EUROPE BIOBANK WEEK

SEPTEMBER 13-16, 2016
VIENNA - AUSTRIA

Loes Linsen: "Pre-examination process requirements for European biobanks: focus on venous whole blood"

BBMRI-ERIC® gateway for health

BBMRI.at Biobanking and BioMolecular resources Research Infrastructure Austria

European, Middle Eastern & African Society for Biopreservation & Biobanking

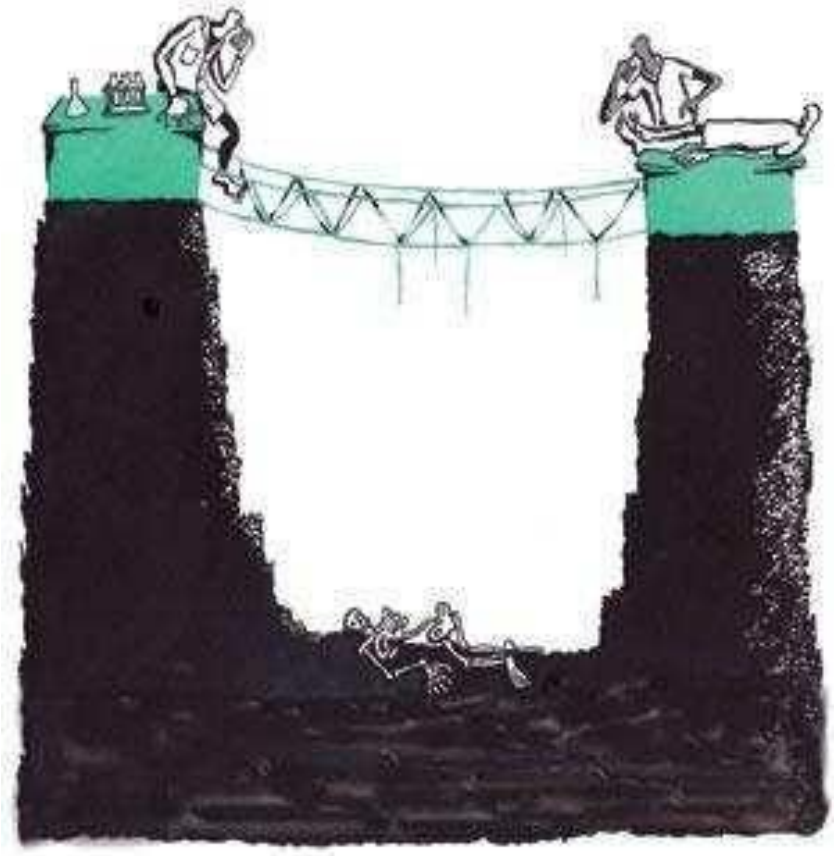
Pre-examination process requirements for European biobanks: focus on venous whole blood

Loes Linsen

On behalf of BBMRI-ERIC WP4 – Quality Workgroup 3 – venous whole blood

Translational Research Gap

- No confirmation of research results



Root causes for irreproducibility

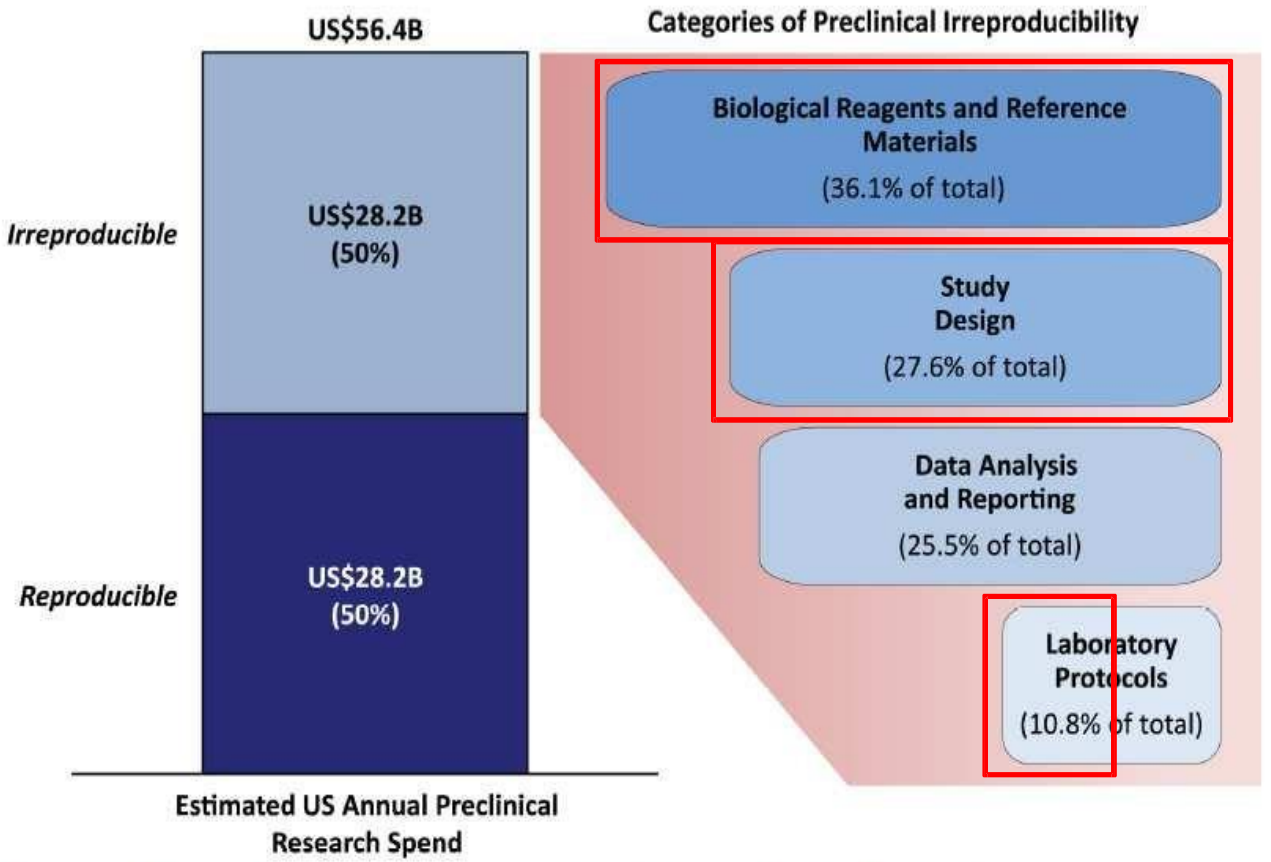


Fig 2. Estimated US preclinical research spend and categories of errors that contribute to irreproducibility. Note that the percentage value of error for each category is the midpoint of the high and low prevalence estimates for that category divided (weighted) by the sum of all midpoint error rates (see S1 Dataset). Source: Chakma et al. [18] and the American Association for the Advancement of Science (AAAS) [19].

(Freedman, L. et al. (2015) Plos Biology 13, e1002165.)

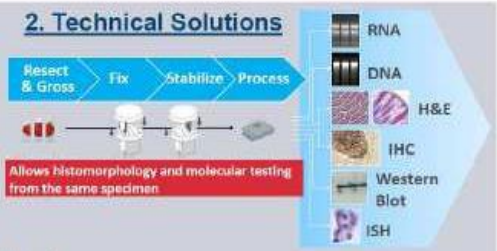
The Road to Standardization

- 2014: 8 new projects for ISO Standards approved in ISO/TC 212 „*Clinical laboratory testing and in vitro diagnostic test systems*"

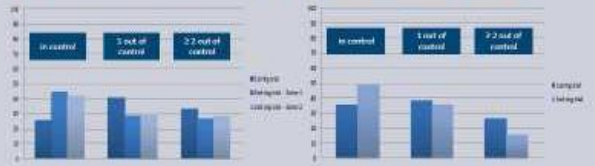
- 2015: 9 CEN Technical Specifications to be published
- 2013: 9 new projects approved in CEN/TC 140 „*In vitro diagnostic medical devices*"
- 2010: Start of standardization work

1. Problem - Errors in Diagnostics

2. Technical Solutions



3. Ring-Trials – Blood RNA (l.) and DNA (r.)



SEVENTH FRAMEWORK PROGRAMME

European Conference. Standards: Your Innovation Bridge. Brussels (2014). SPIDIA Booth.

CEN/TS molecular in vitro diagnostic examination - 16835

- Specifications for pre-examination processes for venous whole blood
  - Part 1: Isolated cellular RNA
  - Part 2: Isolated genomic DNA
  - Part 3: Isolated circulating cell free DNA from plasma

BBMRI WP4: quality - WG3

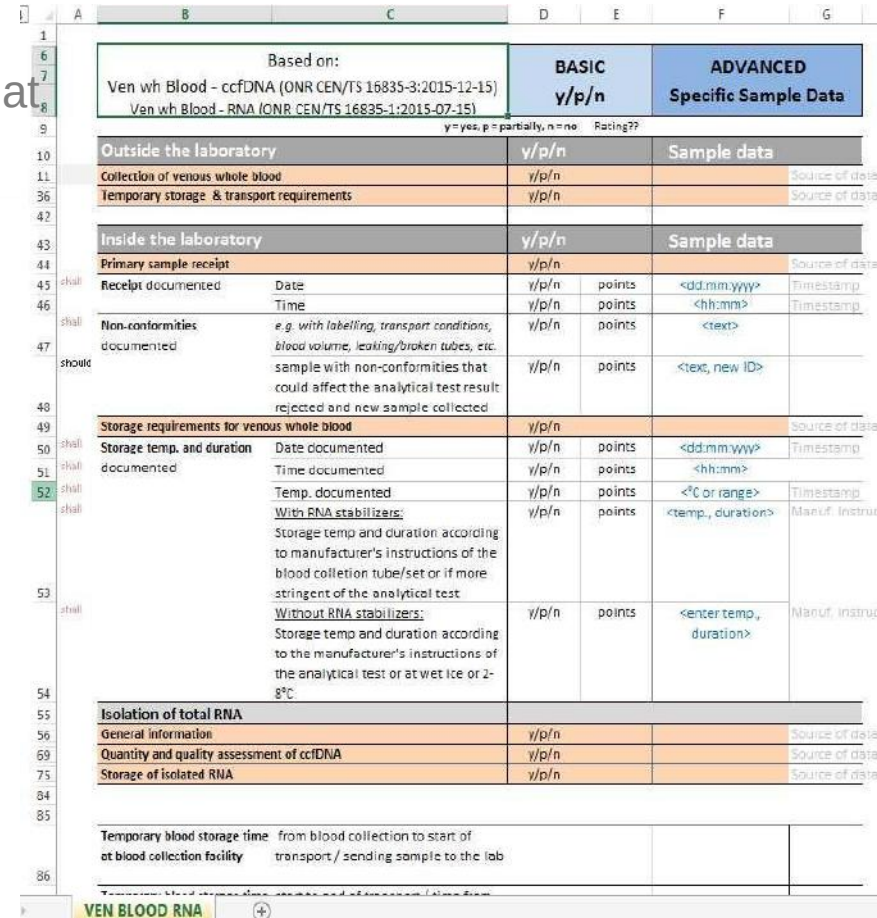
- WG 3 members: 14/17 NN
  - BBMRI.at, .be, .de, .ee, .fi, .it, .mt, .nl, .no, .pl, .se, .tr, IARC, BBMRI-ERIC
- Aims
  - Intra- & interbiobank benchmark
    - Current status
    - Hurdles for implementation
  - Self Assessment Tool
    - Current compliance
    - BBMRI quality flag

CEN/TS assessment

- Molecular in vitro diagnostic examinations > ISO15189
- Validate full process from collection to final test result
- “SPREC”: timings and conditions
- RNA
  - Stability of specific blood cellular RNA profile should be investigated
  - Stabilizer tubes should be used
- DNA
  - Blood should be collected on EDTA or ACD
  - Recommendation on storage before processing
- cfDNA
  - Stability of specific blood ccfDNA profile should be investigated
  - Stabilizer tubes recommended (or EDTA)

Intra/Interbiobank benchmark

- Based on assessment excel bbmri.at
  - Courtesy of C. Stumptner, bbmri.at
- WG 3 members
  - Benchmark
  - Compliance: Y/N/P
  - 11/7 NN responses



	Based on: Ven wh Blood - ccfDNA (ONR CEN/TS 16835-3:2015-12-15) Ven wh Blood - RNA (ONR CEN/TS 16835-1:2015-07-15)		BASIC y/p/n		ADVANCED Specific Sample Data	
	y = yes, p = partially, n = no		Rating??			
	Outside the laboratory		**y/p/n**		**Sample data**	
	Collection of venous whole blood		y/p/n			Source of data
	Temporary storage & transport requirements		y/p/n			Source of data
	Inside the laboratory		**y/p/n**		**Sample data**	
	Primary sample receipt		y/p/n			Source of data
shall	Receipt documented	Date	y/p/n	points	<dd:mm:yyy>	Timestamp
		Time	y/p/n	points	<hh:mm>	Timestamp
shall	Non-conformities documented	*e.g. with labelling, transport conditions, blood volume, leaking/broken tubes, etc.*	y/p/n	points	<text>	
should		sample with non-conformities that could affect the analytical test result rejected and new sample collected	y/p/n	points	<text, new ID>	
	Storage requirements for venous whole blood		y/p/n			Source of data
shall	Storage temp. and duration documented	Date documented	y/p/n	points	<dd:mm:yyy>	Timestamp
shall		Time documented	y/p/n	points	<hh:mm>	
shall		Temp. documented	y/p/n	points	<°C or range>	Timestamp
shall		With RNA stabilizers: Storage temp and duration according to manufacturer's instructions of the blood colletion tube/set or if more stringent of the analytical test	y/p/n	points	<temp., duration>	Manuf. Instruc
shall		Without RNA stabilizers: Storage temp and duration according to the manufacturer's instructions of the analytical test or at wet Ice or 2-8°C	y/p/n	points	<enter temp., duration>	Manuf. Instruc
	Isolation of total RNA					
	General information		y/p/n			Source of data
	Quantity and quality assessment of ccfDNA		y/p/n			Source of data
	Storage of isolated RNA		y/p/n			Source of data
	Temporary blood storage time at blood collection facility	from blood collection to start of transport / sending sample to the lab				

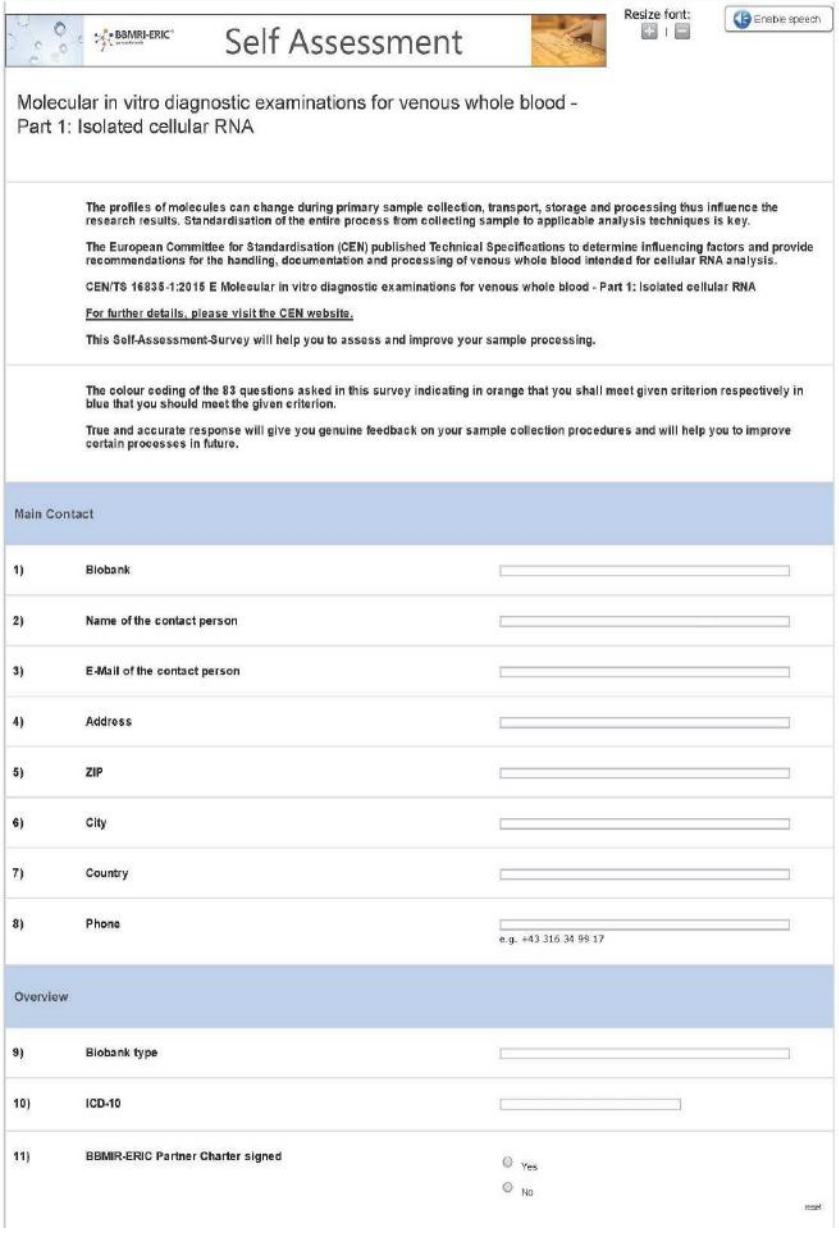
VEN BLOOD RNA

Main issues

- Test driven > implementation for biobanks?
  - Have to validate full process from collection to final test result
- Not all steps of process in hands of biobank “outside the laboratory”
  - Documentation of name/ID of person collecting blood
  - Control? Quality?
- Stabilizer tube use & RNA/cfDNA profile?
  - No stabilizer 100 % efficient/comparable > validate process for molecule of interest
  - Profile? RNA: 4 genes; cfDNA?
- +: collection time shall be documented vs ISO15189 (when needed)
  - HIB, other lab dependencies

➢ Formulate comment to ISO TC with biobank concerns

BBMRI-ERIC Self Assessment Tool



BBMRI-ERIC

Self Assessment

Resize font:

Enable speech

Molecular in vitro diagnostic examinations for venous whole blood - Part 1: Isolated cellular RNA

The profiles of molecules can change during primary sample collection, transport, storage and processing thus influence the research results. Standardisation of the entire process from collecting sample to applicable analysis techniques is key.

The European Committee for Standardisation (CEN) published Technical Specifications to determine influencing factors and provide recommendations for the handling, documentation and processing of venous whole blood intended for cellular RNA analysis.

CEN/TS 16835-1:2015 E Molecular in vitro diagnostic examinations for venous whole blood - Part 1: Isolated cellular RNA

For further details, please visit the CEN website.

This Self-Assessment-Survey will help you to assess and improve your sample processing.

The colour coding of the 83 questions asked in this survey indicating in orange that you shall meet given criterion respectively in blue that you should meet the given criterion.

True and accurate response will give you genuine feedback on your sample collection procedures and will help you to improve certain processes in future.

Main Contact

1)	Biobank	
2)	Name of the contact person	
3)	E-Mail of the contact person	
4)	Address	
5)	ZIP	
6)	City	
7)	Country	
8)	Phone	e.g. +43 316 34 99 17

Overview

9)	Biobank type	
10)	ICD-10	
11)	BBMRI-ERIC Partner Charter signed	Yes / No

Conclusion

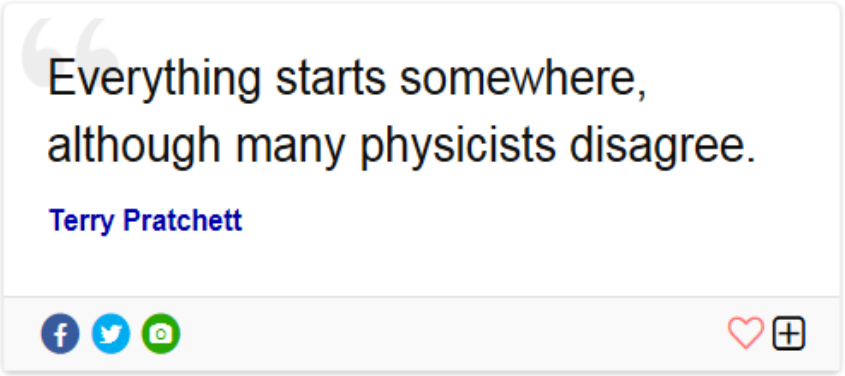
- CEN/TS
  - Majority of criteria are/can be implemented by biobanks
  - Some hurdles identified
  - Comment to be formulated to ISO
- SAT
  - Expected end 2016
  - WG3 validation
- Consensus based SOPs

WG3 Whole Blood

BBMRI-ERIC
Biobanking and BioMolecular resources Research Infrastructure

BBMRI.at	Cornelia Stumptner	Medical University Graz	QM-Coordinator, Lab-technician
	Helmuth Haslacher	Biobank Vienna	Biobank Manager, MD
	Berthold Huppertz	Medical University Graz	CEO and director Biobank Graz
BBMRI.be	Annemieke De Wilde	Antwerp University Hospital	Biobank Manager – focus on quality management
	Sofie Goethals	Antwerp University Hospital	Biobank Manager – sample, project management
	Loes Linsen	University Hospitals Leuven	Biobank expert
BBMRI.de	Bettina Meinung	University Clinic Jena	Quality Manager, BBMRI.de
	Ronny Baber	University Hospital Leipzig	Coordinator of the LIFE-Biobank and Preanalytical Laboratory
	Claudia Schmidt	Helmholtz Zentrum München	Quality management representative of m4 Biobank Alliance
	Romy Kirsten	BioMaterialBank Heidelberg (BMBH)	Head Liquid Biobank NCT Heidelberg
BBMRI.ee	Paula Ann Kivistik	Estonian Genom Center	Biobank expert
	Steven Smit	Estonian Genom Center	Genome sequency Manager
BBMRI.fi	Aulikki Santavuori	Auria Biopankki	Quality Manager
BBMRI.it	Rita Lawlor	ARC-NET, Verona	Biobank quality management
	Alberto Bardelli	IRCC, Candiolo (TO)	Molecular genetics
	Maria Grazia Daidone	INT, Milan	Biomarkers
	Valentina Appierto	INT, Milan	Biobank researcher
BBMRI.mt	Nikola Pace	University of Malta, BBMRI.mt	Molecular Genetics / Clinical Medicine
	Esther Zammit	University of Malta, BBMRI.mt	Research Support Officer, Quality Assistant
BBMRI.nl	Peter Riegman	Erasmus MC tissue bank	Biobank Manager, head of E-MC tissue bank
BBMRI.no	Liv Wenche Thorbjørnsen	Oslo University Hospital	Biobank Manager
	Anne Kari Tveter	National Institute of Health, Norway	Laboratory Manager
	Elin Kyllo	HUNT Biobank/NTNU	Senior engineer
	Lise Norøy	HUNT Biobank/NTNU	Staff engineer
BBMRI.pl	Lukasz Koszera	University of Wroclaw	National Biobanking Coordinator for Poland
	Malgorzata Witon	Swietokrzyski Biobank	Biobank Manager
BBMRI.se	Carita Björkman	KI/BBMRI Biobank	Quality manager
BBMRI.tr	Ayşe Yüzbaşıoğlu	Hacettepe Biobank	Ass. Director
	Yucel Erbilgin	Istanbul University	Experimental medicine
	Meral Ozguc	Hacettepe University DNA/Cell Bank for RD	Director Cell Bank, Management / QA program set up
IARC	Elodie Caboux	IARC	Biobank Expert
BBMRI-ERIC	Andrea Wutte	BBMRI-ERIC	Quality Manager

Questions?


Everything starts somewhere,
although many physicists disagree.
Terry Pratchett