Detection Capability of Faecal Haemoglobin Examinations

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Scottish University of the Year 2017

Berkshire & Surrey Pathology Services

A joint venture between Ashford and St. Peter's Hospitals NHS Foundation Trust, Frimley Health NHS Foundation Trust, Royal Berkshire NHS Foundation Trust and Royal Surrey County Hospital NHS Foundation Trust. Legal entity host Frimley Health NHS Foundation Trust

NHS Pathology Solutions

NHS Cancer Screening Programmes

Possible Conflicts of Interest

CGF

- ***Consultant: Kyowa Medex Co., Ltd, Tokyo, Japan***
- ***Funding for participtionin meetings: Alpha Labs Ltd, Eastleigh, Hants, UK***

SCB

- ***None declared***

Rationale for Interest

Much current interest in "low" faecal haemoglobin concentrations (f-Hb) in CRC screening, in assessment of the future risk of neoplasia, and in assessment of patients presenting with lower abdominal symptoms.

These "low" f-Hb approach the "detection capabilities" of the quantitative FIT systems currently available.

In addition, currently used clinical f-Hb decision limits are close to these detection capabilities, especially for assessment of symptomatic patients.

In consequence, an understanding of the detection capability is very important for f-Hb examinations.

Current Problems

1. ***Use of nomenclature** – many terms used, including: sensitivity, functional sensitivity, analytical sensitivity, detection limit, etc, which is confusing!*

2. ***Numerical f-Hb cited below manufacturer's stated "working range".***

Baseline f-Hb concentration

0 µg Hb/g
> 0-2 µg Hb/g
≥ 2-4 µg Hb/g
≥ 4-6 µg Hb/g
≥ 6-8 µg Hb/g
≥ 8-10 µg Hb/g

***Grobbee EJ, et al. Association between concentrations of hemoglobin determined by fecal immunochemical tests and long-term development of advanced colorectal neoplasia. Gastroenterology 2017;153:12519.e2*.**

3. ***Low f-Hb cited to many significant figures.***

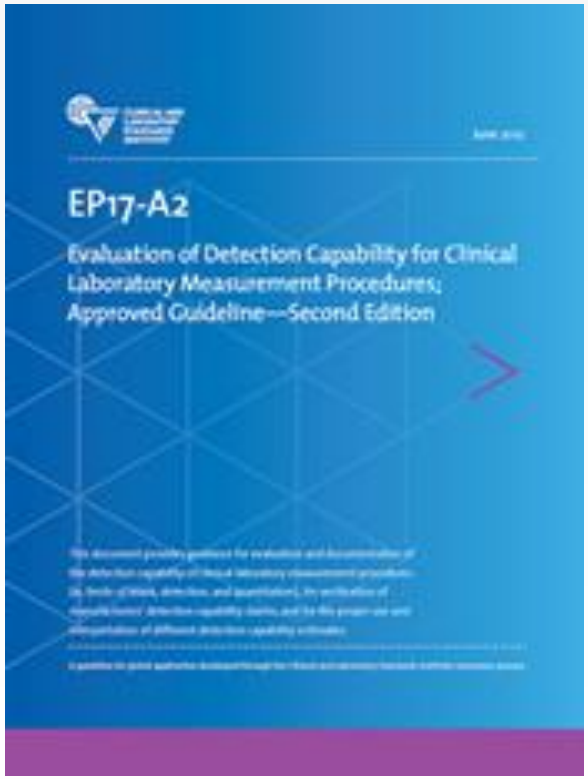
Analytical range [µg Hb/g feces]

0.086 - 50.0
3.75 - 250.0
1.70 - 129.88

Gies A, et al. Direct comparison of diagnostic performance of 9 FIT…… Gastroenterology2018;154:93-104.

One Answer to Perceived Current Problems

CLINICAL AND LABORATORY STANDARDS INSTITUTE ™



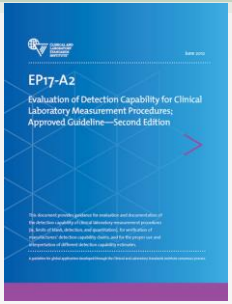
This document provides guidance:

for evaluation and documentation of the detection capability of clinical laboratory measurement procedures,

for verification of manufacturers' detection capability claims, and

for the proper use and interpretation of different detection capability estimates.

Definitions



Limit of Blank (LoB)

LoB is the highest measured result likely to be observed (typically at 95% certainty) for a sample containing no f-Hb (a blank sample).

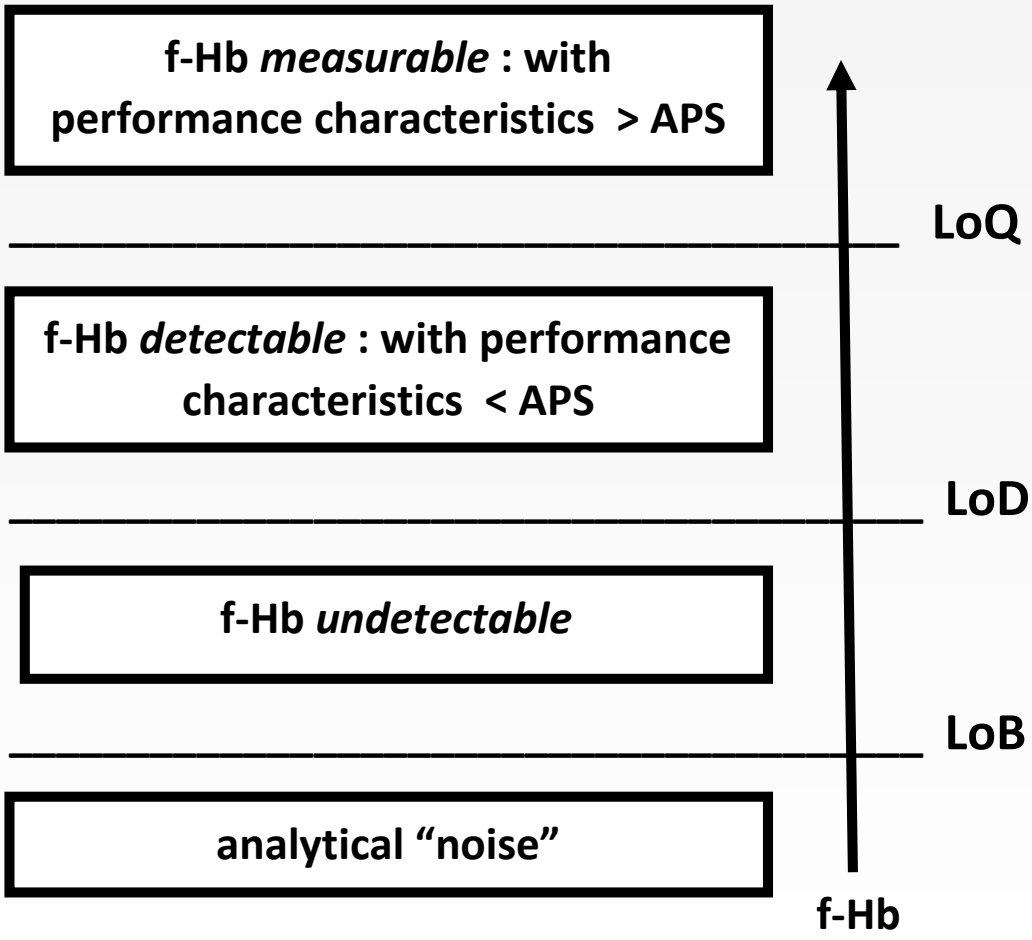
Limit of Detection (LoD)

LoD is the lowest f-Hb that can be detected 95% of the time. It is the lowest f-Hb likely to be reliably distinguished from the intrinsic analytical "noise", the signal produced in the absence of analyte (blank), and at which detection is feasible. Calculated from LoB + 1.645 x SD of low f-Hb samples.

Limit of Quantitation (LoQ)

LoQ is the lowest f-Hb at which the analyte can not only be reliably detected, but at which some predefined goals (analytical performance specifications) for analytical accuracy and MU - are met.

LoB, LoD and LoQ



Setting Analytical Performance Specifications

Consensus Statement:

Sverre Sandberg, Callum G. Fraser, et al.

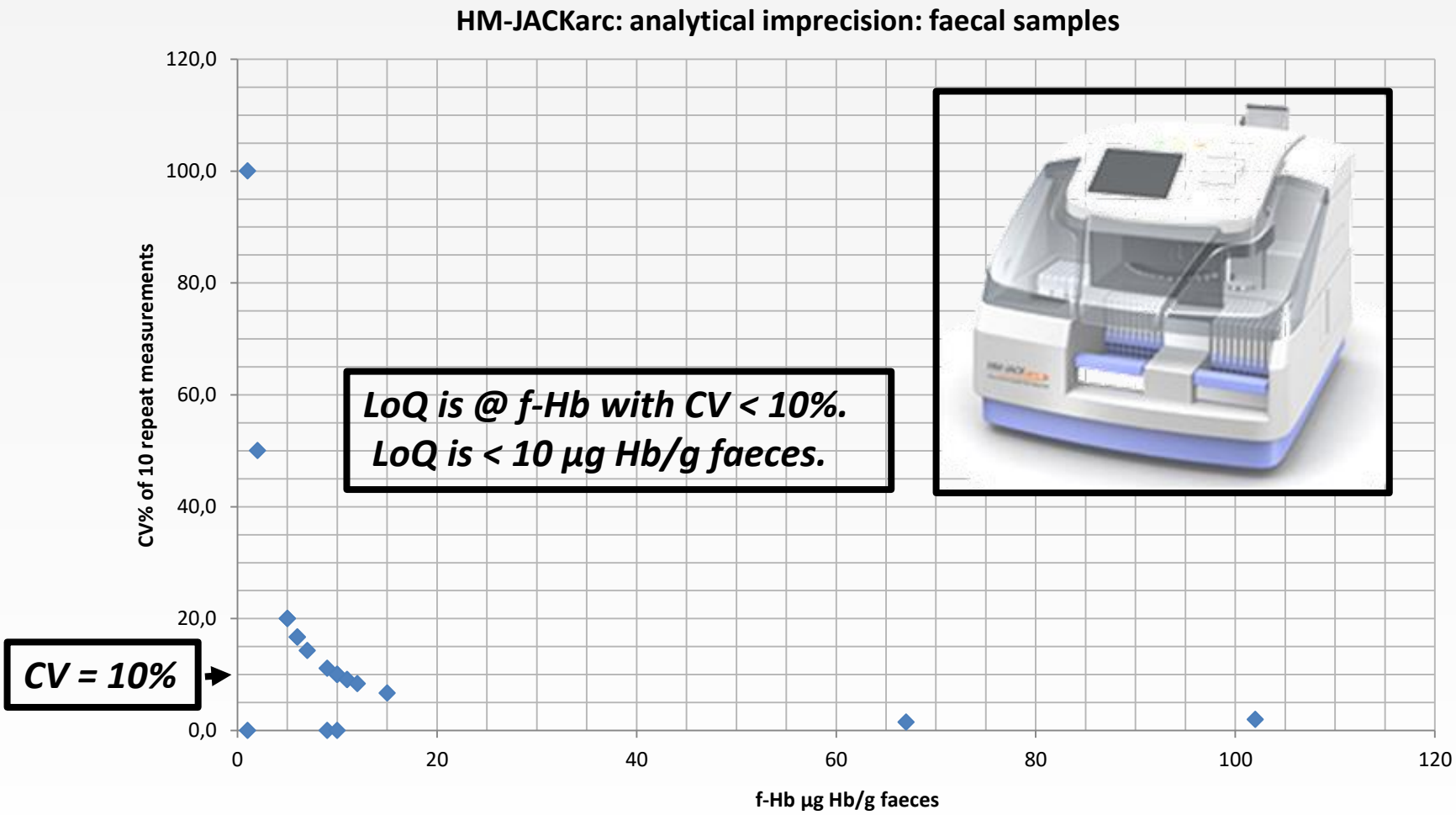
Defining analytical performance specifications….

Clin Chem Lab Med 2015;53: 833–5.

- ***Model 1: Based on the effect of examination performance on clinical outcomes.***
- ***Model 2: Based on components of biological variation of the measurand.***
- ***<u>Model 3: Based on state-of-the-art*</u>***

Our "interim" proposal, from study of literature - CV < 10%.

LoQ Estimated - "Imprecision Profile"



Proposals for Reporting f-Hb

Fraser CG and Benton SC. Clin Chem Lab Med 2018 (Early on-line]

Proposal 1: f-Hb should only be reported to whole integers.

Proposal 2: f-Hb less than the LoD should be termed "undetectable" or "not detected".

Proposal 3: Manufacturers should make imprecision profiles available to all users and detail their derivation. Labs might verify.

Proposal 4: For academic use: f-Hb greater than the LoD could advantageously be documented for research purposes, but the correct LoD should be clearly detailed in all publications.

Proposals for Reporting f-Hb

Proposal 5: Such reports should follow the EWG FITTER guidelines and the analytical performance achieved documented, particularly at/near the LoD.

Proposal 6: For routine clinical use: numerical f-Hb should be reported only when greater than the LoQ: f-Hb less than the LoQ (x), report as:

f-Hb < x µg Hb/g faeces.

Proposal 7: If a more sophisticated reporting system is required, one suggested option is report as

f-Hb < LoD = not detected

f-Hb LoD < result < LoQ = f-Hb detected

f-Hb ≥ LoQ = report the found f-Hb

Proposal 8: Efforts should be made to communicate the correct interpretation of reports of f-Hb to users.

Conclusions

Use of correct nomenclature for the lowest f-Hb that can be used in academic and routine practice is urgently needed, as are reporting strategies, with harmonisation across manufacturers, suppliers, researchers, reviewers, journal editors and all users.

Please feedback your views on our proposals to:

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DE GRUYTER Clin Chem Lab Med 2018; aop

Opinion Paper

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Detection capability of quantitative faecal immunochemical tests for haemoglobin (FIT) and reporting of low faecal haemoglobin concentrations