

## **Expert Working Group – ‘FIT for Screening’**

### **Short Discussion Document No. 1 – FIT Standardisation**

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#### **1. Case for change**

**Nomenclature** – We need to agree and adopt common ‘nomenclature’ for FIT technology because the many names and abbreviations used are confusing and, in some cases, inaccurate.

- iFOBT, FIT, FIT<sup>100</sup>, QFIT, QIFIT, QtFIT<sup>100</sup>
- Immunochemical faecal occult blood test, immunological faecal occult blood test, faecal immunochemical test, immunohistochemical test
- Qualitative, semi-quantitative, quantitative FOBT/FIT

**Standardised analytical information** – The EWG identified 47 distinct FIT products currently on the international market. It is not possible to determine with confidence:

- a) Whether these products are all measuring human haemoglobin (Hb), all its variants and significant degradation products.
- b) How (for quantitative tests) the reported units relate to the concentration of Hb in faeces.
- c) The lowest or highest concentration of Hb in faeces that the device can measure. The analytical precision (repeatability) of the measurements.
- d) The stability characteristics for Hb in the devices.
- e) The mass of faeces picked up by the quantitative devices.
- f) The volume of buffer into which the faeces is transferred.
- g) The standard material and method used to calibrate the test.
- h) The method used for determining the cut-off haemoglobin concentration(s) if provided.
- i) The variability in product characteristics likely/acceptable in manufacture.
- j) The period of notice for product changes that a purchaser can expect.
- k) The level of inaccuracy that should be expected in ‘read by eye’ products.
- l) Whether colour blindness or visual acuity needs to be checked for ‘read by eye’ products.

**Publications** – Published scientific and medical papers typically provide cursory information about the device and the performance characteristics of FIT used in clinical studies. This makes reliable assessment and comparison difficult and potentially misleading.

**Procurement** – The product procurement process does not always identify the key performance characteristics and can place unrealistic expectations upon products and companies.

#### **2. Proposed solution**

**Nomenclature** – *Recommendations*

**Full test name** – Faecal (fecal) Immunochemical Test for Haemoglobin (hemoglobin)

**Abbreviation** – FIT

**Quantitative** – Products that measure and report numerical ‘haemoglobin in faeces’ concentrations across the relevant clinical range should be designated Quantitative FIT (no abbreviation).

**Qualitative** – Products that provide a positive or negative result should be designated Qualitative FIT (no abbreviation).

**Cut-Off** – When the product is being used with a specific analytical cut-off to designate a test being positive or negative then the cut-off concentration (**µg Hb/g faeces not ng Hb/mL buffer**) should be added as a superscript suffix to the abbreviation e.g. Quantitative FIT<sup>20</sup> or Qualitative FIT<sup>30</sup>.

**Standardised analytical information – Recommendations**

- a) We assemble a list of product descriptive/performance information that manufacturers should make available to customers on request.
- b) Whilst manufacturers might wish to quote the concentrations measured in the solutions used by the device/system, the formal unit for reporting is that of concentration of Hb in faeces ( $\mu\text{g/g}$ ).
- c) We agree a study of candidate matrices that might be used in place of faeces for a range of procedures that characterise the FIT product. These might include:
  - measurement of sample mass delivered by faecal sample devices
  - stability measurements
  - quality control and assessment.
- d) We agree the method for measurement of stability, sample mass determination, cross reactivity, reliable analytical range, *etc.*
- e) We identify a WHO traceable standard and method of calibration.
- f) We identify a range of Hb variants that should be used in the determination assay cross reactivity.
- g) We identify chemicals that might cause potential assay interference and for which interference should be assessed.
- h) We identify product and manufacturing quality standards that could reasonably be expected to be shared with customers.
- i) We identify performance attributes necessary for those performing 'read by eye' tests.

**Publications – Recommendations**

Produce a list of items essential when describing use of FIT in a medical publication.

**Procurement – Recommendations**

Produce a list of key issues that should be considered when procuring a FIT product for population-based screening.

**3. Issues for consideration**

- Gaining support from diagnostics companies and the analytical community in developing the standards.
- Adoption of the standards by manufacturers.
- Independent verification of product claims.
- Adoption of the standardised approach by product users.
- Stimulating the development and adoption of new FIT products.

**4. Relevant publications**

Benson VS, Atkin WS *et al.* Towards standardizing and reporting colorectal cancer screening indicators on an international level: The international colorectal cancer screening network (ICRCSN). *Int J Cancer* 2012;130:2961-73.

Duffy MJ, van Rossum LG *et al.* Use of faecal markers in screening for colorectal neoplasia: a European group on tumour markers position paper. *Int J Cancer* 2011;128:3-11.

Fraser CG, Allison JE, Halloran SP, Young GP. A proposal to standardize reporting units for fecal immunochemical tests for hemoglobin. *J Natl Cancer Inst* 2012, doi: 10.1093/jnci/djs190.

Guittet L, Guillaume E *et al.* Analytical comparison of three quantitative immunochemical faecal occult blood tests for colorectal cancer screening. *Cancer Epidemiol Biomarkers Prev* 2011;20:1492-1501.

Halloran S, Launoy G, Zappa M. Fecal occult blood testing. In: Segnan N, Patnick J, von Karsa L, editors. *European guidelines for quality assurance in colorectal cancer screening*. First ed. Luxembourg: Publications Office of the European Union; 2010. p. 165-206.

Rabeneck L, Rumble RB *et al.* Fecal immunochemical tests compared with guaiac fecal occult blood tests for population-based colorectal cancer screening. *Can J Gastroenterol* 2012;26:131-47.

Van Roon AHC, Hol L *et al.* Are fecal immunochemical test characteristics influenced by sample return time? A population-based colorectal cancer screening trial. *Am J Gastroenterol* 2012;107:99-107.