ISBER Biospecimen Science Working Group

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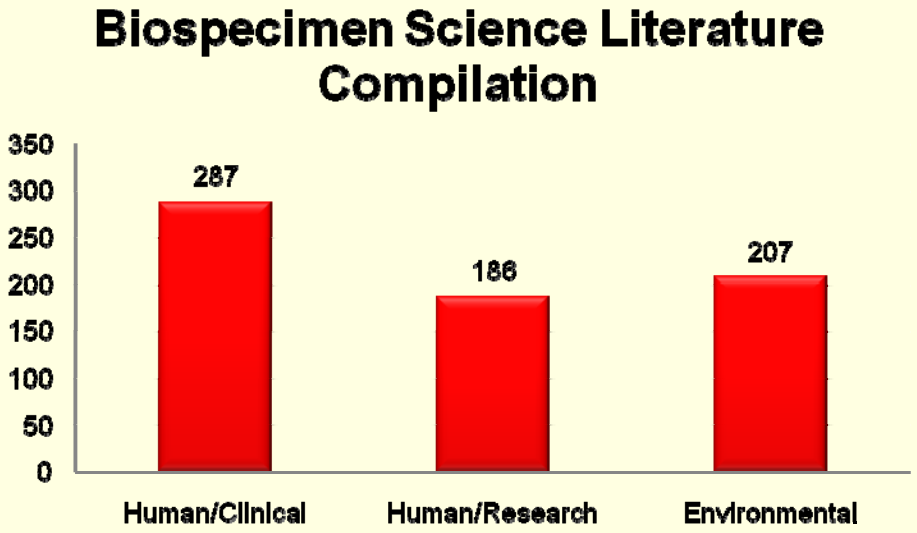
The Goal of the Working Group

- Biospecimen Science
  - Scientific knowledge about the biomolecular quality of samples
- Biospecimen Research

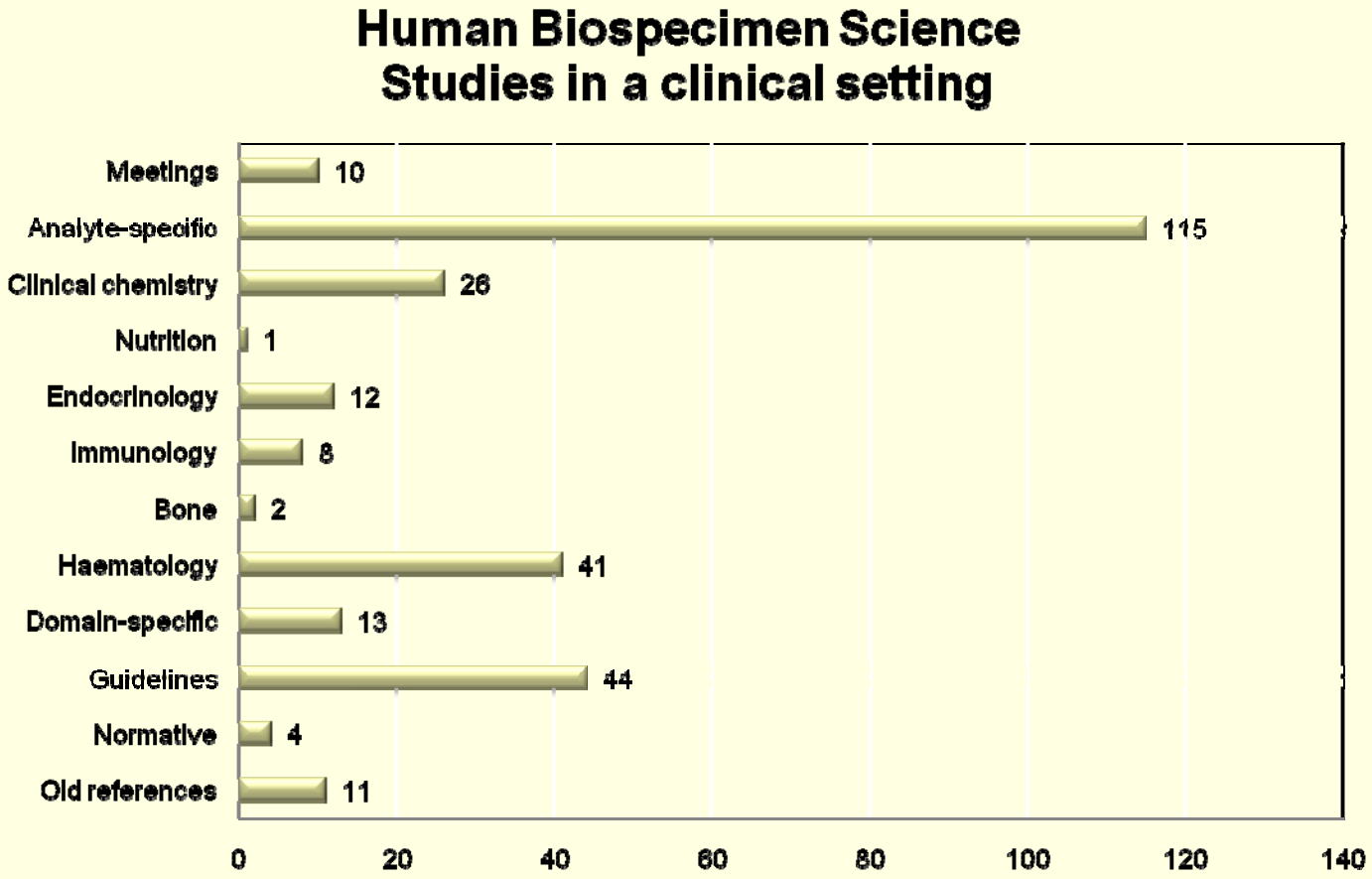
1st action

- **Biospecimen Research literature compilation**
  - Justification
    - A lot of data already published, but not always easy to find
  - Results :
    - **385 references (2009)**
    - **680 references (2010)**

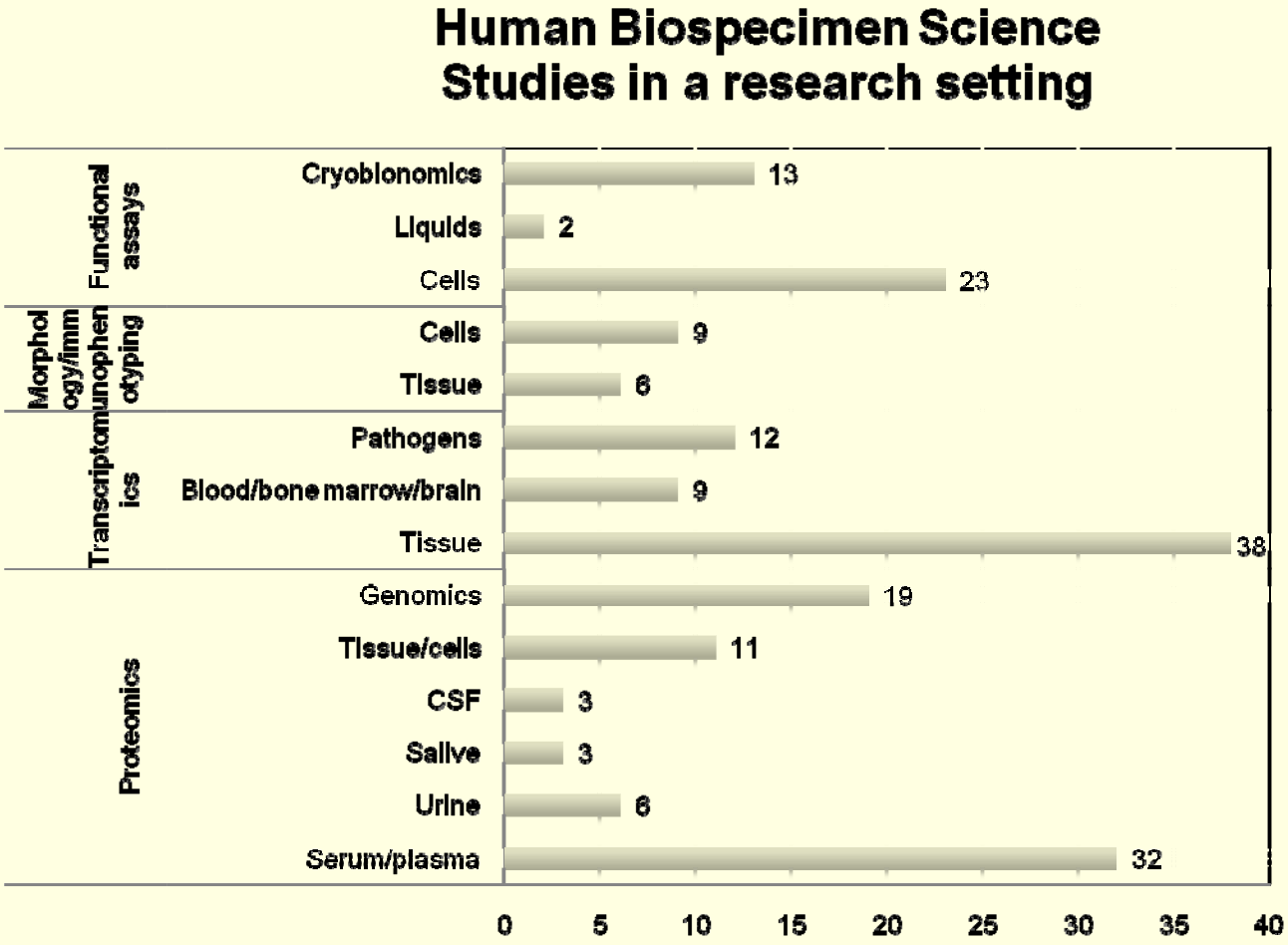


http://www.isber.org/wg/BS-WG-LitComp.html

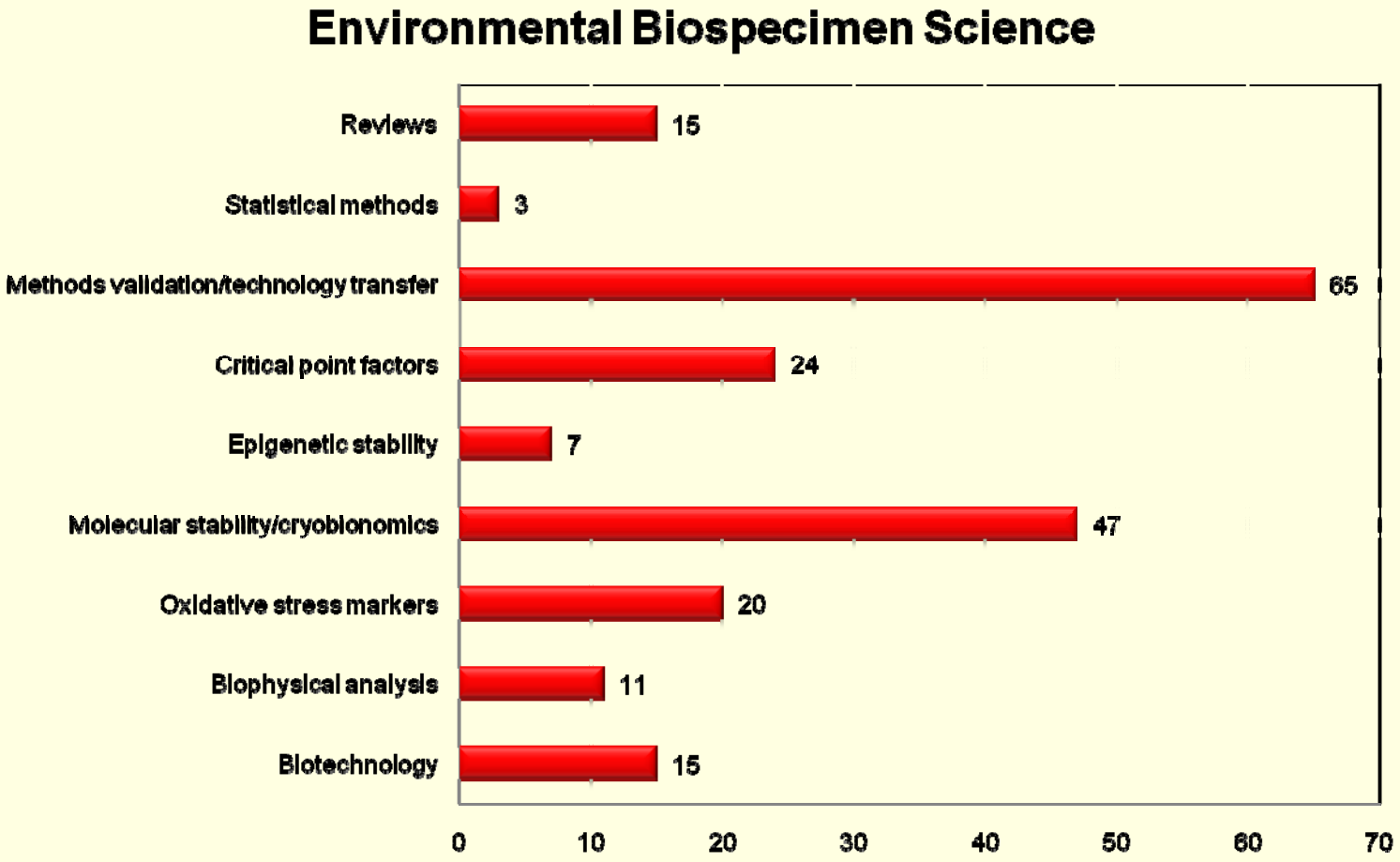
Human Biospecimen Science
Studies in a clinical setting



Human Biospecimen Science
Studies in a research setting



Environmental Biospecimen Science



2nd action

- **Standard Biospecimen Research Experimental Protocol**
  - Justification
    - Extreme variability in experimental designs makes comparing results very difficult
    - Example
  - Results : experimental protocol including standardized options, for application in:
    - Preclinical exploratory phase
    - Clinical assay validation phase

Cancer Epidemiology Biomarkers and Prevention 2009;18:1017-1025

Standard Biospecimen Research Experimental Protocol options

- **Plasma** sample

Pre-centrifugation:
•Type of tube: **EDTA**, Heparin, ACD, Citrate, Sodium Fluoride/ Sodium Oxalate, Micro Tube with gel
•Delay time 1 (Δt1): **<2h**, 2h, 4h, 8h, 24h, 48h, 72h
•Temperature: 20-25°C, **3-7°C**, 35-38°C
Centrifugation:
•Temperature: **20-22°C**, 3-7°C
•Number of centrifugations: 1, **2**
Post-centrifugation:
•Delay time 2 (Δt2): **<1h**, 2h, 4h, 8h, 24h, 48h, 72h
•Pre-aliquoting temperature: 22-25°C, **3-7°C**, 35-38°C
•Storage temperature: -20°C, **-80°C**, vapor-phase liquid nitrogen
•Number of freeze-thaws: **1**, 2, 4, 10, 20, 30
•Storage duration (years): **1.5**, 3, 6, 9, 12, n
•Secondary container: **Polypropylene tube**, plastic straw, glass vial

Standard Biospecimen Research Experimental Protocol options

- **Urine** sample

Pre-centrifugation:
•Type of collection: First void, Later void, 12h, **24h**
•Type of container: With protease inhibitors, **Without protease inhibitors**
•Delay time 1 (Δt1): **<2h**, 2h, 4h, 8h, 24h, 48h
•Temperature: 20-25°C, **3-7°C**, 35-38°C, -80°C
Centrifugation:
•Temperature: **20-22°C**, 3-7°C
•g, Delay time 2 (Δt2) : 1000g 10min, **2000g 10min**, 4000g 10min
•Number of centrifugations: 1, **2**
Post-centrifugation:
•Secondary container: **Polypropylene microtube**, Plastic straw, Polypropylene 5ml tube
•Delay time 3 (Δt3): **<2h**, 2h, 4h, 8h, 24h, 48h, 72h
•Pre-aliquoting temperature: 22-25°C, **3-7°C**, 35-38°C
•Storage temperature: -20°C, **-80°C**, vapor-phase liquid nitrogen
•Number of freeze-thaws: **1**, 2, 4, 10, 20, 30
•Storage duration (years): **1**, 3, 6, 9, 12, n

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Standard Biospecimen Research Experimental Protocol options

- **Solid tissue** sample

Pre-fixation:
•Warm ischemia time: 0, **≤10min**, 15-20min, 25-30min, 50-60min
•Cold ischemia time (delay time 1 (Δt1) before fixation): 2min, 15min, **30min**, 60min, 120min
Fixation:
•Type of fixation :
  •Cryopreservation: **Snap Freezing**, OCT embedding
  •No cryopreservation: RNA-Later, **Buffered formalin**, Zinc
Post-fixation:
•Delay time 2 (Δt2) from OCT embedding to freezing: 0, 15min, **4-8h**, 24h, 48h, 72h
•Storage temperature (for cryopreservation): **-80°C**, vapor-phase liquid nitrogen
•Storage duration (years): **1**, 3, 6, 9, 12, n

Standard Biospecimen Research Experimental Protocol

- **Impact**
  - Harmonization of Biospecimen research and comparability of results
  - Identification and validation of new quality control tools
  - Development of standard nomenclature for sample collection / processing / storage procedures

3rd action

- **Logistics and Sample Transport**
  - Justification
    - While *in-vitro* preanalytical factors can be controlled, shipping / logistics factors are out of the repository's control and may have severe impacts on the sample's quality
  - Results
    - Overview, recommendations, validation protocol

http://www.isber.org/wg/BS-WG-LogTransp.html

4th action

- **Standard PREanalytical Coding for Biospecimens : SPREC**
  - Justification
    - Traceability of biospecimen preanalytical variations
  - Results
    - Details on pre-analytical sample processing
    - 7-element-long biospecimen characterization code
    - Easy to implement
    - Flexible

Cancer Epidemiology Biomarkers and Prevention 2010, *in press*

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SPREC-01

Fluid samples

TYPE OF SAMPLE	TYPE OF PRIMARY CONTAINER	PRE-CENTRIFUGATION	CENTRIFUGATION	SECOND CENTRIFUGATION	POST-CENTRIFUGATION	STORAGE
• ASC	• ACD	• RT <2h A	• RT 10mn <3000g nb A	• RT 10mn <3000g A	• <1h 3-7°C A	• PP 2ml -80°C A
• AMN	• CPD	• 3-7°C <2h B	• RT 10mn <3000g b B	• RT 10mn <3000g b B	• <1h RT B	• PP 2ml -20°C B
• BAL	• HEP	• RT 2-4h C	• 4°C 10mn <3000g C	• 4°C 10mn <3000g C	• 1-2h 3-7°C C	• Cryo 2ml LN C
• BLD	• HIR	• 3-7°C 2-4h D	• 4°C 10mn <3000g b D	• 4°C 10mn <3000g b D	• 1-2h RT D	• Cryo 2ml -80°C D
• BMA	• ORG	• RT 4-8h E	• RT 10mn 3-6000g b E	• RT 10mn 3-6000g b E	• 2-8h 3-7°C E	• Cryo 2ml PRF -135C E
• BMK	• PAX	• 3-7°C 4-8h F	• 4°C 10mn 3-6000g b F	• 4°C 10mn 3-6000g b F	• 2-8h RT F	• Straw LN F
• BUC	• PED	• RT 8-12h G	• RT 10mn 6-10000g b G	• RT 10mn 6-10000g b G	• 8-24h 3-7°C G	• Straw -80°C G
• BUF	• PI1	• 3-7°C 8-12h H	• 4C 10mn 6-10000g b H	• 4°C 10mn 6-10000gbH	• 8-24h RT H	• Straw -20°C H
• CEL	• PIX	• RT 12-24h I	• RT 10mn >10000g b I	• RT 10mn >10000g b I	• >24h 3-7°C I	• Straw PRF -135°C I
• CEN	• PPS	• 3-7°C 12-24h J	• 4°C 10mn >10000g b J	• 4°C 10mn >10000g b J	• >24h RT J	• PP 5ml -80°C J
• CLN	• PXD	• RT 24-48h K	• No centrifugation N	• No 2nd centrifugation N	• X	• PP 5ml -20°C K
• CRD	• PXR	• 3-7°C 24-48h L	• X	• X	• Z	• Mplate -80°C L
• CSF	• SCI	• RT >48h M	• Z	• Z		• Mplate -20°C M
• NAS	• SED	• 3-7°C >48h N				• Paraffin RT P
• PEL	• SPO	• 35-38°C <2h O				• X
• PEN	• SST	• X				• Z
• PFL	• TEM	• Z				
• PL1	• TRC					
• PL2	• XXX					
• SAL	• ZZZ					
• SEM						
• SER						
• SPT						
• STL						
• SYN						
• TER						
• U24						
• URN						
• ZZZ						

Cancer Epidemiology Biomarkers and Prevention 2010, *in press*

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Solid samples

TYPE OF SAMPLE	TYPE OF COLLECTION	WARM ISCHEMIA TIME	COLD ISCHEMIA TIME	FIXATION TYPE	FIXATION TIME	STORAGE
• CEN	• A06	• <2min A	• <2min A	• ACA	• <15min A	• PP 2ml -80°C A
• CLN	• A12	• 2-10min B	• 2-10min B	• ALD	• 15min-1h B	• PP 2ml -20°C B
• FNA	• A24	• 10-20min C	• 10-20min C	• ETH	• 1-4h C	• Cryo 2ml LN C
• HAR	• A48	• 20-30min D	• 20-30min D	• FOR	• 4-8h D	• Cryo 2ml -80°C D
• LCM	• A72	• 30-60min E	• 30-60min E	• SNP	• 8-24h E	• Cryo 2ml PRF -135C E
• PEN	• BPS	• >60min F	• >60min F	• NAA	• 24-48h F	• Straw LN F
• TIS	• FNA	• X	• X	• NBF	• 48-72h G	• Straw -80°C G
• LCM	• PUN	• N	• N	• OCT	• X	• Straw -20°C H
• ZZZ	• SRG	• Z	• Z	• RNL	• Z	• Straw PRF -135°C I
	• SWB			• XXX		• PP 5ml -80°C J
	• ZZZ			• ZZZ		• PP 5ml -20°C K
						• Mplate -80°C L
						• Mplate -20°C M
						• Paraffin RT P
						• X
						• Z

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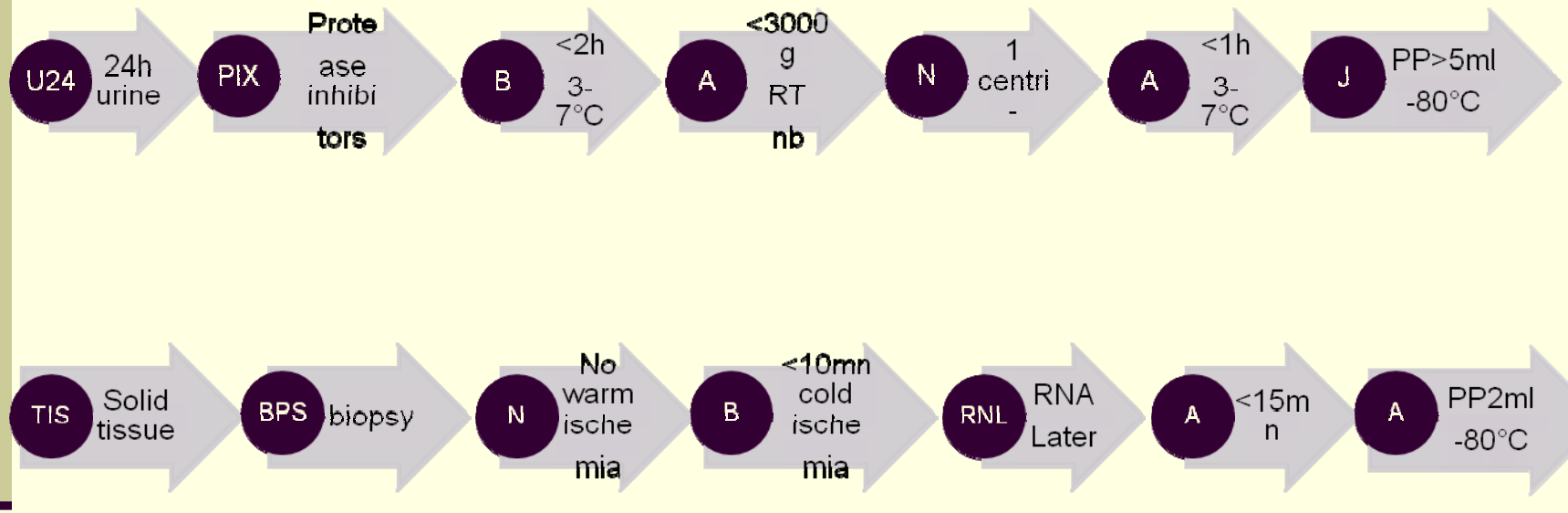
Scope of application

- Primary samples
  - Specimens directly collected from the donor
- Simple derivatives
  - Samples prepared by simple laboratory manipulation
- Complex derivatives, out of scope
  - Cell disruption
  - Cell selection
  - Multi-step chemical manipulation
    - Acidification
    - Digestion
    - Precipitation
    - Deproteinisation
    - Desalting

SPREC-01

Biospecimen description examples



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Impact

- Get incorporated in databases and QMS
- Facilitate and consolidate biomarker identification research
- Support biospecimen research
- Support laboratory accreditation

- Complement reporting recommendations
  - STARD
  - « baseline data »
  - « baseline demographic and clinical characteristics »
  - www.consort-statement.org/initiatives/newstand.htm
  - STROBE
  - « descriptive data »
  - www.strobe-statement.org/index.html
  - REMARK
  - « type of biological material used, methods of preservation and storage »
  - J Nat Cancer Inst 2005;97:1180-84

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Future actions

- Proficiency Testing programs development for assessment of Quality Control assay performance
- Inter-laboratory evaluation of novel technologies for sample collection, processing, storage, transport

Thank you!!!

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Biospecimen Science Working Group


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David Horsfall


Elaine Gunter


Kathi Shea


Mike Barnes


Cynthia Kleeberger

James Eliason


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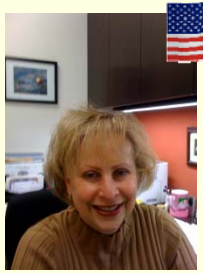
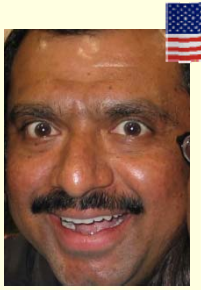

Barbara Glazer


Fay Betsou

Fiorella Guadagni


Anil Prasad


Garry Ashton