Azienda Ospedaliero Universitaria Careggi

Principali criticità evidenziate nelle risposte dai campioni del programma VEQ Sangue Occulto

Stefano Rapi AOU Careggi

VEQ Ciclo 2017 – RISULTATI 1

Ematologia, G6PDH, coagulazione, screening Hb patologiche, HbA1C, elettroforesi proteine, sangue occulto

Consensus Meeting

15 Maggio 2018

Ore 14.30-18.30

Sede: Pad 3, piano terreno, AulaMagna

Azienda Ospedaliero Universitaria Careggi

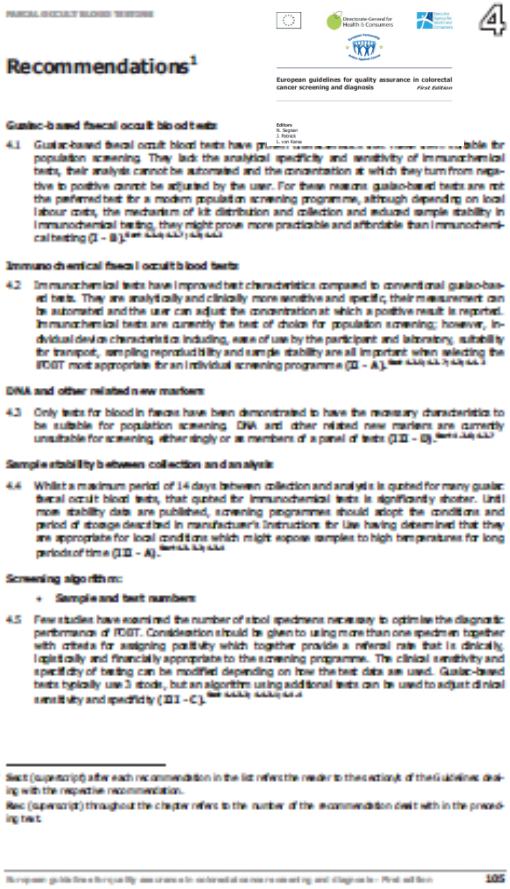
Sangue Occulto

Immunochemical faecal occult blood tests

4.2 Immunochemical tests have improved test characteristics compared to conventional guaiac-based tests.

They are analytically and clinically more sensitive and specific, their measurement can be automated and the user can adjust the concentration at which a positive result is reported.

Immunochemical tests are currently the test of choice for population screening; however, individual device characteristics including, ease of use by the participant and laboratory, suitability for transport, sampling reproducibility and sample stability are all important when selecting the iFOBT most appropriate for an individual screening programme **(II - A).Sect 4.2.5; 4.2.7;**



4

Recommendations[1]

European guidelines for quality assurance in colorectal cancer screening and diagnosis *First Edition*

Guaiac-based faecal occult blood tests

4.1 Guaiac-based faecal occult blood tests have pr[illegible] ible for population screening. They lack the analytical specificity and sensitivity of immunochemical tests, their analysis cannot be automated and the concentration at which they turn from negative to positive cannot be adjusted by the user. For these reasons guaiac-based tests are not the preferred test for a modern population screening programme, although depending on local labour costs, the mechanism of kit distribution and collection and reduced sample stability in immunochemical testing, they might prove more practicable and affordable than immunochemical testing (I - B).[illegible]

Immunochemical faecal occult blood tests

4.2 Immunochemical tests have improved test characteristics compared to conventional guaiac-based tests. They are analytically and clinically more sensitive and specific, their measurement can be automated and the user can adjust the concentration at which a positive result is reported. Immunochemical tests are currently the test of choice for population screening; however, individual device characteristics including, ease of use by the participant and laboratory, suitability for transport, sampling reproducibility and sample stability are all important when selecting the iFOBT most appropriate for an individual screening programme (II - A).[illegible]

DNA and other related new markers

4.3 Only tests for blood in faeces have been demonstrated to have the necessary characteristics to be suitable for population screening. DNA and other related new markers are currently unsuitable for screening, either singly or as members of a panel of tests (III - B).[illegible]

Sample stability between collection and analysis

4.4 Whilst a maximum period of 14 days between collection and analysis is quoted for many guaiac faecal occult blood tests, that quoted for immunochemical tests is significantly shorter. Until more stability data are published, screening programmes should adopt the conditions and period of storage described in manufacturer's instructions for use having determined that they are appropriate for local conditions which might expose samples to high temperatures for long periods of time (III - A).[illegible]

Screening algorithm:

- **Sample and test numbers**

4.5 Few studies have examined the number of stool specimens necessary to optimise the diagnostic performance of FOBT. Consideration should be given to using more than one specimen together with criteria for assigning positivity which together provide a referral rate that is clinically, logistically and financially appropriate to the screening programme. The clinical sensitivity and specificity of testing can be modified depending on how the test data are used. Guaiac-based tests typically use 3 stools, but an algorithm using additional tests can be used to adjust clinical sensitivity and specificity (III - C).[illegible]

[1] Sect (superscript) after each recommendation in the list refers the reader to the section of the Guidelines dealing with the respective recommendation.
Rec (superscript) throughout the chapter refers to the number of the recommendation dealt with in the preceding text.

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Standardizzazione dei test

WEO World Endoscopy Organization

World Endoscopy Organization
Colorectal Cancer Screening Committee

Expert Working Group – 'FIT for Screening'

Short Discussion Document No. 1 – FIT Standardisation

Prepared by: Prof Stephen Halloran and Dr Michelle Young, Bowel Cancer Screening Programme Southern Hub, Guildford, UK (e-mail: s.halloran@nhs.net)

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^{100}, QFIT, QIFIT, QtFIT^{100}
- 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:

2012

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Espressione risultati

WEO World Endoscopy Organization

World Endoscopy Organization
Colorectal Cancer Screening Committee

Expert Working Group – 'FIT for Screening'

Short Discussion Document No. 2 – FIT Reporting Units

Prepared by:

Callum G Fraser, Centre for Research into Cancer Prevention and Screening, University of Dundee, Ninewells hospital and Medical School, Dundee DD1 9SY, Scotland (e-mail: callum.fraser@nhs.net)

1. Case for change

Faecal immunochemical tests (FIT) for haemoglobin are replacing traditional guaiac faecal occult blood tests (gFOBT) in population screening programmes. However, the many available FIT differ with regard to a number of key factors. In particular, the methods for sampling, the mass of faeces collected, and the volume and characteristics of the buffer used in the sampling device differ among FIT. This makes comparisons of analytical and clinical test performance characteristics difficult. FIT results may be expressed as the haemoglobin concentration in the sampling device buffer and, sometimes, albeit rarely, as the mass of haemoglobin per mass of faeces. The current lack of consistency in units for reporting haemoglobin concentration is particularly problematic because apparently similar haemoglobin concentrations obtained with different FIT devices can lead to very different clinical interpretations. This also makes selection of the best test for a programme difficult. These considerations apply to both qualitative and quantitative FIT.

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Stabilità matariale biologico

WEO World Endoscopy Organization

World Endoscopy Organization
Colorectal Cancer Screening Committee

Expert Working Group – 'FIT for Screening'

Short Discussion Document No. 3 – Stability of haemoglobin

Prepared by: Prof Stephen Halloran, Dr Helen Seaman and Dr Michelle Young,
Bowel Cancer Screening Programme Southern Hub, Guildford, UK (e-mail: s.halloran@nhs.net)

1. Case for change

The application of faecal samples to absorbent paper and drying before analysis confers relative stability upon haemoglobin (Hb) in faeces (Young, 1996) and therefore upon guaiac occult blood tests (gFOBT).

gFOBT detect the presence of the chemically robust iron-containing pyrrole ring, the haem component of Hb. Faecal immunochemical tests for Hb (FIT), clinically superior tests, detect the protein globin in Hb and, in quantitative FIT, the amount of Hb is also measured. FIT confer the opportunity for

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Materiali per CQi e VEQ

WEO World Endoscopy Organization

World Endoscopy Organization
Colorectal Cancer Screening Committee

Expert Working Group (EWG) – 'FIT for Screening'

Short Discussion Document No. 4 – Internal Quality Control & External Quality Assessment

Prepared by: Callum G Fraser, University of Dundee, Ninewells Hospital and Medical School, Dundee DD1 9SY, Scotland (e-mail: callum.fraser@nhs.net)

1. Reasons for change

- To ensure acceptable international analytical performance in CRC screening.
- To enable screening programmes to provide evidence that analysis is of adequate quality.
- To enable and encourage publications that describe the use of FIT to include standardised information about analytical performance and quality.

2. Proposed solution

(a) **Standardised units of reporting.** Subject to a separate discussion document.

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Uniformare studi e report di valutazione metodi

WEO World Endoscopy Organization

World Endoscopy Organization
Colorectal Cancer Screening Committee

Expert Working Group – 'FIT for Screening'

Short Discussion Document No. 5

A Standard for Faecal Immunochemical TesTs for Haemoglobin Evaluation Reporting (FITTER)

A standard and check-list endorsed by the Colorectal Cancer Screening Committee, World Endoscopy Organization, for those preparing, reviewing and editing manuscripts on studies using Faecal Immunochemical Tests for haemoglobin (FIT).

Callum G Fraser,[1] Stephen P Halloran,[2] James E Allison[3] and Graeme P Young.[4]

[1]Centre for Research into Cancer Prevention and Screening, University of Dundee, Scotland, UK.

[2]NHS Bowel Cancer Screening Programme, Southern Hub, Royal Surrey County Hospital NHS Foundation Trust and University of Surrey, Guildford, Surrey, UK.

[3]Division of Gastroenterology, University of California San Francisco, San Francisco, California, USA.

[4] Flinders Centre for Innovation in Cancer, Flinders University of South Australia, Bedford Park, Australia.

Introduction

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Uniformare gestione 'appalti'

WEO World Endoscopy Organization

World Endoscopy Organization
Colorectal Cancer Screening Committee

Expert Working Group – 'FIT for Screening'

Short Discussion Document No. 6 – Quantitative FIT Procurement

Prepared by: Prof Stephen Halloran, NHS Bowel Cancer Screening Programme Southern Hub, Guildford, UK (e-mail: s.halloran@nhs.net).

Quantitative FIT Device Procurement

The first section is a checklist to be used to help in the preparation of FIT procurement.

The second section is a series of recommendations that describe the information that should be requested from any company submitting a proposal to supply FIT.

Whilst the document has been developed primarily to aid the effective procurement of sample collection and measurement devices, it describes other facilities and services that might form part of a 'system' procurement.

Definitions

1. Sample collection device – *test kit as used by the invitee/participant.*
2. Measuring device – *analytical instrument and ancillary reagents and consumables as used by the laboratory.*

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Risultati esercizi VEQ 2018

Quantitativi	n	E1	E2	E3	E4	E5	E6
Eiken m±ds	89	134 ± 16	325 ± 44	161 ± 36	143 ±1 8	83 ± 14	240 ± 25
Alfresa m±ds	9	231 ± 33	209 ± 13	99 ± 14	84 ± 11	46 ± 10	141 ± 21
Sentinel m±ds *	15	372 ± 90	439 ± 110	281 ± 62	205 ± 40	134 ± 30	318 ± 55
negativi	tutti	0	0	6	9	52	1
<100	tutti	2	1	15	14	96	2
Qualitativi							
Positivi		111	116	108	112	103	119
negativi		4	2	9	5	14	0

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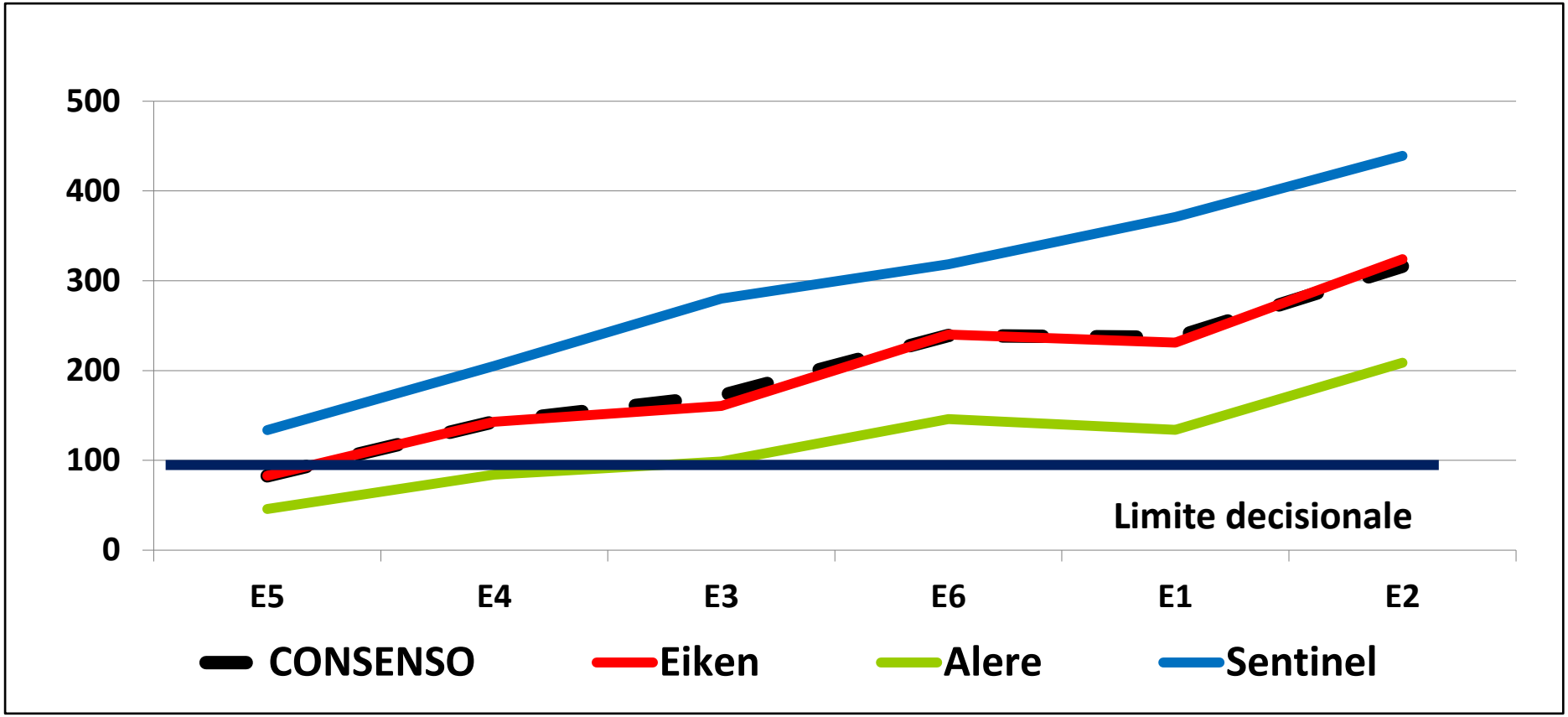
VEQ 2018



Limiti decisionali dichiarati

Eiken	50-70-85-90-99-100
Alfresa	50-80-100
Sentinel	50-80-99-100

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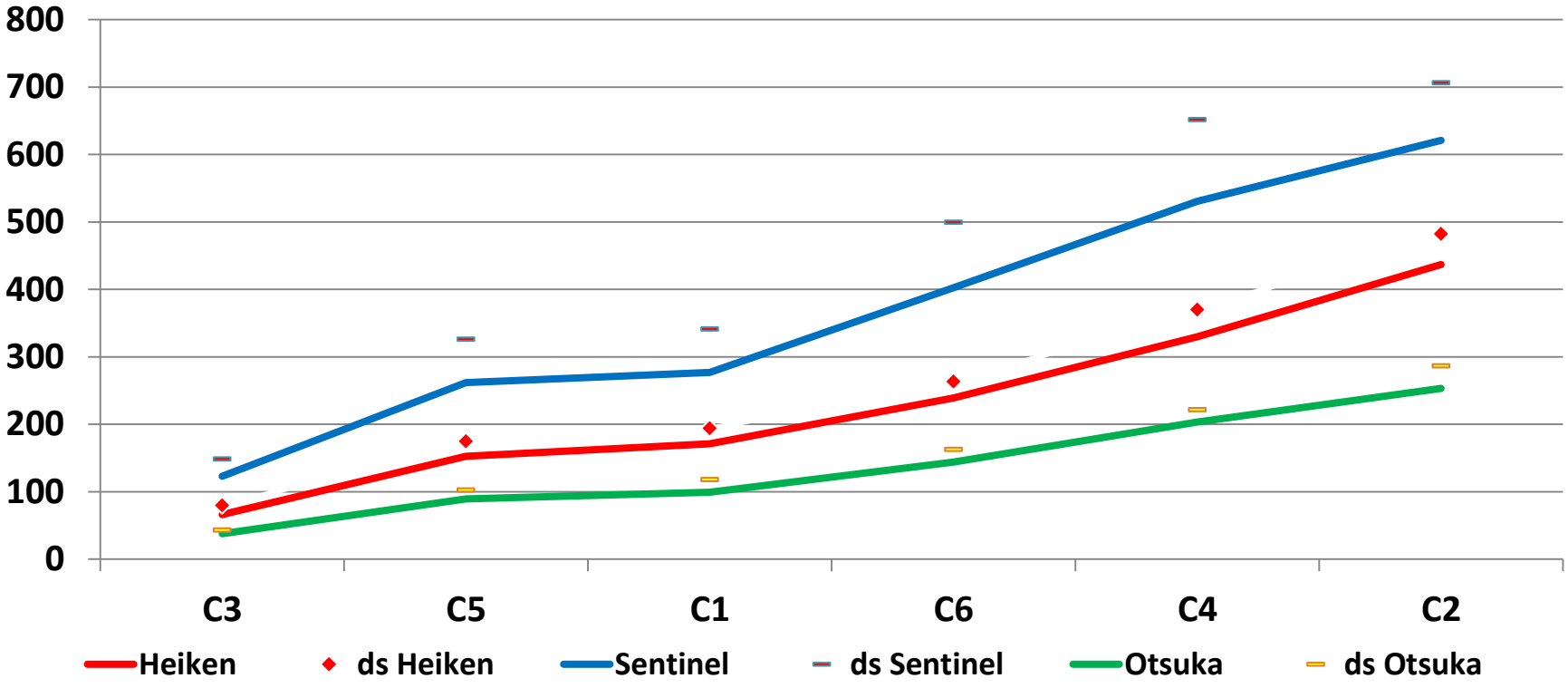
Nessuna differenza significativa dagli esercizi precedenti. ☹

VEQ 2016

	M OC-Sensor	M NS-PLUs	M FOB-Gold	M Chroma
I	171.12 ± 23	99.2 ± 18	276.68 ± 64	nd
II	436.9 ± 45	253.22 ± 33	620.79 ± 85	801.07 ± 98
III	66.09 ± 13	37.78 ± 5	122.77 ± 26	122.77 ± 26
IV	329.7 ± 40	203.33 ± 18	530.84 ± 121	nd
V	152.57 ± 22	89.22 ± 13	261.74 ± 64	nd
VI	238.84 ± 24	143.78 ± 19	402.37 ± 97	nd



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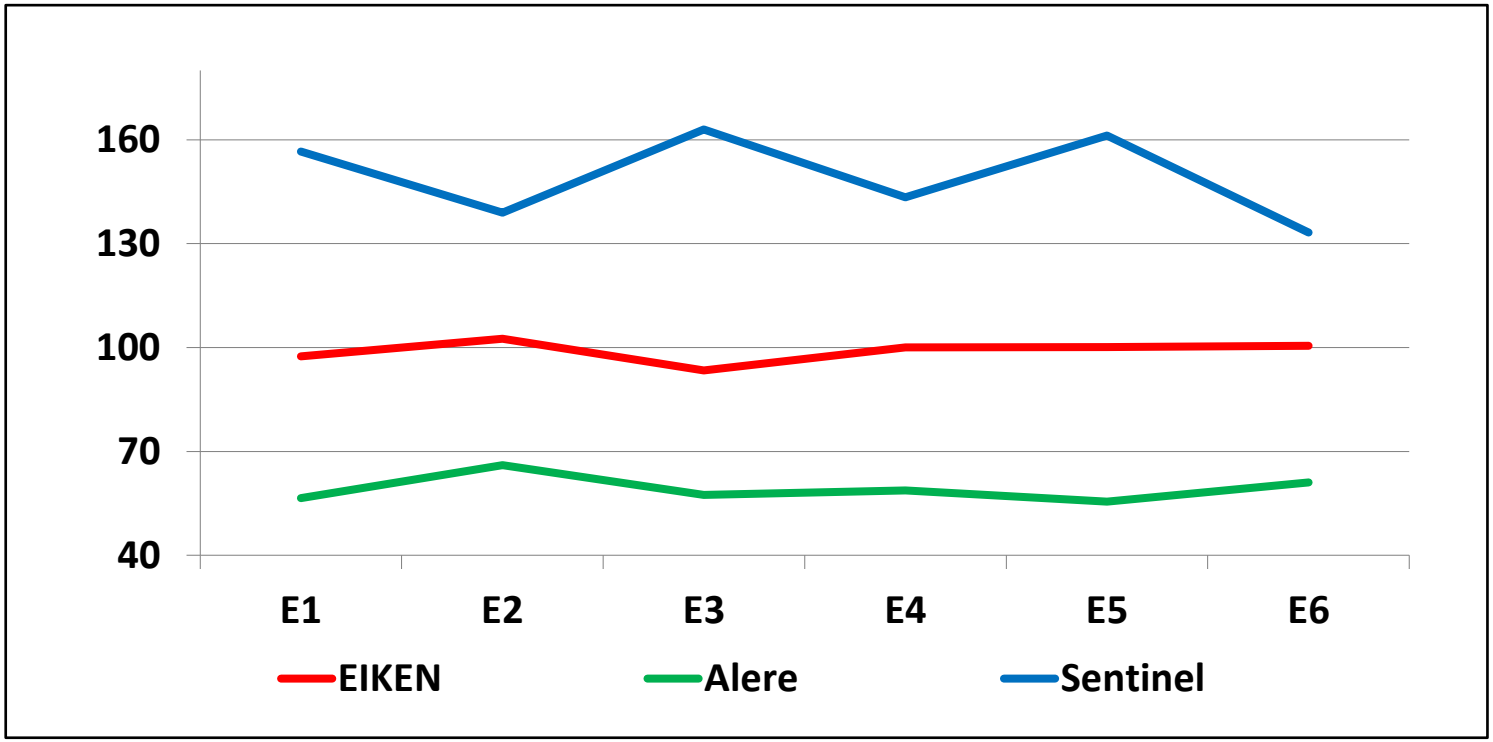
Differenze % tra metodi



* Strumento non allineato coi risultati metodo !

	E1	E2	E3	E4	E5	E6
Sentinel m±ds	372±90	439±110	281±62	205±40	134±30	318±55
Strumento Fu E%	154	144	154.5	142.9	126.5	172.6

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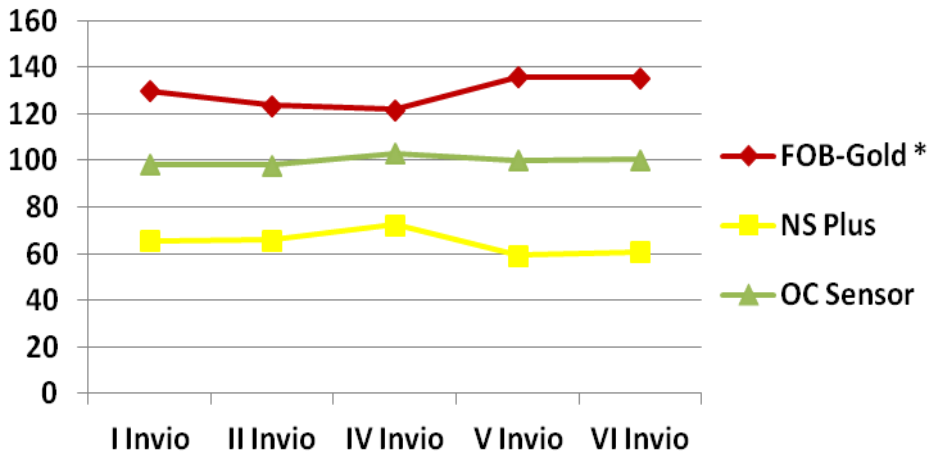
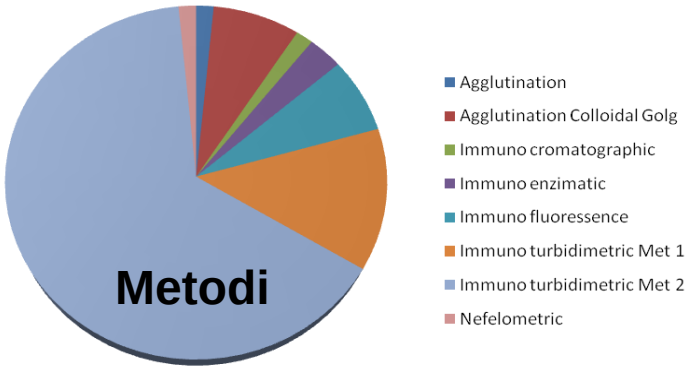
Differenze fase analitica

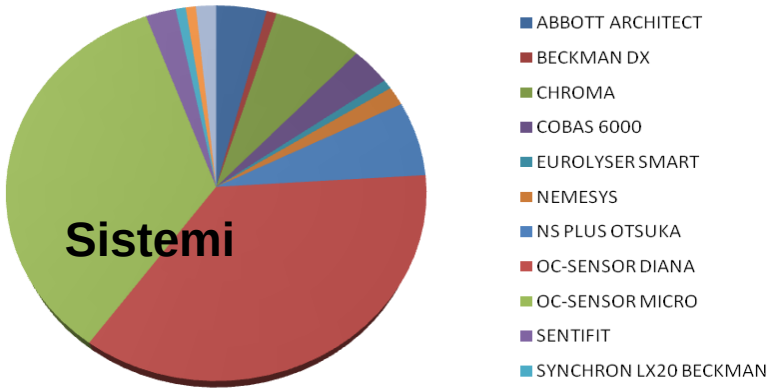


Differenze (%) tra medie consenso

Dati VEQ 2014 CRR Regione Toscana
n = 135

Reagenti diversi (lattice, oro colloidale).
Riferimenti e standards di calibrazione non dichiarati
Metodiche lettura (nefelometria, rifrattometria).



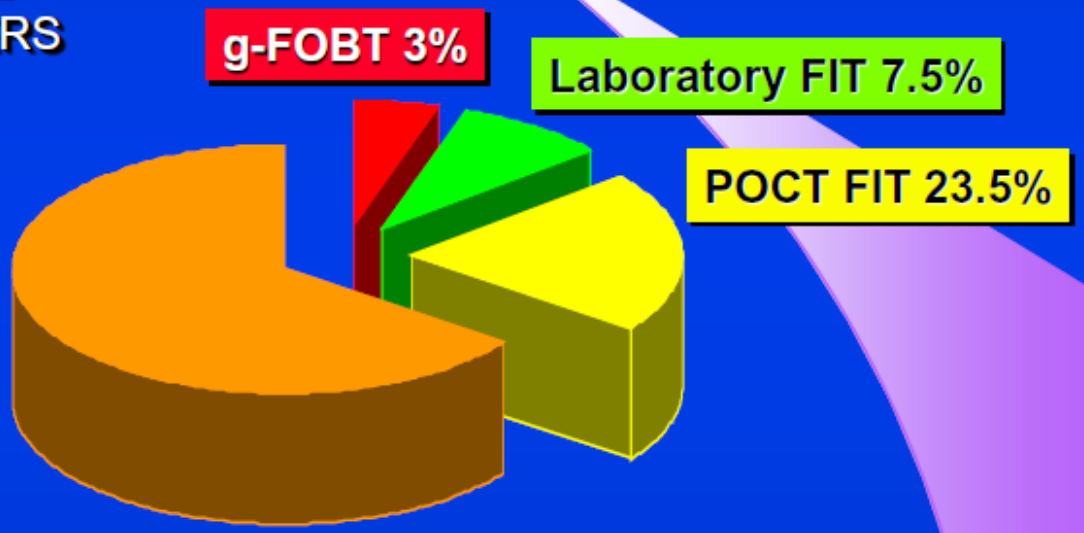


Stato dell'arte Europa. Metodi in uso

1. LÉKAŘSKÁ FAKULTA
UNIVERZITY KARLOVY V PRAZE

FIT REALIZED BY GENERAL PRACTITIONER IN CZECH - 2014

QUESTIONNAIRE
FOR PRACTITIONERS
n = 522



Qualitative FIT 66% - 13 different methods - rapid tests

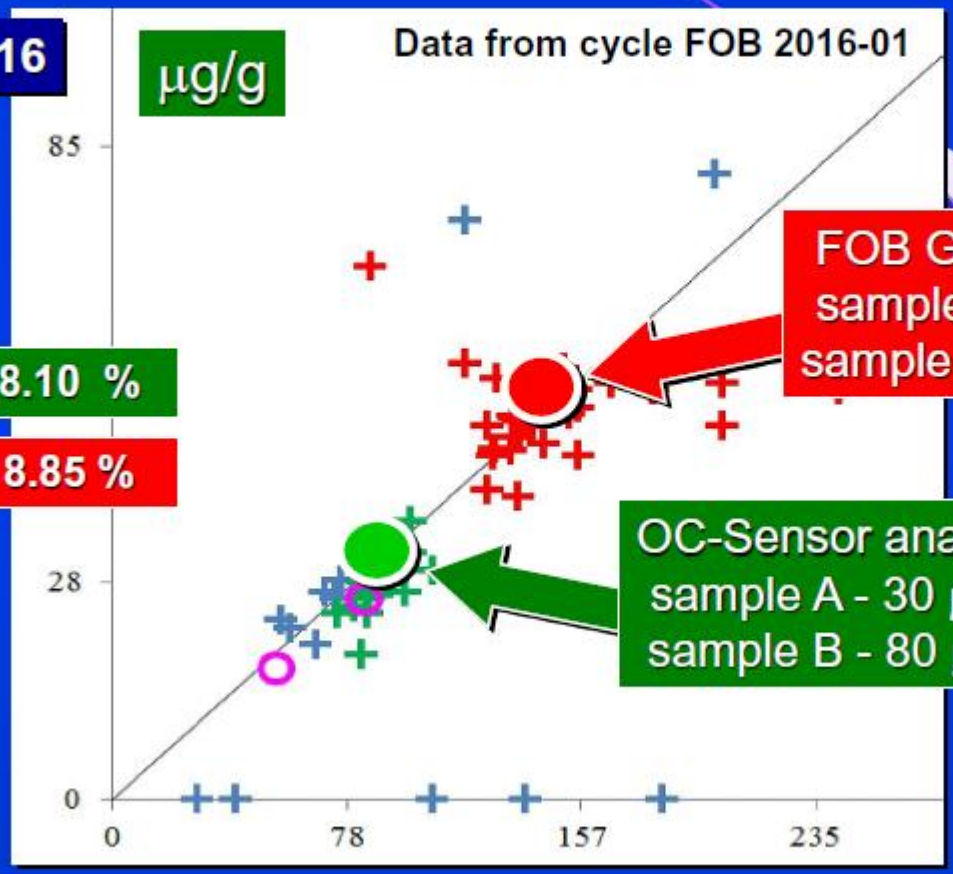
Král N., Seifert B., Korcová M.: Variability tests for occult blood used by general practitioners in screening for colorectal cancer in the Czech Republic. Gastroent Hepatol 2015 69(3): 255–258

Stato dell'arte: VEQ Europa

FIRST FACULTY OF MEDICINE
CHARLES UNIVERSITY IN PRAGUE

FIT EXTERNAL QUALITY ASSESSMENT IN CZECH REPUBLIC

April 2016



Eiken OC-Sensor

Sentinel FOBGold

CV - 8.10 %

CV - 8.85 %

FOB Gold analysis
sample A - 50 µg/g
sample B - 140 µg/g

1,6x higher

OC-Sensor analysis
sample A - 30 µg/g
sample B - 80 µg/g

13

Kocna P., Zima T., Budina M., Ichiyanagi T.: External Quality Assessment (EQA) for Quantitative Fecal Blood in Stool (FIT). Biochimica Clinica, 2013, 37, 423

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Stato dell'arte: fase analitica

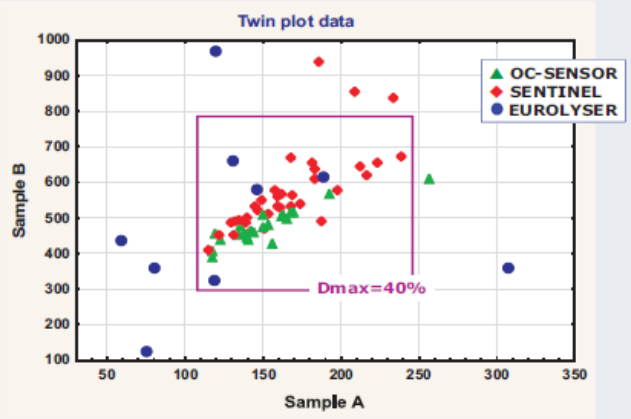
External Quality Assessment (EQA) for Quantitative Fecal Blood in Stool (FIT)

Kocna Petr, Zima Tomáš, Budina Marek, Ichiyanagi Takuo

Institute of Medical Biochemistry & Laboratory Diagnostics, 1st Faculty of Medicine, General Faculty Hospital, Charles University, SEKK, Pardubice, Czech Republic, Eiken Chemical Co. Ltd. Tokyo, Japan

ÚLBLD VFN a 1.LF UK SEKK EIKEN CHEMICAL CO., LTD.

SEKK FOB - EHK 2011/2012

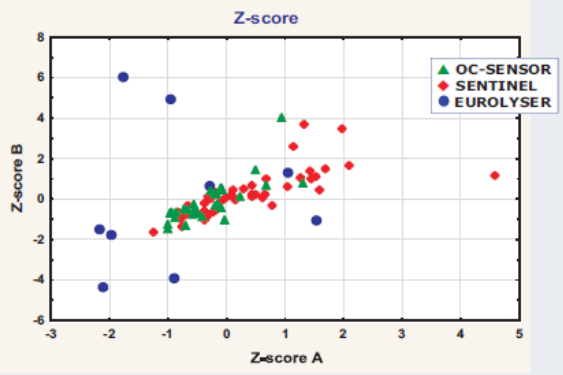


SEKK - EQA - FOB quality, programme design

SEKK is EQA/PT provider accredited according to ISO 17043. SEKK started in 1996 and currently operates in Czech and Slovak Republics and offers EQA programmes in the fields of clinical chemistry, haematology, immunology, nuclear medicine, transfusion medicine, and pathology. The 5 year history of statistical evaluations of all EQA rounds I s freely available at www.sekk.cz.

SEKK is full member of EQALM organisation and closely cooperates with other EQA providers (e.g. RfB - Germany, ECAT – The Netherlands, UK NEQAS - Great Britain).

SEKK FOB - EHK 2011/2012



EIKEN - EQCS - OC SENSORs

EIKEN OC-SENSORs history:
1989 - OC-SENSOR I
1996 - OC-SENSOR II, OC-SENSOR Micro (CE/FDA)
2001 - OC-SENSOR Neo
2007 - OC-SENSOR Diana (CE/FDA)
2010 - OC-SENSOR io (CE/FDA)

These are OC-SESNOR dedicated automatic analysers, more than 1,200 facilities over the world. Six years after releasing the first generation of automatic analyser, we started External Quality Assessment service, which is named EQCS.

EIKEN started quality control service for OC-SENSOR users of Japanese domestic customer from 1995 and now it is expanding for international customers. Its aim is to offer an external quality assessment service to report customers relative positions of their measurements.
At each facilities working OC-SESNOR series analysers, 2 samples are measured 3 times on a day, for 2days. 6 times in total. And the results written on report forms are sent back to Eiken.

In 2008, we started to use liquid samples for this External Quality Assessment program and SD values are lower in 2008 than 2007 when lyohilised samples were used. This means liquid control can reduce variation due to human manipulations.

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Stato dell'arte: Corea

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J Lab Med Qual Assur - 10/2016

- External quality control in Korea - in 2015
- EQA analysis was conducted 3x during the year - 1,250 participants
- Qualitative tests - 569 participants (71%) - 9 different methods
- Qualitative tests provide false-positive results
- The success of the qualitative samples for negative sample was only 11%

- Quantitative FIT test - 235 participants (29%) - 7 different analyzers
- Totally different results depending on the technique used - in ng/ml

Chang-Ho Jeon and A-Jin Lee, J Lab Med Qual Assur 2016;38:120-128
Annual Report on the External Quality Assessment Scheme for Urinalysis and Faecal Occult Blood Testing in Korea (2015)

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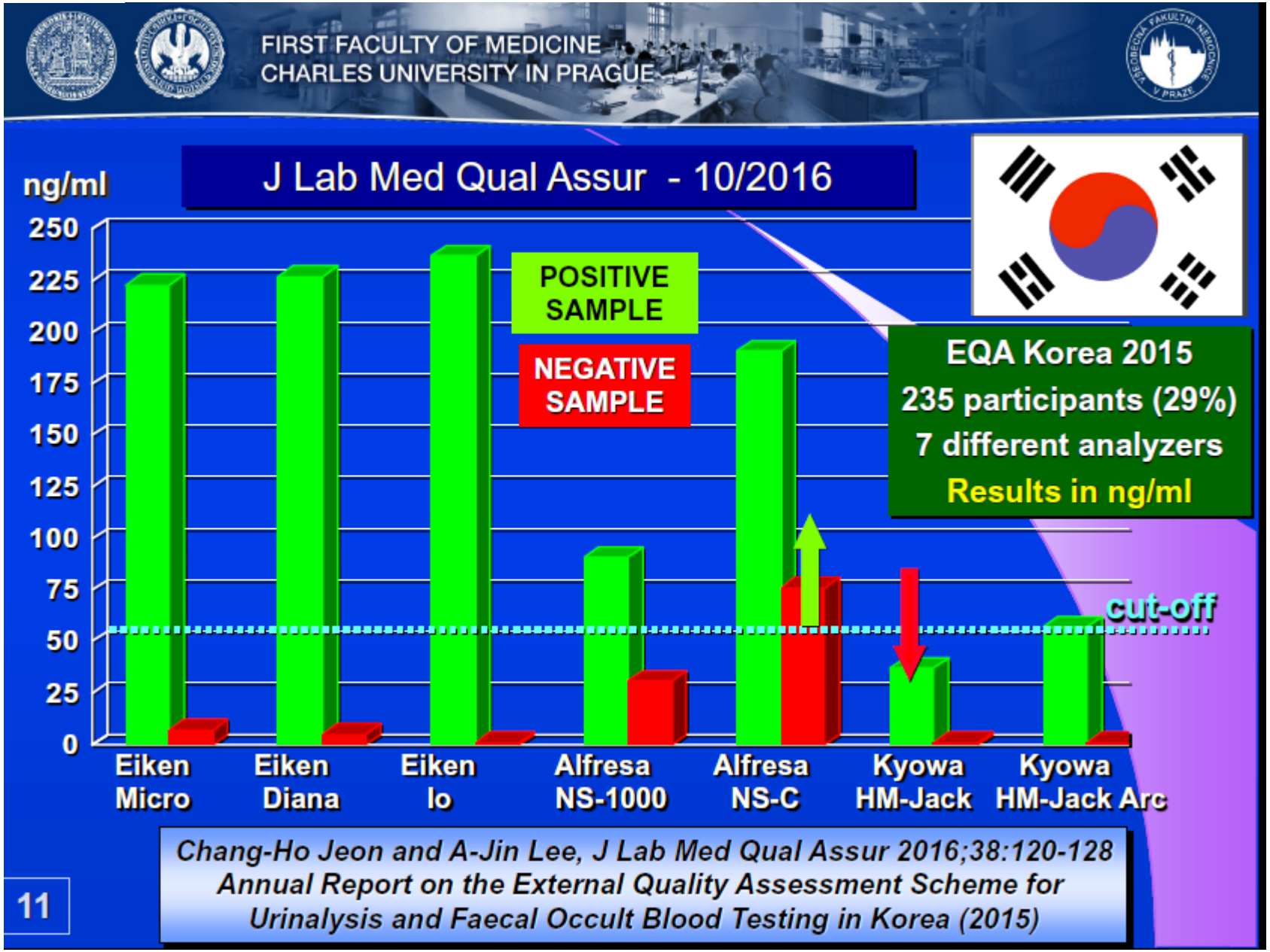
Stato dell'arte: Quantitativi Corea



Gastroenterology - 03/2017

Screening with cut-off 15 µg/g according to OC-Sensor - Eiken study

Predicted positivity - 6.3 %

Screening done with the test FOB Gold - Sentinel

FIT test positivity - 12.2 %

Cut-off has been modified to 47 µg/g to effort positivity 6.3 %

Toes-Zoutendijk E, van Leerdam ME, Dekker E et all. : Real-Time Monitoring of Results During First Year of Dutch Colorectal Cancer Screening Program and Optimization by Altering Fecal Immunochemical Test Cut-Off Levels. Gastroenterology 2017;152:767–775

Dal 2006 non abbiamo risolto nessuna delle criticità emerse

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NSC UK National Screening Committee

14/383

UK National Screening Committee

Screening for Bowel Cancer

19 November 2015

Eppure

Aim

1. To ask the UK National Screening Committee to make a recommendation, based upon the evidence presented in this document, on whether to replace guaiac occult blood testing (gFOBt) with the faecal immunochemical testing (FIT).
2. This document provides background on the items addressing the proposed modification to the NHS Bowel Cancer Screening programme.

The UK NSC recommends a change to the test used in the Bowel Cancer Screening Programmes. The use of Faecal Immunochemical Test as the primary test for bowel cancer should replace guaiac Faecal Occult Blood Test.

As colonoscopy capacity grows or screening uptake increases, the UK NSC and programmes should review and recommend alteration of the cut offs to increase the number of cancers detected.

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Richieste: assistenziali

The quantitative nature of FIT offers, however, new options for screening, which have not been fully explored.

To improve the performance of FIT in CRC screening programs, it was suggested that f-Hb concentration, eventually combined with screenee's age and gender, could be used to categorize different risk groups for advanced neoplasia (AN - advanced adenoma, or CRC), which then be offered tailored protocols, adopting risk based screening intervals and colonoscopy referral criteria.

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Official Journal L 117
of the European Union

English edition Legislation Volume 60 5 May 2017

Contents

I Legislative acts

REGULATIONS

* Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (1) 1

* Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU (1) 176

Richieste: normative

There are specific features of *in vitro* diagnostic medical devices, in particular in terms of risk classification, conformity assessment procedures and clinical evidence, and of the *in vitro* diagnostic medical device sector which require the adoption of specific legislation, distinct from the legislation on other medical devices, whereas the horizontal aspects common to both sectors should be aligned.

Azienda Ospedaliero Universitaria Careggi

Official Journal of the European Union L 117

English edition Legislation Volume 60 5 May 2017

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I Legislative acts

REGULATIONS

* Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (1) 1

* Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU (1) 176

Richieste: normative

Key elements of the existing regulatory approach, such as the supervision of notified bodies, risk classification, conformity assessment procedures, performance evaluation and performance studies, vigilance and market surveillance should be significantly reinforced, whilst provisions ensuring transparency and traceability regarding *in vitro* diagnostic medical devices should be introduced, to improve health and safety.

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VEQ: include fase campionamento

UK NEQAS
International Quality Expertise

Birmingham Quality

BIRMINGHAM QUALITY

Birmingham Quality
PO Box 3909
Birmingham
B15 2UE

birminghamquality@uhb.nhs.uk
www.birminghamquality.org.uk

0121 414 7300
FAX 0121 414 1179

N:\REGI7\PLEU.DOCX; V 1.0

January 2017

SUBSCRIPTION CHARGES FOR 2017-2018
EUROPEAN LABORATORIES

Subscription charges for the new financial year are listed below for Schemes operated from Birmingham

Chemistry special package	A	B	C
Clinical Chemistry	£714	£714	£643
Lipid Investigations ①	£428	£385	£346
Urine Chemistries	£596	£537	£483
GFR Estimation	£371	£334	£301

* If the Chemistry special package does not apply

Hormone special package	A	D	E
Thyroid Hormones	£714	£643	£579
Steroid Hormones ① - 1 analyte	£360	£324	£292
Steroid Hormones - 2 analytes	£563	£506	£456
Steroid Hormones - 3 analytes	£816	£734	£661
Steroid Hormones - 4 analytes	£1,058	£952	£857
Steroid Hormones - 5 analytes	£1,288	£1,159	£1,043
Steroid Hormones - 6 analytes	£1,508	£1,357	£1,221
Steroid Hormones - 7 analytes	£1,710	£1,539	£1,385
Steroid Hormones - 8 analytes	£1,901	£1,711	£1,540
Steroid Hormones - 9 analytes	£2,093	£1,883	£1,695
Steroid Hormones - 10 analytes	£2,250	£2,025	£1,823
Steroid Hormones - 11 analytes	£2,419	£2,177	£1,959
Steroid Hormones - 12 analytes	£2,531	£2,278	£2,050

UK NEQAS for Interpretative ② Comment in Clinical Chemistry	A
Individual participation	£135

Other Schemes	A	B
Haematinics①	£641	£577
Erythropoietin	£332	£299
Holotranscobalamin	£332	£299
Intrinsic Factor Antibodies	£354	£319
Glycated Haemoglobins①	£557	£501
Fructosamine①	£557	£501
Specific Proteins	£422	£380
Tox and TDM [Tox analytes] ①	£332	£299
Tox and TDM [TDM analytes] ①	£332	£299
Newborn Screening	£1,727	£1,554
Neonatal Screening (PKU & TSH)	£591	£532
Paediatric Bilirubin	£394	£354
Quantitative Phenylalanine	£394	£354
Sweat Testing	£371	£334
Urinary Orotic Acid	£332	£299
Urinary Catecholamines	£371	£334
Urine Dipsticks ②	£248	£223
Thyroglobulin	£371	£334
Vitamin Assays ①	£332	£299
Cholinesterase Investigations	£478	£430
Lead & Cadmium in Blood	£523	£471
Faecal Markers of Inflammation	£613	£552
Faecal Haemoglobin (FOB/FIT)	£281	£253
Colorectal Cancer Screening	£90	
Antibiotics ②	charged by	

Weqas

FOB & FIT EQA

WEQAS
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Llanishen
Cardiff, UK
CF14 5DU
Tel: +44 (0) 2920 314750
Fax: +44 (0) 2920 314760
E-mail: office@weqas.com

INTENDED USE
Weqas Faecal Occult Blood and Faecal Immunochemical Testing (FOB & FIT) EQA samples are for in-vitro diagnostic use as an external quality assessment material for testing for the presence of Haemoglobin in faeces.

SUMMARY
External Quality Assessment (EQA), or proficiency Testing (PT) is an essential part of providing quality laboratory diagnostic services, and participation in EQA is required for laboratory accreditation to ISO 15189 and ISO 17025. EQA is the inter laboratory comparison and performance evaluation that extends throughout all phases of the healthcare diagnostic testing cycle.

PRODUCT DESCRIPTION
Material is dispensed aseptically into 0.3g aliquots and stored at -20°C until dispatched. The base material is organic material which closely mirrors the basic constituents of human faeces. This material is then spiked with human whole blood (Hb) to cover the pathological and analytical range for Qualitative guaiac based tests (FOB) and Faecal Immunochemical tests (FIT).

STORAGE AND STABILITY
Unopened samples are stable for 9 months at -20°C.

The samples are dispatched frozen as a 10 week batch of material and should be stored at -20°C on arrival. Samples should be removed from the freezer at set intervals, determined by the schedule of distributions, and brought to room temperature before assay.

PROCEDURE
The samples should be treated the same as patient specimens and run in accordance with the instructions accompanying the test system being used.
TWO SAMPLES SHOULD BE ANALYSED PER FORTNIGHT; EITHER AS A PAIR PER FORTNIGHT OR ONE PER WEEK IF PATIENT SAMPLES ARE BEING TESTED WEEKLY.

1. Wear gloves and handle the sample as a normal patient sample.
2. Carefully remove the blue lid from the universal container; the sample is on the scoop.
3. Apply the sample to the testing device as per the manufacturer instructions for your kit.
4. Safely dispose of excess sample in accordance with local waste policy guidelines.

Always wear gloves to avoid contamination.

LIMITATIONS OF PROCEDURE
The Weqas FOB & FIT EQA samples should be analysed according to the instructions within this document. If there is evidence of microbial or fungal contamination in the product, discard the vial.

The Weqas FOB & FIT EQA samples require storage as described in STORAGE AND STABILITY and handling as described in PROCEDURE.

Accurate and reproducible results are dependent upon properly functioning instruments and reagents and the use of correct procedures.

APPROXIMATE RANGE COVERED
The Weqas FOB & FIT EQA samples cover a relevant pathological and analytical range as outlined below.

Analyte	Approx Range
FOB	0 – 3.5 mg / g
hs FOB	0 – 3.5 mg / g
Qualitative FIT*	0 – 800 µg / g

* - Not Accredited

! CAUTION !
Human source material.
The base material is organic material spiked with human whole blood (Hb).

Although every effort is made to ensure that the material is free from any known infectious agent, the samples should be handled as for clinical specimens.

Filename: SI-QL1-FOBFITIntUse	Approved by: G. Davies	Version: 1.0	Date of Issue: 24/03/17	Page: 1 of 1

Azienda Ospedaliero Universitaria Careggi

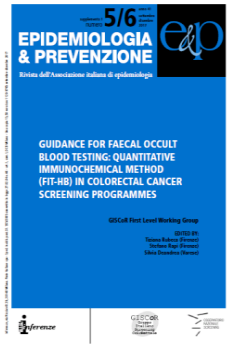
Fase pre-analitica

con comparazioni interlaboratorio;

9. considerando le criticità legate alla corretta gestione della fase pre-analitica, si raccomanda il massimo coinvolgimento del laboratorio nella stesura e nella verifica dei protocolli e delle IdL relativi alle fasi di campionamento, conservazione e invio del materiale biologico; particolare attenzione dovrà essere prestata alla comunicazione all'utente delle modalità di corretta gestione del campione per la sua consegna al laboratorio (ISO/TS 20658 4.3; ISO 15189 5.4.4.2; ISO 15189 5.4.4.3).[5]

A questo proposito viene fortemente raccomandato il massimo coordinamento con il centro screening, il quale dovrà fornire all'utente informazioni esaustive su:

1. modalità di raccolta del materiale biologico, specifiche per il metodo in uso; le modalità ottimali di campionamento sono legate alla forma del bastoncino di prelievo e sono quindi diverse a seconda del metodo utilizzato: risulta quindi utile un intervento specifico al fine di ridurre al massimo le non conformità legate ai campioni "non valutabili" per materiale in eccesso o in difetto;
2. temperatura di conservazione del materiale biologico (per i metodi attualmente in uso è consigliabile la conservazione a 4° C); nel caso in cui il dispositivo campionato non possa essere "immediatamente" consegnato al centro raccolta, dovrà essere indicato al paziente come evitare la degradazione dell'Hb;[11]
3. utilizzo di frigoriferi e contenitori refrigerati presso i centri di raccolta e durante il trasporto del materiale; quest'ultima raccomandazione si rende necessaria al fine di evitare la degradazione dell'Hb contenuta nel dispositivo di campionamento. Dal Congresso GISCoR del 2014 è emerso che solo nel 19,7% dei centri screening il trasporto del materiale fino al laboratorio è eseguito a temperatura controllata, mentre nel 23,7% il trasporto è fatto a temperatura ambiente e nel 56,6% è misto;[25]
4. registrazione della data di raccolta del campione.[14]



Azienda Ospedaliero Universitaria Careggi

Materiali commutabili per CQi

Table 3. Experimental results obtained with the various instruments, using third-party control materials. The following data are included: duration of the investigation, number of values included, mean and standard deviation values (ng/mL), and the range of bias (%) obtained.

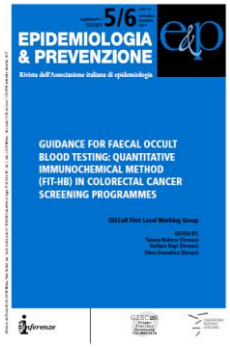
	OC Sensor Diana				HM Jack arc				FOBGOLD				NS Plus			
batches	days	No.	mean±sd	bias (%)	days	No.	mean±sd	bias (%)	days	No.	mean±sd	bias (%)	days	No.	mean±sd	bias (%)
Poly1*	9	24	67±1.9	-2.4÷3.6	7	22	38±1.9	-5.6÷9	6	16	33±5.0	-7.6÷6.6	nv	nv	nv	nv
Poly2*	9	24	378±23.4	-3.6÷4.2	7	22	199±6	-7÷1.8	8	26	376±22.0	-10÷2.1	9	26	63±6.9	-11.1÷14.8
Care1**	9	26	129±1.1	-1.6÷0.7	8	24	130±2.3	-4.2÷1.9	9	26	578±5.4	-1.8÷0.6	8	24	166±23.1	-23.2÷9.9
Care2**	9	26	793±8.0	-1.4÷0.9	8	24	794±6.6	0.1÷0.9	9	26	1.660±22	-2.6÷0.2	8	24	10.6±244.1	-37.2÷25.6
Lyo1***	9	28	198±15.1	-9÷-1.7	7	22	219±7.1	0÷7.7	9	26	170±8.4	-4.7÷4.7	8	14	44±6.0	-21.6÷18.9
Lyo2***	9	28	130±3.8	-3.4÷5.4	7	22	141±3.9	-3.5÷5.5	9	26	77±7.8	12.3÷8.5	nv	nv	nv	nv
Lyo3***	9	28	179±7.3	-5.8÷5.3	7	22	190±11.4	-7.5÷2.5	9	26	152±9.5	-4.7÷7.4	nv	nv	nv	nv

nv: not evaluable
* ready-to-use Polymed controls (Polymed Srl, Florence - Italy)
** ready-to-use Care controls (Care Srl, Genoa - Italy)
*** freeze-dried Polymed controls (Polymed Srl, Florence - Italy)

Table 3 shows the "experimental" results obtained from an investigation of certain third-party control materials found in Italy. The information collected confirms the lack of a standard reference for different analytical methods and the difficulties related to the procurement of usable third-party material. The data provided in Table 3 is intended to provide the preliminary guidance for selecting adequate materials and setting analytical targets for different methods.

The experiment was conducted over eight days with material stored at 4°C. The freeze-dried controls were reconstituted with the buffer used by the analytical system (as indicated by the manufacturer). The results obtained confirmed the inability to interchange control materials and the absence of a standard reference for analytical methods – particularly when they are based on different analytical strategies.

It is therefore desirable to develop new control materials to address the current shortcomings.



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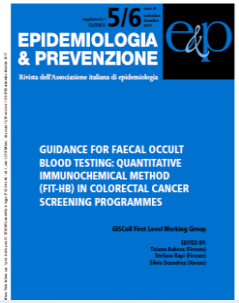
Cqi materiali non di terza parte

Table 2. IQC operating ranges on quantitative analytical systems used by screening laboratories in Italy. The following data are included: duration of verification, number of batches used and analytical ranges. In detail ranges of targets set by manufacturers, bias and coefficients of variation (CV).

	No. OF MONTHS	No. OF BATCHES	No. OF SESSIONS	TARGET	BIAS (%)	CV
OC Sensor Diana						
low	12	6	8÷38	127÷137	-1.5÷3.4	1.6÷4.4
high	12	6	8÷38	432÷453	-3.1÷7.5	0.89÷2.3
HM Jack arc						
low	6	1	108	24	-2.1÷3.1	2.8÷5.9
high	6	1	108	95	-0.5÷7.4	2.3÷4.9
FOBGOLD						
low	12	5	15÷71	78÷90	-10.4÷8.9	5.6÷11.5
high	12	5	15÷71	309÷318	-10.7÷ 5.6	1.7÷7.8
NS Plus						
low	12	3	42÷198	96÷101	-3.8÷9.9	2.9÷7.8
high	12	3	42÷198	246÷264	-5.3÷8.0	2.4÷6.1



Si ritiene quindi auspicabile lo sviluppo di nuovi materiali di controllo in grado di sopperire alle attuali carenze.

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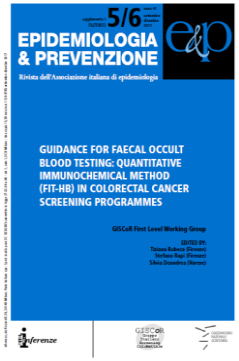
Gestione appalti

laboratori siano coinvolti nella valutazione preliminare dei dispositivi di prelievo. In particolare, si suggerisce di inserire in fase di stesura dei capitolati di gara una valutazione comparativa specifica con l'attribuzione di punteggi qualitativi associati alle seguenti informazioni:

1. capacità del tampone di stabilizzare l'Hb;
2. praticità del dispositivo di prelievo;
3. qualità (completezza, semplicità) delle informazioni fornite per l'auto-campionamento;
4. caratteristiche prestazionali dei dispositivi di campionamento forniti;
5. volume di campionamento del dispositivo;
6. volume di tampone utilizzato;
7. frasi di rischio del materiale contenuto all'interno del dispositivo (come definito in: Annex III of European Union Directive 67/548/EEC: Nature of special risks attributed to dangerous substances and preparations).



Epidemiol Prev 2017; 41 (5-6) Suppl1: 1-32. doi: 10.19191/EP17.5-6S1.P001.101

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Report risultati

POST-ESAME (FASE POST-ANALITICA)

Le linee guida internazionali richiedono che i risultati siano espressi in modalità qualitativa binaria POSITIVO/NEGATIVO[14] con l'indicazione di sottoporsi a colonscopia in caso di risultato positivo e alla ripetizione dopo 2 anni in caso di risultato negativo dell'esame.

In caso di risultato positivo è auspicabile, pur personalizzando la risposta, che il centro screening dia indicazioni esaustive per l'esecuzione dell'approfondimento.[6]

Sebbene non vi sia consenso sulle modalità di espressione dei risultati quantitativi, è fortemente consigliato l'uti[illegible] µg Hb/g feci come unità di misura per riportare i dati quantitativi. Tuttavia, appare auspicabile in futuro il progressivo u[illegible] µg Hb/ml di materiale campionato,[13] sia perché scientificamente corretto (il materiale non viene pesato ma ottenuto per auto-campionamento mediante riempimento di una specifica regione del dispositivo), sia perché consente di fornire indicazioni sulle caratteristiche dei dispositivi di prelievo alle aziende produttrici.[29]

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Qualità - Processo

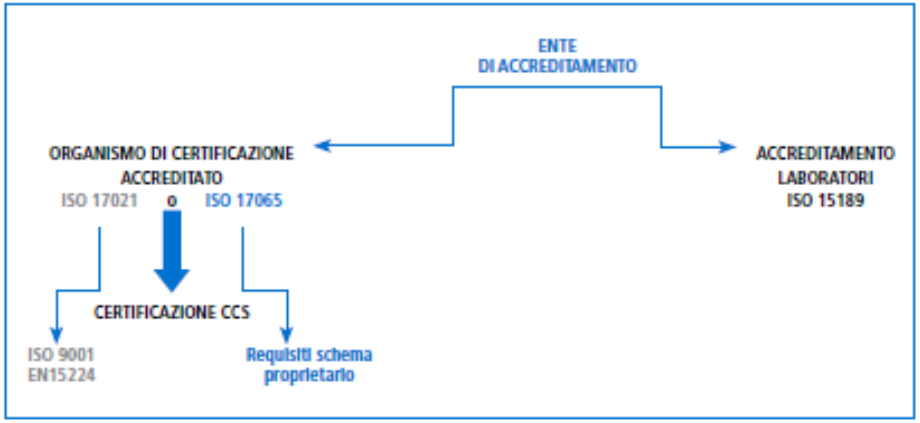
LA CERTIFICAZIONE DEL PROCESSO DI SCREENING

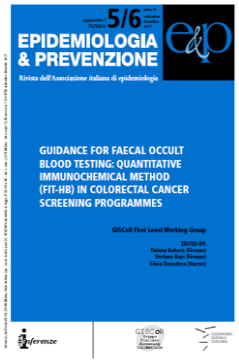
Il processo di screening e diagnosi è composto sostanzialmente da due sotto-processi:

- servizi collegati all'avvio e al termine del processo;
- servizi di medicina di laboratorio.

Poiché strettamente correlati, ai fini della qualità complessiva del macro-processo entrambi dovrebbero essere sottoposti a valutazione da una terza parte indipendente.
Non essendoci norme di accreditamento per la valutazione del primo processo, esso dovrà essere sottoposto a una certificazione di tipo generale secondo i requisiti generali già fissati dalle normative ISO 9001 o EN 15224 – specifica per il settore sanitario che ricade nei requisiti di accreditamento ISO 17021, oppure, in modo più specifico, potrà essere sottoposto a certificazione di "processo"/"servizio", accreditata secondo la norma ISO 17065, con requisiti fissati direttamente dal "proprietario" dello schema.
Il secondo ricade sotto la norma di accreditamento ISO 15189, ove lo stesso "proprietario" dello schema potrà fissare requisiti specifici per i processi/le discipline oggetto di accreditamento.

Figura 1. Schema dei riconoscimenti di terza parte indipendente.





Epidemiol Prev 2017; 41 (5-6) Suppl1: 1-32. doi: 10.19191/EP17.5-6S1.P001.101

WEO
Expert Working Group (EWG)
Colorectal Cancer Screening Committee (CRC SC)

WEO
World Endoscopy Organization

First WG-FIT Meeting
Euromedlab Athens 14. June 2017

ifcc
International Federation of Clinical Chemistry and Laboratory Medicine

IFCC
Scientific Division Working Group
Fecal Immunochemical Testing (WG-FIT)

To harmonise and/or standardise analysis of haemoglobin in faecal samples by immunochemistry (FIT)

TAKE HOME MESSAGE

- ✓ Efforts to change qualitative FIT to quantitative FIT
- ✓ Efforts to change units from ng/ml to µg/g of stool
- ✓ Standardization of FIT methods according to IFCC committee
- ✓ Essential requirement for FIT external quality control
- ✓ Personalized approach to FIT analysis of Hb in faeces
- ✓ Screening programs modifications using FIT values

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8.3.56

WG-FIT (Fecal Immunochemical Testing): The WG was established from the last IFCC SD EC meeting (Nov 2016) and has started its activities.

This WG has established the following Terms of Reference:

- To harmonize and/or standardize analysis of hemoglobin in fecal samples by immunochemistry (FIT)
- To standardize the pre-analytical phase
- To establish EQA and 3rd party IQC programs.
- To determine impact of assay interference of Hb variants and other factors 10
- To determine the feasibility of developing reference materials and/or commutable calibrators The first meeting of the WG will be held on Wednesday June 14th at the EuroMedLab/ IFCC congress in Athens.

The core members group includes invited experts in the field of FIT testing from around the world.

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8.3.56 WG –
Key outcomes of the first meeting;

• Development of a reference material/ method for FIT: a reference lab in Belgium to collate information via surveying all the FIT companies. This has been carried out and results to be discussed at the next FIT meeting in October 2017 to enable progression. 11

• Challenges of EQA schemes include the pre-analytical variation of a stool sample being loaded into a collection device so the group has discussed making a formal recommendation that EQA schemes have two parts (1) sample pre-loaded to only assess the performance of the analyzer (2) provide sample to assess whole pathway from sample loading to result.
This needs further discussion and ratification at the next meeting.

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Richieste: normative

Introduction

ISO 15189 (Medical laboratories—Requirements for quality and competence) requires the sources of variation to be assessed in all phases of the examination process. "Section 5.5.1.4. Measurement uncertainty of measured quantity values" requires the laboratory to "determine measurement uncertainty for each measurement procedure in the examination phase used to report measured quantity values on patients' samples" (1). The laboratory shall define the performance requirements for the measurement uncertainty of each measurement procedure and regularly review estimates of uncertainty measurement.

Editorial

Is it possible to correctly assess the pre-analytical characteristics of faecal tests?

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Dobbiamo decidere dove allocare questi device

Conclusions

Classification of devices and methods for faecal tests according to the incoming European (EU) *in vitro* diagnostic medical devices regulation (10) is not as yet defined, and also the class of this test is not as yet defined. The introduction of faecal tests based on self-sampling among those methods with full metrological and clinical performances assessed before the introduction on the market is unlikely (III or IV class). **Documentation in these more restrictive classes of devices should be justified by the use of test to assess the risk in individuals.**

J Lab Precis Med 2018. http://dx.doi.org/10.21037/jlpm.2018.04.06

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Dobbiamo decidere 'dove allocare' questi device

A more detailed use of f-Hb concentrations requires a more accurate investigation of tests before their application in clinical settings. **In particular, the evidence of an increased risk of CRC (11) in subjects with f-Hb concentrations between the limits of detection and quantification of quantitative methods requires further attention to the standardisation of many aspects of FIT.** Therefore, the presentation of the **appropriate Clinical Laboratory Standards Institute (CLSI) protocols to standardise and assure quality and metrology on both pre-analytical and analytical phases of faecal tests (12) should be a main issue for the IFCC Scientific Division Working Group on FIT (13).**

J Lab Precis Med 2018. http://dx.doi.org/10.21037/jlpm.2018.04.06