Biospecimen Reporting for Improved Study Quality (BRISQ)

Biospecimen Reporting for Improved Study Quality (BRISQ)

Helen M. Moore, Ph.D., Office of Biorepositories and Biospecimen Research, National Cancer Institute
Andrea B. Kelly, Ph.D., Rose Li and Associates, Inc.
Scott D. Jewell, Ph.D., The Ohio State University, Department of Pathology and Comprehensive Cancer Center, Biorepository and Biospecimen Resource
Lisa M. McShane, Ph.D., Biometric Research Branch, National Cancer Institute
Douglas P. Clark, M.D., Johns Hopkins Hospital
Renata Greenspan, M.D., U.S. Military Cancer Institute
Daniel F. Hayes, M.D., University of Michigan Comprehensive Cancer Center
Pierre Hainaut, Ph.D., M.S., International Agency for Research on Cancer, World Health Organization
Paula Kim, Translating Research Across Communities
Elizabeth A. Mansfield, Ph.D., Food and Drug Administration
Olga Potapova, Ph.D., Cureline, Inc.
Peter Riegman, Ph.D., Erasmus MC Tissue Bank
Yaffa Rubinstein, Ph.D., Office of Rare Diseases Research, National Institutes of Health
Edward Seijo, M.S., H. Lee Moffitt Cancer Center & Research Institute
Stella Somiari, Ph.D., Windber Research Institute
Peter Watson, M.B. B.Chir., Vancouver Island Center, British Columbia Cancer Agency
Heinz-Ulrich Weier, Ph.D.,Lawrence Berkeley National Laboratory
Claire Zhu, Ph.D., Division of Cancer Prevention, National Cancer Institute
Jim Vaught, Ph.D., Office of Biorepositories and Biospecimen Research, National Cancer Institute

Cancer Cytopathology, Volume 119, Issue 2, pp. 92-102; April 25, 2011; PMID: 21433001; DOI: 10.1002/cncy.20147

Acknowledgements

This work was supported in parts by a grant from the Director, Office of Energy Research, Office of Health and Environmental Research, U.S. Department of Energy, under contract DE-AC02-05CH11231.

Authors:

Helen M. Moore, Ph.D.
Office of Biorepositories and Biospecimen Research, National Cancer Institute

Andrea Kelly, Ph.D.
Rose Li and Associates, Inc.

Scott D. Jewell, Ph.D.
The Ohio State University
Department of Pathology and
Comprehensive Cancer Center,
Biorepository and Biospecimen Resource

Lisa M. McShane, Ph.D.
Biometric Research Branch,
National Cancer Institute

Douglas Clark, M.D.
Johns Hopkins Hospital

Renata Greenspan, M.D.
U.S. Military Cancer Institute

Daniel F. Hayes, M.D.
University of Michigan Comprehensive
Cancer Center

Pierre Hainaut, Ph.D., M.S.
International Agency for Research on
Cancer, World Health Organization

Paula Kim
Translating Research Across Communities

Elizabeth Mansfield, Ph.D.
Food and Drug Administration

Olga Potapova, Ph.D.
Cureline, Inc.

Peter Riegman, Ph.D.
Erasmus MC Tissue Bank

Yaffa Rubinstein, Ph.D.
Office of Rare Diseases Research, National Institutes of Health

Edward Seijo, M.S.
H. Lee Moffitt Cancer Center & Research Institute

Stella Somiari, Ph.D.
Windber Research Institute

Peter Watson, M.B. B.Chir.
Vancouver Island Center, British Columbia Cancer Agency

Heinz-Ulrich Weier, Ph.D.
Lawrence Berkeley National Laboratory

Claire Zhu, Ph.D.
Division of Cancer Prevention, National Cancer Institute

Jim Vaught, Ph.D.
Office of Biorepositories and Biospecimen Research, National Cancer Institute

Abstract

Human biospecimens are subjected to collection, processing, and storage that can significantly alter their molecular composition and consistency. These biospecimen preanalytical factors, in turn, influence experimental outcomes and the ability to reproduce scientific results. Currently, the extent and type of information specific to the biospecimen preanalytical conditions reported in scientific publications and regulatory submissions varies widely. To improve the quality of research that uses human tissues, it is crucial that information on the handling of biospecimens be reported in a thorough, accurate, and standardized manner. The Biospecimen Reporting for Improved Study Quality (BRISQ) recommendations outlined herein are intended to apply to any study in which human biospecimens are used. The purpose of reporting these details is to supply others, from researchers to regulators, with more consistent and standardized information to better evaluate, interpret, compare, and reproduce the experimental results. The BRISQ guidelines are proposed as an important and timely resource tool to strengthen communication and publications on biospecimen-related research and to help reassure patient contributors and the advocacy community that their contributions are valued and respected.

Introduction

Human biospecimens provide the basis for research leading to better understanding of human disease biology and discovery of new treatments that are tailored to individual patients with cancer or other diseases. These biological materials are subject to a number of different collection, processing, and storage factors that can significantly alter their molecular composition and consistency. These preanalytical factors, in turn, influence experimental outcomes and the ability to reproduce scientific results (Srinivasan et al. 2002; Moore et al. 2009; Espina et al. 2009; Ransohoff and Gourlay 2010). Currently, the extent and type of information specific to the biospecimen preanalytical conditions reported in scientific publications and regulatory submissions varies widely. To improve the quality of research utilizing human tissues it is critical that information regarding the handling of biospecimens be reported in a thorough, accurate, and standardized manner.

The purpose of this article is to make recommendations for the reporting of data elements for human biospecimens, defined as solid tissues and bodily fluids, used in biomedical studies. Cell lines and biospecimen derivatives such as nucleic acids or proteins, although crucial for biomedical research, are not intended to fall within the scope of these recommendations. The Biospecimen Reporting for Improved Study Quality (BRISQ) recommendations are intended to apply to any study in which human biospecimens are used. These include biomedical applications such as translational science, biomarker discovery, clinical trials, technology development, and diagnosticassay and therapeutics development. The recommended data elements would be reported by an author in a journal publication, by a company in a regulatory

submission, or by a biorepository distributing biospecimens. It is intended that the list and the elements within it will be interpreted, modified, and applied according to the context of the study being reported. It is also recognized that information corresponding to all data elements may not be available, but at least for some categories (described below), the known or unknown status of these elements should be documented.

The list of data elements discussed includes general information for consistent documentation of classes of biospecimens but also factors that might influence the integrity, quality, and/or molecular composition of biospecimens. Reporting the details enumerated in the BRISQ list does not guarantee biospecimen quality, and should not be seen as a substitute for empirical quality evaluations. The purpose of reporting these details is to supply others, from researchers to regulatory agencies, with more consistent and standardized information to better evaluate, interpret, compare, and reproduce the experimental results. To maintain consistency with federal regulations on research involving human subjects, information that might enable individual identification of research participants should be withheld.

The BRISQ list has been constructed as an initial step towards defining reporting recommendations. The list will likely evolve as more is learned about the factors that influence biospecimen quality and composition, and in turn their effects on biospecimen analysis. It is envisioned that future iterations of the BRISQ recommendations might include changes to the list of elements and the relative weight thereof in accordance with evidence-based scientific and medical findings and technological developments.

Materials and Methods

A half-day workshop, *Development of Biospecimen Reporting Criteria for Publications*, was held at the National Cancer Institute (NCI) 2009 Biospecimen Research Network Symposium (http://biospecimens.cancer.gov/meeting/brnsymposium) to initiate a discussion on biospecimen reporting recommendations. Workshop attendees included individuals covering a broad range of expertise: laboratory scientists, clinicians, pathologists, statisticians, patient advocates, biobankers, journal editors, leaders of relevant professional societies, and other stakeholders. The attendees noted that reporting guidelines covering many aspects of biomedical studies already exist, particularly guidelines relevant to experimental design and data reporting. (The EQUATOR project [http://www.equator-network.org/] provides an extensive listing of guidelines for health research).

It was proposed that the BRISQ recommendations apply to all studies utilizing human biospecimens, and thus complement existing guidelines by filling a niche concerning reporting of biospecimen pre-analytical variables.

The attendees further proposed that the BRISQ recommendations should broadly encompass solid tissues and bodily fluids, rather than including separate lists for these biospecimen types. It was also agreed that a committee to form biospecimen reporting recommendations should be formed to take the effort forward. Many of the individuals and disciplines participating in the workshop were included when the BRISQ committee was subsequently formed.

Formulation of the recommendations was based on consideration of what biospecimen information could enable a science reviewer to fully evaluate or replicate a reported study. The preliminary list included the most commonly available data elements. The committee considered numerous preanalytical factors, for example, the characteristics of the biospecimens themselves, e.g., the tissue type and the pathology of the sample; patient characteristics that might influence the biospecimens, such as vital and disease states; and the collection and handling of the biospecimens, e.g., the stabilization, shipping, and storage conditions.

The preliminary list of recommendations was refined by consulting the NCI Biospecimen Research Database (http://brd.nci.nih.gov), an online resource compiling peer-reviewed articles that address biospecimen science. The Biospecimen Research Database's terminology for scientific literature curation that was deemed relevant was incorporated into the initial BRISQ list. This terminology served as a starting point for discussion at monthly teleconferences by the BRISQ committee.

Results

The committee composed a list of data elements that represent factors believed to often influence biospecimen quality and thus should be reported, *if known or applicable*, for the particular study (Table 1); supplement 1 includes references that demonstrate the influence a reporting element may have on experimental results. For clarity, these elements are organized according to the lifecycle of the biospecimen (Figure 1), which spans the period immediately prior to removal from the patient through use in a scientific analysis.

Many reporting elements were discussed, but only some were approved by consensus for inclusion in the guidelines. The committee was mindful that certain information, while important to report, may not have direct relevance to the biology or condition of the biospecimen, and therefore, would not be under the purview of the BRISQ recommendations. The committee attempted to carefully balance scientific interest in having access to extensive data about biospecimen collection, processing, and storage against practical challenges in obtaining such detailed information. Each reporting element included in the guidelines is backed by evidence that the factor could have an effect on the structural integrity and molecular characteristics of the biospecimen or on the ability to perform certain assays on the biospecimen and obtain reliable results. While the committee recognizes that collection of data about biospecimens can increase the operational costs to collect and use biospecimens, cost was not factored into the exclusion of data elements that were or should be considered necessary.

The elements in the BRISQ list are prioritized into three tiers according to the relative importance of their being reported. The first tier, "Items recommended to report," includes information such as the organ(s) or the anatomical site from which the biospecimens were derived and the manner in which the biospecimens were collected, stabilized, and preserved; for quick reference, these items are summarized in Table 2. Reporting these items need not be onerous. For example, Beatty et al. (2004) include most BRISQ Tier-1 items in the following excerpts:

- "FNA [fine-needle aspiration] specimens were obtained from 55 surgically removed specimens of breast cancer within 1 hour of resection, before tissue fixation. The aspirates were obtained using a 22- to 25-gauge needle and spread directly on slides and fixed in ethanol or formalin or placed in CytoLyt for preparation of ThinPrep slides according to the manufacturer's protocol. Corresponding FFPE [formalin-fixed, paraffin-embedded] tissue specimens were fixed in 10% neutral buffered formalin for 18 to 24 hours according to routine procedures and embedded in paraffin."
- "All FNA cytologic slides were air dried and stored at room temperature before FISH analysis."
- "Cases with a score of 2+ or 3+ were considered [HER-2] positive only if the 2+ cases demonstrated gene amplification by FISH [fluorescence in situ hybridization] analysis."

"Items beneficial to report" form the second tier. These are data elements an evaluator might find helpful to know but may be slightly less crucial to the scientific contribution or less likely to be annotated, such as the time from biospecimen excision/acquisition to stabilization. "Additional items to report" compose the third tier. These include information about conditions that might be

useful to know concerning the biospecimens but are not known to be as likely to influence research results or are unlikely to be available to researchers, such as environmental factors to which patients were exposed or the type of storage container in which the biospecimens were kept.

The full BRISQ list featured in Table 1 includes each item and its definition along with additional columns that were designed for an author or reviewer to track where the listed items are reported for a particular study. To the right of the "Item Descriptions" is a column assigning each item a unique Roman-numeral/letter/number identification code. The far right column provides space to note where each item may be found in a manuscript or application. The far left "Apply-to" column indicates whether the BRISQ item is applicable to *All* biospecimen types or is more appropriate for solid *Tissue* biospecimens or *Fluid* biospecimens (such as blood, urine, or other fluids). For example, item III.b, "Type of long-term preservation," is pertinent to all types of biospecimens; item III.b.2, "Time in fixative/preservative solution," is more relevant to solid tissue than to fluid biospecimens; and item III.c, "Aliquot volume," applies more often to fluid than to solid tissue biospecimens.

When reporting elements of the BRISQ list, standard operating procedures specifying many of the pertinent details, such as blood-collection protocols, may be provided or referenced; any referenced documents should be publicly available. It is preferable that most Tier I items relevant to the biospecimen and particular scientific study be reported directly in the intended publication rather than be cited from another document. Detailed descriptions that are too lengthy to be accommodated should be made available as supplemental materials online. Whether the

laboratory performing the study was operating under any formal certification or accreditation should be stated if applicable to the study being reported.

The BRISQ committee discussed whether to request information that the biorepository and/or researcher had obtained ethical clearance to collect the biospecimens and perform the study. Clearance from an institutional review board or similar body is important to report in publications, and its reporting is generally required by journals. However, it is not immediately pertinent to the structural integrity and molecular characteristics of the biospecimen and, thus, is not included in the BRISQ recommendations. Similarly, accurate biospecimen-tracking mechanisms are essential to biobanking but not immediately pertinent to the condition of the biospecimen, and thus are also not included in the BRISQ data-elements list.

Surgical parameters, such as type of anesthesia or receipt of blood or other intra-operative infusates, were recognized to be of potential significance to the condition of the biospecimens. However, these data often are not known. When it is available, information about anesthesia and intraoperative treatments that may influence the condition of the biospecimens should be reported. These elements were not included in the BRISQ list because currently such information is rarely available or not required to be recorded as part of biospecimen collection efforts. If or when surgical parameters are determined to be critical through systematic biospecimen research studies these elements will be integrated into future recommendations.

Several preservation parameters known to influence the condition of biospecimens and the results of analyses have been included in the list of recommendations. Researchers should state

the rationale for the chosen preservation parameters. For example, if the type and temperature of the biospecimen preservative were selected to optimize stability, extraction, and analysis of a particular analyte, this should be mentioned.

The BRISQ committee recognized the need for greater specificity in the reported anatomic and histologic details concerning solid tissue biospecimens. The committee agreed that the level of detail with which pathology characteristics are reported should be enough to sufficiently address the scientific research question. These characteristics include not only the tissue site of the biospecimen and the relation of the biospecimen to the pertinent clinical diagnosis within the tissue site but also the composition and pathology within the biospecimen where relevant.

The BRISQ committee included members of the NCI Office of Biorepositories and Biospecimen research (OBBR), participants from the OBBR Biospecimen Research Network Symposium, and members of the International Society for Biological and Environmental Repositories (ISBER) and the committees responsible for the REporting recommendations for tumor MARKer prognostic studies (REMARK; McShane et al 2005) and STrengthening the Reporting of OBservational studies in Epidemiology (STROBE; van Elm et al 2008) guidelines. Essential harmonization with similar efforts underway by these groups is ongoing.

Discussion

An adage in the business community states, “That which is measured improves. That which is measured and reported improves exponentially.” The BRISQ reporting recommendations represent the product of extensive discussion and input from researchers with varied types of expertise and from many stakeholders, all of whom share the common goal of improving biospecimen reporting and, by extension, fields in which biospecimens are used. The committee believes that by providing details concerning preanalytical factors that could affect assay results, investigators will further improve the quality of biomedical studies, including research for developing cancer biomarkers for screening, early detection, and treatment.

Adoption of the BRISQ recommendations is expected to help authors, reviewers, editors, and regulatory officials evaluate whether sufficient information about the biospecimens has been provided to enable assessment of the influence of pre-analytical biospecimen factors on study results. If reported, this information will allow improved evaluation, interpretation, comparison, and reproduction of the results from studies that employ human biospecimens. Although Tier-3 items might not be available or might not be considered significant to report, increased awareness of their potential influence on biospecimen studies might lead to improved tracking and reporting in the future.

The BRISQ recommendations may be implemented by anyone reporting on studies involving biospecimens. Reviewers, editors, and regulatory officials might also employ the list as a tool for evaluating whether sufficient biospecimen information has been included in a manuscript or

application. In addition, the recommendations could be used by investigators requesting biospecimens from a biospecimen resource: essential items on the list might be checked off to indicate that they are required annotations for the desired samples. Elements of BRISQ that document preanalytical variables for tissue biospecimens could be economically captured by using a reporting system such as the Standard PREanalytical Code, or SPREC, which was recently published by the ISBER Working Group on Biospecimen Science (Betsou et al. 2010).

BRISQ reporting items will not necessarily be applicable to every study, and authors and reviewers are urged to use their judgment to decide which factors are essential. It is not always possible for investigators to ascertain every recommended element for every biospecimen, even for Tier 1 items, but unknown elements relevant to the study being reported should be fully acknowledged with a discussion of possible implications that the missing information might have on the study conclusions. Unknown or unreported Tier 1 data elements should not be considered a reason for automatic dismissal of a report or conditional for the award of a grant. The final decision on acceptability of missing Tier 1 information should be specific to the study context.

When consulting the BRISQ list, researchers should evaluate the importance of each item in the context of the study, and adjust their reporting accordingly. An item such as “method of enrichment for relevant components,” listed here as Tier 2 might—for example, in the context of a study comparing the efficacy of various enrichment methods—be essential to report and should thus be considered Tier 1 for that study. The converse may also be true, when, for example, an item listed here as Tier 2—such as “temperature between acquisition and stabilization”—is less

pertinent to the study at hand—perhaps because the time at this temperature was negligible—and should be considered Tier 3.

It is hoped that consideration of the BRISQ recommendations will sensitize the biobanking and research communities and their funding agencies to the importance of tracking pre-analytical variables, leading to more judicious selection and handling of experimental human specimens and thus improved study quality. Anecdotally, recommendations such as REMARK seem to have had the effect of spurring researchers to consider the recommendations in advance of conducting their investigations, with the result that researchers might take greater care in the design, conduct, and analysis of their studies. The BRISQ committee envisions a similar trajectory for pre-analytical biospecimen data elements. Thus, not only might overall quality of publications improve, but the quality of human-biospecimen-dependent investigation in general might improve over time with the formation and adoption of publication recommendations. It is anticipated that biobanks might use these recommendations to improve on their existing standard operating procedures and annotation thereof. Such improvements could include the acquisition of additional relevant biospecimen data based on the BRISQ recommendations and the release of all such data to researchers as a standard procedure. In this way, biobanks might become major players in the universal application of these recommendations.

Patient contribution of biospecimens for research is a voluntary, generous action aimed at helping advance scientific discovery and progress. The research team, pathologist, and biorepository systems, as the stewards of these biospecimens, have a responsibility to be vigilant and persistent in using methods and practices that protect and preserve the highest possible

quality biospecimen and associated data. The BRISQ guidelines are proposed as an important and timely resource tool to strengthen communication and publications around biospecimen-related research and help reassure patient contributors and the advocacy community that the contributions are valued and respected. Researchers are further encouraged to strengthen public outreach and education around the use and potential of human biospecimens and the biorepository community as these are emerging and potentially misunderstood areas.

FUNDING SOURCES

This project has been funded in whole or in part with federal funds from the National Cancer Institute, National Institutes of Health, under Contract No. HHSN261200800001E.]

CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

References

Beatty BG, Bryant R, Wang W, Ashikaga T, Gibson PC, Leiman G, Weaver DL. HER-2/neu detection in fine-needle aspirates of breast cancer: fluorescence in situ hybridization and immunocytochemical analysis. Am J Clin Pathol. 2004;122(2):246-55. PubMed PMID: 15323142.

Betsou F, Lehmann S, Ashton G, Barnes M, Benson EE, Coppola D, DeSouza Y, Eliason J, Glazer B, Guadagni F, Harding K, Horsfall DJ, Kleeberger C, Nanni U, Prasad A, Shea K, Skubitz A, Somiari S, Gunter E; International Society for Biological and Environmental Repositories (ISBER) Working Group on Biospecimen Science. Standard preanalytical coding for biospecimens: defining the sample PREanalytical code. Cancer Epidemiol Biomarkers Prev. 2010;19(4):1004-11. PubMed PMID: 20332280.

Espina V, Muelle C, Edmiston K, Sciro M, Petricoin E, Liotta L. Tissue is alive: New technologies are needed to address the problems of protein biomarker pre-analytical variability. Proteomics Clin. Appl. 2009;3:874–882. Not currently indexed for MEDLINE.

McShane LM, Altman DG, Sauerbrei W, Taube SE, Gion M, Clark GM; Statistics Subcommittee of the NCI-EORTC Working Group on Cancer Diagnostics. Reporting recommendations for tumor marker prognostic studies (REMARK). J Natl Cancer Inst. 2005 17;97(16):1180-4. PubMed PMID: 16106022.

Moore, HM, Compton, CC, Lim, MD, Vaught, J, Christiansen, KN, and Alper, J; 2009 Biospecimen Research Network Symposium: Advancing Cancer Research through Biospecimen Science. Cancer Res. 2009; 69: 6770-6772. PubMed PMID 19706749.

Ransohoff DF, Gourlay ML. Sources of Bias in Specimens for Research About Molecular Markers for Cancer. J Clin Oncol 2010;28(4):698-704. PMID: 20038718.

Srinivasan M, Sedmak D, Jewell S. Effect of fixatives and tissue processing on the content and integrity of nucleic acids. Am J Pathol. 2002;161(6):1961-71. PubMed PMID: 12466110.

von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008;61(4):344-9. PubMed PMID: 18313558.

Figure 1.

Figure 1. The lifecycle of the biospecimen is illustrated. The preanalytical phase of the lifecycle of the biospecimen includes each stage from patient to distribution. Preanalytical variables are addressed in the BRISQ list.

Table 1. BRISQ Recommended Information to Report in Publications that Employ Human Biospecimens

BIOSPECIMEN REPORTING FOR IMPROVED STUDY QUALITY (BRISQ):

ITEMS TO REPORT IF KNOWN AND APPLICABLE

Bold: Tier 1 - Recommended to report
Plain: Tier 2 - Beneficial to report
Italics: Tier 3 - Additional items to report

I. PRE-ACQUISITION				
Apply to	Tier #	Item Description	Item #	Location
All	Tier 1	**Biospecimen type. Solid tissue, whole blood, serum/plasma, isolated cells, urine, secretions, or another product derived from a human being.**	I.a.	_____
All	Tier 1	**Anatomical or collection site. In standard terminology, organ(s) of origin or site of blood draw.**	I.a.1.	_____
All	Tier 1	**Biospecimen disease status. From controls or individuals with the disease of interest; in the case of solid tissue, whether it is from disease site or normal adjacent (not involved but from the same anatomical site as a disease specimen in the same patient).**	I.a.2.	_____
All	Tier 1	**Clinical characteristics of patients. In standard terminology, available medical information known or believed to be pertinent to the condition of the biospecimens.**	I.b.	_____
All	Tier 1	**Vital state. Alive or deceased when biospecimens were obtained**	I.b.1	_____
All	Tier 3	*Disease state. Patient condition relative to disease and treatment, if known (e.g. during- or post-therapy; acute, chronic, or terminal stage).*	I.b.1.1.	_____
All	Tier 3	*Cause of death. For postmortem biospecimens, the cause of death and other diseases present at the time of death.*	I.b.1.2.	_____
All	Tier 3	*Agonal state. The patients' physical condition immediately preceding death (e.g. prolonged degeneration or relatively healthy)*	I.b.1.3.	_____

All	Tier 1	**<u>Diagnosis</u>. Patient diagnoses pertinent to the study being conducted, using an accepted system of standards (e.g. the Systemized Nomenclature of Medicine or the International Classification of Diseases). Please note that clinical and pathology diagnoses are not always the same.**	I.b.2.	_____
All	Tier 1	**<u>Clinical</u>. Patient clinical diagnoses (determined by medical history, physical examination, and analyses of a biospecimen) pertinent to the study being conducted.**	I.b.2.1.	_____
All	Tier 1	**<u>Pathology</u>. Patient pathology diagnoses (determined by macro and/or microscopic evaluation of a biospecimen at the time of diagnosis and/or prior to research use) pertinent to the study being conducted.**	I.b.2.2.	_____
All	Tier 2	<u>Time between diagnosis and sampling</u>. The time or range of time between disease diagnosis and sample acquisition.	1.b.2.3	_____
All	Tier 3	*<u>Exposures</u>. Neoadjuvant therapy, other current or past medical treatments or environmental factors that might influence the condition of the biospecimen (e.g. chemo-and radiation therapy, blood thinner, smoking status).*	I.b.3.	_____
All	Tier 3	*<u>Reproductive status</u>. The hormonal or reproductive state of the patients (e.g. pregnant, pre-pubescent, post-menopausal).*	I.b.4.	_____
All	Tier 2	<u>Patient demographic information</u>. Demographic information that might be relevant to the condition of the biospecimens (e.g. age range, gender).	I.c.	_____
All	Tier 2	<u>Accrual scheme</u>. Whether the biospecimens were obtained for the study being conducted or for a generalized collection (i.e. retrospective or prospective procurement); whether any standard operating procedures (SOPs) were employed and whether these SOPs are available to others upon request. Reference any clinical trials relevant to the accrual scheme.	I.d.	_____
All	Tier 2	<u>Nature of the biobanking institution(s)</u>. The biobanking context in which the biospecimens were obtained (e.g. as part of an internal collection or a biospecimen-acquisition network); include name, location, and primary contact details such as email address or Web site and reference to any pertinent SOPs.	I.e.	_____

II. ACQUISITION				
Apply to	Tier #	Item Description	Item #	Location
All	Tier 1	**Collection mechanism and parameters. How the biospecimens were obtained (e.g. fine needle aspiration, pre-operative blood draw).**	II.a.	_____
Tissue	Tier 3	*Time from cessation of blood flow in vivo to biospecimen excision/acquisition. The time or range of times that the biospecimens were ischemic in the body.*	II.b.	_____
All	Tier 2	Time from biospecimen excision/acquisition to stabilization. The time or time-range between when the biospecimens were obtained (e.g. blood drawn or tumor surgically removed) and when they were stabilized. *For postmortem biospecimens*, list the postmortem interval range (i.e. the time from death to stabilization of the biospecimen).	II.c.	_____
All	Tier 2	Temperature between biospecimen excision/acquisition and stabilization. The temperature or range thereof at which biospecimens were kept between when biospecimens were obtained (e.g. blood drawn or tumor surgically removed) and when they were stabilized. *For postmortem biospecimens*, the temperature at which the cadaver was stored during the postmortem interval.	II.d.	_____
Fluid	Tier 2	Collection container. The kind of tube into which biospecimens were captured as they left the body.	II.e.	_____
III. STABILIZATION/PRESERVATION				
Apply to	Tier #	Item Description	Item #	Location
All	Tier 1	**Mechanism of stabilization. The initial process by which biospecimens were stabilized during collection [e.g. snap or controlled-rate freezing, fixation, additive (heparin, citrate, or EDTA), none].**	III.a.	_____
All	Tier 1	**Type of long-term preservation. The process by which the biospecimens were sustained after collection (e.g. freezing and at which temperature; formalin fixation, paraffin embedding; additive; none). Please note, this might or might not differ from the mechanism of stabilization.**	III.b.	_____

All	Tier 1	**Constitution and concentration of fixative/preservation solution. The make-up of any formulation employed to maintain the biospecimens in a non-reactive state (e.g. 10 percent neutral-buffered formalin or 10 USP Heparin Units/mL).**	III.b.1.	_____
Tissue	Tier 2	Time in fixative/preservation solution. The time or range thereof that biospecimens were exposed to the preservation medium.	III.b.2.	_____
Tissue	Tier 2	Temperature during time in preservation solution. The temperature of the medium during the preservation process.	III.b.3.	_____
Fluid	Tier 2	Aliquot volume. The amount in each liquid biospecimen sample.	III.c.	_____
Tissue	Tier 2	Specimen size. The approximate size or weight of solid biospecimen samples processed(e.g. cubes approximately 0.5 cm on a side, 0.5 gram).	III.d.	_____
		IV. STORAGE/TRANSPORT		
Apply to	Tier #	Item Description	Item #	Location
		Storage parameters. The conditions under which the biospecimens were maintained until analysis.		
All	Tier 1	**Storage temperature. The temperature or range thereof at which the biospecimens were maintained until distribution or analysis.**	IV.a.1	_____
All	Tier 1	**Storage duration. The time or range thereof between biospecimen acquisition and distribution or analysis.**	IV.a.2.	_____
All	Tier 2	Storage details. Other conditions under which specimens were maintained during storage (e.g. to minimize oxidation).	IV.a.3.	_____
All	Tier 3	*Type of storage container. The vessel in which biospecimens were kept.*	IV.a.4	_____
All	Tier 3	*Type of slide. The microscope slides to which biospecimens were affixed.*	IV.a.5	_____
		Shipping parameters. The conditions to which biospecimens were exposed during each shipment or inventory management.		
All	Tier 1	**Shipping temperature(s). The temperature or range thereof at which biospecimens were maintained during each shipment or relocation.**	IV.b.1.	_____
All	Tier 2	Shipping duration. The time, estimate, or range thereof that the biospecimens spent in shipment each time they were transported.	IV.b.2.	_____

All	Tier 3	*Type of transport container. The type of vessel (e.g. pre-manufactured shipping container, polystyrene box) and the packing material in which the biospecimens were transported.*	IV.b.3.	_____
All	Tier 3	*Shipping parameters. Other conditions under which the biospecimens were transported (e.g. vacuum sealing, desiccant, packing material). Please note any deviations from standard operating procedures that might influence the condition of the biospecimens (e.g. shipping anomalies that exposed paraffin blocks to high temperatures).*	IV.b.4.	_____
		Freeze-thaw parameters. The conditions to which biospecimens were subjected during any thaw events.		
Fluid	Tier 2	Number of freeze-thaw cycles. The number, estimate, or range thereof of unfreeze-refreeze events to which biospecimens were subjected prior to analysis.	IV.c.1.	_____
Fluid	Tier 3	*Duration of thaw events. The amount of time or range thereof the biospecimens spent thawed prior to the final thaw before processing.*	IV.c.2.	_____
Fluid	Tier 3	*Time from last thaw to processing. The time or range of times between unfreezing and analysis.*	IV.c.3.	_____
All	Tier 3	*Temperature between last thaw and processing. The temperature at which biospecimens were kept between unfreezing and analysis.*	IV.c.4.	_____
V. QUALITY ASSURANCE MEASURES RELEVANT TO THE EXTRACTED PRODUCT AND PROCESSING PRIOR TO ANALYTE EXTRACTION AND EVALUATION				
Apply to	Tier #	Item Description	Item #	Location
All	Tier 1	**Composition assessment and selection. Any parameters that were used to evaluate and/or choose biospecimens for inclusion in the study.**	V.a.	_____
All	Tier 2	Gross and microscopic review. The anatomical characteristics of the biospecimens in the study and the relevant qualifications of the individual performing the review (e.g. anatomist, pathologist, hematologist, microbiologist, or researcher).	V.a.1.	_____
Tissue	Tier 2	Proximity to primary pathology of interest. Whether the biospecimen was taken from a region adjacent to or distal from another region of interest, such as a tumor or area of necrosis. Give approximate distances if known.	V.a.2.	_____

All	Tier 2	Method of enrichment for relevant component(s). The method by which pertinent portions of the biospecimen were separated from the rest of the biospecimen (e.g. laser-capture microdissection of tissue, block selection for region of lesion, centrifugation of blood).	V.a.3	_____
All	Tier 2	Details of enrichment for relevant component(s). The parameters used to separate pertinent portions of the biospecimen from the rest of the biospecimen, if applicable (e.g. centrifugation speed and temperature).	V.a.4	_____
Tissue	Tier 3	*Embedding reagent/medium. Any formulation used to enclose the biospecimens (e.g. paraffin).*	V.b.	_____
All	Tier 2	Quality assurance measures. Any methods used to assess the quality of the biospecimens relevant to the biomolecular analyte, when these methods were employed (e.g. prior to long-term storage or immediately before experimental analysis), and the results (e.g. RNA integrity number, hemolysis assessment).	V.c	_____

Table 2. Quick-reference BRISQ Summary/Checklist: Tier 1 items to report if known and applicable.

	Data Elements	Examples
❒	**Biospecimen type** *Solid tissue, whole blood, or another product derived from a human being*	Serum, Urine
❒	**Anatomical site** *Organ of origin or site of blood draw*	Liver, Antecubital area of the arm
❒	**Disease status of patients** *Controls or individuals with the disease of interest*	Diabetic, Healthy control
❒	**Clinical characteristics of patients** *Available medical information known or believed to be pertinent to the condition of the biospecimens*	Pre-menopausal breast cancer patients
❒	**Vital State of patients** *Alive or deceased patient when biospecimens were obtained*	Postmortem
❒	**Clinical diagnosis of patients** *Patient clinical diagnoses (determined by medical history, physical examination, and analyses of the biospecimen) pertinent to the study*	Breast cancer
❒	**Pathology diagnosis** *Patient pathology diagnoses (determined by macro and/or microscopic evaluation of the biospecimen at the time of diagnosis and/or prior to research use) pertinent to the study*	Her2-negative intraductal carcinoma
❒	**Collection mechanism** *How the biospecimens were obtained*	Fine needle aspiration, Pre-operative blood draw
❒	**Type of stabilization** *The initial process by which biospecimens were stabilized during collection*	Heparin, On ice
❒	**Type of long-term preservation** *The process by which the biospecimens were sustained after collection*	Formalin fixation, freezing
❒	**Constitution of preservative** *The make-up of any formulation used to maintain the biospecimens in a non-reactive state*	10% neutral-buffered formalin, 10 USP Heparin Units/mL
❒	**Storage temperature** *The temperature or range thereof at which the biospecimens were kept until distribution/analysis.*	-80 °C, 20 to 25 °C
❒	**Storage duration** *The time or range thereof between biospecimen acquisition and distribution or analysis.*	8 days, 5 to 7 years
❒	**Shipping temperature** *The temperature or range thereof at which biospecimens were kept during shipment or relocation.*	-170 °C to -190 °C
❒	**Composition assessment & selection** *Parameters used to choose biospecimens for the study*	Minimum 80% tumour nuclei & maximum 50% necrosis

Supplement 1. BRISQ table with references that exemplify each data element's influence on experimental results. This is not intended to be an exhaustive list.

I. PRE-ACQUISITION				
Apply to	Tier #	Item Description	Item #	Example
All	Tier 1	**Biospecimen type. Solid tissue, whole blood, serum/plasma, isolated cells, urine, secretions, or another product derived from a human being.**	I.a.	Di Nunno, Humphreys-Beher, Barton
All	Tier 1	**Anatomical or collection site. In standard terminology, organ(s) of origin or site of blood draw.**	I.a.1.	Centeno, Hoff-Olsen, Yan, Heinrich
All	Tier 1	**Biospecimen disease status. From controls or individuals with the disease of interest; in the case of solid tissue, whether it is from disease site or normal adjacent (not involved but from the same anatomical site as a disease specimen in the same patient).**	I.a.2.	Weis
All	Tier 1	**Clinical characteristics of patients. In standard terminology, available medical information known or believed to be pertinent to the condition of the biospecimens.**	I.b.	Tantipaiboonwong
All	Tier 1	**Vital state. Alive or deceased when biospecimens were obtained**	I.b.1	He, Jones
All	Tier 3	*Disease state. Patient condition relative to disease and treatment, if known (e.g. during- or post-therapy; acute, chronic, or terminal stage).*	I.b.1.1.	Pinder
All	Tier 3	*Cause of death. For postmortem biospecimens, the cause of death and other diseases present at the time of death.*	I.b.1.2.	Tomita, Preece, Johnston
All	Tier 3	*Agonal state. The patients' physical condition immediately preceding death (e.g. prolonged degeneration or relatively healthy)*	I.b.1.3.	Tomita, Preece, Johnston
All	Tier 1	**Diagnosis. Patient diagnoses pertinent to the study being conducted, using an accepted system of standards (e.g. the Systemized Nomenclature of Medicine or the International Classification of Diseases). Please note that clinical and pathologic diagnoses are not always the same.**	I.b.2.	Webster

All	Tier 1	**Clinical. Patient clinical diagnoses (determined by medical history, physical examination, and analyses of a biospecimen) pertinent to the study being conducted.**	I.b.2.1.	Tantipaiboonwong
All	Tier 1	**Pathologic. Patient pathologic diagnoses (determined by macro and/or microscopic evaluation of a biospecimen at the time of diagnosis and/or prior to research use) pertinent to the study being conducted.**	I.b.2.2.	Ellis
All	Tier 2	Time between diagnosis and sampling. The time or range of time between disease diagnosis and sample acquisition.	1.b.2.3	_____
All	Tier 3	*Exposures. Neoadjuvant therapy, other current or past medical treatments or environmental factors that might influence the condition of the biospecimen (e.g. chemo-and radiation therapy, blood thinner, smoking status).*	I.b.3.	Pinder, Webster
All	Tier 3	*Reproductive status. The hormonal or reproductive state of the patients (e.g. pregnant, pre-pubescent, post-menopausal).*	I.b.4.	Reyna
All	Tier 2	Patient demographic information. Demographic information that might be relevant to the condition of the biospecimens (e.g. age range, gender).	I.c.	Papale
All	Tier 2	Accrual scheme. Whether the biospecimens were obtained for the study being conducted or for a generalized collection (i.e. retrospective or prospective procurement); whether any standard operating procedures (SOPs) were employed and whether these SOPs are available to others upon request. Reference any clinical trials relevant to the accrual scheme.	I.d.	_____
All	Tier 2	Nature of the biobanking institution(s). The biobanking context in which the biospecimens were obtained (e.g. as part of an internal collection or a biospecimen-acquisition network); include name, location, and primary contact details such as email address or Web site and reference to any pertinent SOPs.	I.e.	Barnes, Karsan
II. ACQUISITION				
Apply to	Tier #	Item Description	Item #	Location
All	Tier 1	**Collection mechanism and parameters. How the biospecimens were obtained (e.g. fine needle aspiration, pre-operative blood draw).**	II.a.	Sung, Morrison, Schaub

Tissue	Tier 3	*Time from cessation of blood flow in vivo to biospecimen excision/acquisition. The time or range of times that the biospecimens were ischemic in the body.*	II.b.	Smith
All	Tier 2	Time from biospecimen excision/acquisition to stabilization. The time or time-range between when the biospecimens were obtained (e.g. blood drawn or tumor surgically removed) and when they were stabilized. *For postmortem biospecimens*, list the postmortem interval range (i.e. the time from death to stabilization of the biospecimen).	II.c.	Heinrich, Visvikis, Micke, Burke, Spruessel, Espina
All	Tier 2	Temperature between biospecimen excision/acquisition and stabilization. The temperature or range thereof at which biospecimens were kept between when biospecimens were obtained (e.g. blood drawn or tumor surgically removed) and when they were stabilized. *For postmortem biospecimens*, the temperature at which the cadaver was stored during the postmortem interval.	II.d.	van Maldegem, Langebrake, Micke, Espina
Fluid	Tier 2	Collection container. The kind of tube into which biospecimens were captured as they left the body.	II.e.	Yucel, Drake, Preissner
		III. STABILIZATION/PRESERVATION		
Apply to	Tier #	Item Description	Item #	Location
All	Tier 1	**Mechanism of stabilization. The initial process by which biospecimens were stabilized during collection [e.g. snap or controlled-rate freezing, fixation, additive (heparin, citrate, or EDTA), none].**	III.a.	Frank, Scicchitano
All	Tier 1	**Type of long-term preservation. The process by which the biospecimens were sustained after collection (e.g. freezing and at which temperature; formalin fixation, paraffin embedding; additive; none). Please note, this might or might not differ from the mechanism of stabilization.**	III.b.	Rogers, Greer, Beatty, Kouri
All	Tier 1	**Constitution and concentration of fixative/preservation solution. The make-up of any formulation employed to maintain the biospecimens in a non-reactive state (e.g. 10 percent neutral-buffered formalin or 10 USP Heparin Units/mL).**	III.b.1.	Zsilka, Ferry
Tissue	Tier 2	Time in fixative/preservation solution. The time or range thereof that biospecimens were exposed to the preservation medium.	III.b.2.	Macabeo-Ong, Meithing
Tissue	Tier 2	Temperature during time in preservation solution. The temperature of the medium during the preservation process.	III.b.3.	Micke

Fluid	Tier 2	Aliquot volume. The amount in each liquid biospecimen sample.	III.c.	Ferry
Tissue	Tier 2	Specimen size. The approximate size or weight of solid biospecimen samples processed(e.g. cubes approximately 0.5 cm on a side, 0.5 gram).	III.d.	Gillio-Tos
IV. STORAGE/TRANSPORT				
Apply to	Tier #	Item Description	Item #	Location
		Storage parameters. The conditions under which the biospecimens were maintained until analysis.		Visvikis, Sigurdson, Atkins
All	Tier 1	**Storage temperature. The temperature or range thereof at which the biospecimens were maintained until distribution or analysis.**	IV.a.1	Visvikis, Sigurdson, Atkins, Zhou, Ahmad
All	Tier 1	**Storage duration. The time or range thereof between biospecimen acquisition and distribution or analysis.**	IV.a.2.	Visvikis, Sigurdson, Paik, Atkins, Ahmad
All	Tier 2	Storage details. Other conditions under which specimens were maintained during storage (e.g. to minimize oxidation).	IV.a.3.	Visvikis, Sigurdson
All	Tier 3	*Type of storage container. The vessel in which biospecimens were kept.*	IV.a.4	Ferry, Isaksson, Preissner
All	Tier 3	*Type of slide. The microscope slides to which biospecimens were affixed.*	IV.a.5	Kaupinnen
		Shipping parameters. The conditions to which biospecimens were exposed during each shipment or inventory management.		Visvikis, Guder
All	Tier 1	**Shipping temperature(s). The temperature or range thereof at which biospecimens were maintained during each shipment or relocation.**	IV.b.1.	Guder, Timms
All	Tier 2	Shipping duration. The time, estimate, or range thereof that the biospecimens spent in shipment each time they were transported.	IV.b.2.	Guder, Timms
All	Tier 3	*Type of transport container. The type of vessel (e.g. pre-manufactured shipping container, polystyrene box) and the packing material in which the biospecimens were transported.*	IV.b.3.	_____
All	Tier 3	*Shipping parameters. Other conditions under which the biospecimens were transported (e.g. vacuum sealing, desiccant, packing material). Please note any deviations from standard operating procedures that might influence the condition of the biospecimens (e.g. shipping anomalies that exposed paraffin blocks to high temperatures).*	IV.b.4.	_____

		Freeze-thaw parameters. The conditions to which biospecimens were subjected during any thaw events.		Visvikis
Fluid	Tier 2	Number of freeze-thaw cycles. The number, estimate, or range thereof of unfreeze-refreeze events to which biospecimens were subjected prior to analysis.	IV.c.1.	Chan, Fiedler
Fluid	Tier 3	*Duration of thaw events. The amount of time or range thereof the biospecimens spent thawed prior to the final thaw before processing.*	IV.c.2.	Kirk
Fluid	Tier 3	*Time from last thaw to processing. The time or range of times between unfreezing and analysis.*	IV.c.3.	_____
All	Tier 3	*Temperature between last thaw and processing. The temperature at which biospecimens were kept between unfreezing and analysis.*	IV.c.4.	Kuelzo
V. QUALITY ASSURANCE MEASURES RELEVANT TO THE EXTRACTED PRODUCT AND PROCESSING PRIOR TO ANALYTE EXTRACTION AND EVALUATION				
Apply to	Tier #	Item Description	Item #	Location
All	Tier 1	**Composition assessment and selection. Any parameters that were used to evaluate and/or choose biospecimens for inclusion in the study.**	V.a.	_____
All	Tier 2	Gross and microscopic review. The anatomical characteristics of the biospecimens in the study and the relevant qualifications of the individual performing the review (e.g. anatomist, pathologist, hematologist, microbiologist, or researcher).	V.a.1.	_____
Tissue	Tier 2	Proximity to primary pathology of interest. Whether the biospecimen was taken from a region adjacent to or distal from another region of interest, such as a tumor or area of necrosis. Give approximate distances if known.	V.a.2.	_____
All	Tier 2	Method of enrichment for relevant component(s). The method by which pertinent portions of the biospecimen were separated from the rest of the biospecimen (e.g. laser-capture microdissection of tissue, block selection for region of lesion, centrifugation of blood).	V.a.3	Mojica, Umar
All	Tier 2	Details of enrichment for relevant component(s). The parameters used to separate pertinent portions of the biospecimen from the rest of the biospecimen, if applicable (e.g. centrifugation speed and temperature).	V.a.4	Breit

Tissue	Tier 3	*Embedding reagent/medium. Any formulation used to enclose the biospecimens (e.g. paraffin).*	V.b.	Coudry
All	Tier 2	Quality assurance measures. Any methods used to assess the quality of the biospecimens relevant to the biomolecular analyte, when these methods were employed (e.g. prior to long-term storage or immediately before experimental analysis), and the results (e.g. RNA integrity number, hemolysis assessment).	V.c	Webster, Sanchez-Carbayo

BRISQ Item References

Ahmad S, Sundaramoorthy E, Arora R, Sen S, Karthikeyan G, Sengupta S. Progressive degradation of serum samples limits proteomic biomarker discovery. Anal Biochem. 2009;394(2):237-42. PubMed PMID: 19632190.

Apweiler R, Aslanidis C, Deufel T, Gerstner A, Hansen J, Hochstrasser D, Kellner R, Kubicek M, Lottspeich F, Maser E, Mewes HW, Meyer HE, Müllner S, Mutter W, Neumaier M, Nollau P, Nothwang HG, Ponten F, Radbruch A, Reinert K, Rothe G, Stockinger H, Tárnok A, Taussig MJ, Thiel A, Thiery J, Ueffing M, Valet G, Vandekerckhove J, Wagener C, Wagner O, Schmitz G. Approaching clinical proteomics: current state and future fields of application in cellular proteomics. Cytometry A. 2009;75(10):816-32. PubMed PMID: 19739086.

Apweiler R, Aslanidis C, Deufel T, Gerstner A, Hansen J, Hochstrasser D, Kellner R, Kubicek M, Lottspeich F, Maser E, Mewes HW, Meyer HE, Müllner S, Mutter W, Neumaier M, Nollau P, Nothwang HG, Ponten F, Radbruch A, Reinert K, Rothe G, Stockinger H, Tarnok A, Taussig MJ, Thiel A, Thiery J, Ueffing M, Valet G, Vandekerckhove J, Verhuven W, Wagener C, Wagner O, Schmitz G. Approaching clinical proteomics: current state and future fields of application in fluid proteomics. Clin Chem Lab Med. 2009;47(6):724-44. PubMed PMID: 19527139.

Atkins D, Reiffen KA, Tegtmeier CL, Winther H, Bonato MS, Störkel S. Immunohistochemical detection of EGFR in paraffin-embedded tumor tissues: variation in staining intensity due to choice of fixative and storage time of tissue sections. J Histochem Cytochem. 2004;52(7):893-901. PubMed PMID: 15208356.

Barnes RO, Parisien M, Murphy LC, Watson PH. Influence of evolution in tumor biobanking on the interpretation of translational research. Cancer Epidemiol Biomarkers Prev. 2008;17(12):3344-50.PMID: 19064549.

Barton RH, Nicholson JK, Elliott P, Holmes E. High-throughput 1H NMR-based metabolic analysis of human serum and urine for large-scale epidemiological studies: validation study. Int J Epidemiol. 2008;37 Suppl 1:i31-40. PubMed PMID: 18381391.

Beatty BG, Bryant R, Wang W, Ashikaga T, Gibson PC, Leiman G, Weaver DL. HER-2/neu detection in fine-needle aspirates of breast cancer: fluorescence in situ hybridization and immunocytochemical analysis. Am J Clin Pathol. 2004;122(2):246-55. PubMed PMID: 15323142.

Breit S, Nees M, Schaefer U, Pfoersich M, Hagemeier C, Muckenthaler M, Kulozik AE. Impact of pre-analytical handling on bone marrow mRNA gene expression. Br J Haematol. 2004;126(2):231-43. PubMed PMID: 15238145.

Burke WJ, O'Malley KL, Chung HD, Harmon SK, Miller JP, Berg L. Effect of pre- and postmortem variables on specific mRNA levels in human brain. Brain Res Mol Brain Res. 1991; 11(1):37. PubMed PMID: 1662743.

Carruthers M, Trinick TR, Wheeler MJ. The validity of androgen assays. Aging Male. 2007;10(3):165-72. Review. PubMed PMID: 17701661.

Centeno BA, Enkemann SA, Coppola D, Huntsman S, Bloom G, Yeatman TJ. Classification of human tumors using gene expression profiles obtained after microarray analysis of fine-needle aspiration biopsy samples. Cancer. 2005 25;105(2):101-9. PubMed PMID: 15643601.

Chan KC, Yeung SW, Lui WB, Rainer TH, Lo YM. Effects of preanalytical factors on the molecular size of cell-free DNA in blood. Clin Chem. 2005;51(4):781-4. PubMed PMID: 15708950.

Cohn JS, Rodriguez C, Jacques H, Tremblay M, Davignon J. Storage of human plasma samples leads to alterations in the lipoprotein distribution of apoC-III and apoE. J Lipid Res. 2004;45(8):1572-9. PMID: 15145987

Coudry RA, Meireles SI, Stoyanova R, Cooper HS, Carpino A, Wang X, Engstrom PF, Clapper ML. Successful application of microarray technology to microdissected formalin-fixed, paraffin-embedded tissue. J Mol Diagn. 2007;9(1):70-9. PubMed PMID: 17251338.

Di Nunno N, Costantinides F, Cina SJ, Rizzardi C, Di Nunno C, Melato M. What is the best sample for determining the early postmortem period by on-the-spot flow cytometry analysis? Am J Forensic Med Pathol. 2002;23(2):173-80. PubMed PMID: 12040264.

Drake SK, Bowen RA, Remaley AT, Hortin GL. Potential interferences from blood collection tubes in mass spectrometric analyses of serum polypeptides. Clin Chem. 2004;50(12):2398-401. PubMed PMID: 15563493.

Ellis M, Davis N, Coop A, Liu M, Schumaker L, Lee RY, Srikanchana R, Russell CG, Singh B, Miller WR, Stearns V, Pennanen M, Tsangaris T, Gallagher A, Liu A, Zwart A, Hayes DF, Lippman ME, Wang Y, Clarke R. Development and validation of a method for using breast core needle biopsies for gene expression microarray analyses. Clin Cancer Res. 2002;8(5):1155-66. PubMed PMID: 12006532.

Espina V, Edmiston KH, Heiby M, Pierobon M, Sciro M, Merritt B, Banks S, Deng J, VanMeter AJ, Geho DH, Pastore L, Sennesh J, Petricoin EF 3rd, Liotta LA. A portrait of tissue phosphoprotein stability in the clinical tissue procurement process. Mol Cell Proteomics. 2008;7(10):1998-2018. PubMed PMID: 18667411.

Espina V, Muelle C, Edmiston K, Sciro M, Petricoin E, Liotta L. Tissue is alive: New technologies are needed to address the problems of protein biomarker pre-analytical variability. Proteomics Clin. Appl. 2009;3:874–882.

Ferry JD, Collins S, Sykes E. Effect of serum volume and time of exposure to gel barrier tubes on results for progesterone by Roche Diagnostics Elecsys 2010. Clin Chem. 1999;45(9):1574-5. PubMed PMID: 10471667.

Fiedler GM, Baumann S, Leichtle A, Oltmann A, Kase J, Thiery J, Ceglarek U. Standardized peptidome profiling of human urine by magnetic bead separation and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. Clin Chem. 2007;53(3):421-8. PubMed PMID: 17272489.

Frank M, Döring C, Metzler D, Eckerle S, Hansmann ML. Global gene expression profiling of formalin-fixed paraffin-embedded tumor samples: a comparison to snap-frozen material using oligonucleotide microarrays. Virchows Arch. 2007;450(6):699-711. PubMed PMID: 17479285.

Gillio-Tos A, De Marco L, Fiano V, Garcia-Bragado F, Dikshit R, Boffetta P, Merletti F. Efficient DNA extraction from 25-year-old paraffin-embedded tissues: study of 365 samples. Pathology. 2007;39(3):345-8. PubMed PMID: 17558863.

Greer CE, Lund JK, Manos MM. PCR amplification from paraffin-embedded tissues: recommendations on fixatives for long-term storage and prospective studies. PCR Methods Appl. 1991;1(1):46-50. PubMed PMID: 1842921.

Guder WG. Preanalytical factors and their influence on analytical quality specifications. Scand J Clin Lab Invest. 1999;59(7):545-9. PubMed PMID: 10667696.

He S, Wang Q, He J, Pu H, Yang W, Ji J. Proteomic analysis and comparison of the biopsy and autopsy specimen of human brain temporal lobe. Proteomics. 2006;6(18):4987-96. PubMed PMID: 16912969.

Heinrich M, Matt K, Lutz-Bonengel S, Schmidt U. Successful RNA extraction from various human postmortem tissues. Int J Legal Med. 2007;121(2):136-42. PubMed PMID: 17115174.

Hoff-Olsen P, Jacobsen S, Mevåg B, Olaisen B. Microsatellite stability in human post-mortem tissues. Forensic Sci Int. 2001;119(3):273-8. PubMed PMID: 11390139.

Humphreys-Beher MG, King FK, Bunnel B, Brody B. Isolation of biologically active RNA from human autopsy for the study of cystic fibrosis. Biotechnol Appl Biochem. 1986;8(5):392-403. PubMed PMID: 3768147.

Isaksson HS, Nilsson TK. Preanalytical aspects of quantitative TaqMan real-time RT-PCR: applications for TF and VEGF mRNA quantification. Clin Biochem. 2006;39(4):373-7. PubMed PMID: 16546153.

Johnston NL, Cervenak J, Shore AD, Torrey EF, Yolken RH. Multivariate analysis of RNA levels from postmortem human brains as measured by three different methods of RT-PCR. Stanley Neuropathology Consortium. J Neurosci Methods. 1997 7;77(1):83-92. Erratum in: J Neurosci Methods 1998 Feb 20;79(2):233. Cerevnak J [corrected to Cervenak J]. PubMed PMID: 9402561.

Jones RF, Sunheimer R, Friedman H, Miller D, Ginsburg R, Jumbelic M, Threatte G, Haas GP. Comparison of ante- and post-mortem PSA levels for epidemiological studies. Anticancer Res. 2005;25(2B):1263-7. PubMed PMID: 15865076.

Karsan A, Eigl BJ, Flibotte S, Gelmon K, Switzer P, Hassell P, Harrison D, Law J, Hayes M, Stillwell M, Xiao Z, Conrads TP, Veenstra T. Analytical and preanalytical biases in serum proteomic pattern analysis for breast cancer diagnosis. Clin Chem. 2005;51(8):1525-8. PubMed PMID: 15951319.

Kauppinen T, Martikainen P, Alafuzoff I. Human postmortem brain tissue and 2-mm tissue microarrays. Appl Immunohistochem Mol Morphol. 2006;14(3):353-9. PubMed PMID: 16932029.

Kirk MJ, Hayward RM, Sproull M, Scott T, Smith S, Cooley-Zgela T, Crouse NS, Citrin DE, Camphausen K. Non-patient related variables affecting levels of vascular endothelial growth factor in urine biospecimens. J Cell Mol Med. 2008;12(4):1250-5. PubMed PMID: 18782189.

Kouri T, Malminiemi O, Penders J, Pelkonen V, Vuotari L, Delanghe J. Limits of preservation of samples for urine strip tests and particle counting. Clin Chem Lab Med. 2008;46(5):703-13. PubMed PMID: 18839472.

Kueltzo LA, Wang W, Randolph TW, Carpenter JF. Effects of solution conditions, processing parameters, and container materials on aggregation of a monoclonal antibody during freeze-thawing. J Pharm Sci. 2008;97(5):1801-12. PubMed PMID: 17823949.

Langebrake C, Günther K, Lauber J, Reinhardt D. Preanalytical mRNA stabilization of whole bone marrow samples. Clin Chem. 2007;53(4):587-93. PubMed PMID: 17289802.

Macabeo-Ong M, Ginzinger DG, Dekker N, McMillan A, Regezi JA, Wong DT, Jordan RC. Effect of duration of fixation on quantitative reverse transcription polymerase chain reaction analyses. Mod Pathol. 2002;15(9):979-87. PubMed PMID: 12218216.

Micke P, Ohshima M, Tahmasebpoor S, Ren ZP, Ostman A, Pontén F, Botling J. Biobanking of fresh frozen tissue: RNA is stable in nonfixed surgical specimens. Lab Invest. 2006;86(2):202-11. PubMed PMID: 16402036.

Miething F, Hering S, Hanschke B, Dressler J. Effect of fixation to the degradation of nuclear and mitochondrial DNA in different tissues. J Histochem Cytochem. 2006;54(3):371-4. PubMed PMID: 16260588.

Mojica WD, Stein L, Hawthorn L. An exfoliation and enrichment strategy results in improved transcriptional profiles when compared to matched formalin fixed samples. BMC Clin Pathol. 2007;7:7. PubMed PMID: 17683544.

Morrison C, Palatini J, Riggenbach J, Radmacher M, Porcu P. Fine-needle aspiration biopsy of non-Hodgkin lymphoma for use in expression microarray analysis. Cancer. 2006;108(5):311-8. PubMed PMID: 16944538.

Narayanan S. Considerations in the application of selected molecular biology techniques in the clinical laboratory: preanalytical and analytical issues. Rinsho Byori. 1996;Suppl 103:262-70. PubMed PMID: 9128356.

Paik S, Kim CY, Song YK, Kim WS. Technology insight: Application of molecular techniques to formalin-fixed paraffin-embedded tissues from breast cancer. Nat Clin Pract Oncol. 2005;2(5):246-54. PubMed PMID: 16264960.

Papale M, Pedicillo MC, Thatcher BJ, Di Paolo S, Lo Muzio L, Bufo P, Rocchetti MT, Centra M, Ranieri E, Gesualdo L. Urine profiling by SELDI-TOF/MS: monitoring of the critical steps in sample collection, handling and analysis. J Chromatogr B Analyt Technol Biomed Life Sci. 2007;856(1-2):205-13. PubMed PMID: 1761328.

Pinder SE, Provenzano E, Earl H, Ellis IO. Laboratory handling and histology reporting of breast specimens from patients who have received neoadjuvant chemotherapy. Histopathology. 2007;50(4):409-17. PubMed PMID: 17448015.

Preece P, Virley DJ, Costandi M, Coombes R, Moss SJ, Mudge AW, Jazin E, Cairns NJ. An optimistic view for quantifying mRNA in post-mortem human brain. Brain Res Mol Brain Res. 200319;116(1-2):7-16. PubMed PMID: 12941456.

Preissner CM, Reilly WM, Cyr RC, O'Kane DJ, Singh RJ, Grebe SK. Plastic versus glass tubes: effects on analytical performance of selected serum and plasma hormone assays. Clin Chem. 2004;50(7):1245-7. PubMed PMID: 15229156.

Reyna R, Traynor KD, et al. Repeated freezing and thawing does not generally alter assay results for several commonly studied reproductive hormones. Fertil Steril 2001;76:823–5. PMID: 11591421

Rosenling T, Slim CL, Christin C, Coulier L, Shi S, Stoop MP, Bosman J, Suits F, Horvatovich PL, Stockhofe-Zurwieden N, Vreeken R, Hankemeier T, van Gool AJ, Luider TM, Bischoff R. The effect of preanalytical factors on stability of the proteome and selected metabolites in cerebrospinal fluid (CSF). J Proteome Res. 2009;8(12):5511-22. PMID: 19845411

Sanchez-Carbayo M, Saint F, Lozano JJ, Viale A, Cordon-Cardo C. Comparison of gene expression profiles in laser-microdissected, nonembedded, and OCT-embedded tumor samples by oligonucleotide microarray analysis. Clin Chem. 2003;49(12):2096-100. PubMed PMID: 14633888.

Schaub S, Wilkins J, Weiler T, Sangster K, Rush D, Nickerson P. Urine protein profiling with surface-enhanced laser-desorption/ionization time-of-flight mass spectrometry. Kidney Int. 2004;65(1):323-32. PubMed PMID: 14675066.

Scicchitano MS, Dalmas DA, Bertiaux MA, Anderson SM, Turner LR, Thomas RA, Mirable R, Boyce RW. Preliminary comparison of quantity, quality, and microarray performance of RNA extracted from formalin-fixed, paraffin-embedded, and unfixed frozen tissue samples. *J Histochem Cytochem.* 2006;54(11):1229-37. PMID: 16864893.

Sigurdson AJ, Ha M, Cosentino M, Franklin T, Haque KA, Qi Y, Glaser C, Reid Y, Vaught JB, Bergen AW. Long-term storage and recovery of buccal cell DNA from treated cards. Cancer Epidemiol Biomarkers Prev. 2006;15(2):385-8. PubMed PMID: 16492933.

Smith JL, Pillay SP, de Jersey J, Hardie IR. Effect of ischaemia on the activities of human hepatic acyl-CoA:cholesterol acyltransferase and other microsomal enzymes. Clin Chim Acta. 1989;184(3):259-68. PubMed PMID: 2575465.

Spruessel A, Steimann G, Jung M, Lee SA, Carr T, Fentz AK, Spangenberg J, Zornig C, Juhl HH, David KA. Tissue ischemia time affects gene and protein expression patterns within minutes following surgical tumor excision. Biotechniques. 2004;36(6):1030-7. PubMed PMID: 15211754.

Srinivasan M, Sedmak D, Jewell S. Effect of fixatives and tissue processing on the content and integrity of nucleic acids. Am J Pathol. 2002;161(6):1961-71. PubMed PMID: 12466110

Stankovic AK, DiLauri E. Quality improvements in the preanalytical phase: focus on urine specimen workflow. Clin Lab Med. 2008;28(2):339-50.PubMed PMID: 18436075.

Sung MT, Lin H, Koch MO, Davidson DD, Cheng L. Radial distance of extraprostatic extension measured by ocular micrometer is an independent predictor of prostate-specific antigen recurrence: A new proposal for the substaging of pT3a prostate cancer. Am J Surg Pathol. 2007;31(2):311-8. PubMed PMID: 17255778.

Tammen H. Specimen collection and handling: standardization of blood sample collection. Methods Mol Biol. 2008;428:35-42. PubMed PMID: 18287766.

Tantipaiboonwong P, Sinchaikul S, Sriyam S, Phutrakul S, Chen ST. Different techniques for urinary protein analysis of normal and lung cancer patients. Proteomics. 2005;5(4):1140-9. PubMed PMID: 15693063.

Timms JF, Arslan-Low E, Gentry-Maharaj A, Luo Z, T'Jampens D, Podust VN, Ford J, Fung ET, Gammerman A, Jacobs I, Menon U. Preanalytic influence of sample handling on SELDI-TOF serum protein profiles. Clin Chem. 2007;53(4):645-56. PubMed PMID: 17303688.

Tomita H, Vawter MP, Walsh DM, Evans SJ, Choudary PV, Li J, Overman KM, Atz ME, Myers RM, Jones EG, Watson SJ, Akil H, Bunney WE Jr. Effect of agonal and postmortem factors on gene expression profile: quality control in microarray analyses of postmortem human brain. Biol Psychiatry. 2004;55(4):346-52. PubMed PMID: 14960286.

Umar A, Dalebout JC, Timmermans AM, Foekens JA, Luider TM. Method optimisation for peptide profiling of microdissected breast carcinoma tissue by matrix-assisted laser desorption/ionisation-time of flight and matrix-assisted laser desorption/ionisation-time of flight/time of flight-mass spectrometry. Proteomics. 2005;5(10):2680-8. PubMed PMID: 15892168.

van Maldegem F, de Wit M, Morsink F, Musler A, Weegenaar J, van Noesel CJ. Effects of processing delay, formalin fixation, and immunohistochemistry on RNA Recovery From Formalin-fixed Paraffin-embedded Tissue Sections. Diagn Mol Pathol. 2008;17(1):51-8. PubMed PMID: 18303406.

Visvikis S, Schlenck A, Maurice M. DNA extraction and stability for epidemiological studies. Clin Chem Lab Med. 1998;36(8):551-5. PubMed PMID: 9806458.

Webster MJ. Tissue preparation and banking. Prog Brain Res. 2006;158:3-14. PubMed PMID: 17027689.

Weis S, Llenos IC, Dulay JR, Elashoff M, Martínez-Murillo F, Miller CL. Quality control for microarray analysis of human brain samples: The impact of postmortem factors, RNA characteristics, and histopathology. J Neurosci Methods. 2007;165(2):198-209. PubMed PMID: 17628689.

Yang ZW, Yang SH, Chen L, Qu J, Zhu J, Tang Z. Comparison of blood counts in venous, fingertip and arterial blood and their measurement variation. Clin Lab Haematol. 2001;23(3):155-9. PubMed PMID: 11553055.

Yucel A, Karakus R, Cemalettin A. Effect of blood collection tube types on the measurement of human epidermal growth factor. J Immunoassay Immunochem. 2007;28(1):47-60. PubMed PMID: 17236396.

Zhou H, Yuen PS, Pisitkun T, Gonzales PA, Yasuda H, Dear JW, Gross P, Knepper MA, Star RA. Collection, storage, preservation, and normalization of human urinary exosomes for biomarker discovery. Kidney Int. 2006;69(8):1471-6. PubMed PMID: 16501490.

Zsikla V, Baumann M, Cathomas G. Effect of buffered formalin on amplification of DNA from paraffin wax embedded small biopsies using real-time PCR. J Clin Pathol. 2004;57(6):654-6. PubMed PMID: 15166276.