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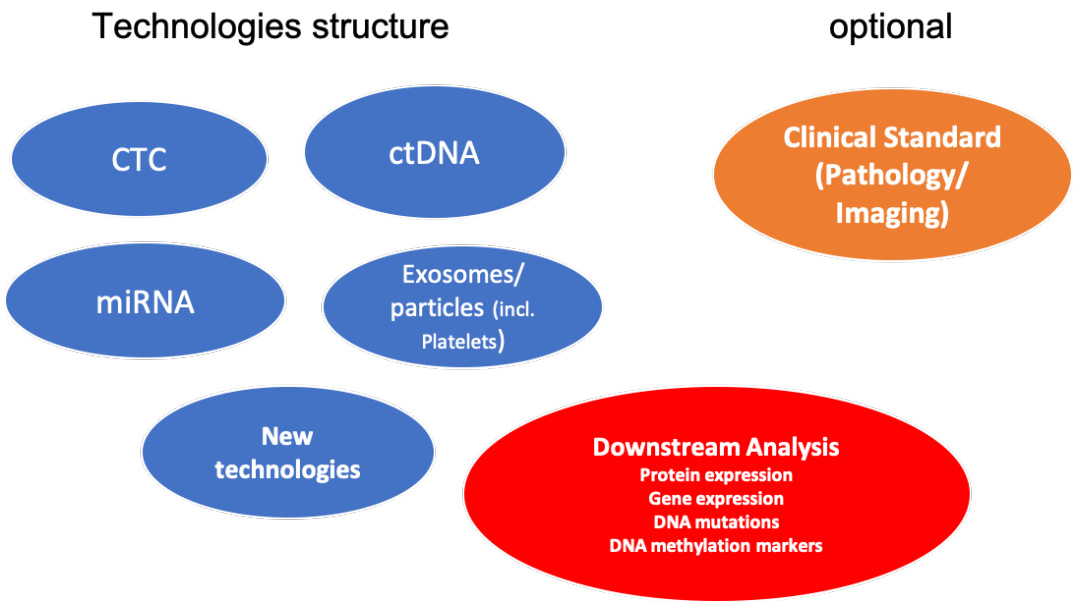
Technologies



Short-term goals

- To form working groups based on the suggested structure with two (or more) responsible organizers for each working group
- To make an inventory of all technologies, analytes and biomarkers used in the labs of ELBS members (questionnaire prepared)
- **To validate novel technologies in terms of sensitivity, specificity and robustness with the platforms established within CANCER-ID and extend this beyond NSCLC**
- To establish networks with common aims to identify funding opportunities and facilitate common funding

Long-term goals

- prepare a list of validated LB technologies, based on the clinical question to be answered
- standardization of LB tests (ISO-15189) at the pre-analytical and analytical steps
- establishment of external quality control schemes in collaboration with the ELBS standardization group

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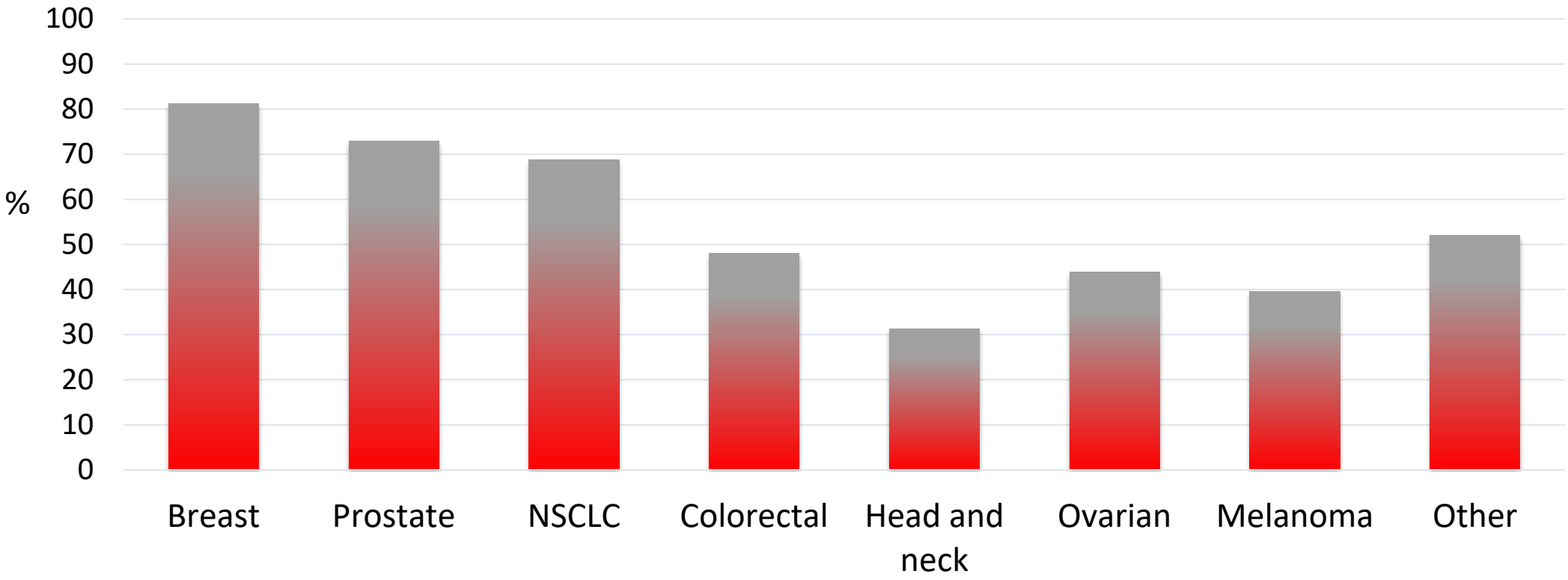
ELBS – cancer types investigated



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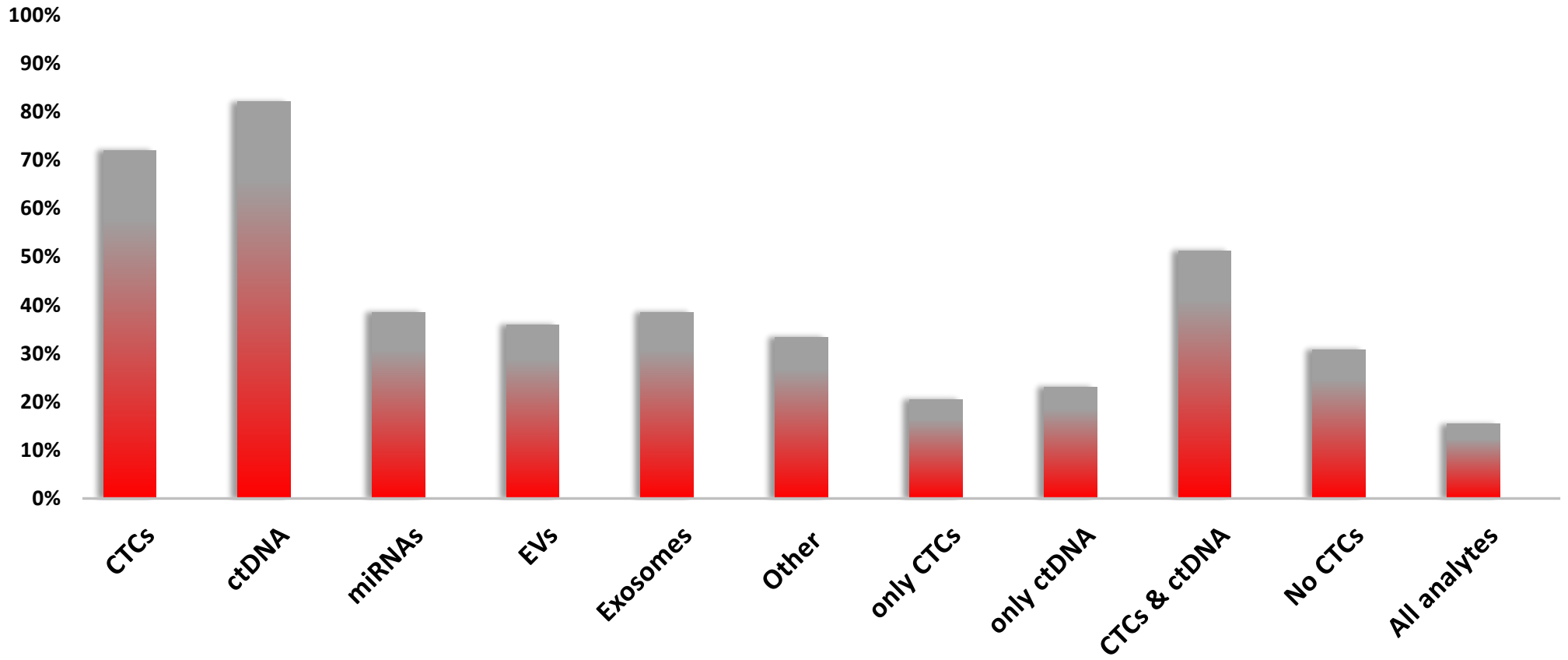
ELBS - Liquid biopsy analytes



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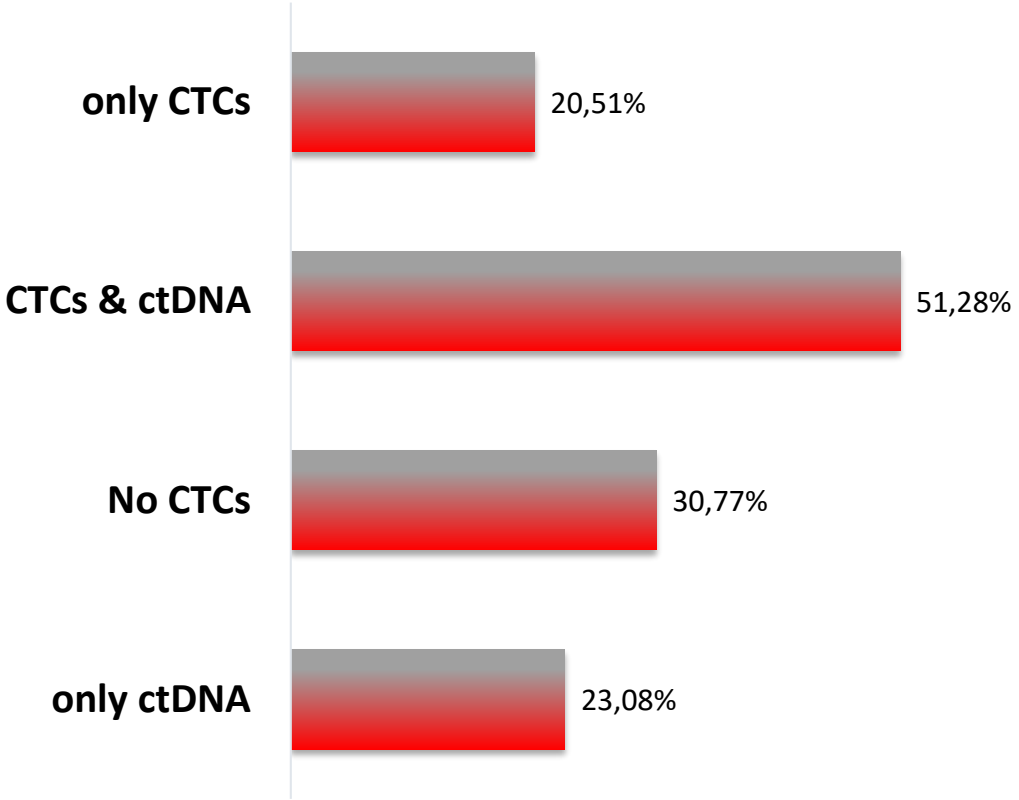
ELBS - Liquid biopsy analytes



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CTC

Evi Lianidou

Nick Stoecklein

Working towards accreditation and reimbursement

- Markers of immediate interest for ISO15189 certification
- Establishment of a validation pipeline
- Distribution of protocols and support for certification

→ ELBS ”certified” labs

Ring trials and technology assessment

- Frequency of ring trials
- “Pre-competitive arena” for companies
- Cross comparisons between technologies

→ ELBS “approved” technologies

Networking

- “open channel” for discussion of technologies and issues
- Exchange between users and companies

Please contribute
→ chair a task

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ELBS CTC technologies meeting
26th May 2021

ISO15189 certification requirements step by step

Evi Lianidou
ACTC Lab, University of Athens, Greece

ACCREDITATION ACCORDING TO ISO 15189:2012 STANDARD

- procedure by which an authoritative body gives formal recognition that a clinical laboratory is performing in accordance with the requirements of ISO 15189:2012 standard and is competent to carry out specific analyses

- Useful tool for clinical laboratories that allows them to provide qualitative services to clinicians and patients by ensuring the generation of accurate and reliable results.

- A key step to obtain accreditation according to ISO 15189:2012 is the constant and periodic participation in External Quality Assessment (EQA) schemes.

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ICS › 03 › 03.120 › 03.120.10

ISO 15189:2012

Medical laboratories — Requirements for quality and competence

- **Scope:** to guide laboratories to develop a quality management system that regulates the whole testing procedure, thus ensuring constant quality services of patient care.

- The ISO15189:2012 describes which procedures and aspects must be included regarding pre-analytical, analytical and post-analytical phase, in order to design a proper quality management system.

- This International Standard can be used by medical laboratories in developing their quality management systems and assessing their own competence. It can also be used for confirming or recognizing the competence of medical laboratories by laboratory customers, regulating authorities and accreditation bodies.

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ISO 15189: 2012 REQUIREMENTS

Management requirements

Organization and management responsibility
Quality management system
Document control
Service agreements
Examination by referral laboratories
External services and supplies
Advisory services
Resolution of complaints
Identification and control of nonconformities
Corrective action
Preventive action
Continual improvement
Control of records
Evaluation and audits
Management review

Technical Requirements

Personnel
Accommodation and environmental conditions
Laboratory equipment, reagents, and consumables
Pre-examination processes
Examination processes
Ensuring quality of examination results
Post-examination processes
Reporting of results
Release of results

EXTERNAL QUALITY ASSESSMENT SCHEMES

- Crucial for the harmonization and standardization of the processes by ensuring the evaluation and monitoring of the comparability of test results across different laboratories and over time.

- The purpose of EQA programs includes
  (a) the evaluation of laboratory performance for specific tests and its continuous monitoring,
  (b) the identification of interlaboratory differences,
  (c) the evaluation of method/diagnostic system performances,
  (d) the degree of comparability between methods/diagnostic systems and
  (e) the monitoring of the success of harmonization/standardization efforts for improving results comparability.

  (*Sciacovelli et al. Clin Chem Lab Med 2018; 56(10): 1644–1654*)

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EXTERNAL QUALITY ASSESSMENT (EQA) scheme providers

- IQNPATH
  http://www.iqnpath.org/

  EQA-European Society of Pathology
  http://lung.eqascheme.org/

  EMQN
  https://www.emqn.org/

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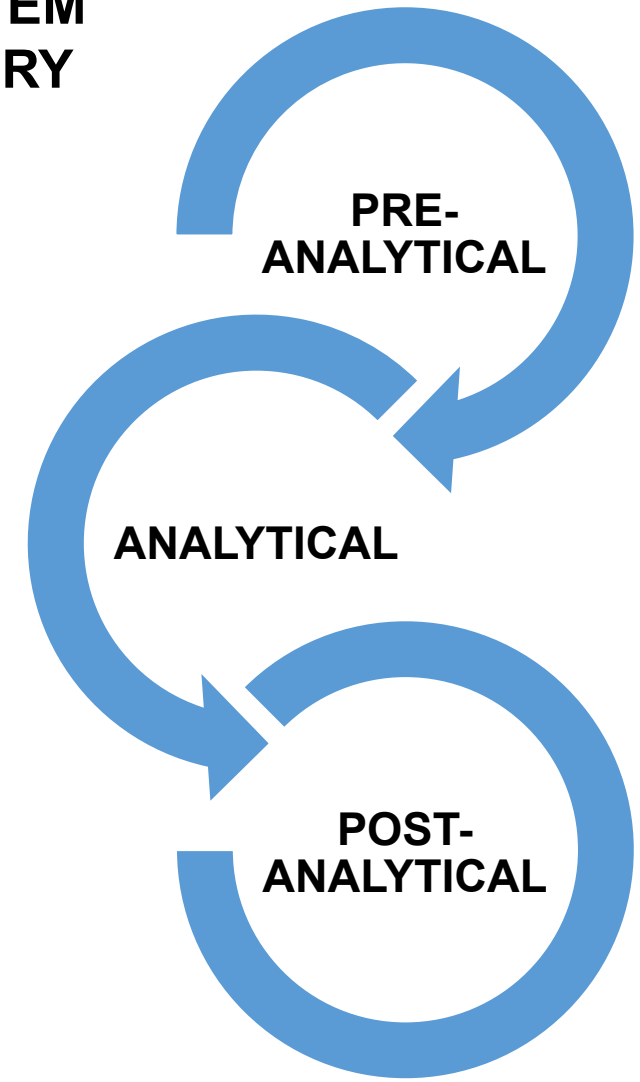
QUALITY MANAGEMENT SYSTEM OF THE CLINICAL LABORATORY



- Identification of patient
- Whole blood sampling
- Transportation
- Sample processing

- Quality control assessment
- Review of analytical procedure (SOPs)

- Review of results
- Storage of clinical material
- Sample and waste disposal
- Reporting and releasing of results
- Retention of results

EQA SCHEMES IN LIQUID BIOPSY

- Standardization of all procedures, and pre-analytical factors are essential for the implementation of liquid biopsy assays in routine clinical practice

- Several external quality assessments and multi-laboratory comparisons have been completed so far mainly on ctDNA isolation and analysis

- EGFR mutation analysis in plasma cfDNA is the only available EQA scheme in liquid biopsy so far and thus could consist a paradigm of the implementation of further liquid biopsy EQA schemes

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EQA SCHEMES IN LIQUID BIOPSY

- Standardization of all procedures, and pre-analytical factors are essential for the implementation of liquid biopsy assays in routine clinical practice
- ISO-15189 certification for specific liquid biopsy assays is essential for reimbursement purposes
- Liquid biopsy:
- ctDNA: FDA approved companion diagnostic tests in plasma, external quality schemes are available (EGFR, PIK3CA starting)
- **CTCs: no EQA available so far!! ELBS????**

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DE GRUYTER

Clin Chem Lab Med 2017; aop

Verena Haselmann*, Parviz Ahmad-Nejad, Wolf J. Geilenkeuser, Angelika Duda, Merle Gabor, Romy Eichner, Simon Patton and Michael Neumaier*

Results of the first external quality assessment scheme (EQA) for isolation and analysis of circulating tumour DNA (ctDNA)

Virchows Arch
DOI 10.1007/s00428-017-2226-8

ORIGINAL ARTICLE

EGFR T790M mutation testing of non-small cell lung cancer tissue and blood samples artificially spiked with circulating cell-free tumor DNA: results of a round robin trial

Jana Fassunke[1] · Michaela Angelika Ihle[1] · Dido Lenze[2] · Annika Lehmann[2] · Michael Hummel[2] · Claudia Vollbrecht[2] · Roland Penzel[3] · Anna-Lena Volckmar[3] · Albrecht Stenzinger[3] · Volker Endris[3] · Andreas Jung[4] · Ulrich Lehmann[5] · Silke Zeugner[6] · Gustavo Baretton[6] · Hans Kreipe[5] · Peter Schirmacher[3] · Thomas Kirchner[4] · Manfred Dietel[2] · Reinhard Büttner[1] · Sabine Merkelbach-Bruse[1]

The Journal of Molecular Diagnostics, Vol. 20, No. 4, July 2018

ELSEVIER

the Journal of Molecular Diagnostics
jmd.amjpathol.org

Detection of *EGFR* Variants in Plasma

A Multilaboratory Comparison of a Real-Time PCR EGFR *Mutation Test in Europe*

Cleo Keppens,* John F. Palma,† Partha M. Das,‡ Sidney Scudder,‡ Wei Wen,‡ Nicola Normanno,§ J. Han van Krieken,¶ Alessandra Sacco,§ Francesca Fenizia,§ David Gonzalez de Castro,‖** Selma Hönigschnabl,†† Izidor Kern,‡‡ Fernando Lopez-Rios,§§ Maria D. Lozano,¶¶ Antonio Marchetti,‖‖ Philippe Halfon,*** Ed Schuuring,††† Ulrike Setinek,‡‡‡ Boe Sorensen,§§§ Phillipe Taniere,¶¶¶ Markus Tiemann,‖‖‖ Hana Vosmikova,**** and Elisabeth M.C. Dequeker*

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Keppens et al. BMC Cancer (2018) 18:804
https://doi.org/10.1186/s12885-018-4694-x

BMC Cancer

RESEARCH ARTICLE Open Access

International pilot external quality assessment scheme for analysis and reporting of circulating tumour DNA

Cleo Keppens[1,2*], Elisabeth M. C. Dequeker[1,2], Simon J. Patton[3], Nicola Normanno[4], Francesca Fenizia[4], Rachel Butler[5], Melanie Cheetham[3], Jennifer A. Fairley[6], Hannah Williams[6], Jacqueline A. Hall[7,8], Ed Schuuring[2,9], Zandra C. Deans[6] and On behalf of IQN Path ASBL

Virchows Archiv
https://doi.org/10.1007/s00428-019-02571-3

ORIGINAL ARTICLE

IQN path ASBL report from the first European cfDNA consensus meeting: expert opinion on the minimal requirements for clinical ctDNA testing

Zandra C. Deans[1] · Rachel Butler[2] · Melanie Cheetham[3] · Elisabeth M. C. Dequeker[4,5] · Jennifer A. Fairley[1] · Francesca Fenizia[6] · Jacqueline A. Hall[7] · Cleo Keppens[4] · Nicola Normanno[6] · Ed Schuuring[8] · Simon J. Patton[3]

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Multicenter Study > Clin Chem Lab Med. 2019 Apr 24;57(5):e97-e101.
doi: 10.1515/cclm-2018-0676.

A pilot plasma-ctDNA ring trial for the Cobas® EGFR Mutation Test in clinical diagnostic laboratories

Aliki Ntzifa [1], Christos Kroupis [2], Alexander Haliassos [3], Evi Lianidou [4]

➢**10 identical cfDNA reference standards in synthetic plasma:**

- ISO-certified for cfDNA analysis
- purchased from *Horizon Discovery, Cambridge, UK*
- *EGFR* mutations*:* T790M, E746-A750del*,* L858R in different allelic frequencies: 5%, 0.5%, 0.05%, 0% (wild type)

•shipped on dry ice to each laboratory by a courier ISO 9001:2015 certified for biological sample transportations
•All samples in codes
•All labs in codes

➢**8 diagnostic laboratories in Greece, received 10 identical samples for analysis**

- 6/8 were ISO15189-accredited for EGFR testing in tissues with various techniques
- 3/6 also in plasma matrix
- Only 1/8 was ISO15189-accredited for EGFR testing in plasma ctDNA with Cobas®

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RESULTS

Table 1: Plasma *EGFR* mutation results for the eight participating laboratories.[a]

Horizon reference standards	Mutations and percentage in Horizon certified standards	Enrolled laboratories							
		1	2	3	4	5	6	7	8
#1	0.5% T790M	T790M	T790M	T790M	T790M	T790M, **Exon19 Del**	T790M	T790M	T790M
#2	5% T790M	T790M	T790M	**No mutation detected**	T790M	T790M	T790M	T790M	T790M
#3	0.5% L858R	L858R	L858R	L858R	L858R	L858R	**No mutation detected**	L858R	L858R
#4	0.05% E746-A750del	Exon19 Del	Exon19 Del	Exon19 Del	Exon19 Del	Exon19 Del	Exon19 Del	Exon19 Del	Exon19 Del
#5	0.5% E746-A750del	Exon19 Del	Exon19 Del	Exon19 Del	Exon19 Del	Exon19 Del	**No mutation detected**	Exon19 Del	Exon19 Del
#6	Wild type	Wild type	Wild type	Wild type	Wild type	Wild type	**T790M**	Wild type	Wild type
#7	0.5% T790M, L858R	T790M, L858R	T790M, L858R	T790M, L858R	T790M, L858R	T790M, L858R	T790M, L858R	T790M, L858R	T790M, L858R
#8	5% T790M, L858R	T790M, L858R	T790M, L858R	T790M, L858R	T790M, L858R	T790M, L858R	T790M, L858R	T790M, L858R	T790M, L858R
#9	0.5% T790M, E746-A750del	T790M, Exon19 Del	T790M, Exon19 Del	T790M, Exon19 Del	T790M, Exon19 Del	T790M, Exon19 Del	T790M, Exon19 Del	T790M, Exon19 Del	T790M, Exon19 Del
#10	5% T790M, E746-A750del	T790M, Exon19 Del	T790M, Exon19 Del	T790M, Exon19 Del	T790M, Exon19 Del	T790M, Exon19 Del	T790M, Exon19 Del	T790M, Exon19 Del	T790M, Exon19 Del

[a]Cobas® EGFR Mutation Test v2 offers only qualitative genotyping result and also does not refer to the exact nature of exon19 deletion (e.g. e746-750). In bold are the wrong results, that were not expected since these were not the correct answers according to the standards provided.

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FDA approves alpelisib for metastatic breast cancer

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On May 24, 2019, the Food and Drug Administration approved alpelisib (PIQRAY, Novartis Pharmaceuticals Corporation) in combination with fulvestrant for postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after an endocrine-based regimen.

FDA U.S. FOOD & DRUG ADMINISTRATION

EMQN

Participating in EQA

EMQN launches pilot External Quality Assessment (EQA) scheme for PIK3CA testing in Advanced Breast Cancer

Posted 1 year ago

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Diagnostics (Basel). 2020 Oct 18;10(10):837. doi: 10.3390/diagnostics10100837.

Managing Deviating EQA Results: A Survey to Assess the Corrective and Preventive Actions of Medical Laboratories Testing for Oncological Biomarkers

Analysis in tissues

Cleo Keppens [1], Ed Schuuring [2], Elisabeth Mc Dequeker [1]

EQA participants from the European Society of Pathology between 2014 and 2018 for lung and colorectal cancer were contacted, if they had at least one analysis error or test failure in the provided cases, to complete a survey.

For 72.4% of 514 deviating EQA results, an appropriate action was performed, most often including staff training (15.2%) and protocol revisions (14.6%).

The majority of participants adhered to ISO 15189 and implemented suitable actions by designated staff, not limited to accredited laboratories.

However, for 27.6% of cases (by 20 laboratories) no corrective action was taken, especially for pre-analytic problems and complex techniques.

The surveys were feasible to request information on results follow-up and further recommendations were provided.

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Volume 66, Issue 1
January 2020

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Multicenter Evaluation of Circulating Cell-Free DNA Extraction and Downstream Analyses for the Development of Standardized (Pre)analytical Work Flows

Rita Lampignano, Martin H.D Neumann, Sabrina Weber, Vera Kloten, Andrei Herdean, Thorsten Voss, Daniel Groelz, Anna Babayan, Marco Tibbesma, Martin Schlumpberger ...
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Clinical Chemistry, Volume 66, Issue 1, January 2020, Pages 149–160,
https://doi.org/10.1373/clinchem.2019.306837
Published: 30 December 2019 **Article history**

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Multicenter Evaluation of Circulating Plasma MicroRNA Extraction Technologies for the Development of Clinically Feasible Reverse Transcription Quantitative PCR and Next-Generation Sequencing Analytical Work Flows

Vera Kloten, Martin H.D. Neumann, Francesca Di Pasquale, Markus Sprenger-Haussels, Jonathan M. Shaffer, Martin Schlumpberger, Andrei Herdean, Fay Betsou, Wim Ammerlaan, Taija af Hällström, Elina Serkkola, Tarja Forsman, Evi Lianidou, Robert Sjöback, Mikael Kubista, Sebastian Bender, Rita Lampignano, Thomas Krahn, Thomas Schlange, for the CANCER-ID consortium

DOI: 10.1373/clinchem.2019.303271 Published September 2019

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Evaluation of Preanalytical Conditions and Implementation of Quality Control Steps for Reliable Gene Expression and DNA Methylation Analyses in Liquid Biopsies

Martha Zavridou, Sofia Mastoraki, Areti Strati, Eleni Tzanikou, Maria Chimonidou, Evi Lianidou

DOI: 10.1373/clinchem.2018.292318 Published September 2018

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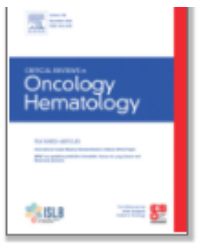
Critical Reviews in Oncology/Hematology

Volume 156, December 2020, 103112



European School of Oncology – Review

International liquid biopsy standardization alliance white paper

Dana Connors [a], Jeff Allen [b], J.D. Alvarez [c], Jennifer Boyle [d], Massimo Cristofanilli [e], Carolyn Hiller [c], Susan Keating [f], Gary Kelloff [g], Lauren Leiman [h], Robert McCormack [i], Diana Merino [b], Emily Morgan [a], Klaus Pantel [j], Christian Rolfo [k], Maria Jose Serrano [l], A. Pia Sanzone [d], Thomas Schlange [m], Caroline Sigman [f], Mark Stewart [b]

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https://www.iso.org/standard/69800.html

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ICS › 11 › 11.100 › 11.100.10

ISO 20186-3:2019

Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for venous whole blood — Part 3: Isolated circulating cell free DNA from plasma

ABSTRACT PREVIEW

This document provides recommendations and requirements on the handling, storage, processing and documentation of venous whole blood specimens intended for circulating cell free DNA (ccfDNA) examination during the pre-examination phase before an analytical test is performed. This document covers specimens collected in venous whole blood collection tubes.

This document is applicable to any molecular in vitro diagnostic examination performed by medical laboratories. It is also intended to be used by laboratory customers, in vitro diagnostics developers and manufacturers, biobanks, institutions and commercial organizations performing biomedical research, and regulatory authorities.

Different dedicated measures are taken for stabilizing blood genomic DNA, which are not described in this document. Blood genomic DNA is covered in ISO 20186-2.

Different dedicated measures are taken for preserving DNA in circulating exosomes, which are not described in this document.

NOTE ccfDNA obtained from blood by the procedures cited in this document can contain DNA originally present in exosomes[8][9].

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FORMAT	LANGUAGE
✔ PDF + EPUB	English
PAPER	English

CHF 88 BUY

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Clinical Chemistry

Proficiency Testing to Assess Technical Performance for CTC-Processing and Detection Methods in CANCER-ID

Rui P L Neves, Wim Ammerlaan, Kiki C Andree, Sebastian Bender, Laure Cayrefourcq, Christiane Driemel, Claudia Koch, Merlin Verena Luetke-Eversloh, Marianne Oulhen, Elisabetta Rossi ... Show more

Clinical Chemistry, Volume 67, Issue 4, April 2021, Pages 631–641,
https://doi.org/10.1093/clinchem/hvaa322

CANCER ID

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CTC analysis in ELBS

CellSearch, FACS	Enumeration	28/50
Parsortix/ANGLE, ISET, Genesis/Bio-Rad, Filtration, DEPArray, VyCAP, AF4-MALS, CTCapture Chip, Magnetic bead based separation (MACS), ClearCell FX	Enrichment	35/50
RT-qPCR, BioRAD/droplet ddPCR & CFX96, QX200, QXOne Droplet Digital PCR System, WGA, SafeSEQ & OncoBEAM ctDNA mutation analysis	Molecular assays both CTCs and ctDNA	40/50

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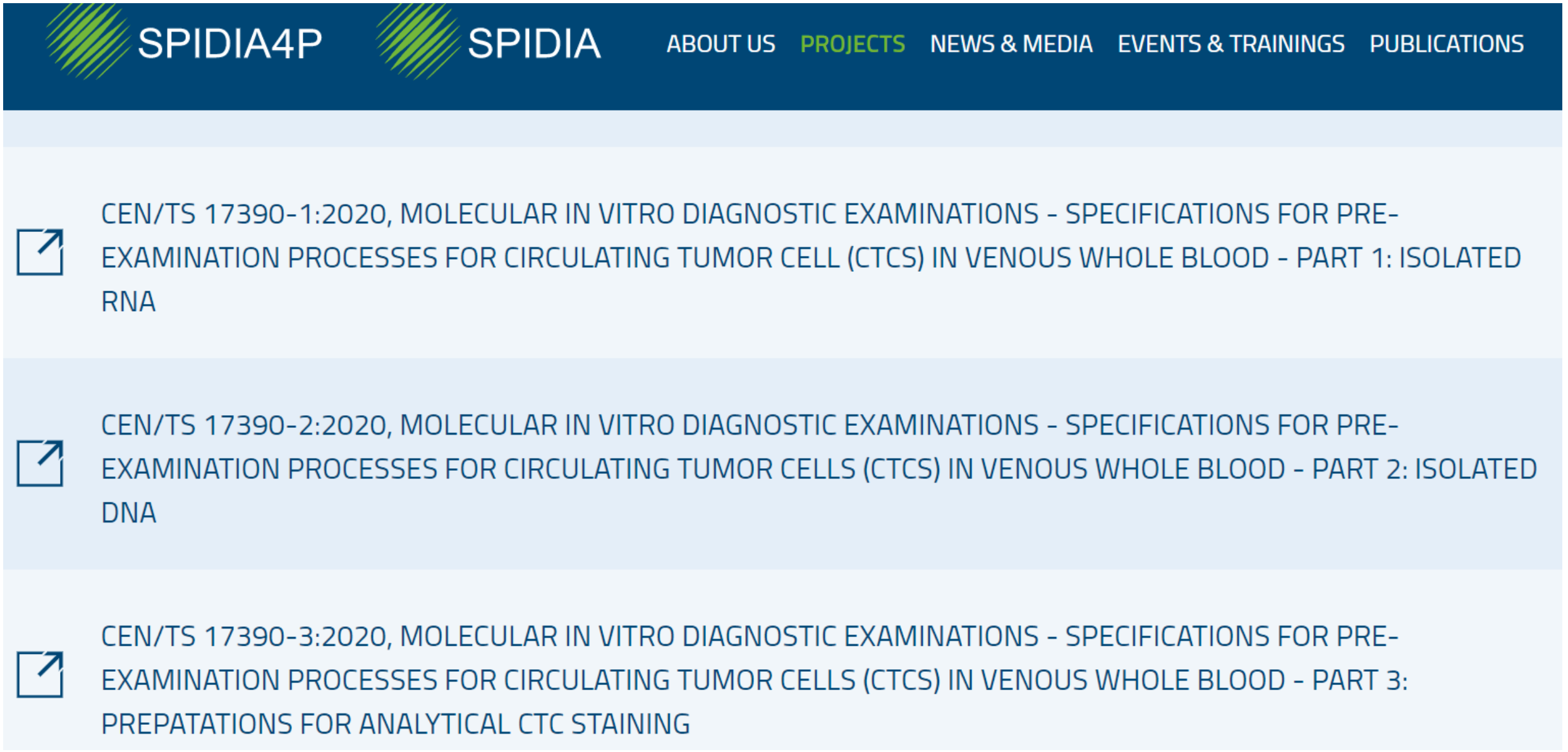
SPIDIA4P (https://www.spidia.eu/projects/standard-documents)



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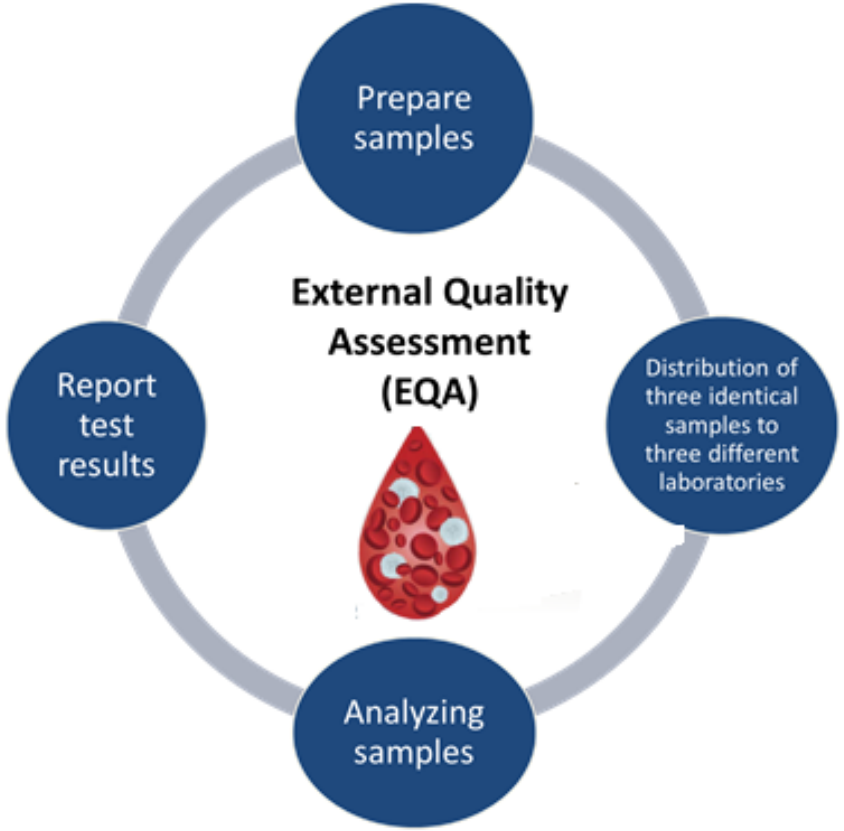
ISO-15189 ACCREDITATION
CTC analysis main issues



Identification of CTC assays to be ISO-15189 certified (clinical utility), eg:

- **CTC enumeration**
- **AR-V7,**
- **PD-L1,**
- **HER-2, ….**

Identification of ELBS labs that want to be ISO-15189 certified for specific assays and use identical technologies (ELBS questionnaires)

Preparation of spiked samples (CANCER ID Experience!!)

Organize ring trials providing the same blood samples to all in a coded format

Use of ISO certified couriers to ship the samples

Analysis and report test results (all documentation needed)

Ask for ISO-15189 certificate from the local agencies in European Countries

Main goal for ELBS!
Reimbursement of liquid biopsy tests by the National Health System of each country

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ACTC lab : ISO-15189 ACCREDITATION For CellSearch CTC enumeration

Εθνικό Σύστημα Διαπίστευσης

ΕΣΥΔ

ACCREDITATION CERTIFICATE No. 1108

The Hellenic Accreditation System S.A. (ESYD), as the national accreditation body of Greece in accordance with the Law 4468/2017

ACCREDITS

of the

Analysis of Circulating Tumor Cells lab

of the

Department of Chemistry

of the

National and Kapodistrian University of Athens

in Zografou, Attiki, Greece

under the terms of the ELOT EN ISO 15189: 2012 Standard and the ESYD Criteria, to carry out tests, as specified in the attached Scope of the Accreditation, which may be revised by decisions of ESYD.

This Certificate is valid until 28.12.2021, provided that the accredited body will comply with the above Standard and the ESYD Criteria.

Athens, December 28th, 2017

Konstantinos Voutsinas
Managing Director, ESYD

ESYD is a signatory of the European co-operation for Accreditation (EA) Multilateral Agreement for the activities covered by this certificate

Hellenic Accreditation System

ΕΣΥΔ

Annex G1/1 to the Certificate No. **1108**

SCOPE of ACCREDITATION
of the
Analysis of Circulating Tumor Cells lab
of the
Department of Chemistry,
of the
National and Kapodistrian University of Athens

Tested materials/ products	Types of test/ Properties to be measured	Applied Standards/ Techniques to be used
Biological testing		
1. Peripheral blood, plasma (EDTA), (Liquid Biopsy)	1. Detection of somatic mutations in exons 18, 19, 20, και 21 of the EGFR gene in patients with Non-Small Cell Lung cancer (NSCLC) CE-IVD approved FDA cleared assay EGFR MUTATIONS G719X (2156G>C, 2155G>A, 2155G>T) Ex19Del: 2240_2251del12, 2239_2247del9, 2238_2255del18, 2235_2249del15, 2236_2250del15, 2239_2253del15, 2239_2256del18, 2237_2254del18 2240_2254del15, 2240_2257del18, 2239_2248TTAAGAGAAG>C, 2239_2251>C, 2237_2255>T, 2235_2255>AAT, 2237_2252>T, 2239_2258>CA, 2239_2256>CAA, 2237_2253>TTGCT, 2238_2252>GCA, 2238_2248>GC, 2237_2251del15, 2236_2253del18, 2235_2248>AATTC, 2235_2252>AAT, 2235_2251>AATTC, 2253_2276del24, 2237_2257>TCT, 2238_2252del15, 2233_2247del15	**Cobas z 480 Analyzer, ROCHE DIAGNOSTICS*** Real time PCR for the semi-quantitative measurement of mutations. COBAS® EGFR Mutation Test v2 CE-IVD approved FDA cleared assay

Tested materials/ products	Types of test/ Properties to be measured	Applied Standards/ Techniques to be used
1. Peripheral blood, plasma (EDTA), (Liquid Biopsy) cont.	S768I (2303G>T) T790M (2369C>T) Ex20Ins 2307_2308ins9GCCAGCGTG, 2319_2320insCAC, 2310_2311insGGT, 2311_2312ins9GCGTGGACA, 2309_2310AC>CCAGCGTGGA L858R 2573T>G, 2573_2574TG>GT L861Q (2582T>A)	
2. Peripheral blood (Cellsave Preservative Tubes) (Liquid Biopsy)	Identification and enumeration of Circulating Tumor Cells (CTCs)	**CELLSEARCH SYSTEM CIRCULATING TUMOR CELL KIT, Menarini*** CE-IVD approved FDA cleared assay

**Reference to the commercial name of a specific analyzer/kit, refers to a specific analytical method and protocol*

Site of assessment: **Laboratory permanent premises: Department of Chemistry, National and Kapodistrian University of Athens, University Campus, 157 71 Zografou, Attiki, Greece.**
Approved signatory: **E. Lianidou**

The Accreditation Certificate No. **1108**, to ELOT EN ISO 15189:2012, is valid until 28.12.2021.

Athens, December 28th, 2017

Konstantinos Voutsinas
Managing Director, ESYD

ISO-15189 ACCREDITATION
CellSearch CTC enumeration

- **ACTC lab is accredited for the CTC enumeration using the CellSearch system according to ISO 15189:2012**

An example when EQA schemes for liquid biopsy analyses are not available

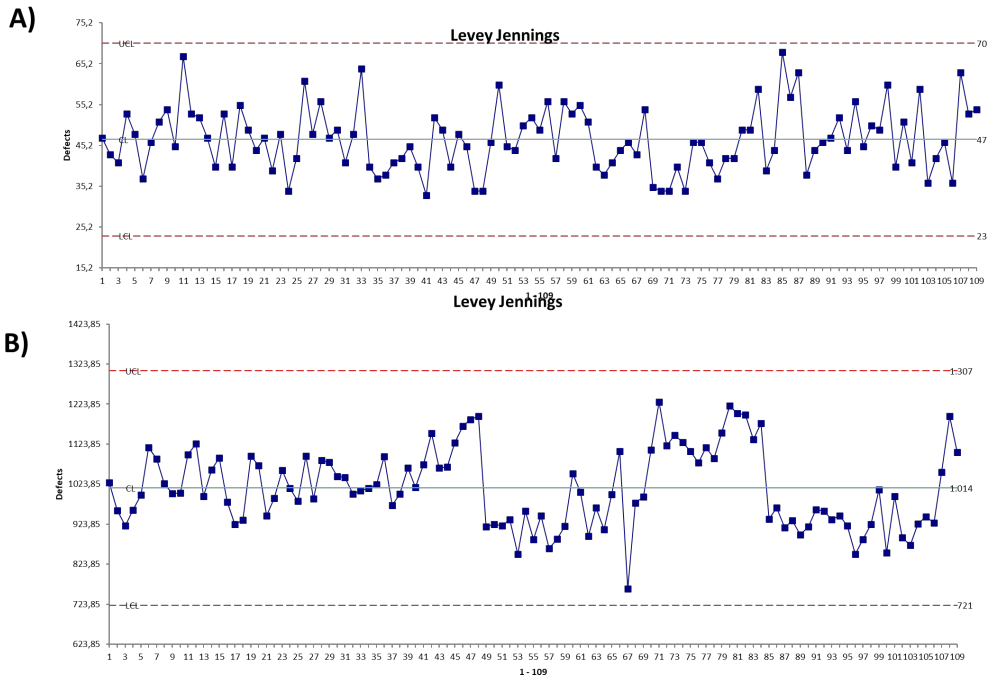
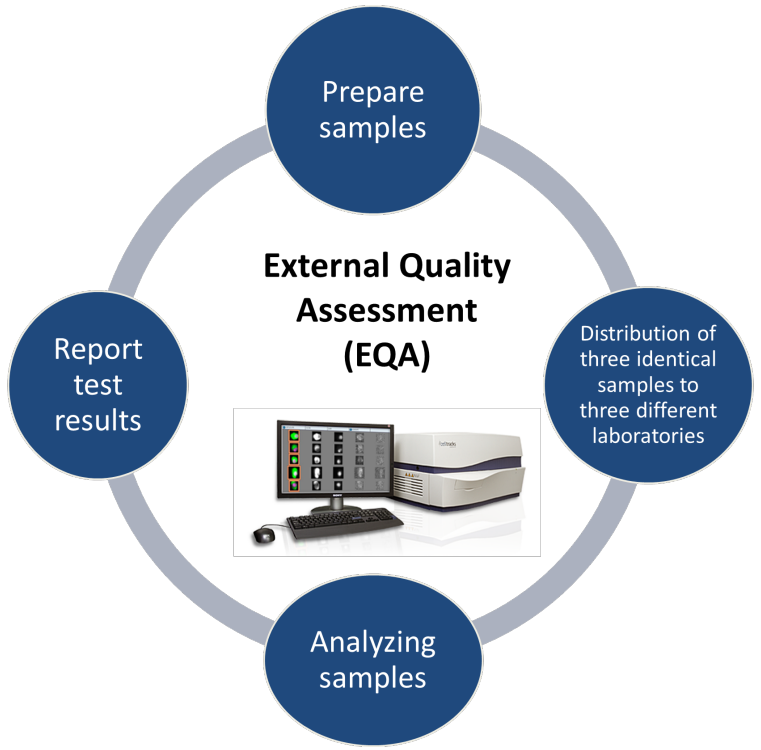


Figure 3. Quality control of CellSearch analysis (Levey–Jennings graphs): A) Low control, B) High Control



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Day to day repeatability: CellSearch® Circulating Tumor Cell Control

	Low CTC numbers			High CTC numbers		
Day	median	range	result	median	range	result
1	48	25-71	36	971	819-1123	927
2	48	25-71	46	971	819-1123	943
3	48	25-71	42	971	819-1123	925
4	48	25-71	36	971	819-1123	871
5	48	25-71	59	971	819-1123	890
6	48	25-71	41	971	819-1123	993
7	48	25-71	51	971	819-1123	853
8	48	25-71	40	971	819-1123	1010
9	48	25-71	60	971	819-1123	923
10	48	25-71	49	971	819-1123	886
11	48	25-71	50	971	819-1123	849
12	48	25-71	45	971	819-1123	920
13	48	25-71	56	971	819-1123	945
14	48	25-71	44	971	819-1123	935
15	48	25-71	52	971	819-1123	957
16	48	25-71	47	971	819-1123	960
Median value			47			924
Standard deviation (SD)			7,4			46
(CV%)			16			5,0

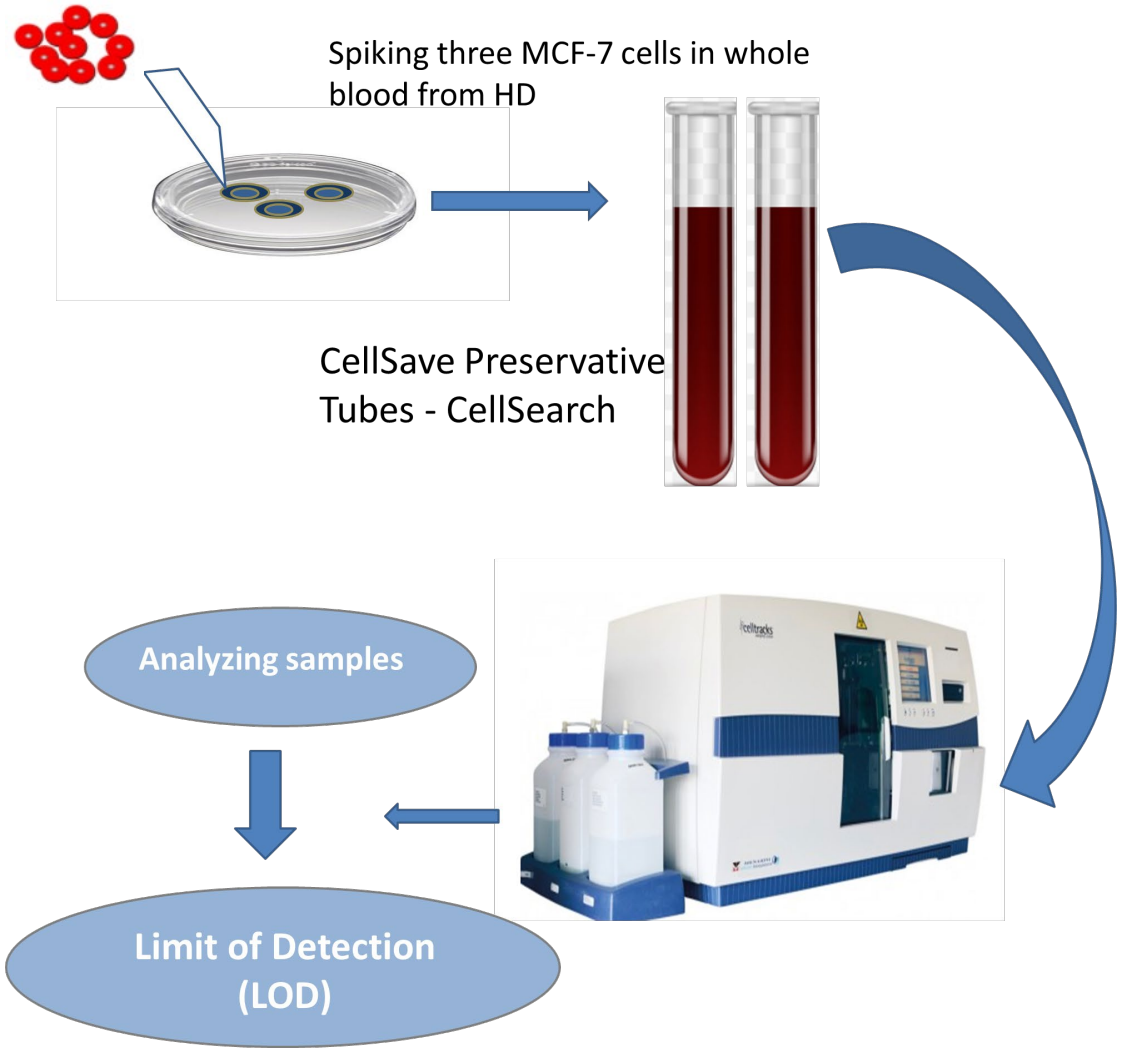

Table 1. Intra-operator repeatability for CTC enumeration

Number of spiked MCF-7 cells	Enumeration of CTCs	Recovery (%)
100	92	92%
100	80	80%
100	74	74%
Mean	82	
SD	9,2	
CV	11%	

Table 2. Validation of the LOD of the CellSearch System

Number of spiked MCF-7 cells	Enumeration of CTCs	Recovery (%)
3	3	100%
3	3	100%
Mean	3	

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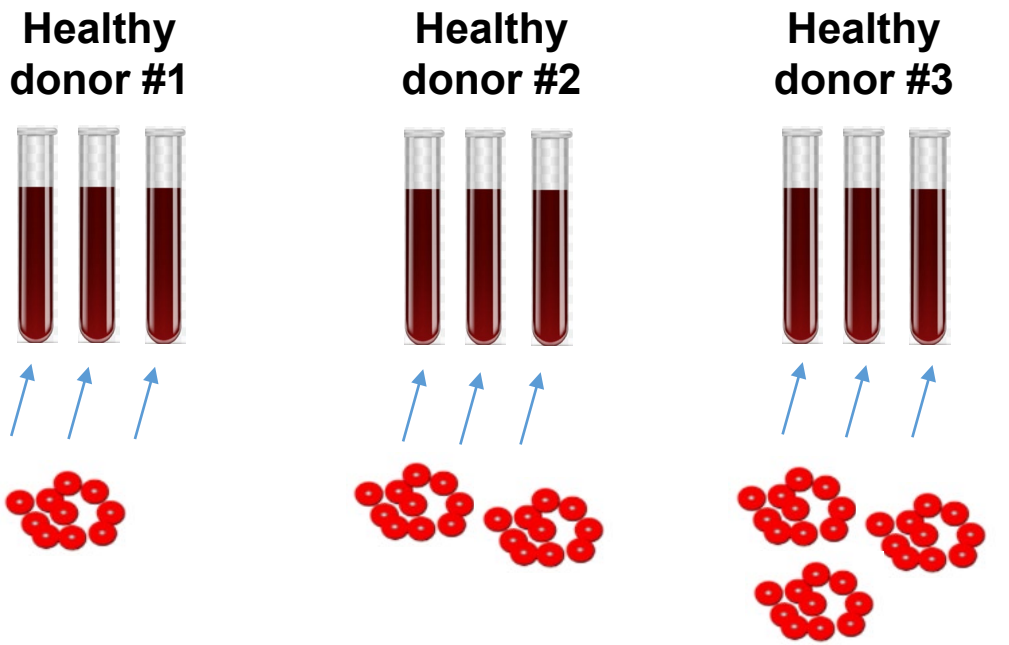
Preparation of samples: Spiking MCF-7 cells in healthy donors blood samples



EQA 2017 RESULTS

Participating labs: E. Lianidou, K. Pantel, L. Terstappen

Table 3. External Quality Assessment Schemes for CellSearch testing for the year 2017

Samples	Lab#1	Lab#2	Lab#3	Mean	SD	CV%
Sample 1	51	37	34	41	9,1	22,3
Sample 2	12	12	3	9	5,2	57,7
Sample 3	0	0	0	0	0,0	
Sample 4	90	64	62	72	15,6	21,7

EQA 2019 RESULTS

Participating labs: E. Lianidou, R. Zamarchi, N. Stoecklein

Table 4. External Quality Assessment Schemes for CellSearch testing for the year 2019

Samples	Lab#1	Lab#2	Lab#3	Mean	SD	CV%
Sample 1	7,0	0,0	4,0	3,7	3,5	95,8
Sample 2	3,0	2,0	1,0	2,0	1,0	50,0
Sample 3	9,0	7,0	8,0	8,0	1,0	12,5

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BENEFITS OF ISO-15189 ACCREDITATION

- Harmonization of results for the same liquid biopsy assays in different labs that use exactly the same technology
- Highly important to establish a network of ISO-15189 certified labs for specific liquid biopsy tests within ELBS
- Validation of liquid biopsy protocols and their implementation in the clinical setting
- Reimbursement of liquid biopsy tests by the National Health System (example: AR-V7, Epic assay, USA)
- Evaluation of novel technologies by comparing results for the same samples in ISO-15189 labs

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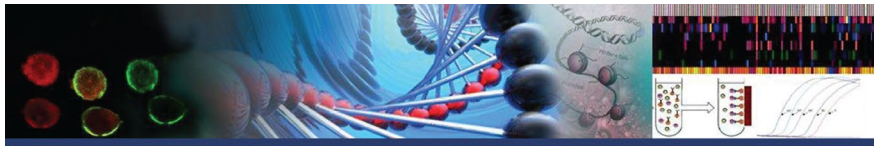
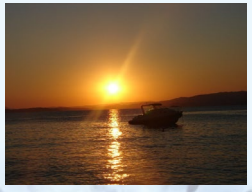


SAVE THE DATE!!!!

5th ACTC meeting
Advances in Circulating Tumor Cells
"Liquid Biopsy in its best"




Kalamata, Greece

Venue: Filoxenia Conference Center

September 22-25, 2021

Organizers
- **Evi Lianidou, University of Athens**
- **Hellenic Society of Liquid Biopsy**

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