- THE TRUSTED CLINICAL TRIALS BUSINESS RESOURCE -
APPLIED CLINICAL TRIALS

Point of View: Traceability and Transparency Should be Mandatory for All Human Biospecimens

May 08, 2017

By Ann Cooreman [1], Elena Bravo [2], Alain J. van Gool [3], Pascal Puchois [4], Michael H. A. Roehrl [5], Paul Hofman [6]

Human biospecimens and derivatives (e.g., FFPE, serum, plasma, tissue microarrays, cell lines, organoids, etc.) are invaluable for drug discovery and biomarker discovery, and for clinical and analytical validation of new medical devices or in vitro diagnostic (IVD) companion diagnostics. In this paper, we will raise the issue of traceability of biospecimens that are used by scientists in their studies, which can be pivotal for publishing or filing. When biospecimens are collected as part of clinical trials on drugs, the traceability of all samples is guaranteed by the regulations that govern clinical trials (e.g., GCP guidelines). However, in preclinical research, scientists (academic and private) who need biospecimens to support their R&D programs often use human samples from sources—mainly commercial ones—that do not necessarily disclose where, when, or how the samples have been collected. That contrasts the collection practices of academic biobanks. Many scientists blindly believe that what will be delivered was obtained at the collection site ethically and in line with all state-of-the-art procedures as well as local and international regulations, and, therefore, their selection of a biospecimen provider is often based on financial criteria alone.

Traceability as good practice in using human biospecimens

Biobanking is now a science and academic biobanks have played a pivotal role in providing guidelines for collecting, processing, preserving, storing, and even transporting human biospecimens. These are crucial components of the biomedical research field and enable the discovery, validation and development of clinically relevant biomarkers.1,2 Several biobank organizations such as the Public Population Project in Genomics and Society (P^{3}G), the International Society for Biological and Environmental Repositories (ISBER), the Biobanking and Biomolecular Resources Research Infrastructure linked with the European Research Infrastructure Consortium (BBMRI-ERIC), the European and Middle Eastern Society for Biopreservation and Biobanking (ESBB), the National Cancer Institute (NCI) and the Australian Biospecimen Network (ABN) have worked to develop appropriate policies and guidelines to improve sample quality. These documents focus on operational, technical, ethical, legal, and policy best practices for biospecimen resources and a comparison of selected reference guidelines carried out by P^{3}G (P^{3}G, 2014) showed that these guidelines cover most biobanking processes (e.g., ISBER Best Practices for Repositories, 2012). Importantly, all of them underline the importance of the traceability of the biosamples when associated with translational research program developments. Given the critical role of collecting sites, they should have robust procedures in place that allow any end user of these specimens to ascertain that these samples have been collected properly, including maintaining control of pre-analytic variables and respect for ethical and legal regulations.

The ethical and legal regulations are, on the whole, followed by all biobanks, including those regulations regarding the need for obtaining consent from donors (in line with the regulations of IHC Helsinki [2013], the Common Rule in the U.S., the UK Human Tissues Act [2006], the pre-2018 Rule, which will replace the Common Rule, etc.) and protecting their identity by either anonymizing or pseudo-anonymizing any clinical and medical data that accompany the donated specimens (in line with the Health Insurance Portability and Accountability Act [HIPAA] privacy

regulations, the Data Protection Act of 1998 in the UK and the General Data Protection Regulation, which comes into effect in the EU in 2018). Depending on the country where biospecimens with accompanying data are collected, using non-identified specimens in research does not necessarily require consent from donors and may not even require approval from an institutional review board (IRB) or ethical committee. In the U.S., according to the Common Rule, researchers who receive grant funding from U.S. government sources (e.g., NIH) are required to apply for IRB approval while industry-based research does not have this legal requirement imposed on them, although it is generally thought to be a good idea especially when the researcher plans to publish or plans to use the research as a basis for an Investigational new drug application (IND). According to the Common Rule in the U.S. and the proposed changes to this rule (the pre-2018 rule), the use of anonymized samples for research does not necessarily require consent from the donors. The situation is different in clinical trials where the FDA requires both IRB approval and donor consent. The situation is very different in the UK, for instance, where only a small set of exceptions exist to the general rule that donor consent is required by law (UK Human Tissue Act 2006).

Most, if not all, biobanks recognize the necessity of obtaining both IRB or ethical approval and consent from donors. Currently, many pharmaceutical companies demand proof of both before accepting samples from a biobank, yet they do not require the exact provenance of the collected samples.

Considering the huge efforts made by the biobanks, especially academic biobanks,[3,4] to diligently track the process of biospecimen collection, one would expect that any end user of human biospecimens should be able to retrace this information. However, astonishingly, today this is not mandatory. In many other industry projects, traceability of source materials and transparency of the "manufacturing process" is of high importance (e.g., in pharmaceutics, agriculture, cosmetics, food processing, aerospace and automobile industries, etc.); tracking is an obligatory part of the process. Similarly, the ability of the end user to trace biospecimens regardless of the type of source should be required.

Reasons for asking for traceability

There are multiple reasons why end users of biospecimens should want to know the provenance of these crucial raw materials.

One of the most important reasons is to enable the clinical biomarker researcher to review the collection process and determine pre-analytical variables that potentially introduce unintended artifacts or pitfalls in the downstream analysis of the samples. Researchers must be confident that the raw material used is appropriate to enable them to interpret the research results correctly and that the research data will not vary from study to study depending on the collecting site. This would certainly mean a tremendous savings on research that is otherwise unreproducible.[5,6,7,8] Often, relevant information about biospecimens, including sample site collection, provenance, associated clinical data and tracked sample handling data, is lacking. Astonishingly, this is accepted by many researchers in the biomedical field, which, in our opinion, is largely caused by an unchallenged trust in the source of the biospecimens. An example of this lack of interest from scientists in ensuring the authenticity and the provenance of biological material is the current use and misuse of cancer cell lines. Freedman *et al*.[6]and more recently Cosme *et al*.[9] report misidentification and cross-contamination events estimated to range from 15% to 36%. Despite accepted and inexpensive ways of authenticating these cells, only one-third of labs typically perform identity tests. The cost to the NIH for research in which misidentified or contaminated cell lines are purportedly used, is projected to be over $1 billion annually.[6] Reducing this by proper identification of the cell lines would ensure a more effective use of government funds and ultimately speed up research and the development of new treatments for disease. The same holds true for antibodies and other lab reagents that cannot easily be checked by simple quality controls.

Knowing where the biospecimen source is located is crucial for an end user to allow direct interactions with the team who collected the samples in case additional details about the pre-analytical steps (and even more clinical data details) are needed. Knowing the original sites where the biospecimens are collected also allows potential future audits of these sites by authorities or—why not?—by the end user himself. The practice of auditing clinical sites is well-established in clinical drug trials, where sponsors and regulatory bodies such as the FDA demand to know who the participating investigators are and audits on the participating sites must be possible. Why should the same information not be available for the collection of human biospecimens that are used in biomarker and drug development research?

Secondly, not knowing the geographical location of the source material may leave investigators open to

incidental findings based on different local laboratory practices. For instance, in the field of cancer and anatomo-cytopathology for tumour classification, used nomenclature and/or classification might vary from country to country. It is also now well recognized that, if not known, environmental, socio-economic and genetic factors may lead to misinterpretation of some biomarker results.[10,11,12] For instance, recently, Lin *et al.*[12] reported that Asian and non-Asian gastric cancers exhibit distinct tumor immunity signatures related to T-cell function, which, therefore, might have a strong impact on the identification and validation of novel targets and biomarkers in immuno-oncology (including PD-1 and PD-L1) depending on the geographical location from which the samples are collected. Therefore, depending on the origin of the tissues, their use may have a significant impact on the final selection of new drug targets or biomarkers (for instance, Asian versus Caucasian) and caution must be taken with commercial tissue microarrays, for example, even if commercialized by well-known companies that are headquartered in the U.S. If geographical location of where samples are collected has an impact on the discovery process and it is also crucial for the validation process of biomarkers, as underlined by FDA guidance documents issued in summer 2016 (FDA Document number 1500626 and Document number 1400027), companies developing drugs, medical devices or companion diagnostics should make sure that results obtained are not compromised by a non-representative population and not biased by the ethnicity of patients.

Thirdly, this lack of transparency around biospecimen sourcing channels might put end users at risk of infringing upon local or national regulations without realizing it. For example, in some countries (e.g., China, India, Russia), exporting biospecimens is forbidden unless a specific license is obtained. Local authorities might consider the violation of this regulation a criminal act, and have made it clear that they would take legal action against all stakeholders locally and abroad if such a case is pursued. Not asking a biospecimen provider for proof that this licensing process has been followed in order to potentially claim ignorance is not only weak legally, but could be a breach of guidelines and laws. Because of the corporate risk they incur, companies using human biospecimens should be very careful and should always request proof that tissues and their derivatives (TMA, cell lines, etc.) have been exported respecting the laws of the country where the specimens were collected originally.

In addition to using in-house collections (e.g., samples acquired during their own clinical trials) or obtaining biospecimens from independent academic or virtual biobanks,[13] the pharmaceutical and biotech industries currently source a large part of their biospecimens from commercial biobanks or brokers. The process of obtaining biospecimens from commercial sources is shown to be both faster and easier.[14] Some of these commercial sources act as genuine contract research organizations (CROs), keeping the process from collecting site to end user transparent; some act simply as brokers between industry and collecting sites (hospitals, clinics, etc.) and, finally, some are retailers merely selling specimens as lab reagents on the Internet or in the research market place, even offering discounts as special events. In the two latter cases, the link between those who collect and those who use the material is removed and the exact source of the biospecimens is hidden so the end user is oblivious to where his samples are coming. In most, if not all of these cases, information about the pre-analytical conditions under which the samples were collected is lacking.

Often different vendors obtain samples from the same original collection site and it is, therefore, not surprising that end users sometimes receive specimens from the same donor but via different supply channels without realizing they are in danger of double dipping. Researchers should be made responsible for ensuring they know where each biospecimen has been sourced and they should ascertain, when performing a study, that biospecimens from different donors are indeed from different individuals and not obtained twice from the same donor via different vendors. Biospecimen suppliers, by the same token, whether academic or commercial, should make this information available if the end user requests to know the original source of the biological samples.

Some end users have a blind trust in retailers who keep their sources hidden and may use these vendors exclusively, arguing that by not knowing where the samples have been collected they are sure to respect the rules of HIPAA, that are applicable in the US, and other data protection regulations in other countries. We take the position that this is a misguided interpretation of these rules. Not knowing where biospecimens are collected is no guarantee that the rules of data protection are followed since donor identifiers may still be present in data that accompany biospecimens. We maintain that knowing the source of biospecimens is an essential element of quality assurance and does not in any way flout the data protection rules.

A fourth reason for knowing the origin of the biospecimens is based on ethical considerations: donors consent to provide their specimens freely, trust the access policy in place at the institutions and share some of their clinical data with the sample collectors (at private or public sites). It is good practice, and some national guidelines even require, that donors are informed what their specimens and data are used for and where. However, if researchers do not know where biospecimens come from, how could donors possibly know for what purposes their contribution is being used and by whom? For this reason, we strongly believe that any biobank or biospecimen collecting site should know who uses their samples and for what purposes. It is interesting to note that most high quality academic biobanks and some tissue procurement organizations require this information as part of their governance process and ask that a material transfer agreement (MTA) be established directly between them and the end user.[4] These biobanks, when providing specimens, legitimately require that they contribute to a sponsored research program; they do not provide a simple consumable comparable to a reagent or other lab material, as some retailers might do on the Internet or other market places with a catalogue listing human specimens.

Existing initiatives

We believe that traceability should be the standard in the use of biosamples. While good laboratory practices govern research and provide control over reagents and raw materials, we question whether a set of good practices should not be designed specifically for human biospecimens. There are several on-going initiatives in this field, including ISO276/WG2 on Biobanks and Bioresources[15] and efforts by the BBMRI linked with the European Research Infrastructure Consortium (BBMRI-ERIC), but so far not one of these initiatives have been completed.

The requirement of traceability and transparency is also stressed in a document proposed in December 2015 by the Committee on Bio-Ethics of the Council of Europe, *"Recommendation on research on biological materials of human origin."*[16] The recommendation for biobanks to know the end user and vice versa is implied (see articles 8, 10, 16, 18, 19 and 23, approved by the Council of Europe in 2015) relating to Information (for donors and the public), governance principles, access, trans-border flows and availability of results respectively.

With the current state of global political unease, new programs are being introduced in the U.S. and elsewhere to control imported goods, in particular regarding a recent awareness for potential terrorist activities. In this timely context, knowing the origins of the biospecimens would enable American companies to participate in the Customs-Trade Partnership Against Terrorism (C-TPAT) program initiated by the U.S. Department of Customs and Border Protection. However, whether this program, which is currently run on a voluntary basis, will become obligatory in the future, and whether similar programs will be initiated in other countries, remains to be seen. Regardless, if the end user knows the origin of the raw materials it will enable companies to perform due diligence to ascertain any potential threats and respect customs rules.

To help with transparency and oversight and to give credit where credit is due in terms of the resources and technical knowledge required by the biobanking community, efforts are being made toward proper acknowledgement of contributing biobanks in publications. The initiative toward a bioresource research impact factor as an incentive to share human bioresources[17] and the progress from there toward a systematic way of citing bioresources in journal articles[18,19] are commendable examples of changes that are slowly being implemented.

Making traceability of biospecimen mandatory in the future

Transparency regarding the source of biospecimens would improve quality of research, reproducibility, and translational use of the acquired knowledge, as well as save money in case of irreproducibility of results.[20] Scientific robust publications, dissemination and communication are central in this[21,22,23] and reporting guidelines play an essential role toward scientific literature that is transparent, complete, open and reproducible. We believe that regulatory bodies should also demand this information in their evaluations. Whoever is collecting samples for research purposes, should know who is the end user of the collected samples and vice versa and both should keep this information as part of the documented records. This requirement for traceability should be designed, implemented and regulated by health authorities throughout the translational value chain.

Ann Cooreman* *is Independent Consultant on Ethics and Regulatory Affairs, Glasgow, Scotland, and with Trans-Hit Biomarkers Inc., email: anncooreman@gmail.com;* ***Elena Bravo*** *is with National Institute of Health, Rome, Italy;* ***Alain J. van Gool*** *is with Laboratory Medicine, Radboud*

University Medical Center, Nijmegen, The Netherlands, and TNO, Zeist, The Netherlands; ***Pascal Puchois*** *is with Trans-Hit Biomarkers Inc.;* ***Michael H. A. Roehrl*** *is with Precision Pathology Biobanking Center, Memorial Sloan Kettering Cancer Center, New York, NY;* ***Paul Hofman*** *is with Laboratory of Clinical and Experimental Pathology, Nice Hospital-Related Biobank BB-0033-00025, Pasteur Hospital, and University Hospital Federation OncoAge, University of Nice Sophia Antipolis, Nice, France*

* To whom all correspondence should be addressed

References

1. Puchois, P. "Finding ways to improve the use of biobanks." Correspondence. *Nature Medicine 19*, Correspondence. *(2013)*
2. Puchois, P, Miranda LB, van Gool AJ. "Introduction: the cardinal role of biobanks and human biospecimen collections in biomarker validation: issues impeding impact of biomarker research outcomes." *RSC Drug Discovery Series No. 33, Comprehensive Biomarker Discovery and Validation for Clinical Application (Eds Horvatovich P. and Bischoff R.)*, Chapter 3, 73-110. *(2013)*
3. Chadwick D, Roehrl MHA. "High-quality biobanking for personalized precision medicine: Biospecimen sciences at the helm." *Diagnostic Histopathology* 19, 447-456 *(2013)*
4. Hofman P, Brechot C, Zatloukal K, Dagher G, Clement B. "Public-Private relationships on biobanking: a still underestimated key component of open innovation." *Virchows Arch* Jan;464(1):3-9 *(2014)*
5. Ioannidis, JPA McNutt, M. "Why most Published Research Findings are False." *Open Access, PLoS Medicine* 2 (8), e124 *(August 2005)*
6. Freedman LP, Cockburn IM, Simcoe TS. "The economics of reproducibility in preclinical research." *Plos Biology* Jun 9;13(6):e1002165 *(2015)*
7. McNutt, M. "Reproducibility (editorial)." *Science* Vol 343. *(2014)*
8. Rockey S, Tabak L. "Rock Talk: enhancing reproducibility in NIH-supported research through rigor and transparency." *Extramural News* NIH Office of Extramural Research *(2015)*
9. Cosme B, Falagan-Lotsch P, Ribeiro M, Napoleão K, Granjeiro JM, Moura-Neto R. "Are your results valid? Cellular authentication a need from the past, an emergency on the present." *In Vitro Cell.Dev.Biol.—Animal* January *(2017)* [Epub ahead of print]
10. Baldassarre D, Nyyssönen K, Rauramaa R, de Faire U, Hamsten A, Smit AJ, Mannarino E, Humphries SE, Giral P, Grossi E, Veglia F, Paoletti R, Tremoli E. "IMPROVE study. Cross-sectional analysis of baseline data to identify the major determinants of carotid intima-media thickness in a European population: the IMPROVE study." *Eur. Heart J.* 31: 614-622 *(2010)*
11. Napolitano M, Santoro F, Puopolo M, Donfancesco C, Galluzzo L, De Grandi A, Cevenini E, De Curtis A, Sevini F, Palmieri L, Mascalzon D, Roazzi P, Scafato E, Pramstaller P, Iacoviello L, Donati MB, Giampaoli S, Franceschi C, Belardelli F, Bravo E. "Development of a pilot project on data sharing among partners of the Italian Hub of Population Biobanks (HIBP): Association between lipid profile and socio-demographic variables." *Biopreserv Biobank*. 12: 225-33 *(2014)*
12. Lin SJ, Gagnon-Bartsch JA, Tan IB, Earle S, Ruff L, Pettinger K, Yistra B, van Grieken N, Rha SY, Chung HC, Lee J-S, Cheong JH, Noh SH, Aoyama T, Miyagi, Y, Tsuburaya A, Yoshikawa T, Ajani JA, Boussioutas A, Yeoh KG, Yong WP, So J, Lee J, Kang WK, Kim S, Kameda Y, Arai T, zur Hausen A, Speed TP, Grabsch HI, Tan P. "Signatures of tumour immunity distinguish Asian and non-Asian gastric adenocarcinomas." *Gut* Nov; 64(11), 1721-31 *(2015)*
13. The International Society for Biological and Environmental Respositories (ISBER) Best Practices for Repositories *(2012)*
14. Cavallo J, Allen D, Kessler J, Simeon-Dubach D, Puchois P. "Challenges For Industry Working with Academic Biobanks: Survey Supported by the ISBER Pharma Working Group (IPWG)." Results from a questionnaire of pharmaceutical companies. Abstract, ISBER Berlin *(2016)*
15. Furata K, Schacter B. "Report on status of ISA276/W2G on biobanking and bioresources: international standards for biobanking." *Biopreserv Biobank* 13(6):452-3 *(2015)*
16. https://rm.coe.int/CoERMPublicCommonSearchServices/DisplayDCTMContent?documentId=0900001680649 2a7
17. Cambon-Thomsen A, Thorisson GA, Mabile L. BRIF Workshop Group. "The role of a

bioresource research impact factor as an incentive to share human bioresources." *Nat Genet*. Jun;43(6):503-4 *(2011)*

18. Napolitani F, Calzolari A, Cambon-Thomsen A, Mabile L, Rossi AM, De Castro P, Bravo E. "Biobankers: treat the poison of invisibility with CoBRA, a systematic way of citing bioresources in journal articles." *Biopreserv Biobank*. Aug;14(4):350-2 *(2016)*
19. Bravo E, Calzolari A, De Castro P, Mabile L, Napolitani F, Rossi AM, Cambon-Thomsen A. "Developing a guideline to standardize the citation of bioresources in journal articles (CoBRA)." *BMC Medicine* 13:33 *(2015)*
20. Andry C, Duffy E, Moskaluk CA, McCall S, Roehrl MHA, Remick D. "Biobanking – Budgets and the role of pathology biobanks in precision medicine." *Academic Pathology* 2017, in press.
21. Meyer GS, Nelson EC, Pryor DB, James B, Swensen SJ, Kaplan GS, Weissberg J, Bisognano M, Yaes GR, Hint GC. "More quality measures versus measuring what matters: a call for balance and parsimony." Viewpoint. *BMJ Qual Saf* 21:964-968 *(2012)*
22. Vasilevsky NA, Brush MH, Paddock H, Ponting L, Tripathy SJ, LaRocca GM, Haendel MA. "On the reproducibility of science: unique identification of research resources in the biomedical literature." PeerJ 1:e148, https://doi.org/10.7717/peerj.148, *(2013)*
23. Freedman LP, Inglese J. "The increasing urgency for standards in basic biologic research." *J. Cancer Res.* Aug 1;74(15):4024-9 *(2014)*

Additional reading

Budimir D, Polasek O, Marusi? A, Kolci? I, Zemunik T, Boraska V, Jeronci? A, Boban M, Campbell H, Rudan I. "Ethical aspects of human biobanks: a systematic review." *Croat Med J.* 52(3): 262–279 *(2011)*

Caulfield T, Burningham S, Joly Y, Master Z, Shabani M, Borry P, Becker A, Burgess M, Calder K, Critchley C, Edwards K, Fullerton SM, Gottweis H, Hyde-Lay R, Illes J, Isasi R, Kato K, Kaye J, Knoppers B, Lynch J, McGuire A, Meslin E, Nicol D, O'Doherty K, Ogbogu U, Otlowski M, Pullman D, Ries N, Scott C, Sears M, Wallace H, Zawati MH. "A review of key issues associated with the commercialization of biobanks." *Journal of Law and the Biosciences* 1(1):94-110 *(2014)*

De Souza, YG, Greenspan JS. 'Biobanking past, present and future: responsibilities and benefits.' *NIH Public Access (January 2014)*

Engel B, Vaught J, Moore HM. "Evidence-based practices: a novel approach to pre-analytical standardization." *Biopreserv Biobank*, Volume 12, Number 2:148-50 *(2014)*

Haddow GL, Laurie G, Cunningham-Burley S, Hunter, KG. "Tackling community concerns about commercialisation and genetic research: a modest interdisciplinary proposal." *Social Science & Medicine* 4, 2:272-82 *(2007)*

Mabile L, Dalgleish R, Thorisson Gudmundur A, Deschenes M, Carpenter J, Bravo E, Filocamo M, Gourraud PA, Harris JR, Hofman P, Kauffmann F, Munoz-Fernandez MA, Pasterk M, Cambon-Thomsen A, BRIF Working Group. "Quantifying the use of bioresources for promoting their sharing in scientific research." *GigaScience* May 1(2):7 *(2013)*

Moore HM, Kelly AB, Jewell SD, McShane LM, Clark DP, Greenspan R, Hayes DF, Hainaut P, Kim P, Mansfield EA, Potapova O, Riegman P, Rubinstein Y, Seijo E, Somiari S, Watson P, Weier HU, Zhu C, Vaught J. "Biospecimen reporting for improved study quality (BRISQ)." *Cancer Cytopathol*. Apr 25;119(2):92-101. doi: 10.1002/cncy.20147 *(2011)*

Moore HM, Compton CC, Lim MD, Vaught J, Christiansen K N, Alper J. "Biospecimen research network symposium: advancing cancer research through biospecimen science - Meeting Report." *Cancer Res; 69: (17). (2009)*

Simeon-Dubach D, Perren A. "Better provenance for biobank samples." *Nature* 475, 454–455 *(July 2011)*

Vaught, Jim. "Developments in biospecimen research." *British Medical Bulletin* 1–10 *(2015)*

Whitworth, M. "Ensuring traceability of clinical information." *Drug discovery and development, (March 2012)*.

Additional links

Biobanking and Biomolecular Resources Research Initiative linked with the European Research Infrastructure Consortium (BBMRI-ERIC): http://www.bbmri-eric.eu/services/other-services

Evaluation and Reporting of Age, Race, and Ethnicity Data in Medical Device Clinical Studies, Draft Guidance for Industry and Food and Drug Administration Staff: Document number 1500626, June 2016

Principles for Co-development of an In Vitro Companion Diagnostic Device with a Therapeutic Product, Draft Guidance for Industry and Food and Drug Administration Staff: Document number 1400027, July, 2016

Health Information Privacy in Research *(2013)* http://www.hhs.gov/hipaa/for-professionals/special-topics/research/index.html

Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors, FDA Inspections of Clinical Investigators, Office of Good Clinical Practice, Office of Special Medical Programs, Office of the Commissioner - Food and Drug Administration *(June 2010)*

Information Sheet Guidance for Sponsors, Clinical Investigators, and IRBs - Frequently Asked Questions – Statement of Investigator (Form FDA 1572) *(2010)*

International Society for Biological and Environmental Repositories (ISBER) Best practices for repositories: Collection, storage, retrieval, and distribution of biological materials for research. *Biopreserv Biobank*. 10:79-161 *(2012)*

NCI Best Practices for Biospecimen Resources. Biorepositories and Biospecimen Research Branch National Cancer Institute, National Institutes of Health, U.S. Department of Health and Human Services. *(March 2016)*

OECD Guidelines on Human Biobanks and Genetic Research Databases. *The Organization for Economic Co-operation and Development (OECD) (2009)*

P3G, 2014 http://www.p3g.org/biobank-toolkit/comparison-chart-guidelines

Recommendation on research on biological materials of human origin, *Approved Document, Committee on Bio-Ethics of the Council of Europe, Strasbourg (December 2015)*