IFCC FIT working group update

Sally C Benton on behalf of the IFCC FIT working group

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Possible conflicts of interest

• None to declare
Essentialism vs Consequentialism

(Prof Patrick Bossuyt)

“the theory that the value of a marker or a medical test should be judged by the ‘trueness’ of its results”

“the theory that the value of a marker or a medical test should be judged by the value of its consequences”

FIT

• No assay standardisation or harmonisation
• Pre-analytical variability
• EQA scheme challenges
• No 3rd party IQC

IFCC working group

• patients are appropriately categorised
Pre-analytical Variability

- Stool
  - isn’t homogenous
  - has variably consistency
- “Pickers” from all manufacturers are different
- Instructions from manufacturers are different
- Inconsistent sampling techniques by patients

Haemoglobin stability
- Storage and transit temperatures
- Buffer composition
FIT laboratory challenges

- No assay standardisation
  - Different buffers
  - Different antibodies
  - Different calibration

- No primary reference material or method

- External Quality Assurance scheme challenges

- No established independent Internal Quality Control

Different methods give different results

Unable to confirm if results are correct
Impact of no method standardisation/harmonisation......
Impact of variability

• Difficult to consolidate evidence from studies that use different FIT methods

• Risk associated with implementing new screening programmes with pilot data using a different analytical method

• Challenges associated with very specific low cut-offs in symptomatic FIT
  – eg 10ug/g NICE guidelines in England
WEO – FIT for screening EWG

• 5 discussion documents (recommendations) published circa 2012

No. 1 – FIT standardisation

No. 2 – FIT Reporting Units

No. 3 - Stability of Hb

No. 4 – Internal Quality Control and External quality assessment

No. 5 – A Standard for Faecal Immunochemical Tests for Hb Evaluation Reporting (FITTER)
WEO – FIT for screening

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IFCC FIT Working Group
(International Federation of Clinical Chemistry & laboratory medicine)

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Terms of Reference
• To attempt to standardize analysis of haemoglobin in faecal samples by immunochemistry (FIT)
• To identify all sources of pre-analytical variation and standardise if possible
• To establish external quality assurance and third party internal quality control programmes
• To determine impact of assay interference of Hb variants and other factors

First meeting held in Athens in June 2017

6th meeting held in Barcelona in October 2019
Progress of IFCC FIT-WG

1. To attempt to standardize analysis of haemoglobin in faecal samples by immunochemistry (FIT)

2. External Quality Assurance (EQA) Schemes

3. Third Party Internal Quality Control (IQC) Material
1. Standardisation of analysis of Hb in Faecal samples by FIT

• 4 different reference standards identified
• Analysed on 4 different manufacturer analysers (Sentinel, Eiken, Alfresa, Kyowa) in the southern hub in Guildford in accordance with protocol written by the EU JRC reference laboratory in Geel.

Outcome
• Decision made to harmonise methods rather than standardise
• A single reference standard has been selected from the 4 tested
• Further work being carried out using the single reference standard to move towards method harmonisation

Considerations
• Impact on established services and the current evidence base if calibration changed and impacts results significantly
2. External Quality Assurance Schemes

- A review of all global EQA schemes was carried out by the FIT WG (2017)
- An EQA scheme send out samples periodically to enable labs to confirm the results they are getting are **accurate** ie the true result
- Two types of sample currently used in EQA schemes
  - lyophilised/liquid
  - faecal like matrix
- An analytical evaluation of 11 different EQA schemes from around the world carried out by the Southern Hub, Guildford UK
- Results presented to and discussed with IFCC FIT-WG

**Conclusions:**
- To assess analytical accuracy liquid EQA is most appropriate due to very poor imprecision with faecal like matrix samples.
- Ideal scheme might include both to enable us to understand impact of pre-analytical variability

**Next stages:**
- Discuss findings of study with EQA schemes.
- Publish work
- Produce recommendations on EQA material required for FIT
3. Third Party Internal Quality Control (IQC) programmes

Current situation:
- No third party IQC material available
- Analysers all quality control daily using IQC material from same manufacturer

Impact:
- No ability to independently verify results on a daily basis

Progress:
- 4 quantitative FIT manufacturers (Sentinel, Eiken, Alfresa, Kyowa) agreed for their IQC material to be tested on all competitors analysers
- Results demonstrate that competitor IQC material could be used on each others analysers

Outcome:
- Manufacturers to consider whether to sell their IQC material as a 3rd party IQC
Summary

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Good progress being made by IFCC FIT-WG
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