
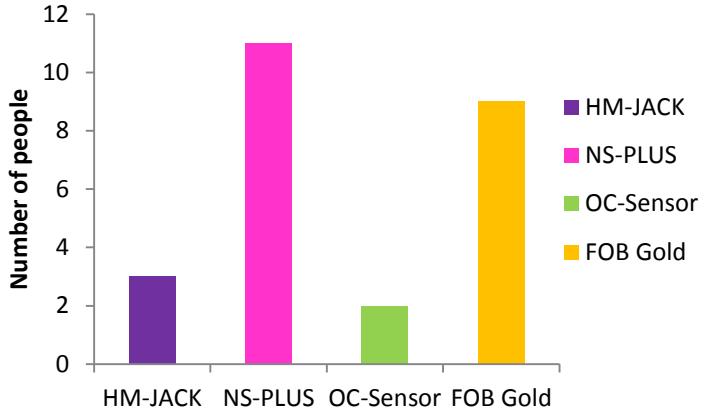


Figure 17: Which is your preferred device?



Analytical system user evaluation

The suppliers and manufacturers were asked to provide a list of current users of their systems who would be willing to complete an evaluation questionnaire. We acknowledge that this may not be a representative sample of users.

Only one reply was received from a laboratory analysing more than 1,000 samples per week; the other replies came from laboratories analysing 50–1,000 samples per week. No replies were received from laboratories using the BioMajesty.

Overall, there were very few technical issues reported, and those reported to the supplier had been dealt with in a timely and satisfactory manner. Most users were happy with their analyser and the support they receive. One user of an NS-PLUS C15 supplied by Alere in Canada, mentioned that consumables were frequently not available when ordered and were placed on 'back order'.

Users stated significant differences in the length of time that they required to perform routine maintenance tasks. Such differences are surprising and it suggests that users were trained differently or that the description of tasks in the user manual may be ambiguous and interpreted differently by different users (instruments affected: HM-JACKarc and NS-PLUS C15).

Ease-of-use

Table 11 compares procedures necessary to use the four analysers and highlights where improvement could be made.

HM-JACKarc

The HM-JACKarc is an easy-to-use bench-top analyser, with a simple touch screen and an easy-to-follow system of menus. Analyser start-up is simple, and it has an automatic feature to prepare the analyser so that it is 'on' and ready for use at a time programmed by the operator. Maintenance is easy to perform and analyser start-up and shut-down procedures are very simple.

GMEC found this analyser simple to use and suitable for use by staff with some laboratory experience. The small capacity of the HM-JACKarc makes it best suited to a small to medium rather than a large screening laboratory.

NS-PLUS C15

The NS-PLUS C15 is a very simple to use bench-top analyser, which is well designed with easy-to-use software. The analyser has good monitoring systems for reagent and waste levels, and barcodes on reagents to make it easy to replenish them during analysis. The software easily records and tracks the use of different reagent LOTs. The water and wash solutions can be topped up easily during analysis, and the waste has a monitor and alarm to alert the user when it needs to be emptied.

The simplicity of the NS-PLUS C15 software and analyser make it suitable for use by staff with limited laboratory experience, as part of a large screening programme.

OC-SENSOR DIANA

The OC-SENSOR DIANA is also an easy-to-use bench-top analyser. Analyser start-up is simple, and it has an automatic feature to prepare the analyser so that it is 'on' and ready for use at a time programmed by the operator. The calibrator and QC material are supplied already prepared, which removes the possibility of introducing errors during the process of reconstitution.

The OC-SENSOR DIANA analyser supplied for the evaluation was replaced during the period of the evaluation due to a failure of internal plumbing. The instrument was replaced within two days of the fault being identified. GMEC noted that the wording on some of the menus was slightly different, which could lead to confusion or the requirement to rewrite standard operating procedures when analysers are changed.

Overall, this analyser is suitable for use by experienced laboratory staff.

FOB Gold/BioMajesty

The BioMajesty is a large floor-standing analyser, which is complex to use, but enables monitoring and checking of systems during operation. The instrument monitors reagent levels and informs the operator when the analysis will be completed. Similar to the OC-SENSOR, the BioMajesty has liquid calibrators and QC materials, which obviates the need for, and potential errors associated with, reconstitution.

Whilst it is possible to connect the BioMajesty to a track system, this facility has not been evaluated by the GMEC team.

Overall, the GMEC team found the BioMajesty a challenging analyser to use; it was unnecessarily complex for the analysis of a single marker (FIT). Staff using the analyser would require extensive training.

Table 11: Ease-of-use of analysers

	HM-JACKarc	*NS-PLUS C15*	*OC-SENSOR DIANA*	*FOB Gold/BioMajesty*
Preparation to use	Analyser start-up simple, one hour warm up but auto-start facility at user-specified time; Reagents are easy to load, though latex buffer requires three primes through reagent line.	Must ensure analyser and computer are switched on in correct order; 12 mins to cool reagent tray; auto-start available (not tested by GMEC).	Analyser start-up is simple; has auto-start facility at user-specified time; buffer requires 30-50 mins to warm if stored refrigerated; samples require one hour warm-up from fridge.	Start-up wash 27-35 mins, which can be part of the automated start-up procedure. Additional initiation and prime routines not part of automatic start-up.
Calibration/QC analysis	Requires reconstitution with accurate pipette and then wait total of 30 mins; two levels of calibrant need to be prepared. Calibrant aliquots can be frozen. Calibration software easy to set-up with handheld barcode reader.	Requires reconstitution with accurate pipette and can use immediately. Single level of calibrant auto-diluted to seven concentrations by analyser. Aliquots can be frozen. Calibration software easy to set-up.	Liquid calibrant and QC – no preparation; easy to dispense with built in dropper and levels are easily identified. Single level of calibrant auto-diluted to seven concentrations by analyser. Calibration software difficult to set up.	Liquid calibrant and QC. Compared with other systems the metal foil lids that cover the rubber stoppers are difficult to remove. Foil lids are different colours but once removed rubber stoppers same colour. Six vials are required for calibration and must be put into cups in correct order. Calibration software difficult to set up.
QC result monitoring	Daily QC results are printed by the analyser on thermo paper and cumulative data are easy to see on screen.	Daily QC results are printed and cumulative data are easy to see on screen.	Daily QC results are printed and cumulative data are easy to see on screen.	Several steps to find daily QC results and more to find cumulative data - not intuitive, data do not print automatically.

Table 11: Ease-of-use of analysers (continued)

	HM-JACKarc	*NS-PLUS C15*	*OC-SENSOR DIANA*	*FOB Gold/BioMajesty*
Sample loading	Racks carry 10 samples. The racks can be easily knocked over when on the bench. Care needed when loading samples to prevent jams; tubes cannot be loaded the wrong way up but barcode can be obscured. Racks are loaded onto analyser one by one.	Racks carry 10 samples and clip together to help transfer to analyser; stable on bench; easy to place samples in racks; samples cannot be loaded the wrong way up; but can be loaded so barcode invisible (easy to enter unread barcodes); racks loaded onto analyser individually.	Racks carry 10 samples. Racks are unstable on bench but secure if loaded in 15 rack transporting tray (150 samples) which clips into loading area; easy to load samples in racks; can be loaded upside down (which damages analyser) and with barcode invisible (barcodes can be edited in).	Samples loaded individually onto the sample ring (takes 84 samples). Must remove lids and align barcodes. Use of analyser track will improve efficiency (not assessed). Manual test request for each individual sample.
Sample unloading	Racks move to different area of analyser when finished. Can then remove 100 samples on a tray.	Blue indicator light shown when racks can be unloaded, (removed individually).	Racks move to different area of analyser when analysed. Can then remove 100 samples on a tray.	Samples need to be unloaded individually and lids replaced (care to avoid cross-sample contamination).
Dilution of out-of-range samples	Automated dilutions are not possible on this analyser.	Analyser dilution can be performed without sample reload - reduces analytical productivity.	Analyser dilution performed after reloading sample on a rack with diluent and dilution cups.	Analyser dilution can be performed without sample reload - reduces analytical productivity.

Table 11: Ease-of-use of analysers (continued)

	HM-JACKarc	*NS-PLUS C15*	*OC-SENSOR DIANA*	*FOB Gold/BioMajesty*
Reagent/consumable management	**Cuvettes:** single use. Used cuvettes are removed from the analyser and replacement cuvettes are picked up from a rack automatically. The analyser does not have a facility to monitor the availability of replacement cuvettes, a rack of which must be loaded manually. **Latex reagent:** analyser holds only one bottle, volume has auto-volume-monitoring, run can be paused to change during analysis. **Buffer:** no auto-volume-monitoring so can run-out without warning. **Liquid waste:** no auto-volume-monitoring so can overflow unless connected to floor drain. Cannot be emptied during analysis.	**Cuvettes:** reusable so no daily replenishment required. **Reagent 1&2:** 3-4 bottles of each stored on analyser, can replenish during analysis. **Diluent:** auto-volume-monitoring, can replenish during analysis. **Liquid waste:** auto-volume-monitoring, can be emptied during analysis. Easy identification and tracking of reagent lot numbers.	**Cuvettes:** reusable so no daily replenishment required. **Latex reagent**: 2 bottles stored on analyser, can replenish when analyser is paused. **Buffer**: auto-volume-monitoring with manual update for new bottles. Inaccurate monitor when using extra buffer priming; it is possible to replenish buffer during analysis. **Liquid waste**: auto-volume-monitoring, cannot be emptied during analysis. Software does not store reagent lot no. information.	**Cuvettes:** reusable so no daily replenishment required. **Reagents:** 3 bottles stored on analyser, can replenish when analyser is paused**.** **Liquid waste:** plumbed directly into main drain. Reagent bottles used in the evaluation had no barcodes, did not fit on analyser and manual transfer of reagent to bottles which did fit the analyser was required. (New bottles under development from Sentinel.)
Maintenance	Quick and easy to perform daily maintenance; minimal additional maintenance	Quick and easy to perform daily maintenance; other maintenance not assessed.	Quick and easy to perform daily maintenance; other maintenance minimal.	Quick and easy to perform daily maintenance; other maintenance not assessed.

Table 11: Ease-of-use of analysers (continued)

	HM-JACKarc	*NS-PLUS C15*	*OC-SENSOR DIANA*	*FOB Gold/BioMajesty*
Close down end of day	Simple.	Simple.	Simple but shut down process takes 17 mins.	Simple but shut down wash takes 27-35 mins.
Instructions for use	Some on-screen help; manual and Quick Use guide easy to use. Improved index of manual required.	On-screen training videos useful and clear, good manual and good package inserts.	On-screen help available and useful; can be difficult to find required section in manual but when found is useful; package inserts good but reagent insert has unnecessary information about other components.	Can be difficult to find required section in paper manual and when found is difficult to understand; good package inserts for FOB Gold.
Troubleshooting	Easy to understand error messages and to find information in manual.	Easy to understand error messages and to find information in manual.	Most error messages easy to understand and find information in manual though some more difficult.	Error messages difficult to understand and difficult to find further information in manual.
Control of analyser	Integrated computer, touch screen, easy to follow software/menu.	Separate PC required, no touch screen, but easy to use software with aid of colour coding and animations.	Integrated computer, touch screen, software menu can be confusing but analysis menu is simple.	Separate PC required, no touch screen, software complex to use.
Staff training and experience required	Can be used by staff with basic analyser training/experience, when supervised by staff experienced with auto-analysers.	Can be used by staff with basic analyser training/experience, when supervised by staff experienced with auto-analysers.	Can be used by staff with intermediate analyser training/ experience, with supervision by staff experienced with auto-analysers.	Needs to be used by experienced laboratory staff provided with extensive analyser training.

Consumables

Table 12 below describes the storage requirements of the reagents and consumables required for each analyser, and the volume each required to perform 5,000 tests, a typical daily total for the BCSP Southern Hub.

The HM-JACKarc would require 25 bottles of latex for a day's work, each placed on the analyser one at a time. The NS-PLUS C15 requires 17 bottles if no dilutions are carried out; four bottles of each reagent can be held on the analyser giving a capacity of 1,200 tests (if dilutions are enabled only three bottles of each reagent can be held on the analyser, reducing onboard capacity to 900 tests). The OC-SENSOR DIANA and the BioMajesty would each require 20 bottles of reagent. The OC-SENSOR DIANA can have two bottles on the analyser at a time (500 tests).

Two of the current Sentinel 20 mL reagent bottles can be emptied into the analyser reagent container and three of these containers can be held on the analyser, providing a capacity of 1,500 tests. Sentinel has now developed replacement bottles for the BioMajesty with three times the volume of reagent, which increases onboard capacity to 2,250 tests. The new containers have a barcode to enable easier loading of the reagents, but these have not been evaluated by GMEC.

The HM-JACKarc produces the largest mass of solid waste. The analyser uses non-recyclable plastic for its single-use cuvettes and single-use cuvette racks.

The three other analysers evaluated use reusable cuvettes, which are cleaned between each analysis. All reusable cuvettes have a recommended lifetime and require replacement: NS-PLUS C15 after 200 analyses in a cuvette which is approximately 10,000 on the analyser (every 2–3 days for the Southern Hub workload); OC-SENSOR DIANA after 100,000 analyses on the analyser (every 20–30 working days for the Southern Hub); BioMajesty every two years, depending on throughput and evidence from quality control monitoring.

Table 12: Consumables and storage conditions required for each analyser, provided by manufacturers (N/A: not applicable)

		HM-JACKarc	*NS-PLUS C15*	*OC-SENSOR DIANA*	*FOB Gold/BioMajesty*
Collection devices	*Before use*	2-30°C until expiry date	1-30°C until expiry date	1-30°C until expiry date (18 mths)	2-30°C until expiry date
	With sample	120 days at 4°C 14 days at 25°C	7 days at 2-8°C 3 days at 18-25°C	14 days at 2-10°C 7 days at 20-25°C	14 days at 2-8°C 7 days at 15-30°C
Latex/Reagent 1	*Unopened*	2-8°C until expiry date	2-8°C until expiry date	2-10°C until expiry date (up to 12 mths)	2-8°C until expiry date
	Opened	2-8°C until expiry date	1 month at 2-8°C	14 days at 2-10°C	30 days at 2-8°C
	On analyser	20 accumulated hours, kept at 2-8°C while not on analyser		7 days	30 days at 2-12°C
	Amount required for 5,000 sample tests	25 bottles (200 tests per bottle)	17 bottles (300 tests per bottle)	20 bottles (250 tests per bottle)	20 bottles (250 tests per bottle)
Buffer/Reagent 2	*Unopened*	2-8°C until expiry date	2-8°C until expiry date	2-10°C until expiry date (up to 12 mths)	2-8°C until expiry date
	Opened	2-8°C until expiry date	1 month at 2-8°C	2-10°C (up to 2 mths)	30 days at 2-8°C
	On analyser	14 accumulated days, with time in between at 2-8°C		1 month	30 days at 2-12°C
	Amount required for 5,000 sample tests	Not provided	17 bottles (300 tests per bottle)	4 bottles (1,250 tests per bottle)	20 bottles (250 tests per bottle)
Diluent	*Unopened*	N/A	2-8°C until expiry date	2-10°C until expiry date (up to 12 mths)	2-8°C until expiry date
	Opened	N/A	2-8°C until expiry date	2-10°C until expiry date (up to 12 mths)	30 days at 2-8°C
	On analyser	N/A	2-8°C until expiry date	N/A	30 days at 2-12°C

Table 12: Consumables and storage conditions required for each analyser, provided by manufacturers (continued) (N/A: not applicable)

		HM-JACKarc	*NS-PLUS C15*	*OC-SENSOR DIANA*	*FOB Gold/BioMajesty*
Wash Solution	*Concentrated solution*	2-25°C until expiry date	1-30°C until expiry date	Domestic bleach room temperature	1-30°C until expiry date
	Diluted	1 month		14 days	
	Amount required for 5,000 sample tests	25 L (25 mL undiluted wash concentrate)		14 litres	
Calibrator	*Unopened*	2-8°C until expiry date	2-8°C until expiry date	2-10°C until expiry date (≤ 12 mths)	2-8°C until expiry date
	Reconstituted	1 week at 2-8°C 1 month at -20°C	Use once only	Ready to use 2-10°C until expiry date (≤ 12 mths)	Open: 4 weeks at 2-8°C Extra 6 mths beyond expiry date if frozen in small aliquots at -20°C
Calibrator Solution	*Unopened*	Uses distilled water	2-8°C until expiry date	N/A	N/A
	Opened		2-8°C until expiry date	N/A	N/A
Quality controls	*Unopened*	2-8°C until expiry date	2-8°C until expiry date	2-10°C until expiry date (up to 12 mths)	2-8°C until expiry date
	Reconstituted	1 week at 2-8°C; 1 month at -30°C	5 days at 2-8°C	Ready to use	Open: 4 weeks at 2-8°C An extra 6 mths beyond expiry date if frozen in small aliquots at -20°C
Cuvettes	*Number required for 5,000 sample tests*	125 racks of cuvettes (40 per rack)	Change whole ring after 10,000 tests	One set (approximately 100,000 reactions)	One set (change every 2 years, or as throughput demands)
Reaction tips	*Number required for 5,000 sample tests*	Reusable probes	Change after 5,000 tests	Reusable probes	Reusable probes

Maintenance and servicing

All analysers evaluated for this report require daily maintenance and cleaning. The BioMajesty is designed for high volume multi-analyte analysis and requires the most cleaning, including two long analyser washes every day (27-35 minutes each). The frequency of refilling wash solution and water bottles, and emptying waste containers depends on the workload, and whether the analysers are connected to mains water and drainage.

The HM-JACKarc required the least cleaning because it had single-use cuvettes; only reagent lines and reagent and sample probes need to be cleaned daily. This analyser therefore created the least liquid waste.

The NS-PLUS C15 and OC-SENSOR DIANA both created more liquid waste because of the need to wash the reusable cuvettes. The OC-SENSOR DIANA had additional wash procedures that used more deionised water and created more liquid waste.

The BioMajesty required washes in addition to those for cuvettes and for conditioning and these washes used more hazardous solutions than those used by the other analysers.

Details of the start-up, daily, weekly and monthly maintenance/procedures, are given in Table 13. Details are also provided on the preparation and frequency of analysis of calibrators and quality control material.

Table 13: Maintenance and servicing of the analysers (N/A: not applicable)

		HM-JACKarc	*NS-PLUS C15*	*OC-SENSOR DIANA*	*FOB Gold/BioMajesty*
Maintenance	*Daily*	Clean all analyser surfaces. Wash (with either buffer or water).	Wipe all analyser surfaces.	Clean with a cloth: the panel and the rack transport system.	Clean all analyser surfaces. Perform a WASH 2 and 3 (one at start, one at end of day). Wipe probes.
	Weekly	Wash through the system after replacing the buffer with water. Remove cuvette waste and replace waste bag.	N/A	Clean external surfaces and the W, R- and S-nozzles, the racks and the trays.	Perform a measurement of the optical density of each cuvette.
	Monthly	Clean probes with warm water.	Clean fan filter. Wash waste bottle. Clean cuvettes and reagent lines.	Soak cell, nozzle soak and perform a cuvette blank measurement. Clean the tanks.	Soak and wash mixing rods (15 mins).
	Start up	One hour wait to allow lamp output to stabilise. 1-3 system washes (if buffer replaced between uses, each wash takes 4 mins).	12 mins to allow analyser to reach correct temperature.	At least 30 mins for the buffer to warm up (can take up to 50 mins).	Initialise, prime reagent lines and wash. Total time 30-40 mins.
	Shut down	One wash, approximately 3 mins. Switch off the analyser.	Switch off the analyser.	Wash takes 10 mins.	Wash, takes 27-35 mins.

Table 13: Maintenance and servicing of the analysers (continued)

		HM-JACKarc	*NS-PLUS C15*	*OC-SENSOR DIANA*	*FOB Gold/BioMajesty*
Calibration	*Preparation of material*	Add distilled water to lyophilised material, leave for 20 mins, mix, leave for further 10 mins.	Add calibrator diluent to lyophilised material, mix.	Provided in liquid form ready to use.	Provided in liquid form ready to use.
	Frequency of calibration	Instructions for use state every 2 days.	At change of reagent LOT.	At change of reagent LOT.	At change of reagent LOT or maximum of 30 days.
Quality Control	*Preparation of material*	Add distilled water to lyophilised material, leave to stand for 20 mins, mix, leave to stand for further 10 mins.	Add diluent to lyophilised material, mix.	Provided in liquid form ready to use.	Provided in liquid form ready to use.
	Frequency of measurement	Daily	Daily	Daily	Daily

Analyser requirements

The five BCSP Hubs in England have different analytical workloads. For an average daily workload of 5,000 samples, such as might be experienced by the Southern Hub, the estimated number of analysers required to comfortably complete the workload on the day of receipt is given in Table 14 (based on an 8-hour working day, during which sample analysis would be undertaken for 7 hours). The number provided includes an extra analyser, which increases capacity and allows for a back-up analyser in case of instrument failure or the need for extensive maintenance or servicing.

Table 14: Number of analysers required to complete an average daily workload of 5,000 sample requests. (Appendix 9 provides a detailed calculation of these numbers; Appendix 10 provides the calculation for extreme workloads of 9,000 samples per day.)

	HM-JACKarc	*NS-PLUS C15*	*OC-SENSOR DIANA*	*FOB Gold/BioMajesty*
Number of analysers required	5	4	4	2

Staff

The process of sample handling is likely to be more complex for FIT than for gFOBT, but this will depend upon the nature of the package used for transport. More staff will be required to receive, open and log the FIT kits.

Once logged, the automated analysis will require fewer staff than is necessary for gFOBT. The staff performing FIT analysis will need more technical knowledge and skills than are currently required. Appropriately trained screening staff who have the necessary technical aptitude would be able to provide routine analysis using all but the BioMajesty analyser. The analytical service will require close supervision by experienced healthcare scientists supported by detailed operating and quality control procedures.

Calibration, quality control and assessment of the analysers and technical validation of results will need to be undertaken or closely supervised by trained healthcare scientists. Validated results can then be uploaded to the BCSP database (Bowel Cancer Screening System [BCSS]).

Economic considerations

A realistic estimate of the cost of using FIT requires detailed cost analysis-based experience obtained from the planned England FIT pilot programme. The cost of the devices will be subject to competitive tendering between at least four potential suppliers. The cost of packaging and postage has yet to be determined and will depend upon the final package design, economies that can be achieved in the mailing system and postal costs that are currently being subject to substantial increases.

In the laboratory, fewer staff will be required to perform the analysis but greater supervision will be necessary from qualified scientific staff. The current time- consuming QC procedure

should take less time but will require more experienced staff. Instrument maintenance and quality checking will be a new activity for the screening Hubs and these procedures can be exacting and demand time from skilled staff. Receipt and computer logging of FIT kits will require more staff time than is currently required for gFOBT; the exact requirement will depend greatly upon the design of the device and packaging.

Whilst the literature has estimates of the cost of the adoption of FIT, figures do not reflect the likely systems and economies of scale that can be realised in the English programme [12,13,14]. The most recent estimates of the cost effectiveness of a population-based FIT bowel cancer screening programme have been made by groups in the Netherlands who will commence their population screening programme in January 2014.

Environmental considerations

Clinical waste

The collection devices are much smaller than current gFOBT kits, however they contain liquid buffer that will be contaminated with faecal material. These must be disposed of as clinical waste.

The HM-JACKarc produces an additional quantity of clinical waste, due to once-only use of the reaction cuvettes. The Southern Hub would therefore typically dispose of 5,000 plastic devices and reaction cuvettes each day. The other analysers use reusable cuvettes, thereby reducing plastic clinical waste.

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Yoshi Itoh, Eiju General Hospital, Japan
Yukata Nara, Saitama Medical Centre, Japan
Yumi Shimizu, Yamanash Kosei Hospital, Japan

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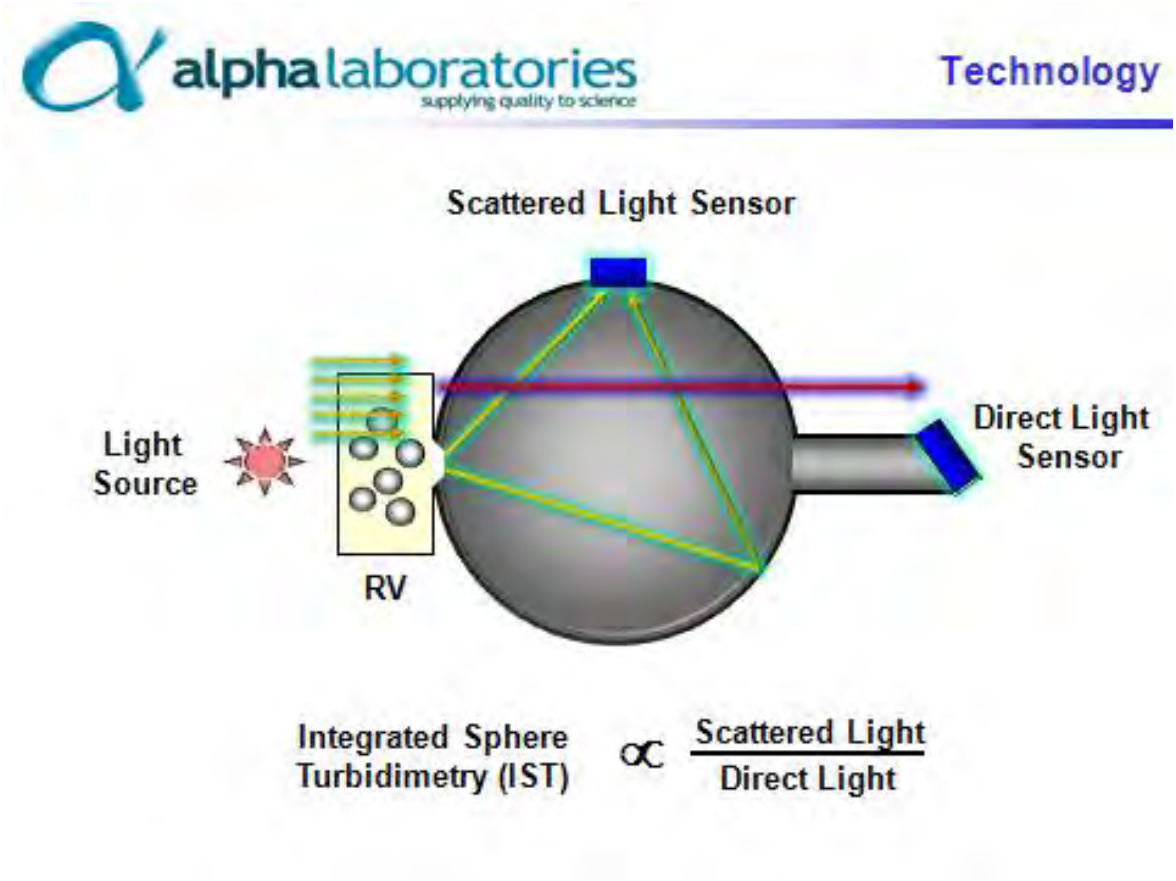
Appendix 1: Integrated sphere turbidimetry (image provided by Alpha Laboratories Ltd)



Appendix 2: Imprecision of the concentration of buffer spiked with haemoglobin (µg Hb/g faeces)

	Expected concentration	*GMEC measured*		
		Average	*SD*	*CV*
HM-JACKarc (µg Hb/g faeces)	11	13.5	1.1	8.2
	56	58.8	2.3	3.9
	280	319.4	8.2	2.6
NS-PLUS C15 (µg Hb/g faeces)	11	8.4	1.3	15.5
	21.5	17.2	1.2	7.1
	41	37.2	1.9	5.1
	78	73.8	7.6	10.3
OC-SENSOR DIANA (µg Hb/g faeces)	26	40.4	2.5	6.2
	90	133.4	8.4	6.3
FOB Gold/BioMajesty (µg Hb/g faeces)	14	19.3	0.8	4.3
	23	32.7	1.7	5.2
	56	86.9	7.3	8.5

Appendix 3: Imprecision of the concentration of faecal samples spiked with haemoglobin (µg Hb/g faeces)

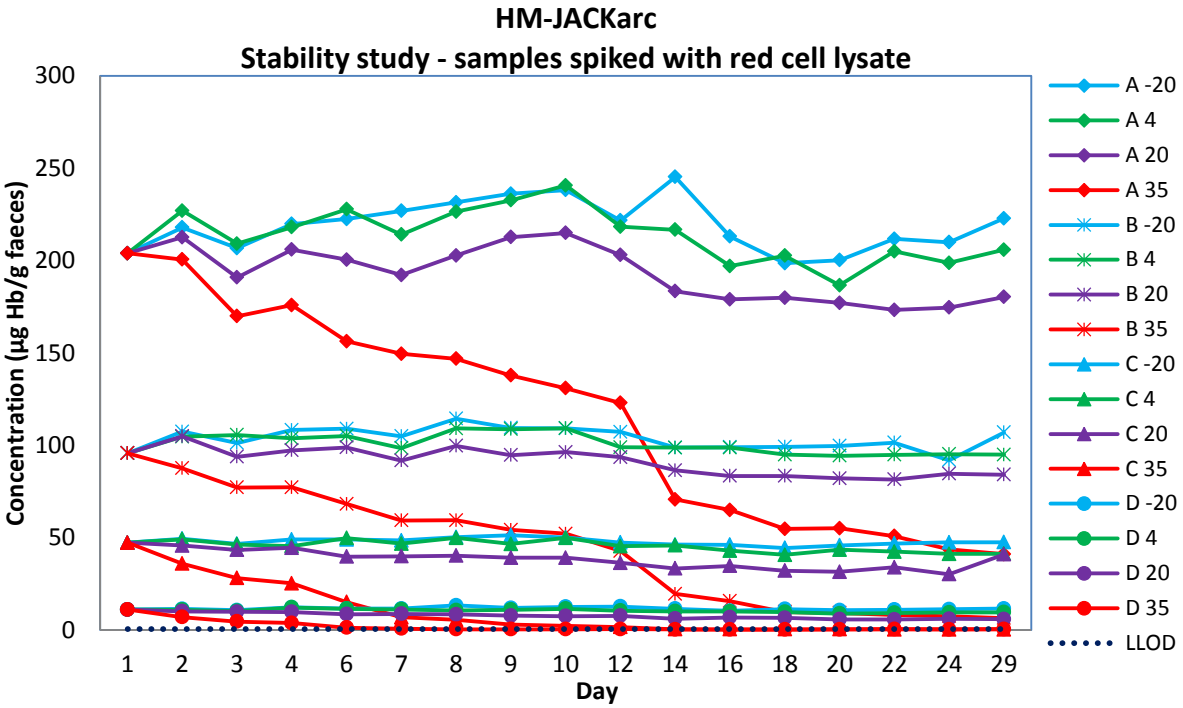
	Expected concentration	*GMEC measured*		
		Average	*SD*	*CV*
HM-JACKarc (µg Hb/g faeces)	20	9.0	2.1	23.2
	50	43.5	16.2	37.3
	150	124.3	6.9	5.6
NS-PLUS C15 (µg Hb/g faeces)	20	5.7	1.6	28.4
	50	36.8	3.8	10.5
	150	104.9	11.1	10.5
OC-SENSOR DIANA (µg Hb/g faeces)	20	8.9	1.4	16.1
	50	44.7	2.4	5.4
	150	144.5	9.8	6.8
FOB Gold/BioMajesty (µg Hb/g faeces)	20	14.1	2.5	18.0
	50	62.5	12.9	20.7
	150	187.2	13.4	7.1

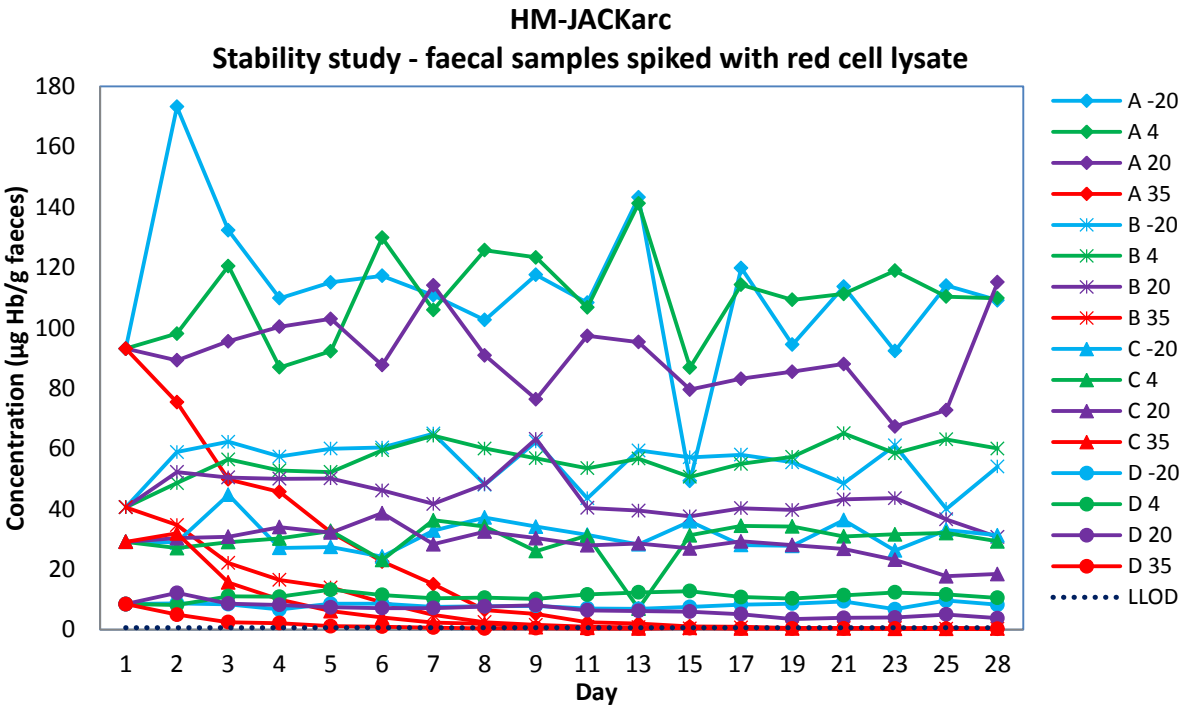
Appendix 4: Precision profile data of buffer samples spiked with haemoglobin (µg Hb/g faeces) (conc – concentration)

Expected conc	*HM-JACKarc*			*NS-PLUS C15*			*OC-SENSOR DIANA*			*FOB Gold/ BioMajesty*		
	Mean	*SD*	*%CV*	*Mean*	*SD*	*%CV*	*Mean*	*SD*	*%CV*	*Mean*	*SD*	*%CV*
400	483.2	8.9	1.8	353.0	42.0	11.9	576.7	24.6	4.3	424.3	6.8	1.6
200	260.7	5.7	2.2	210.0	37.9	18.0	271.8	23.3	8.6	353.9	4.6	1.3
100	124.0	1.4	1.1	100.8	5.5	5.4	146.0	5.1	3.5	196.7	2.6	1.3
75	91.6	1.1	1.2	69.8	2.0	2.8	109.0	3.9	3.6	124. 9	2.1	1.7
50	64.3	0.4	0.7	53.7	1.8	3.4	73.6	1.9	2.6	84.3	1.6	1.9
40	47.5	0.8	1.6	37.8	0.8	2.1	56.8	1.1	2.0	69.4	1.3	1.9
30	34.6	0.6	1.8	28.7	1.2	4.0	44.5	1.0	2.2	47.3	1.0	2.1
20	25.2	0.3	1.3	16.6	0.7	4.2	27.8	0.9	3.2	27.3	0.8	2.8
10	12.3	0.3	2.6	8.1	1.2	14.8	11.3	1.7	14.7	14.5	0.7	5.1
5	5.7	0.3	5.3	3.3	0.7	20.5	5.0	1.3	27.2	7.4	0.6	8.7

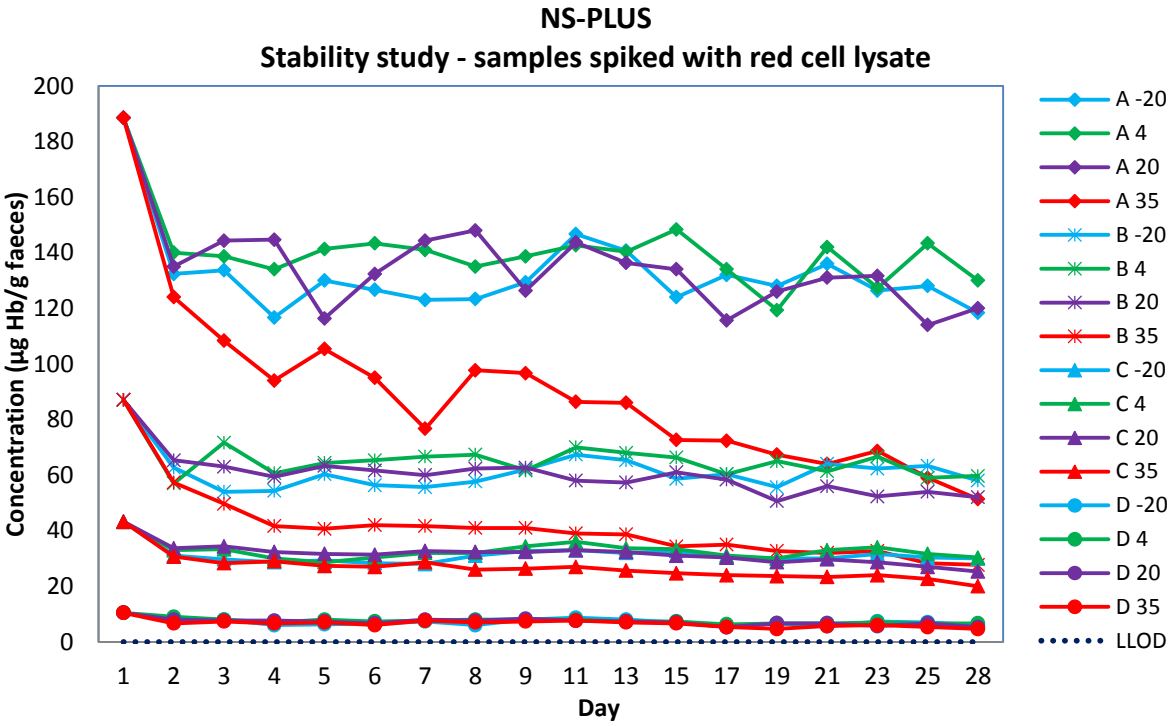
Appendices 5-8 show the stability data for the four analysers. In each case the first graph shows the data from sample collection tubes spiked with known concentrations of Hb (red cell lysate), and the second graph shows the stability of Hb in faecal samples that have been spiked with known concentrations of Hb and then collected into the collection devices. The first result is the mean of 10 samples of the same concentration all measured on the day 1. **Key:** LLOD – Lower limit of detection. A-D – concs, and figures the temperature in ˚C.

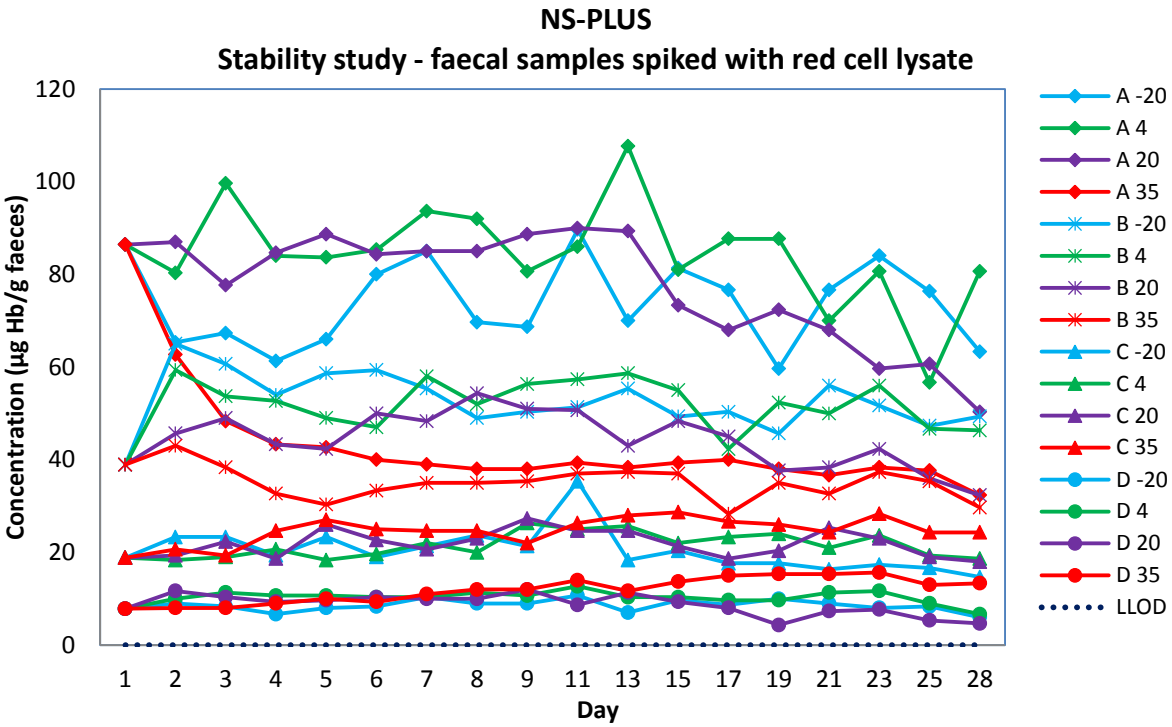
Appendix 5: HM-JACKarc stability data



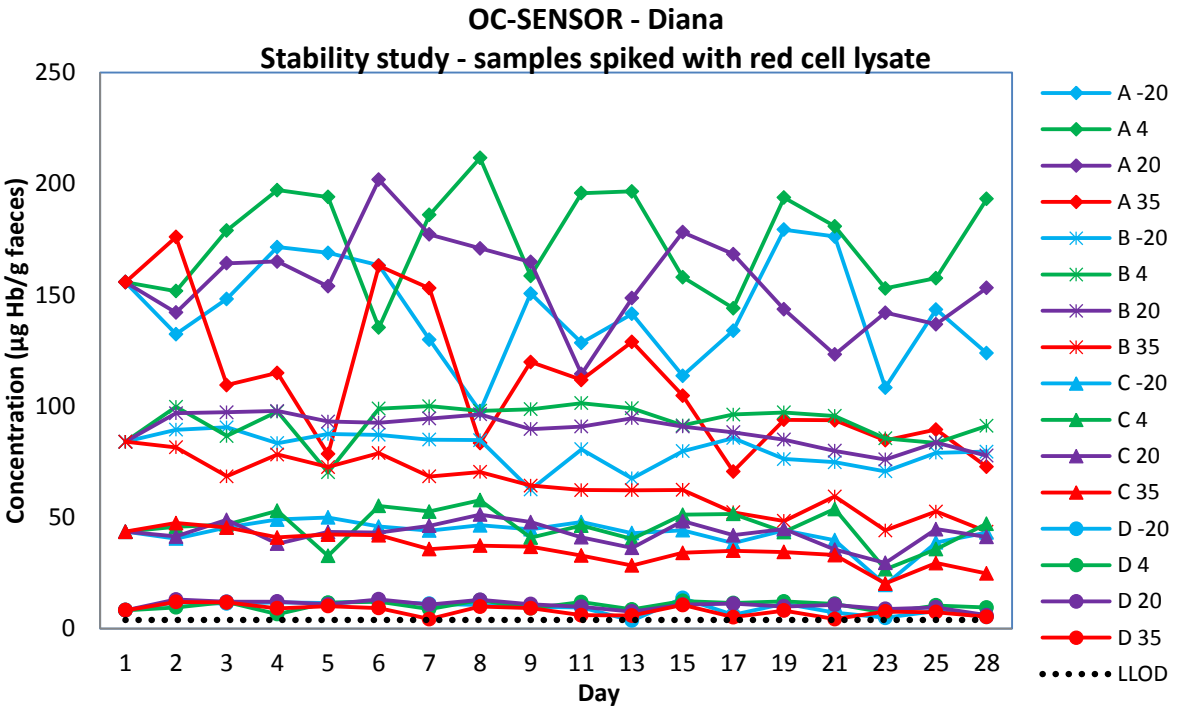


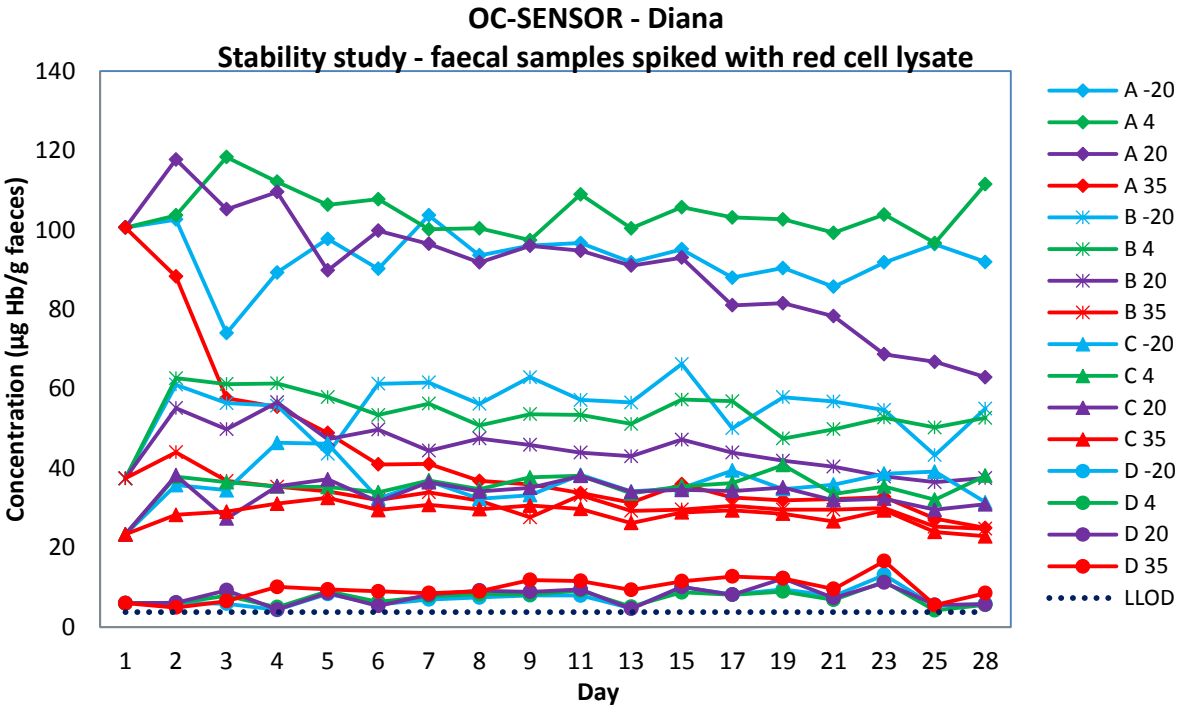
Appendix 6: NS-PLUS C15 stability data



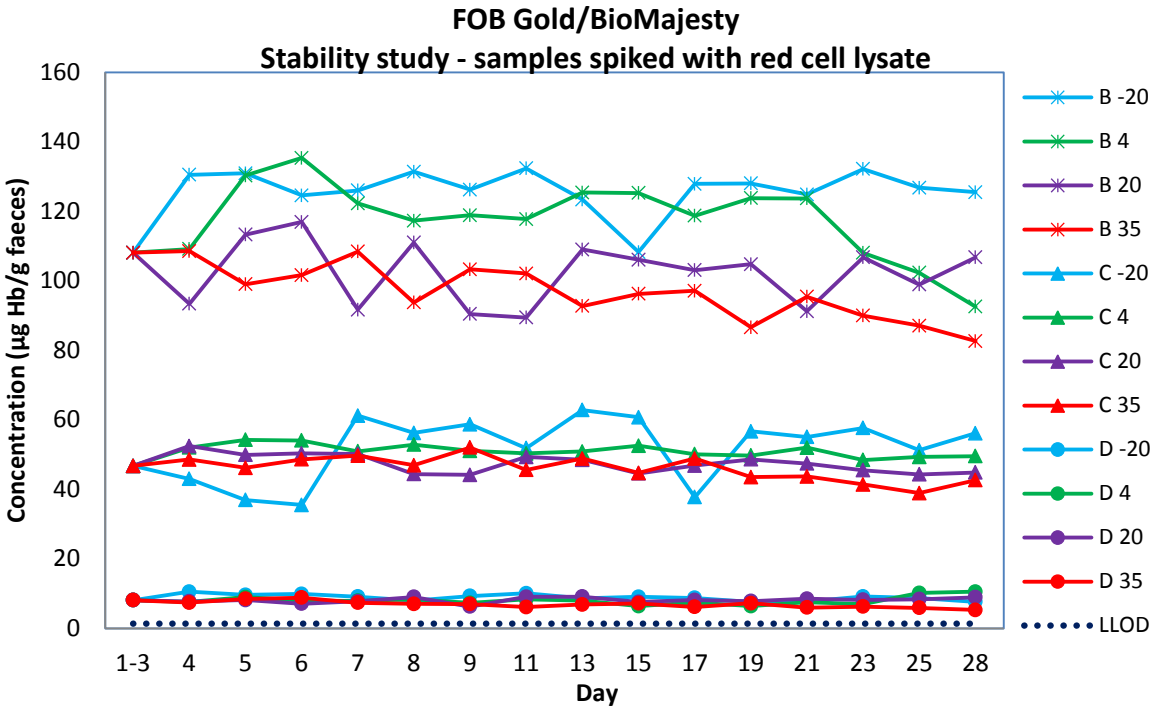


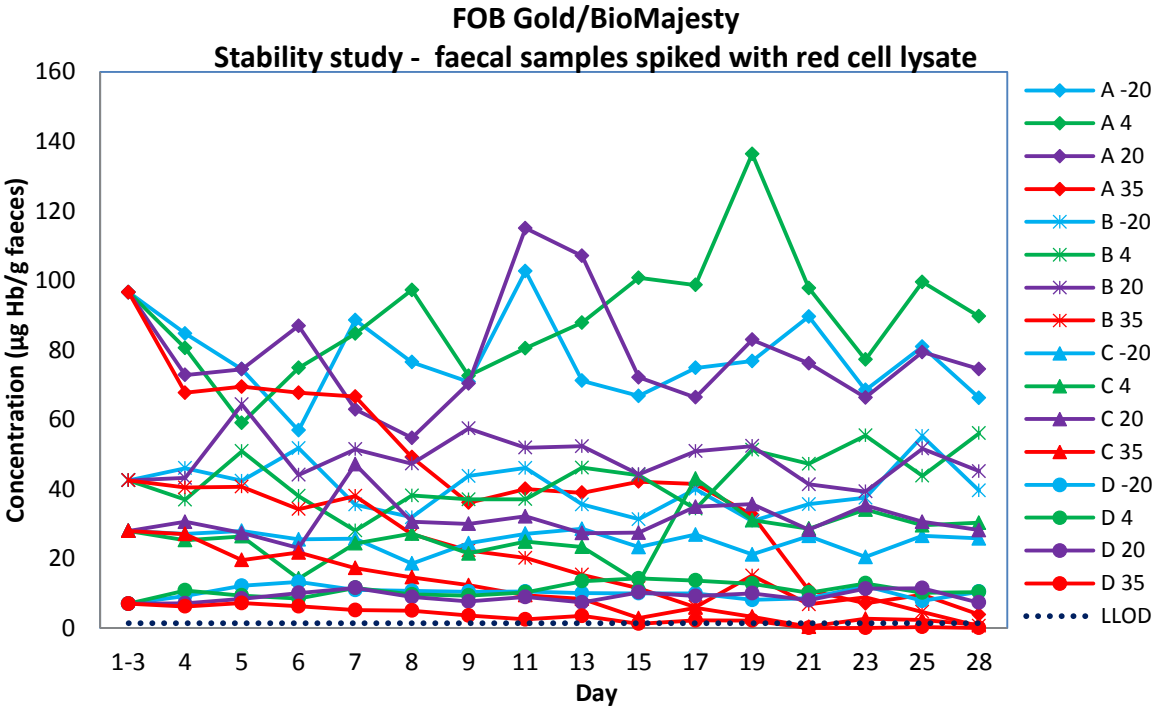
Appendix 7: OC-SENSOR DIANA stability data





Appendix 8: FOB Gold/BioMajesty stability data. The samples more concentrated than 200 µg Hb/g faeces were not diluted, and their reported results gave no indication that they were out-of-range. It was therefore not possible to report the stability of Hb in concentrations greater than 200 µg Hb/g faeces from this study.





Appendix 9: Number of analysers required for an average daily workload of 5,000 samples. (*Figures for FOB Gold/BioMajesty calculated assuming use of a track.)

	HM-JACKarc	*NS-PLUS C15*	*OC-SENSOR DIANA*	*FOB Gold/ BioMajesty**
Number of samples per hour per analyser (a)	200	300	300	800
Number of samples measured in 7 hours (b = a x 7)	1400	2100	2100	5600
Number of analysers required to analyse 5,000 samples (5,000/b)	3.6	2.4	2.4	0.9
Number of analysers required to analyse 5,000 samples in 7 hours (c)	4	3	3	1

If one analyser breaks down there must be sufficient backup within the laboratory to cover the extra workload. Number of analysers required to measure 5,000 samples with enough capacity to ensure that the Hub could cope if one analyser was unavailable:

Total number of analysers required (d)	**5**	**4**	**4**	**2**
Number of hours to process 5,000 samples with 'd' analysers	5 hrs	4 hrs 10 mins	4 hrs 10 mins	3 hrs 8 mins

If one analyser breaks down, how long will it take to analyse the samples using the remaining analysers?

	HM-JACKarc	*NS-PLUS C15*	*OC-SENSOR DIANA*	*FOB Gold/ BioMajesty**
Number of analysers left (e = d-1)	4	3	3	1
total number of samples to analyse (5,000)	5,000	5,000	5,000	5,000
Number of samples per analysers left (f = 5,000/e)	1250	1667	1667	5,000
how many hours (g= f/a)	6 hrs 18 mins	5hrs 36 mins	5hrs 36 mins	6hrs 18 mins

Appendix 10: Number of analysers required for an average daily workload of 9,000 samples. (*Figures for FOB Gold/BioMajesty calculated assuming use of a track.)

	HM-JACKarc	*NS-PLUS C15*	*OC-SENSOR DIANA*	*FOB Gold/ BioMajesty**
Number of samples per hour per analyser (a)	200	300	300	800
Number of samples measured in 7 hours (b = a x 7)	1400	2100	2100	5600
Number of analysers required to analyse 9,000 samples (9,000/b)	6.4	4.3	4.3	1.6
Number of analysers required to analyse 5,000 samples in 7 hours (c)	7	5	5	2

If one analyser breaks down there must be sufficient backup within the laboratory to cover the extra workload. Number of analysers required to measure 9,000 samples with enough capacity to ensure that the Hub could cope if one analyser was unavailable:

Total number of analysers required (d)	**8**	**6**	**6**	**3**
Number of hours to process 9,000 samples with 'd' analysers	5 hrs 38 mins	5 hrs	5 hrs	3 hrs 45 mins

If one analyser breaks down, how long will it take to analyse the samples using the remaining analysers?

	HM-JACKarc	*NS-PLUS C15*	*OC-SENSOR DIANA*	*FOB Gold/ BioMajesty**
Number of analysers left (e = d-1)	7	5	5	2
total number of samples to analyse (9,000)	9,000	9,000	9,000	9,000
per analysers left (f = 9,000/e)	1286	1800	1800	4500
how many hours (g= f/a)	6 hrs 24 mins	6 hrs	6 hrs	5 hrs 36 mins

Appendix 11: Responses from the FIT companies

1. Kyowa Medex

New Developments from Kyowa Medex

New Immunochemical Faecal Occult Blood Analyser: HM-JACK SP

HM-JACK SP
FECAL OCCULT BLOOD TEST ANALYZER

Main Concept:
System integration for "large" programmatic population-based colorectal cancer screening using a faecal immunochemical test for haemoglobin.

Kyowa Medex Co., Ltd., a Japanese based *in vitro* diagnostic manufacturer, has provided ideal solutions to colorectal cancer (CRC) screening for more than 20 years with highly integrated automated immunoturbidimetric analytical systems.

Now, the new concept applied to our successful series of analyzers with excellent performance characteristics has been developed taking expert opinions and customer feedback into account. The HM-JACK SP will be available soon to offer more benefits to large population-based CRC screening laboratories. The planned global launch date will be end of 2014 to early 2015.

Improvements/Benefits are:

- Higher throughput of 260 tests/hour.
- Use of current high sensitivity "HS" reagents to ensure comparability of results over time.
- Loading capacity up to 300 samples.*
- Continuous Rack feeding module.*
- Auto Dilution 1:100, 1:10000 to ensure quantitative faecal haemoglobin concentration data available on all samples.
- Little solid waste due to the re-useable reaction cuvettes.
- Ready-to-use "Liquid Control" rather than lyophilized material requiring reconstitution.
- Flat, easy to use, sample collection device allows small faecal samples to be used minimizing clinical waste and facilitating transport.
- Identity between ng Hb/mL buffer and µg Hb/g faeces units.

** optional*

The HM-JACK series of analysers are known as very simple to use, highly sensitive systems from both analytical and clinical aspects. These are termed middle-sized system in this field. Now, with the HM-JACK SP, we have combined a high throughput module with our highly sensitive measurement system with little clinical waste into the ideal solution.

HM-JACK SP
FECAL OCCULT BLOOD TEST ANALYZER

Reproducibility: haemoglobin spiked buffer solution (ng Hb/mL)

	Sample A	Sample B	Sample C	Sample D	Sample E
1	12.8	27.3	102.0	201.2	401.0
2	13.0	27.2	101.9	200.6	398.6
3	12.9	27.4	102.4	199.9	399.3
4	12.7	27.7	101.7	199.7	399.3
5	12.9	27.0	102.3	199.7	398.2
6	12.6	27.5	102.0	199.2	400.7
7	12.6	27.4	101.7	199.9	398.9
8	13.0	27.5	101.1	202.7	402.4
9	13.1	27.2	101.7	201.6	400.8
10	12.8	27.4	101.1	199.7	400.7
Mean	12.8	27.4	101.8	200.4	400.0
SD	0.18	0.19	0.45	1.10	1.32
CV,%	1.4	0.7	0.4	0.6	0.3

KYOWA KIRIN
Kyowa Medex Co., Ltd.

2. Alere/AlfresaPharma

September 23rd, 2013

RE: *FIT Evaluation Report Follow-up*
AlfresaPharma Corporation launches updated FIT analyzer.

Attention: Dr. Magdalen Carroll
Clinical Biochemist, Project Lead Evaluator

AlfresaPharma Corporation has launched the next generation model of the NS-Plus called the NS-Prime January 2013 in Japan. The new system is identical in terms of intended use, device design, principles of operation and work-flow as those found within the proven NS-Plus.

There are a few key enhancements made to the NS-Prime, which will further streamline the workflow process. Below is a summary of these updates including Table 1 which outlines the differences between the NS-Plus and NS-Prime.

NS-Prime

- Increased maximum sample onboard capacity to 220 samples from 160 samples on the NS-Plus instrument.
- 100-sample rack available for ease of loading.
- 24-hr reagent cooling system allows reagents to be left in the reagent rack for up to 5 days.
- Reagent dispensing nozzle has been modified to metallic instead of carbon containing plastic, increasing durability and replacement life.
- Added capability of managing barcodes for calibrators and controls instead of manual entry.
- Increased onboard reagent capacity.
- The user interface has been updated to allow easier navigation through the software.

Table 1

Product Name	NS-Plus	NS-Prime
Width (mm)	680	805
Depth (mm)	580	620
Height (mm)	430	400
Weight (kg)	58	70
Rated Input Power (Volt-Ampere)	400	Unchanged
Rated Voltage/Frequency	110-120V (50/60Hz) US, Canada 220-240V (50/60Hz) EU, China	100-240V (50/60Hz) – Universal
Throughput Capacity	300 tests per hour	Unchanged
Onboard Sample Capacity	160 Max (including 10 STAT)	220 Max (including 20 STAT)

Sample Rack Configuration	3 Sample racks/tray - Total of 5 trays = 150 samples + Priority Tray (10 samples)	2 racks (10 samples/rack) x 11 trays = 200 samples OR 2 trays (10 sample racks per tray) = 200 samples + Priority tray (20 samples)
Analytes Available	Hemoglobin, Transferrin	Unchanged
Sample Identifier	Barcode Management	Unchanged
Calibrator / Control ID	Manual Input	Barcode Management
Re-test Function	Available	Unchanged
Automatic Re-test function with automatic dilution	Automatic	Unchanged
Prozone Check Function	Available	Unchanged
Optical Source	LED (3 wavelengths – 540nm, 630nm, 660nm)	Unchanged
Detector	Photodiode x3	Unchanged
Reaction Cells	Self-cleaning	Unchanged
Dispensing Nozzles	Sample Nozzle: Metallic Reagent Nozzle: Carbon containing Plastic	Sample Nozzle: Metallic Reagent Nozzle: Metallic
Reagent Cooling Function	Available – cooling function terminates after shut down	Available – software allows user to select shutdown option leaving reagent cooling function operational.
Consumable Level Tracking	Available	Unchanged
Mixing	Rotation by mixing bar	Unchanged
Automatic Start-up/Shut-down	Available	Unchanged
Data Output	RS-232, LAN	RS-232 (LAN optional)
Automatic Printing Function	Available	Unchanged
Reagents	Colloidal Gold	Unchanged
Reagent Loading	3 bottles (x 300 tests) }+ 1 Diluent bottle	5 sets bottles (x 300 tests) + Diluent bottle x 2 sets
Reagent ID	Automatic barcode management (test, lots, remaining volume)	Unchanged
Specimen Collection Container	N/A	No change to specimen collection container

In addition to the above, the reagents and wash solution have been optimized for use with the NS-Prime analyzer. The preservative for Reagent R1 has been modified to be identical to Reagent R2 (NaN_3 0.05%). The antibody of the reagent has not changed and is identical to that which is used for the NS-Plus. The Wash Solution has also been optimized so that less bubbling occurs when used with the analyzer. Finally, there have been no modifications to the Calibrator, Control or Specimen Diluent.

3. Eiken Chemical Co. Ltd.

Comments for the evaluation report from Eiken.

24th September 2013

New analyzer: informal announcement.

Eiken is developing a new OC-SENSOR series analyzer as a successor to the OC-SENSOR DIANA. The new analyzer is expected to be on the market during the second half of 2014 in Japan and the first half of 2015 in the European Union. Please note that these timings are an estimation and not yet committed.

Eiken has not disclosed this information to any party before now, either formally or informally. At the moment we are unable to disclose any further detailed information about the analyzer. Eiken will make a formal announcement regarding the new OC-SENSOR series analyzer in due course.

Tracking system: performance and price (according to technical information from Beckman and Hitachi).

At the moment there is no tracking system available for the OC-SENSOR analyzer. Based on tracking systems currently available in clinical chemistry laboratories, units can analyze 200-300 samples/hour. If a sample needs centrifugation in advance, an additional centrifugation unit is needed, which centrifuges 48 samples in one batch. If a sample needs centrifugation at 1,500 rpm for 15 minutes, the maximum performance of the unit will be 192 samples/hour. The unit price of centrifugation, opening cap and dispensing will be approximately 80,000 EURO.

Takuo Ichiyanagi
Eiken Chemical Co. Ltd.

4. Sentinel Diagnostics (manufacturer of FOB Gold)

The Hb Fecal Immunochemical Test is one of the distinguishing products of Sentinel Diagnostics. The collecting device FOB Gold® tube and the FOB Gold® reagent allow to perform FIT on the major clinical chemistry analyzers, independently from reagent size and format, using CE marked applications developed by Sentinel in its own laboratories. FOB Gold® tube and its universal applicability are well known since more than ten years.

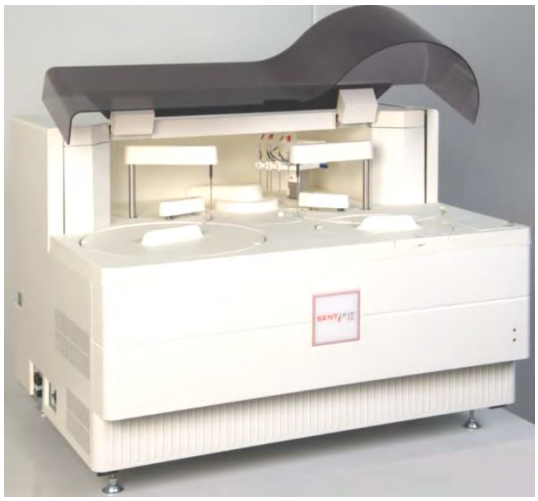
SENTINEL REAGENTS

Considering the screening environment, the collecting device includes a new buffer (Screening System) developed in order to reduce hemoglobin decay at room temperature for many days. During 2013 the following CE marked applications of new FOB Screening System have been released:

Analyzer	Measuring range	Total Imprecision (**)	Calibration	On Board Calibration Stability
BioMajesty JCA-6010	10 to 900(*) ng/mL	3.1% CV (<100 ng/mL) 2.7% CV (>100 ng/mL)	6 points	30 days
Beckman AU series	10 to 800(*) ng/mL	3.1% CV (<100 ng/mL) 2.5% CV (>100 ng/mL)	6 points	30 days
Roche Modular P	14 to 750(*) ng/mL	3.9% CV (<100 ng/mL) 2.3% CV (>100 ng/mL)	6 points	30 days
Abbott Architect series	10 to 800(*) ng/mL	3.1% CV (<100 ng/mL) 3.0% CV (>100 ng/mL)	6 points	30 days
Sentinel SENTiFOB	25 to 750(*) ng/mL	6.4% CV (<100 ng/mL) 4.5% CV (>100 ng/mL)	6 points	30 days
Sentinel SENTiFIT270	10 to 900(*) ng/mL	4.5% CV (<100 ng/mL) 2.2% CV (>100 ng/mL)	6 points	30 days

(*): indicative value, depending on the concentration of highest Calibration level
(**): representative data obtained in defined conditions)

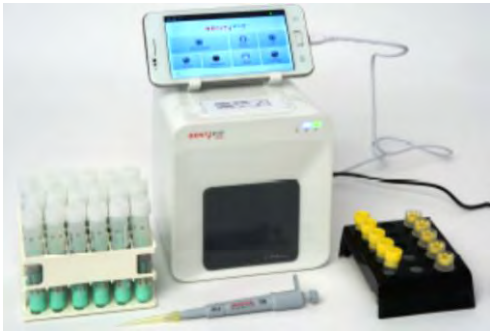
FIT Line Dedicated Systems



SENTiFIT®270 is a recently introduced analyzer, with a dedicated pierceable patented tube. Designed for screening realities, it works with barcode dedicated high yield reagents, and liquid and ready to use calibrators and QCs. The sampling needle's innovative ability to pierce the sampling device allows for laboratory professionals to be protected from biological risks related to sample handling, and makes the pre-analysis phase simpler and quicker.

SENTINEL DIAGNOSTICS

Sentinel is also targeting the market with the **SENTiFIT®*mini***, designed for doctor's office. Extremely easy to use, **SENTiFIT®*mini*** has its own dedicated CE reagent: it is a single test and the calibration curve is available on a card ready to be put on the analyzer.



SENTINEL AUTOMATION VIEW

The connection of laboratory Automation Systems (tracking) with BioMajesty JCA-6010 analyzer, validated in cooperation with Inpeco SA, made the use in large sample turnover environments, such as the FIT screening sites, more easy and time saving. This tracking connectivity approach will allows future applications for a number of analysers to be linked, offering the following process benefits:

- Single input/output modules
- Automated archiving or disposal of samples configurable to site requirements
- Sample de-capping/recapping
- Automated tube rotation and sample identification
- Host connectivity for sample result transfer

FIT LINE POSTERS

FOB Gold® Screen System evaluation on automated platforms Architect C16000, Biomajesty JCA-6010/C and Hitachi Modular P.

M. Gramegna, C. De Cunto, I. D'Agnese, M. Anelli, R. Lucini. *Sentinel CH. SpA, Milan, Italy*
(AACC 2013 Huston, poster accepted, to be published on Clin Chem.)

Evaluation of absence of dietary interferences using FOB Gold® Screen System in the determination of occult blood in fecal samples.

Gramegna M., La Motta M., Longo G., Anelli M.C., Lucini R. *Sentinel CH. SpA, Milan, Italy*
(AACC 2013 Huston, poster accepted, to be published on Clin Chem.)

Evaluation of a new collection tube for at room temperature conservation of human hemoglobin in fecal samples in colorectal cancer screening program.

La Motta M., Longo G., De Cunto C.; D'Agnese I., Anelli M.C. Lucini R. *Sentinel CH. SpA, Milan, Italy*
Biochimica clinica 2013, vol. 37, S667, poster W349 (Euromedlab Milan 2013).

Appendix 12. Revisions made to the original report (revisions published December 2014)

Page 8, Summary

- A new subheading 'Evaluation outcomes: operational performance/considerations' has been included in the Summary.
- Text describing the analysers is the same as the original text for all four analysers.
- A new summary table has been added to assist direct comparison of the analysers' performance and characteristics (entitled 'Evaluation outcomes: technical performance').

The original Summary text included some errors, now corrected in the new summary table:

- HM-JACKarc, Imprecision: *no* within-laboratory imprecision data provided by the manufacturer. Measurement range: Reference to low upper limit to the measurement range removed. There is *no* system for diluting samples that have a high Hb concentration.
- BioMajesty, Imprecision: imprecision of measurement increased (*not 'decreased'*) with increasing Hb concentration.
- OC-SENSOR DIANA, Linearity/measurement range: The upper limit of the undiluted measurement range had been quoted incorrectly as *500 µg Hb/g faeces*, rather than 200 µg Hb/g faeces. The new summary table includes the corrected undiluted measurement range (10-200 µg Hb/g faeces) and a statement that 'Dilution extends the range beyond the undiluted upper limit to 50,000 µg Hb/g faeces'.

Page 11, Introduction

- The Guildford Medical Device Evaluation Centre (GMEC) has undertaken three previous evaluations for the NHS BCSP, *not 'five'*.

Page 26, Table 7 legend

- Inter-day repeatability, *not 'intra-day'*.

Page 27, Linearity

- FOB Gold/BioMajesty was linear in the range 0-120 µg Hb/g faeces (*not 0-200 µg/g*) and non-linear for all concentration >120 µg/g (*not '>200 µg/g'*).

Page 32, Technical Performance, Stability

- The OC-SENSOR was similar to the NS-PLUS C15 in that faecal (*not 'non-faecal'*) Hb degraded faster than Hb diluted in buffer.

Page 44, Operational Performance, Table 11

- OC-SENSOR DIANA, Sample loading: Racks are unstable on bench but secure if loaded in 15 (*not 10*) rack transporting tray (150 [*not 100*] samples).

Page 45, Operational Performance, Table 11

- OC-SENSOR, Buffer replenishment: buffer *can* be replenished during analysis.

Page 48, Operational Performance, Table 12

- OC-SENSOR DIANA, Buffer/Reagent 2, Opened: 2-10°C (up to 2 mths) (*not 'until expiry date'*).

Page 51, Operational Performance, Table 13

- Maintenance and servicing, OC-SENSOR DIANA, Maintenance Daily/Weekly/Monthly:
  - Daily - Clean with a cloth: the panel and the rack transport system.
  - Weekly - Clean external surfaces and the W, R- and S-nozzles, the racks and the trays.
  - Monthly - Soak cell, nozzle soak and perform a cuvette blank measurement. Clean the tanks.