



INTERNATIONAL SOCIETY FOR BIOLOGICAL
AND ENVIRONMENTAL REPOSITORIES

Connecting Repositories Globally through Best Practices
leading since 1999

Making more efficient use of biospecimens

ISBER Contributions and Initiatives

TMF, 3rd National Biobanking Symposium
Berlin, December 3-4, 2014

*by the ISBER Biospecimen Science Working Group,
the ISBER Education and Training Committee and
the ISBER Science Policy Committee,*

presented by Fay Betsou



INTERNATIONAL SOCIETY FOR BIOLOGICAL
AND ENVIRONMENTAL REPOSITORIES

Connecting Repositories Globally through Best Practices
leading since 1999



Mission Statement

ISBER is a global organization which creates opportunities for sharing ideas and innovations in biobanking and harmonizes approaches to evolving challenges for biological and environmental repositories.



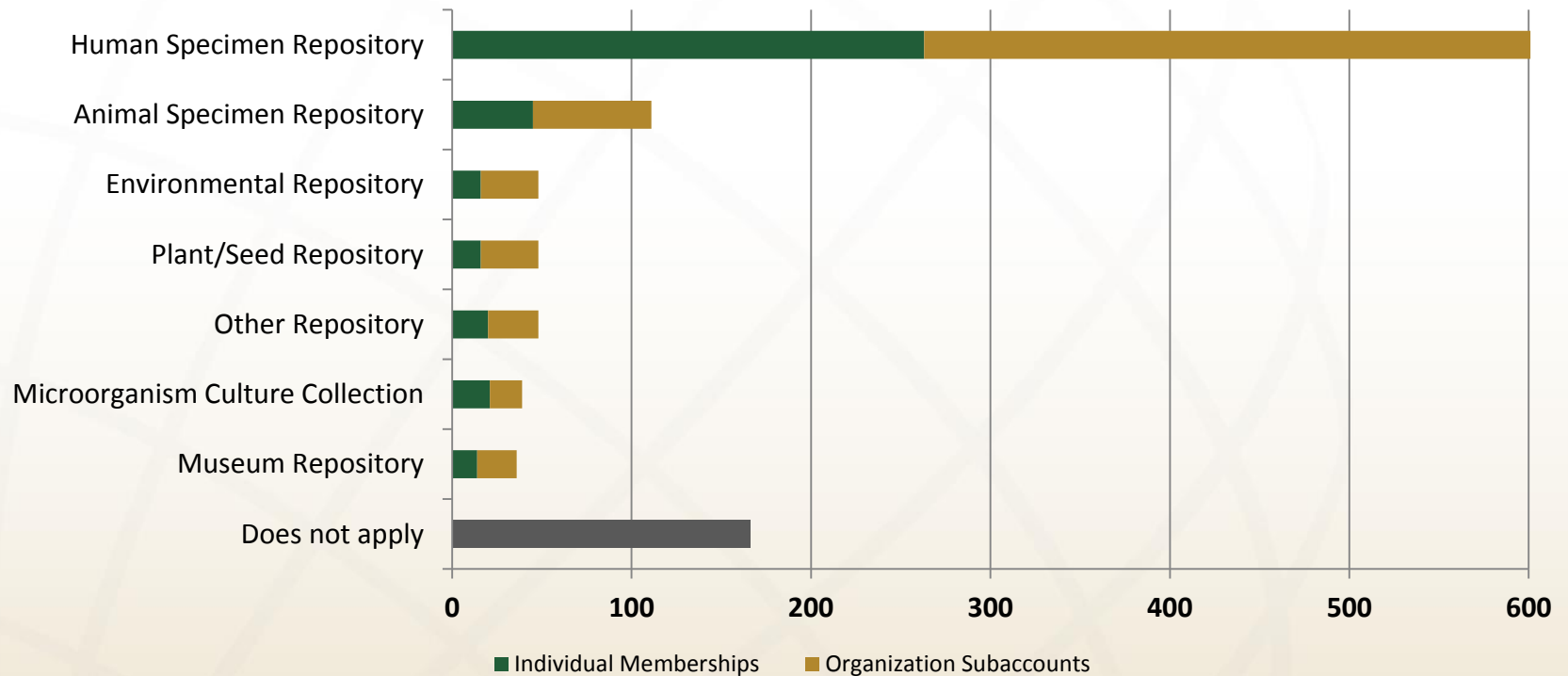
Vision

ISBER will be the leading global forum for promoting harmonized high quality standards, ethical principles, and innovation in the science and management of biorepositories.

SOCIETY GOALS

- Disseminate information on repository management issues
- Educate and share information and tools within the society and with stakeholders
- Act as the voice for repositories to influence regulations and policy
- Develop best practice guidelines
- Provide centralized information about existing repositories
- Bring members together to work on emerging issues

2014 Memberships by Repository Type



ISBER Overview

- ISBER is a global professional scientific society, whose goal is to support biobanks worldwide
 - 2014: 1066 individual and organizational members from 37 countries
- ISBER is a non-profit, 501(c)3 organization whose revenue comes solely from memberships, corporate partnerships, and meeting registration
- ISBER is governed by a Board of Directors with Regional representation
- ISBER Committees, Working Groups, Taskforces

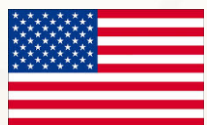
ISBER's ELSI Contributions/Activities

ISBER Best Practices 3rd Edition

- Section L: Legal and ethical issues for biospecimens
 - Collection of human biospecimens
 - Informed consent
 - Protection from research risks
 - Specimens from mentally impaired
 - Specimens from autopsies
 - Pediatric specimens
 - Communities
 - Animal and wildlife biospecimens
 - Sharing and distribution of specimens and data
- Section M: Specimen access, utilization and destruction
 - Access and utilization
 - Data sharing
 - Benefit sharing
 - MTAs
 - Data transfer

ISBER Science Policy Committee

- 2014 members:
 - Co-chairs: Marianna Bledsoe, Nicole Sieffert
 - Members: Lisa Gilbert, William Grizzle, Tyron Hoover, Paula Kim, Yeonhee Lee, Katia Manhaeve, Helen Moore, Helen Morrin, Elena Salvaterra, Amelia Warner, Wendy Wolf
 - Advisor: Nik Zeps



- Communicates and addresses emerging science policy issues that may affect the biorepository community
- Responds to requests for public comment

Comments 2011-2012

- US Department of Health and Human Services proposed changes to the “Common Rule” human subjects regulations
 - *ISBER commented on the importance of allowing left-over tissue to be used with IRB approved waiver of consent under appropriate circumstances and with continued IRB oversight*
 - *Bio specimens should not be considered identifiable in and of themselves.*
- Australian Government National Health and Medical Research Council proposed revisions to Chapter 3.4: Human tissue samples and Chapter 3.6: Human stem cells of the National Statement on Ethical Conduct in Human Research
 - *Full endorsement*

Comments 2013

- Response to the European General Data Protection Regulation Proposal as provided by the European Parliament and the Council of European Union
 - *Noted that the requirement for explicit, specific consent and for compliance with EU data protection regulations for data transfer would hinder global collaborations on important research projects*
- Response to the US Presidential Commission for the Study of Bioethical Issues request for comments on issues related to incidental findings
 - *Encouraged that instead of mandating return of incidental research findings to participants, biobanks should develop policies that are reflected in the IC*
- Response to the request for public comments on the NIH Draft Genomic Data Sharing (GDS) Policy
 - *Noted the need for data standards, for protections for indigenous populations, and allowances for IRB approved waivers of consent under appropriate circumstances*

Comments 2014

- Comments on the International Code of Conduct for genomic and health-related data sharing
 - *Fully supported the draft Code of Conduct but emphasized the importance of allowing for ethics committee waivers of informed consent for retrospective collections under appropriate circumstances*
 - *Comments on case examples are in preparation*
- Comments on the Working Document on Research on Biological Materials of Human Origin to the Committee on Bioethics of the Council of Europe
 - *Noted the need to clarify terms “identifiable” and “future research”*
 - *Urged flexibility in consent models and acceptability of using broad consent*
 - *Recommended allowances for IRB/ethics review waivers of consent under appropriate circumstances when children whose specimens are used in research reach the age of majority and for storage of residual anonymized materials*
 - *Recommended that biobank policies on individual feedback be included in the informed consent*



PRIVACY and PROGRESS in Whole Genome Sequencing

Presidential Commission
for the Study of Bioethical Issues

October 2012

p. 80

BIOBANK RESEARCH

Biobank research raises practical considerations distinct from other research settings. A recent study reviewing biobank policies found that half of the surveyed biobanks address the return of incidental findings, but few suggest that they should be returned. Often, the data stored in biobanks are de-identified such that researchers cannot readily link the data to particular individuals. De-identification makes the return of incidental findings much more difficult. Biobank researchers often lack access to the code that facilitates re-identification, and in many cases agreed that they would not attempt re-identification. A recent study of incidental findings in biobank research estimated the cost to be \$1,322 per disclosure, including the cost of retesting archived DNA samples, providing genetic counseling, contacting participants, and conducting follow up.

“Because one biorepository may supply tissue specimens to hundreds of investigators, the return of incidental findings to participants from the secondary research that follows is impracticable. Hence the biorepository community views any such requirement with great concern. Biorepositories serve as an intermediary between patients from whom specimens are collected and processed, and investigators to whom specimens are provided and who generate research results. Most biorepositories do not have access to secondary research results, and have no infrastructure for the return of incidental findings to participants. Developing such an infrastructure, including informatics necessary to support the return of incidental findings would be extremely costly for biorepositories, most of which have marginal funding.”*

Sources: Wolf, S.M., et al. (2012). Managing incidental findings and research results in genomic research involving biobanks and archived data sets. *Genetics in Medicine*, 14(4), 361-384; Johnson, G., Lawrenz, F., and M. Thao. (2012). An empirical examination of the management of return of individual research results and incidental findings in genomic biobanks. *Genetics in Medicine*, 14(4), 448; Christensen, K.D., et al. (2011). Disclosing individual CDKN2A research results to melanoma survivors: Interest, impact, and demands on researchers. *Cancer Epidemiology, Markers and Prevention*, 20, 522-529; Bledsoe, M.J., et al. (2013). Return of research results from genomic biobanks: Cost matters. *Genetics in Medicine*, 15(2), 103-105.

* Zaayenga, A., President Elect, International Society for Biological and Environmental Repositories (ISBER). (2013, July 8). Comments submitted to the Bioethics Commission.

Other ISBER ELSI Activities

- Working Groups and Task Forces
 - iPSC Task Force
 - Regulatory and Ethics Working Group (new)
 - Regulations Task Force (new)
- Discussions and Workshops at Annual Meetings
 - Governance, Return of Research Results, International Policy Developments, Global Harmonization, Commercial Use and Ownership, Identifiability; Privacy; Genomic Data sharing, Sustainability, Engaging Research Participants

Other ISBER ELSI Activities

- Co-sponsored advanced tissue banking programs with Public Responsibility in Medicine and Research (PRIM&R) to engage and educate the IRB/ethics review committee communities on biobanking activities

Moving Forward: The Challenges

- Broad variation in types of biobanks: one size does not fit all
 - Hospital-based prospective collections, Specific research collections, Use of pathology archives, Population-based biobanks, Other
- Variation in regulations and policies and ethics review committee requirements globally
- Evolving ethical and regulatory landscape
- Education of stakeholders

Moving Forward: Future Initiatives

- Moving forward, how can the experience of ethics and governance bodies be shared and disseminated?
 - ISBER is developing best practices for governance that will be discussed at the 2015 ISBER Annual Meeting
 - ISBER will be continuing to engage IRB/Ethics Committees through collaborations with Public Responsibility in Medicine and Research (PRIM&R)

What is efficient use of biospecimens?

- **Distribute them** to end-users
 - Not burry them
- Distribute them **in time**
 - appropriate stability
- Distribute them **qualified**
 - Accompanied by relevant and verified data
 - Clinical, pathological, epidemiological, preanalytical
 - accurate identity
 - Fit-for-purpose
 - appropriate concentration, integrity, purity, homogeneity
 - Comparable cases and controls

ISBER Education and Training Committee

- 2014 members:
 - Chair: Nicole Sieffert
 - Members: Sheila O'Donoghue, Jane Carpenter, Judith Giri, Lise Matzke, Chi Tarn, Diane McGarvey
 - Advisors: Marianna Bledsoe, Kathy Sexton, Karen Pitt
- This Committee strives to identify ways to ensure that ISBER members have access to state-of-the art information in order to effectively operate repositories and ensure quality preservation of specimens to use for future research and analysis. Wherever possible, the Committee makes available to members information on training courses and other educational opportunities to allow for the dissemination of methods and practices for performing efficient, effective repository activities.

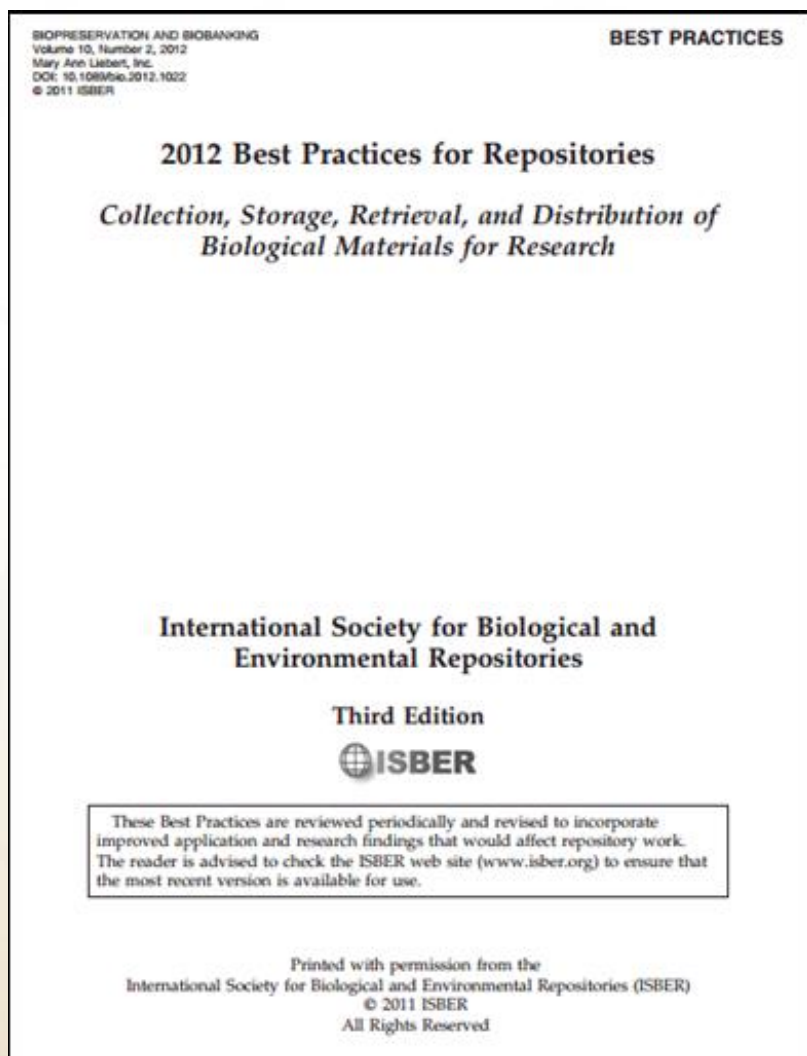


Education and Training

ISBER

- **Best Practices**
 - www.isber.org/bp/
- **Self Assessment Tool**
 - www.isber.org/sat/
- **Certified Repository Technician**
 - www.isber.org/crt/index.cfm
- **Proficiency Testing**
 - www.isber.org/proficiency_testing/
- **Pre-analytical EQA**
 - www.isber.org

ISBER Best Practices for Repositories



**Specimen Collection, Processing,
Storage And Retrieval**
Legal And Ethical Issues in Biobanking
**Specimen Access, Distribution, Use And
Destruction**

Repository Planning

Facilities
Storage Equipment And Environments
Quality Management
Safety
Records Management
Biological Material Tracking

Training
Cost Management & Sustainability

ISBER SAT

Self Assessment Tool

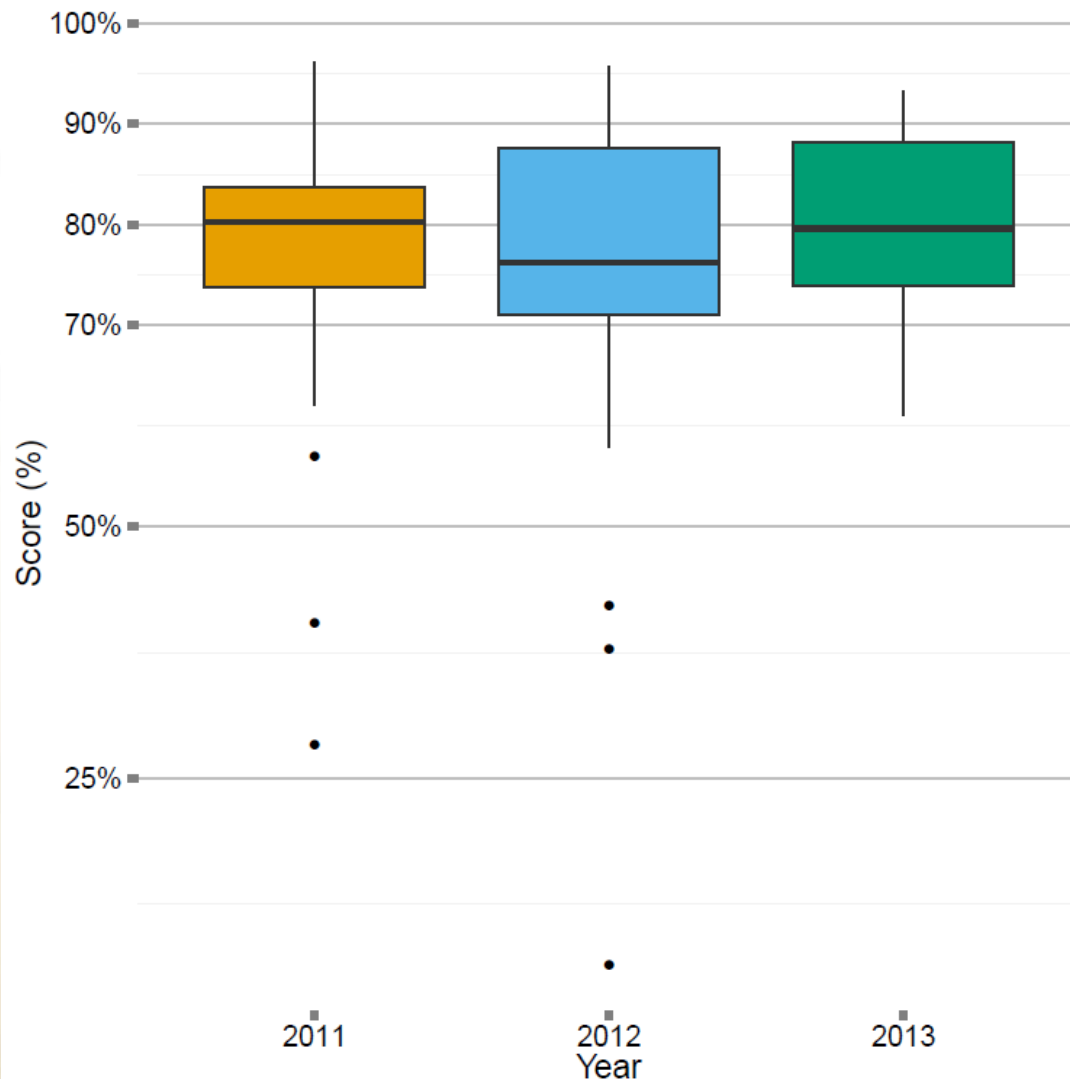
- Based on ISBER BPs 3rd edition
- 158 questions
- Confidential
- Risk balanced global compliance score (%)
- Highlight on highest and intermediate risk items
- Risk evaluation based on
 - Severity
 - Frequency
 - Ease of detection
- Usefulness in
 - Quantitative QI in biobank certification
 - Continuous improvement
 - Accountability to stakeholders
 - Assessment by biobank funding agencies (eg. Australia)

ISBER Self-Assessment Tool (SAT) for Repositories Results from 2011-2013 by Region



Region ● Americas ● Europe, Middle East, and Africa ● Indo-Pacific Rim ● Unknown

ISBER Self-Assessment Tool (SAT) for Repositories Results Summary from 2011-2013



ISBER CRT

Certified Repository Technician

- Educational materials
- Written examination
- ASCP (American Society for Clinical Pathology)

ISBER

Biospecimen Science

Working Group Update:

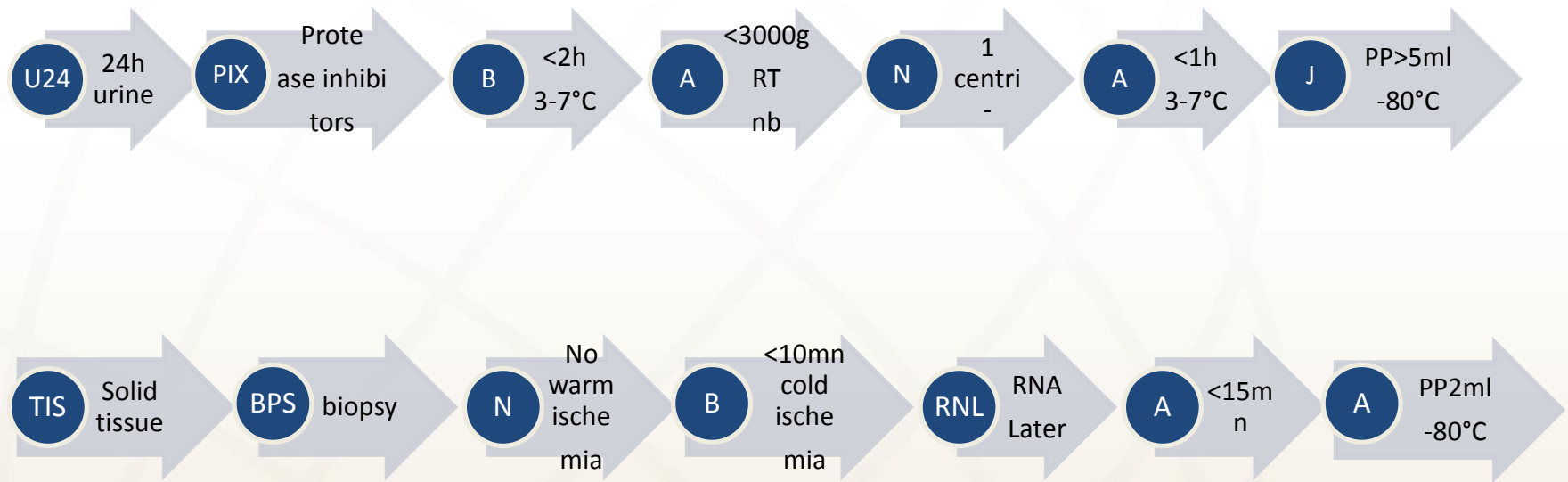
From *in silico* biospecimen research
to external quality assessment

2010-2014 activities and deliverables

- SPREC v01, v02
- SPREC implementation in databases, SPRECalc
- Biospecimen Science literature compilation
- QC tool identification through data mining
- Development of a Proficiency Testing program
- Study of robustness and reproducibility of RT RNA storage
- Study of robustness and reproducibility of viable cell shipping at frozen or RT
- Development of a pre-analytical EQA survey

SPREC-02

Biospecimen preanalytical code



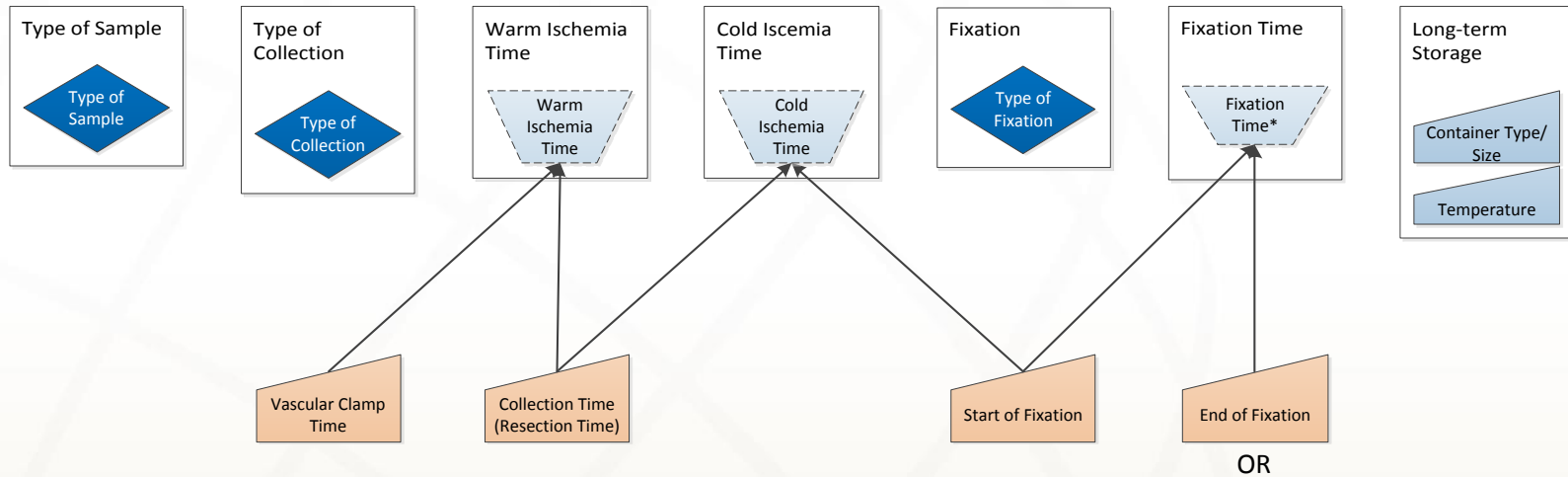
Cancer Epidemiology Biomarkers and Prevention 2010;19:1004-11

SPREC implementation

- Prostate Cancer Bioresource, Australia
- BioBIM, San Raffaele, Italy → **SPRECware tool**: SPREC coding and decoding
- IBBL, Luxembourg → **SPRECalc tool**: SPREC Excel calculator
- Precision, USA
- Quintiles, USA
- Lifegene, Lifelines, MIABIS, TMF?...
- SPREC beyond humans... **“Standard PREanalytical Codes (SPREC): A New Paradigm for Environmental Biobanking Sectors Explored in Algal Culture Collections”, Biopreservation Biobanking, 2012;4:399-410**

SPREC version 2.0

Flowchart for automatic calculation of SPREC v.2 for Solid Samples



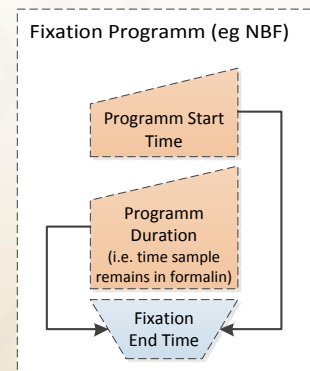
- SPREC 2.0

- More options
- Implementation tools

All time stamps must be in format: ddmmyyyy hh:ss

— — — — — → Calculated value or optional input

* for SNP samples, Fixation Time is per definition: < 15 min.



V1
S. Lehmann
16-Jan-2012

<http://www.isber.org/?page=SPREC>

Contact Us Sign In Join ISBER



**Connecting Repositories
Globally through Best Practices**
Leading since 1999

USERNAME PASSWORD REMEMBER ME

[FORGOT YOUR PASSWORD?](#) [HAVEN'T JOINED YET?](#)

HOME ABOUT ISBER MEMBERSHIP MEETINGS INDUSTRY LEARNING RESOURCES **FORUMS**



ISBER creates opportunities for sharing ideas internationally, and harmonizes approaches to evolving challenges in biobanking, and biological and environmental repository operation.

SITE-WIDE SEARCH
Enter search criteria...
Search »

CALENDAR [more](#)
6/26/2013 » 12/31/2014
BIOBANKING EDUCATION
9/16/2013 » 9/18/2013
INTERNATIONAL BIOBANKING
SUMMIT - II, BMMR/ERIC AND LPC

BREAKING NEWS [more](#)
7/8/2013
TAKE ACTION WITH THE ISBER
SCIENCE POLICY COMMITTEE
5/16/2013
NEW WEBSITE LAUNCH JUNE 3RD

**Welcome to the International Society for
Biological and Environmental Repositories!**

ISBER is the largest international forum that addresses the technical, legal, ethical, and managerial issues relevant to repositories of biological and environmental specimens. ISBER is a professional society of individuals and organizations who share an interest in promoting consistent, high quality standards, ethical principles and innovation in biospecimen banking by uniting the global biobanking community. ISBER invites all sub-components of government, academia, the private sector, and manufacturers to become active participants of the society.

**BEST PRACTICES
for REPOSITORIES**

JOIN isber

isber2014
**ANNUAL MEETING
& EXHIBITS**
Orlando, FL • May 20-24, 2014

Challenges in Biospecimen QC

Difficulty of accessing Biospecimen Science information

<http://www.isber.org/?page=BS>

ISBER BSWG literature compilation

→ 678 references

→ 293 different journals

OBBR database

<https://brd.nci.nih.gov/BRN/brnHome.seam>

Clin Chem	67
CryoLetters	60
Clin Chem Lab Med	28
CEBP	14

Biospecimen science literature

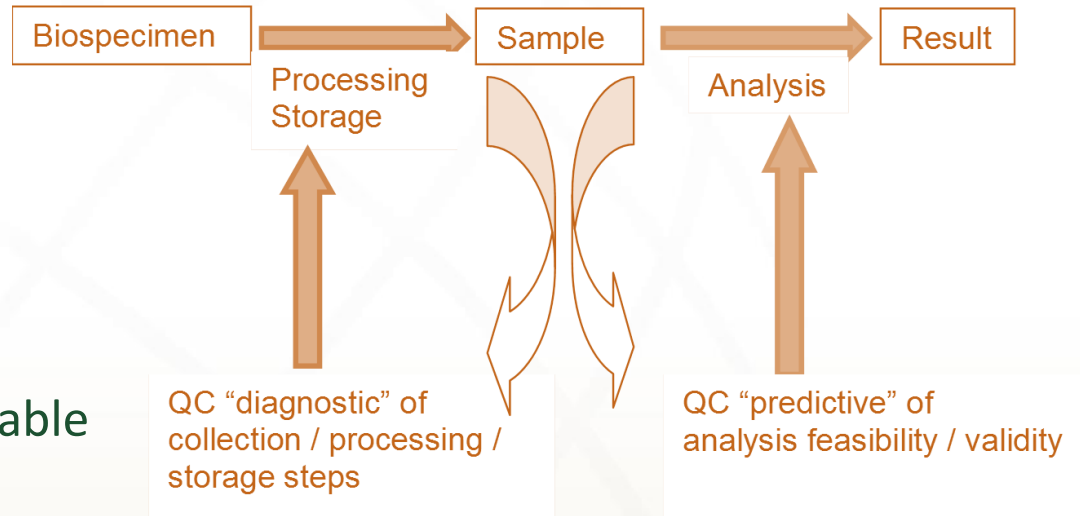
- Update of the biospecimen science literature compilation
<http://www.isber.org/wg/BS-WG-LitComp.html>
- Long term storage and freeze-thaw stability literature information
- Critical reading of ~600 publications to identify biospecimen QC tools (markers/assays) that can be used to define sample quality

Eventual implementation in PT schemes!

In silico biospecimen research

MATRIX including:

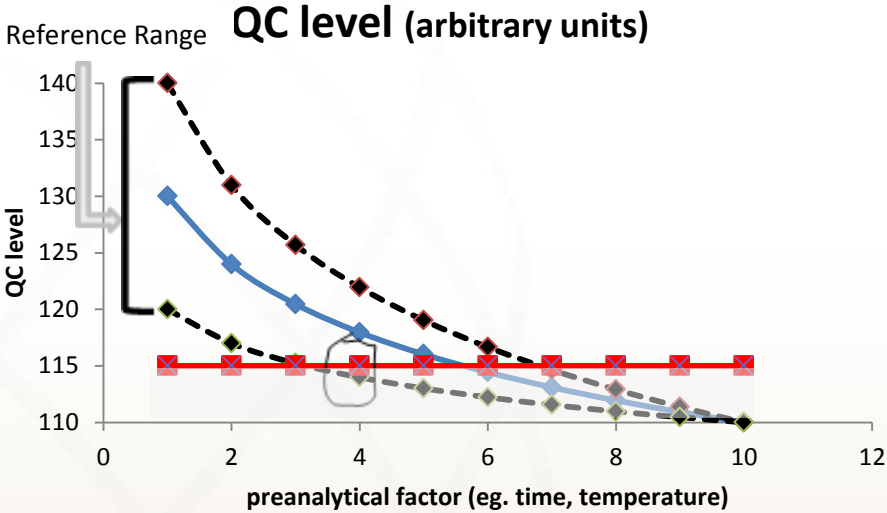
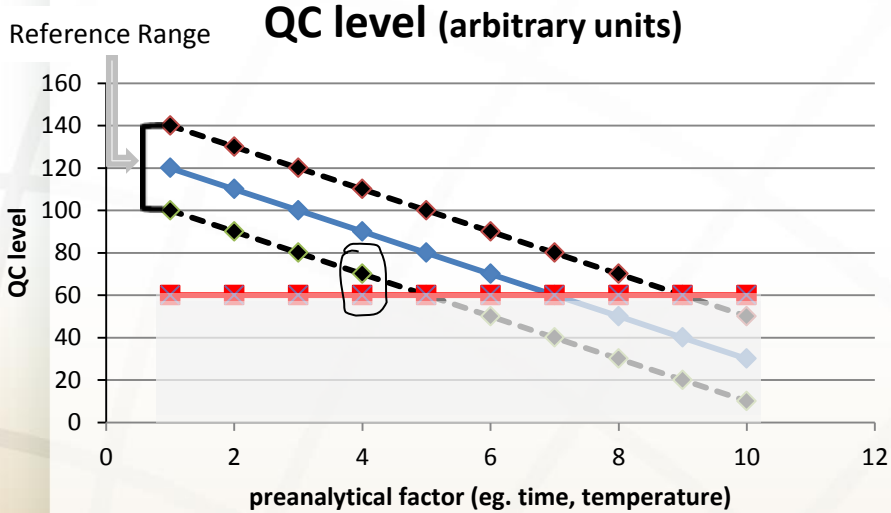
- Reference
- Type(s) of sample
- Pre-analytical variable(s)
- Range of pre-analytical variable
- Pre-analytical “threshold”
- QC tool (marker)
- QC assessment method
- Type of method (qualitative vs quantitative ; simple vs multiplex)
- Range of the QC marker
- Control samples used as baseline
- Reference (control) range



In silico biospecimen research: results

- Type of QC tool
 - Diagnostic
 - Predictive
- Evidence-based
- Applicability grade
 - Immediately applicable
 - Potentially applicable
 - Not immediately applicable
- Accessibility grade
 - Readily accessible
 - Potentially accessible
 - Not immediately accessible

Models of QC tools



Examples of biospecimen molecular diagnostic tools identified

QC tool	Sample type	QC scope	Applicability grade	Accessibility grade	Future research required
K+	Serum	Precentrifugation delay at 4°C	1	1	Plasma
Truncated cystatin C	CSF	Storage conditions	3	3	Produce MAbs once confirmation in other sample types.
DUSP1 expression	Prostate fresh tissue	Warm ischemia time	1	1	other tissue types
Myosin heavy chain	Prostatic tissue	Cold ischemia	3	2	Other tissue types, ref values

Heins M et al. Eur J Clin Chem Clin Biochem 1995;33:231

Carrette O et al. Proteomics 2005;5:3060

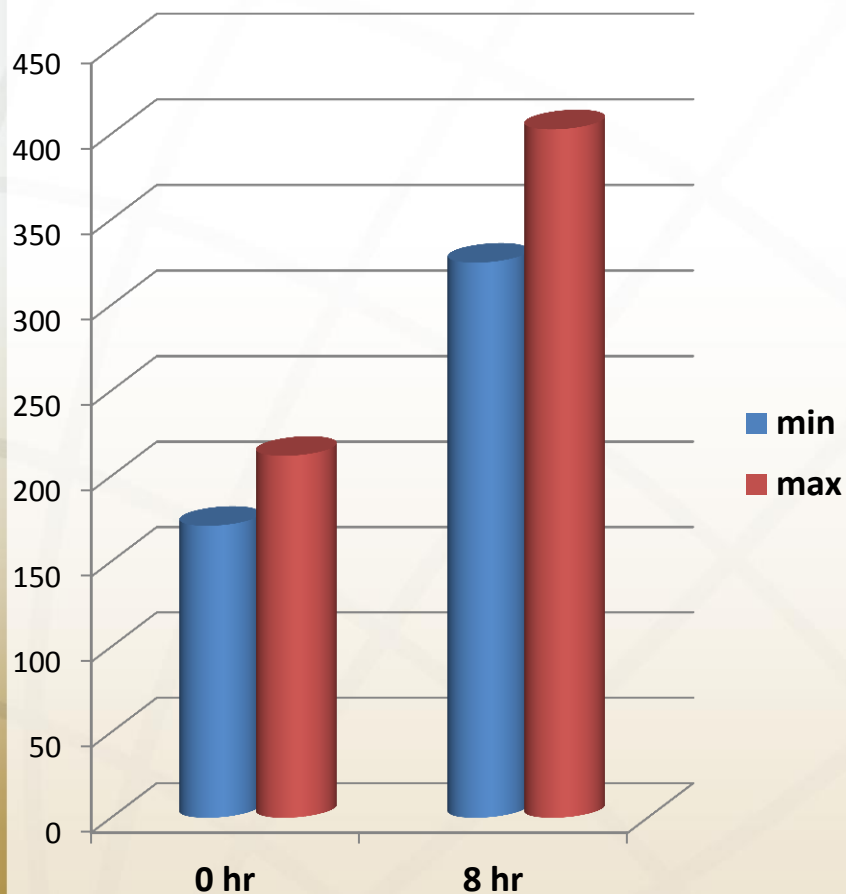
Lin DW et al. J Clin Oncol 2006;24:3763

Jackson D et al. Proteomics 2006;6:3901

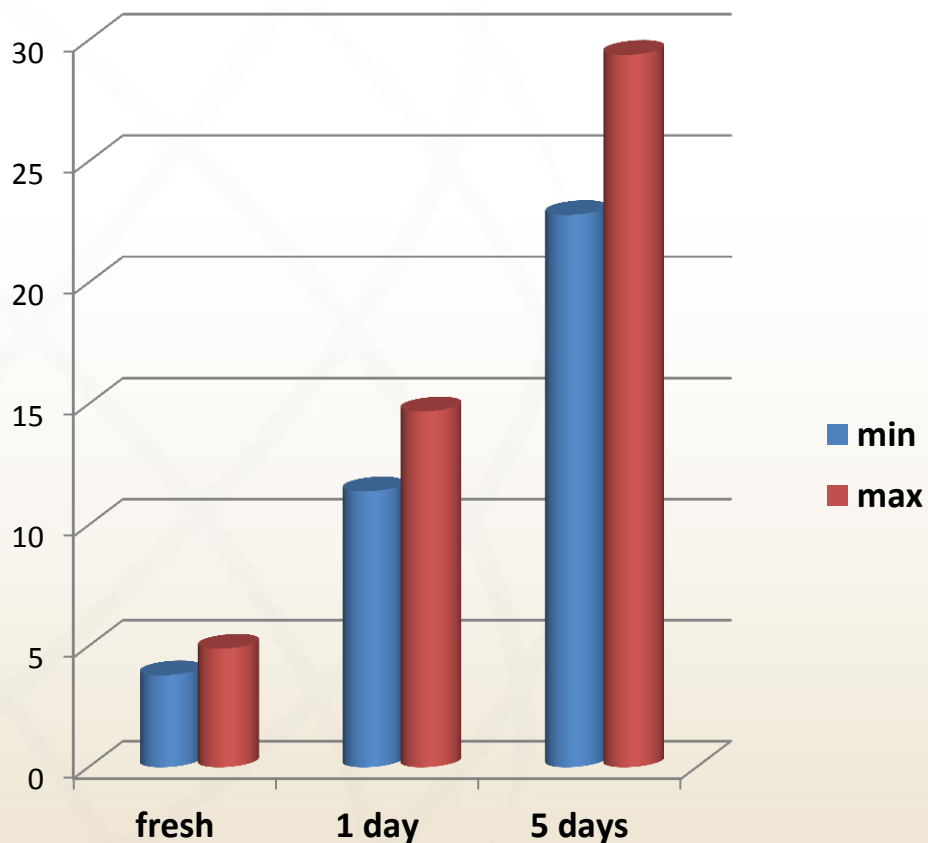
Identification of evidence-based biospecimen quality control tools, *J Mol Diagn* 2012

Serum Pre-Centrifugation Delay

Transferrin receptor ELISA (U/ml)

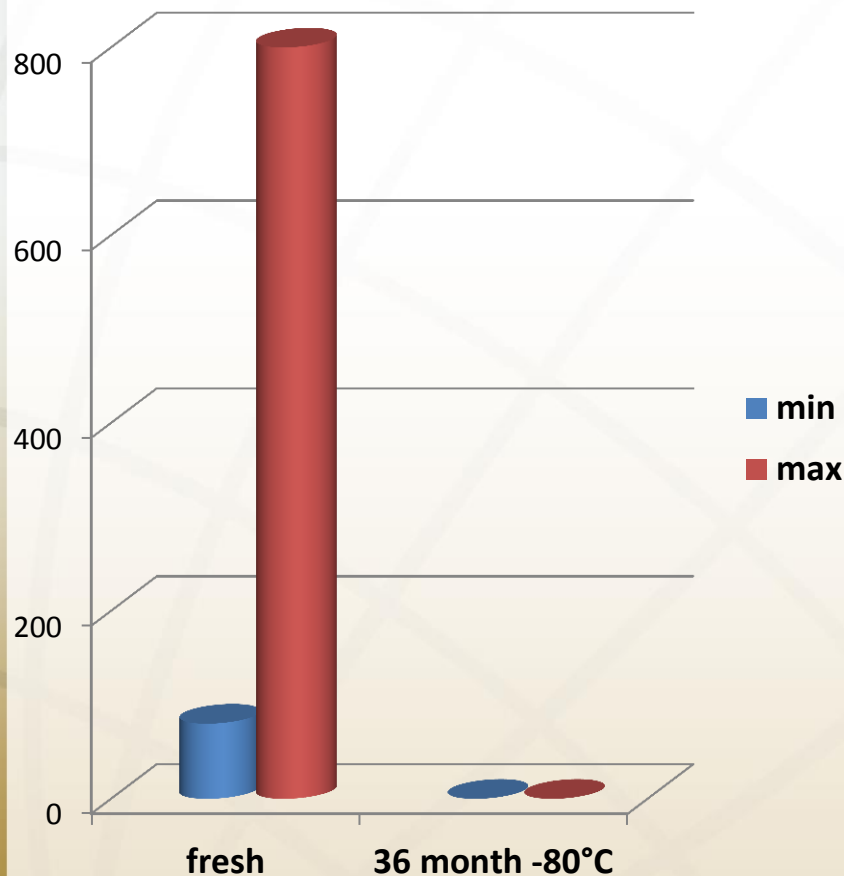


Potassium potentiometry (mmol/L)

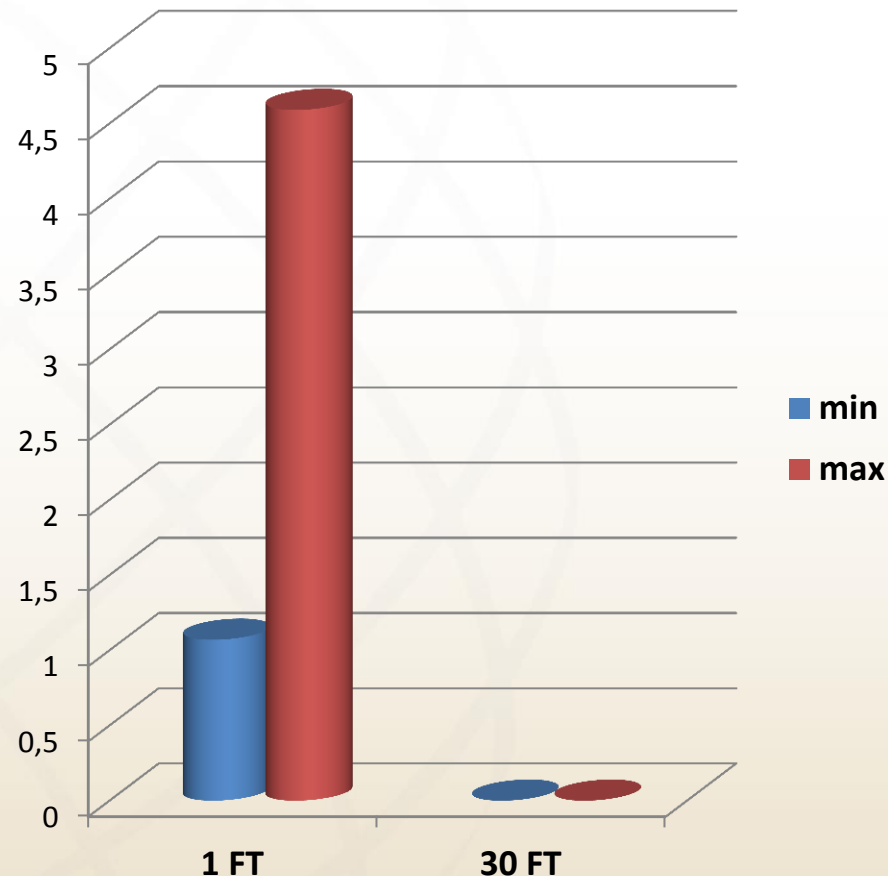


Plasma, Serum Storage Conditions

MMP9 ELISA (ng/ml)

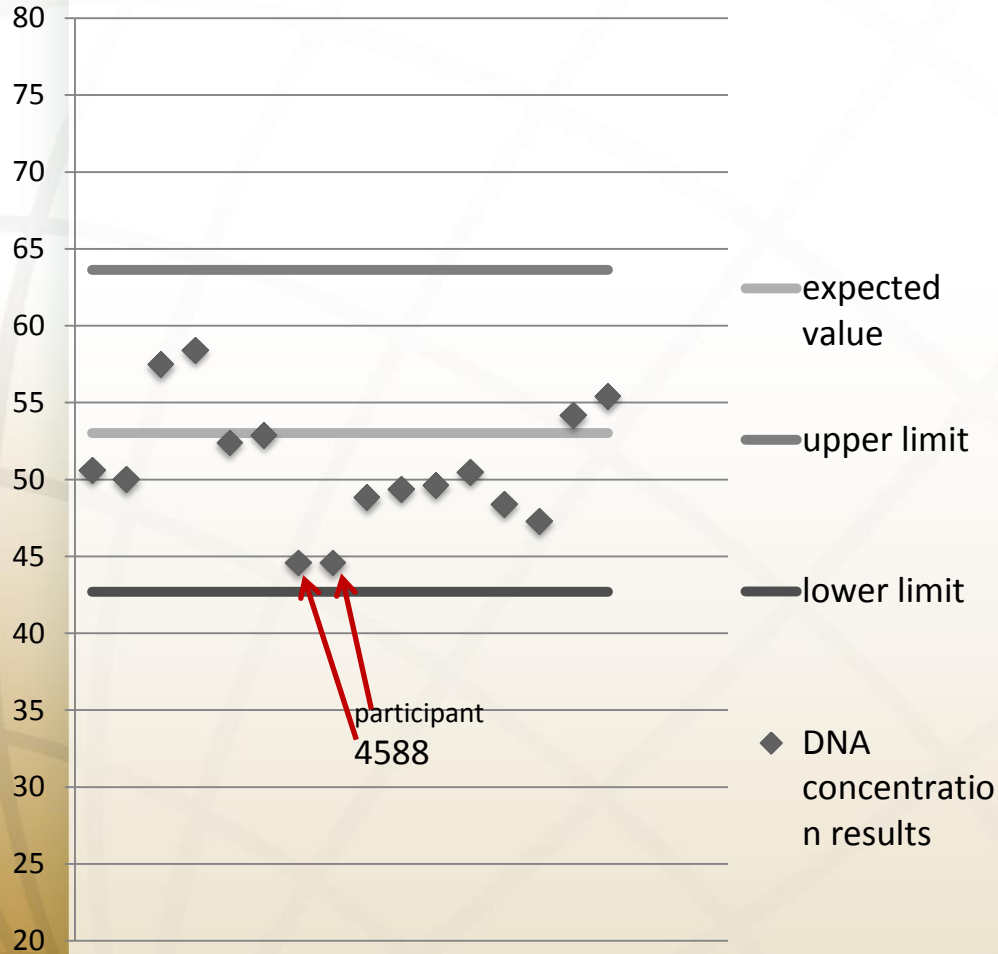


MMP7 ELISA (ng/ml)

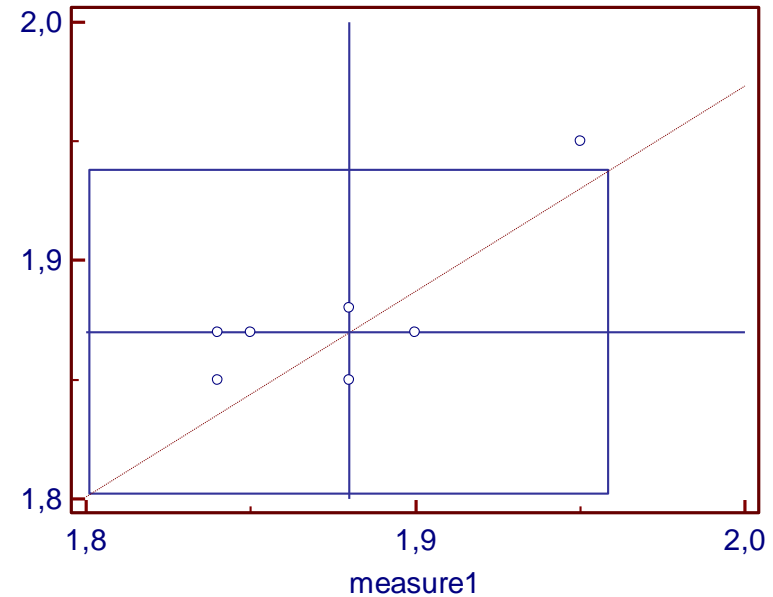


ISBER-endorsed PT (EQA)

PT scheme summary statistics



PT scheme Youden plot

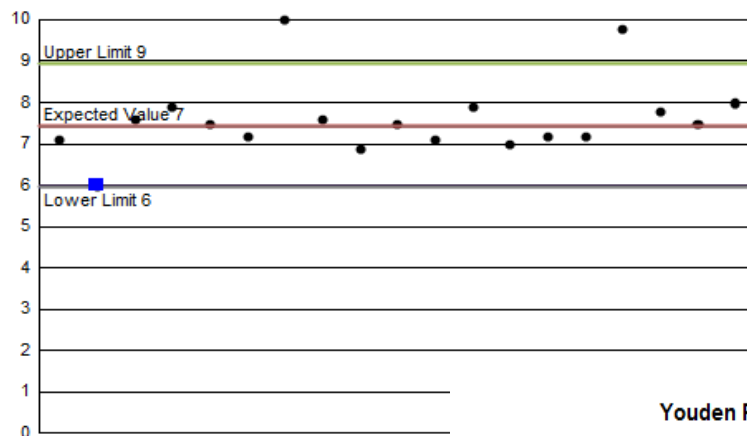


Proficiency Testing

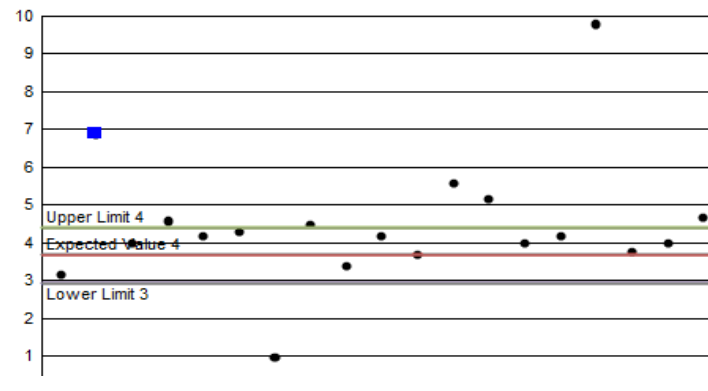
- Biorepositories: highly standardized and accurately characterized biospecimens!
- Efficiency of the specimen processing?
- Accuracy of the sample QC testing?
- Proficiency Testing = inter-laboratory comparisons to
 - Identify problems in laboratories and inter-laboratory differences
 - Determine performance of new QC methods
 - Provide confidence to end-users

RNA Integrity Performance Statistics

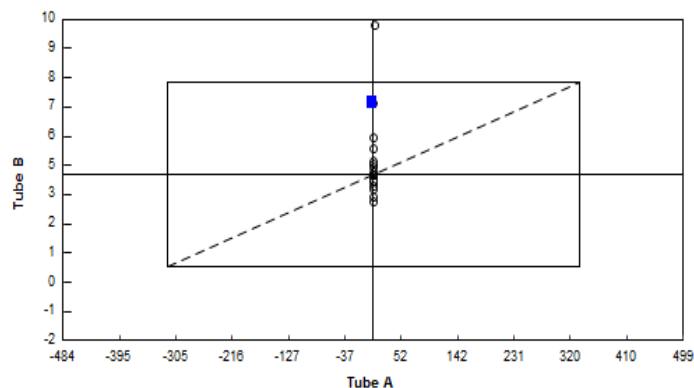
Tube A Results



Tube B Results

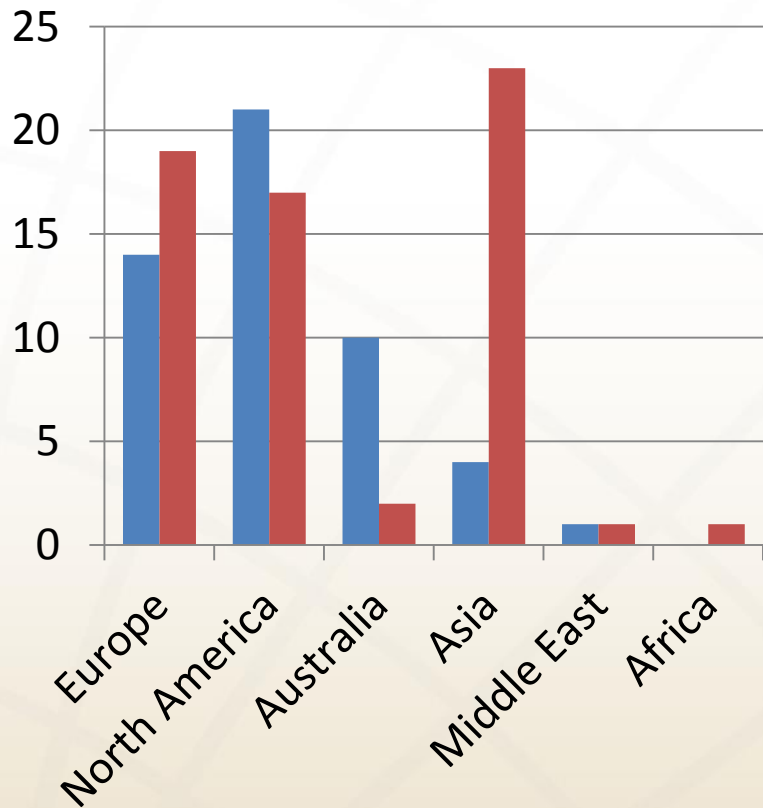


Youden Plot for RNA Integrity



		Assigned value (RIN)	Uncertainty of assigned value	PT Standard Deviation
Bioanalyser	Tube A	7.45	0.09	1.49
	Tube B	3.68	0.15	0.74

Proficiency Testing program 2013



Schemes:

- DNA quantification and purity
- RNA integrity
- Cell viability
- Tissue histology
- DNA extraction from whole blood

ISBER-endorsed PT

PT schemes

2013 PT Schemes:

DNA Quantification and Purity

RNA Integrity

Cell Viability

Tissue Histology

DNA extraction from whole blood

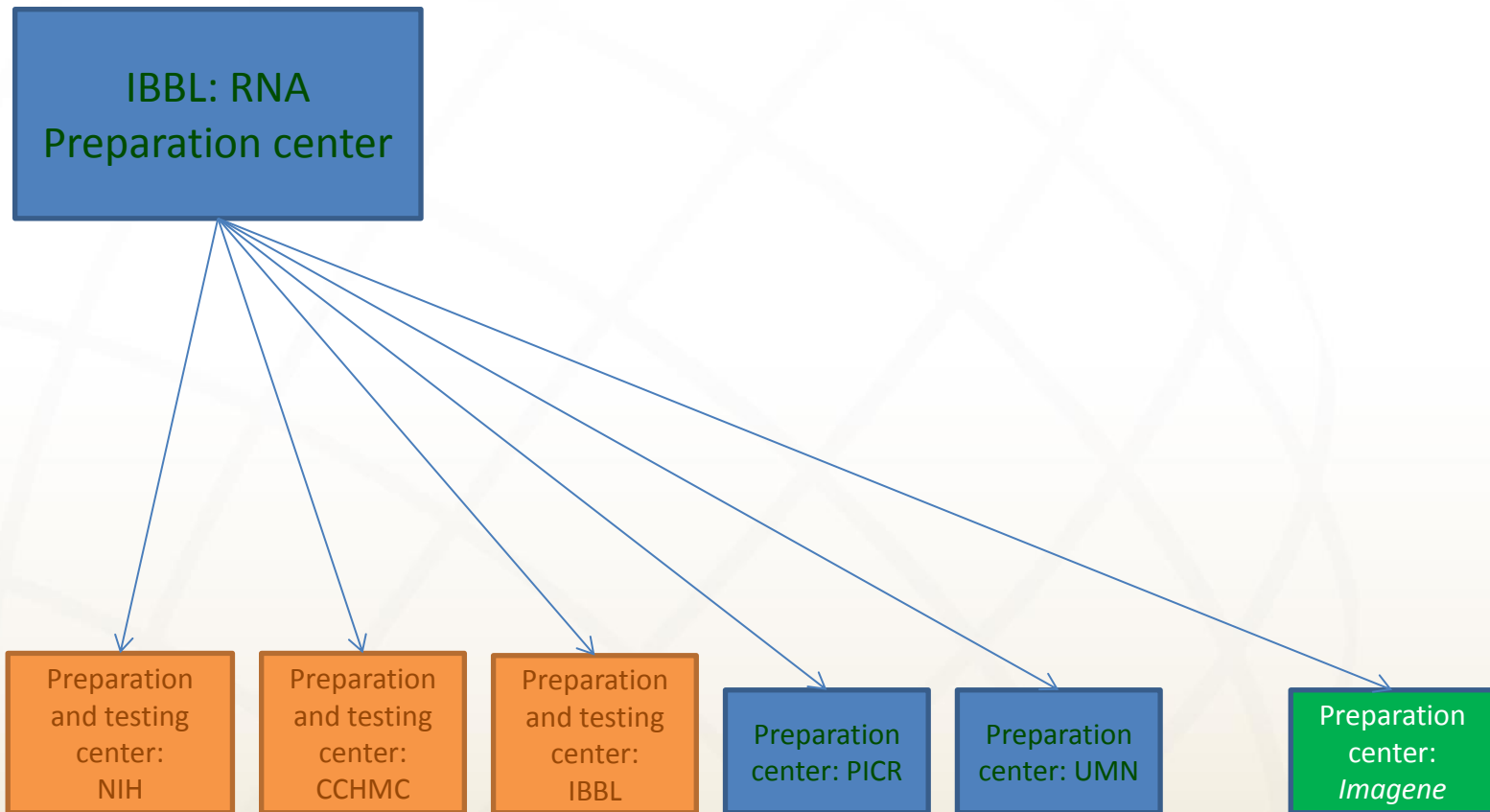
RNA extraction from whole blood

DNA extraction from FFPE tissue

Plasma metabolomics quality assessment

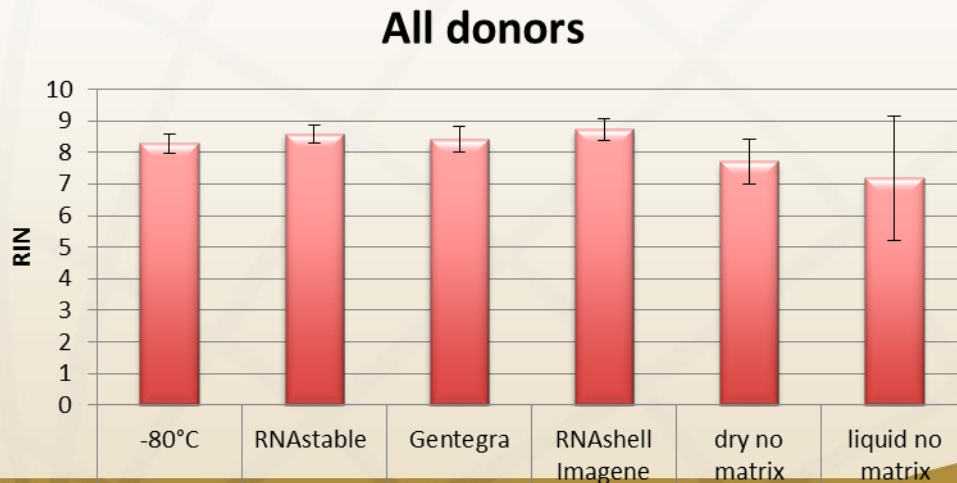
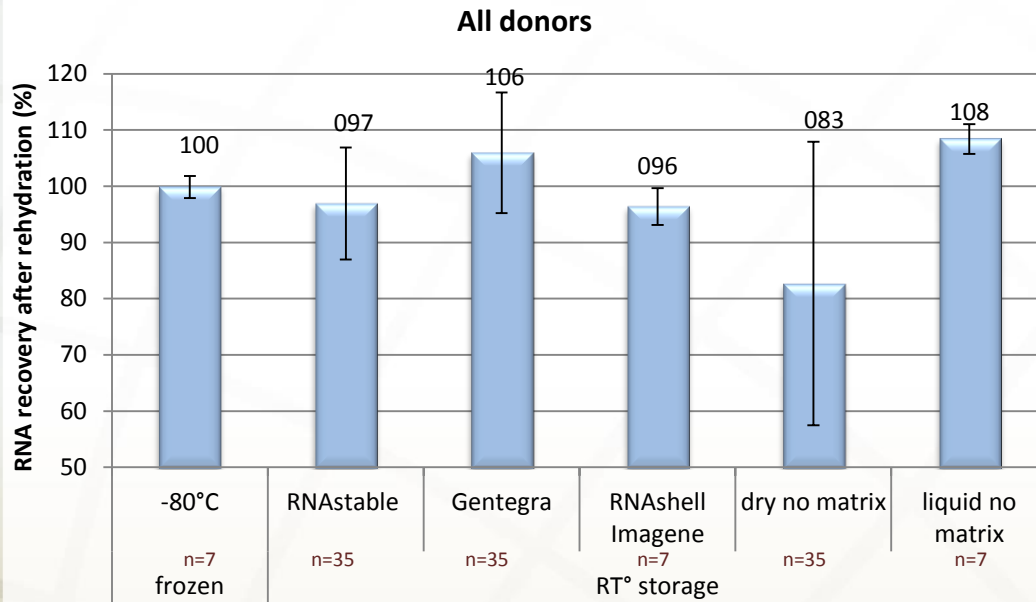


Room temperature RNA stability



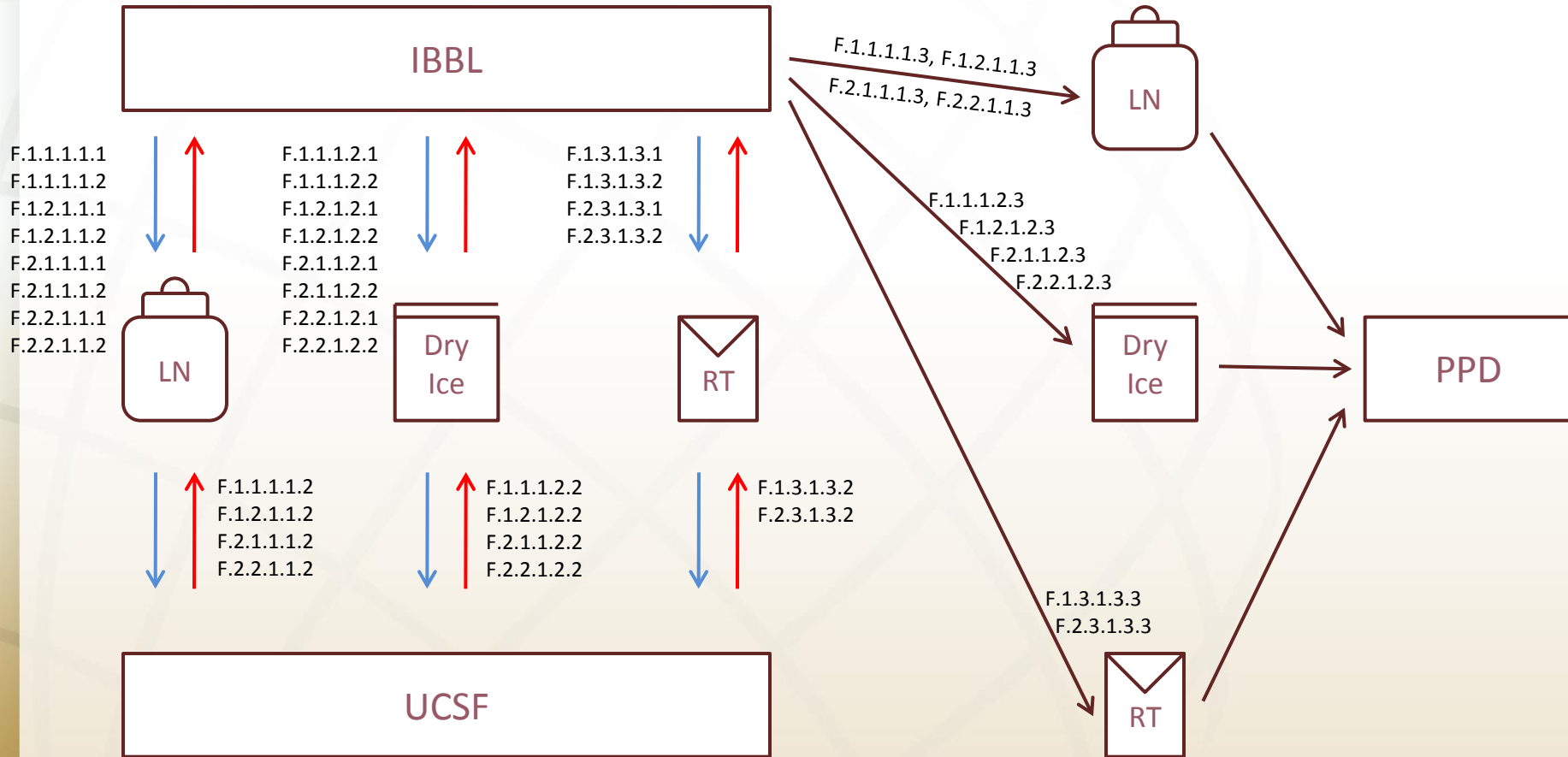
NIH: National Institutes of Health; Advanced Technology Center, Maryland
CCHMC: Cincinnati Children's Hospital, Ohio
PICR: National Biobank of Korea, Korea
UMN: University of Minnesota, Minnesota
Imagene: France

Results: RNA recovery, RIN



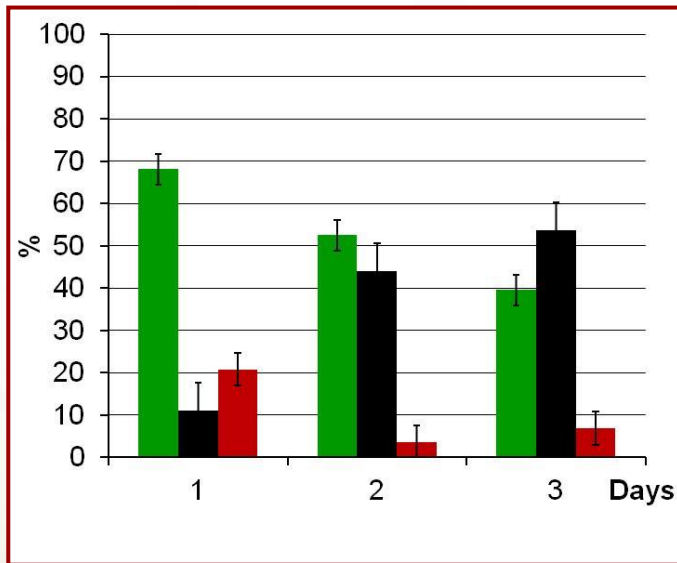
Implementation in PT schemes!

Shipment conditions and cell preservation

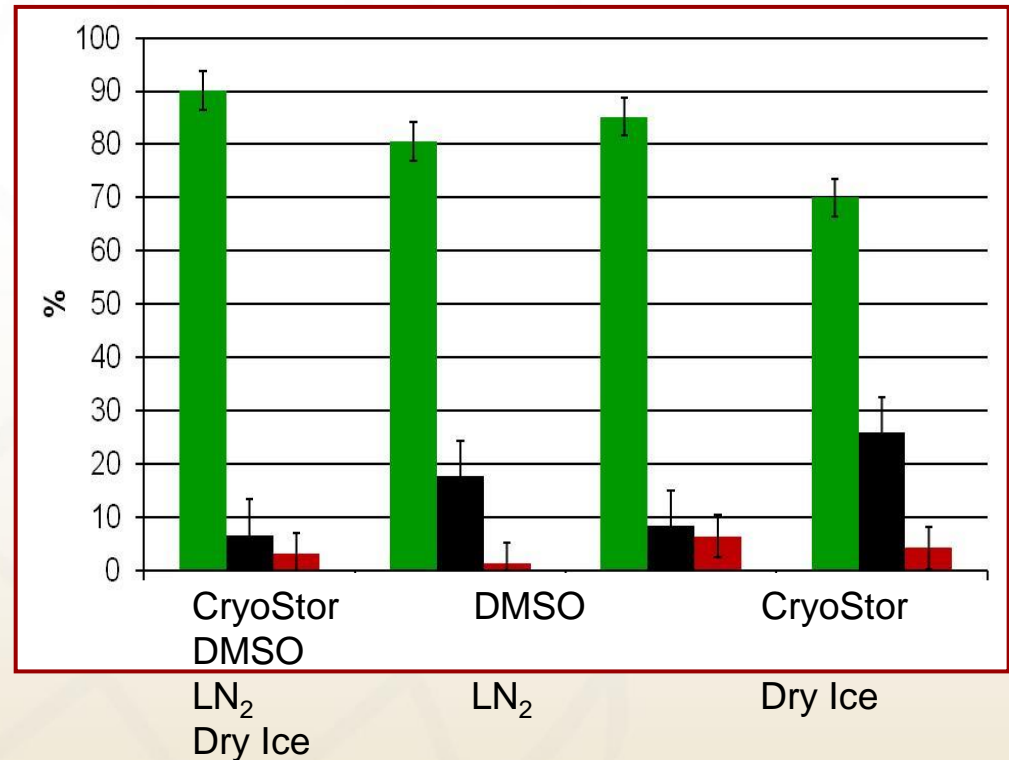


Shipment conditions and cell preservation: results

Room temperature transport media



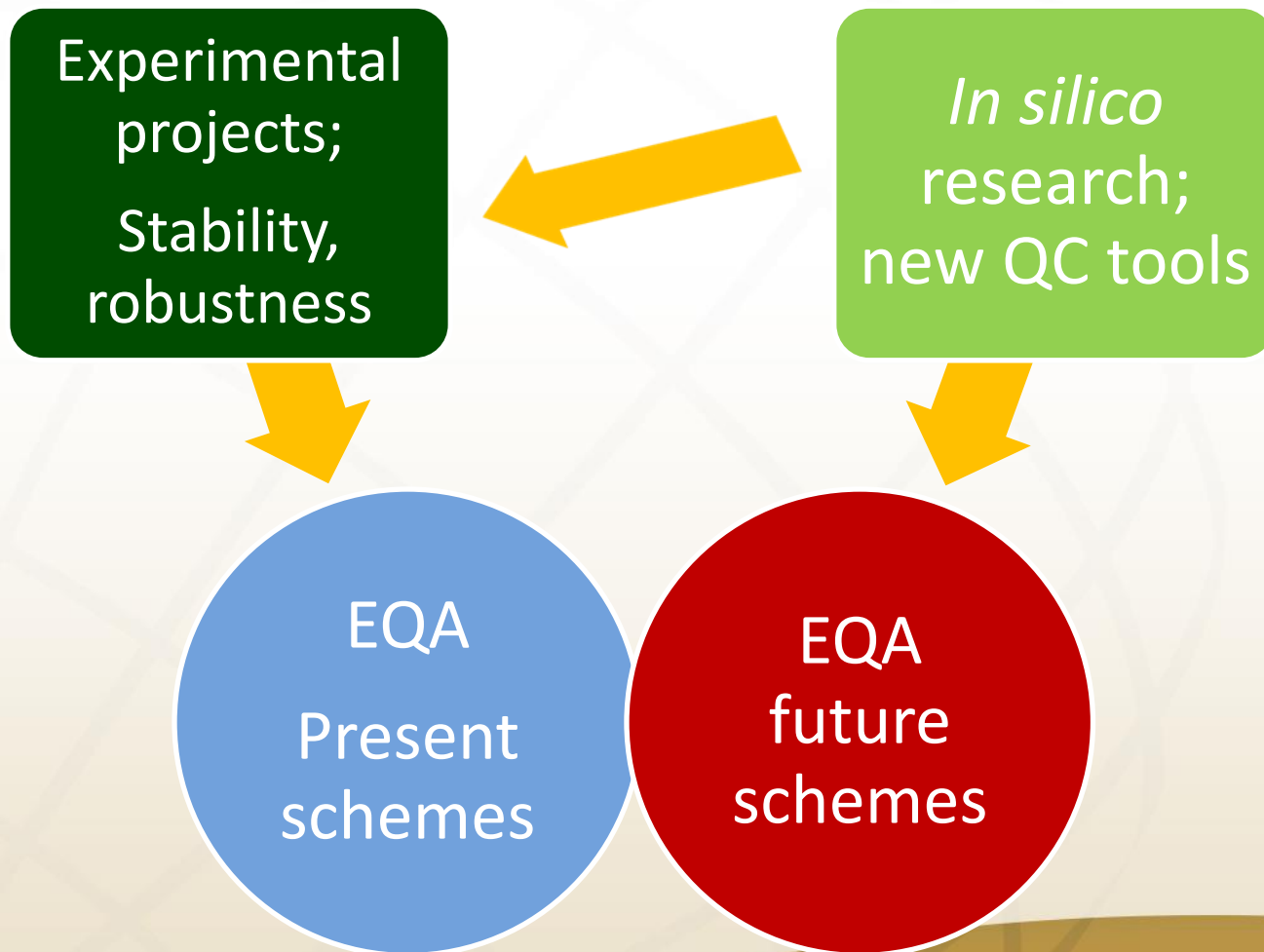
Travelling cells



- Viable cells
- Dead cells
- Early apoptotic cells

Implementation in PT schemes!

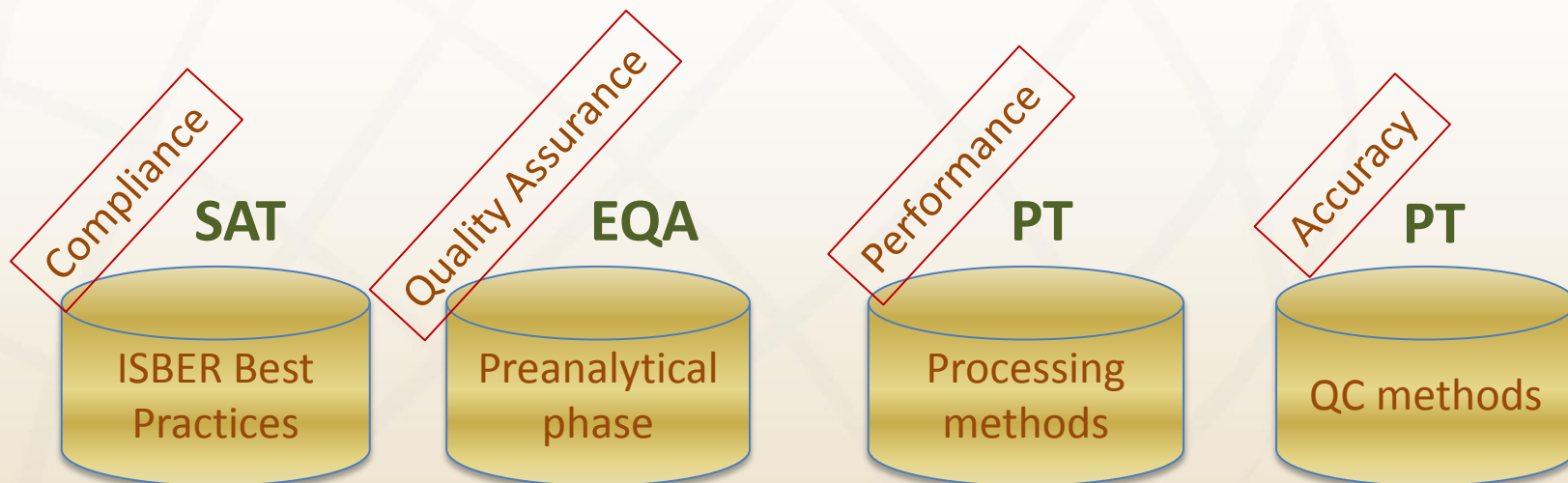
Conclusions



Pre-analytical EQA Survey tool

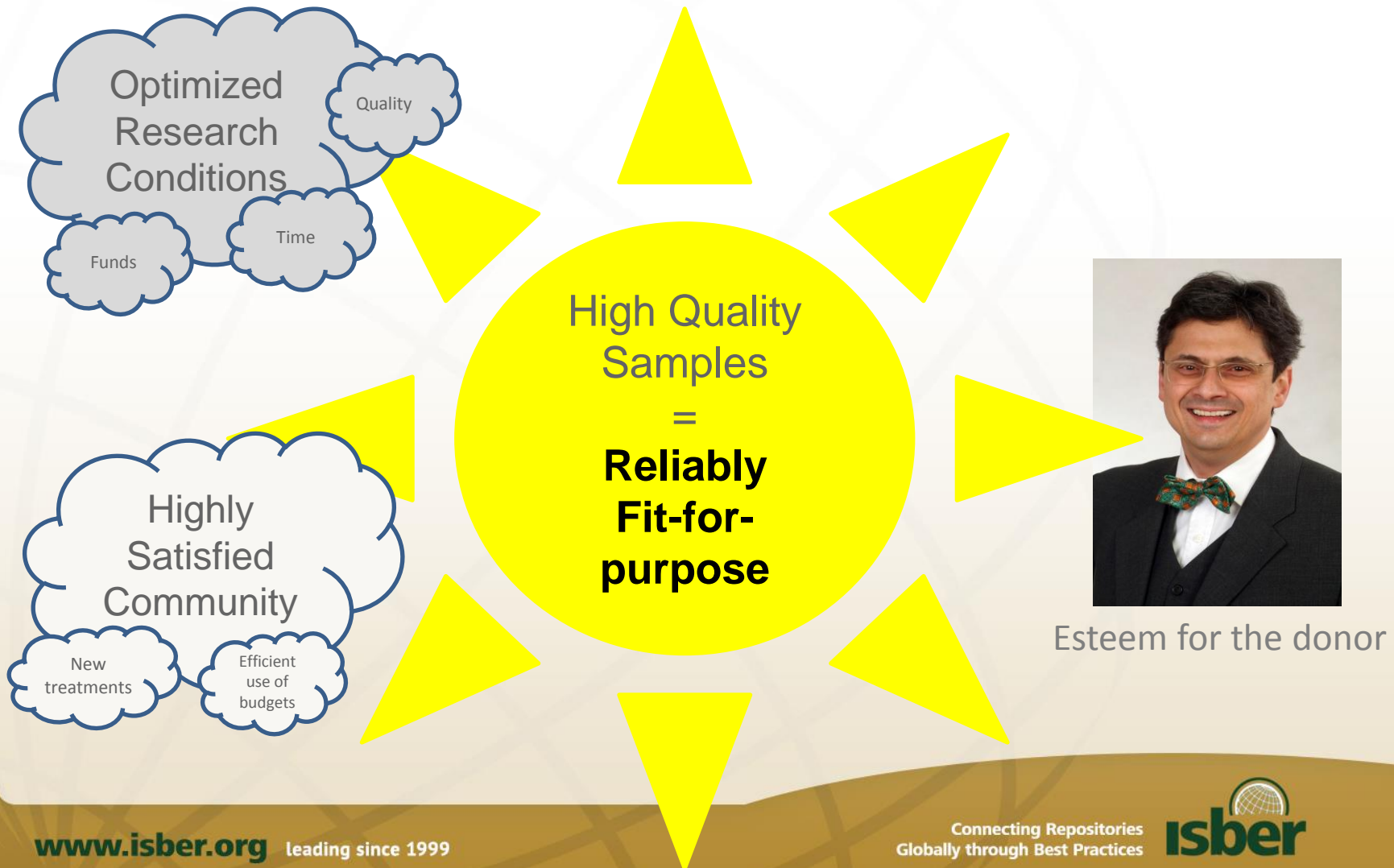
<http://www.isber.org/surveys/?id=BSWG.EQAsurvey>

- Allows biorepositories to assess the quality of the pre-analytical phase
- Contains trans-disciplinary questions
- Complements the SAT and PT



Making more efficient use of biospecimens

WHY ???





isber 2015

SHERATON PHOENIX DOWNTOWN • MAY 5 - MAY 9

ANNUAL MEETING AND EXHIBITS

Join us in Phoenix, Arizona USA
visit isber.org for more information

leading since 1999



isber

INTERNATIONAL SOCIETY FOR BIOLOGICAL
AND ENVIRONMENTAL REPOSITORIES

Acknowledgements

- ISBER Science Policy Committee
- ISBER Education and Training Committee
- ISBER Biospecimen Science Working Group
- ISBER iPSC Task Force
- Marianna Bledsoe and ISBER Board of Directors
- ISBER membership and meeting participants