

NCI Best Practices for Biospecimen Resources

**Revised Draft Document
for Public Review and Comment**

Office of Biorepositories and Biospecimen Research

National Cancer Institute

National Institutes of Health

U.S. Department of Health and Human Services

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Revision and Expansion of the NCI Best Practices

As part of the commitment to maintaining current and scientifically accurate best practices, the National Cancer Institute (NCI) is seeking public comment on a revised version of the *NCI Best Practices for Biospecimen Resources*. This revised version of the *NCI Best Practices* is intended to both respond to comments received from the biospecimen resource community and provide more current and detailed recommendations related to biospecimen and data quality. The revised *NCI Best Practices* was based on recommendations developed at [NCI workshops](#), public input received at the [NCI Best Practices Forums](#), and changes in federal regulations and/or guidance. Major revisions include:

- Technical and Operational Best Practices
 - Addition of a new section “Biospecimen Resource Management and Operations”
 - Updated references and websites for further information throughout
- Ethical, Legal and Policy Best Practices
 - Expanded Custodianship and Informed Consent sections based on NCI workshops
 - Revised informed consent and privacy recommendations to reflect current federal guidance
 - Addition of a new section on “Conflicts of Interest”
- New Appendices
 - Minimal Clinical Data Set
 - Template Governance Plan
 - Additional Resources Related to Ethical, Legal and Policy Issues in Biospecimen Research
 - Sample Material Transfer Agreement

The revised *NCI Best Practices* were developed and reviewed by the trans-NCI Biorepository Coordinating Committee. The entire document was reviewed by the Cancer Biomedical Informatics Grid (caBIG[®]) Tissue Banking and Pathology Tools workspace as well as subject-experts as needed. In addition, the Ethical, Legal and Policy section was reviewed by the caBIG[®] Data Sharing and Intellectual Capital Workspace, the trans-NIH Bioethics Committee Data and Specimen Committee, and the Office for Human Research Protections. Within NIH, the document was reviewed by the Office of Extramural Research, the Office of Technology Transfer, the Office of Intramural Research, the Office of the General Counsel, and the Office of Science Policy. Following receipt and consideration of public comments, the revised *NCI Best Practices* will be launched using an interactive Web format, which will provide a mechanism for more frequent updates and encourage feedback from the community about the *NCI Best Practices*.

To submit comments on the revised NCI Best Practices, please email nciobbr@mail.nih.gov with the subject line “NCI Best Practices”. Please submit all comments by September 21, 2010.

INTRODUCTION

1 Unprecedented advances in biomolecular technology have greatly increased the power and
2 precision of analytical tools used in cancer research and have accelerated the drive toward
3 personalized medicine. Human specimens that are analyzed using these new and developing
4 technology platforms have emerged as a critical resource for basic and translational research in
5 cancer because they are a direct source of molecular data from which targets for therapy,
6 detection, and prevention are identified and molecular taxonomies of cancer are derived. The
7 reliability of molecular data derived from these new analysis platforms is dependent on the
8 quality and consistency of the biospecimens being analyzed. As a result of the increased
9 requirement for biospecimen quality, standardization of biospecimen resources using state-of-
10 the-science approaches has become a pressing need across the research enterprise. The lack of
11 standardized, high-quality biospecimens is widely recognized as a significant roadblock to
12 cancer research.

13 Over the past several years, the National Cancer Institute (NCI) has undertaken an intensive due-
14 diligence process to understand the state of its funded biospecimen resources and the quality of
15 biospecimens used in cancer research. During 2004 and 2005, the NCI first established a
16 transdivisional Biorepository Coordinating Committee and then created the Office of
17 Biorepositories and Biospecimen Research (OBBR) to lead and coordinate a strategic plan to
18 confront and resolve the issues in a stepwise fashion. These efforts culminated with the
19 development of the First-Generation Guidelines for NCI-Supported Biorepositories, a first-
20 iteration document published in the *Federal Register* on April 28, 2006 (71 FR 25184). The
21 Guidelines were subsequently revised based on public comment and input from content experts,
22 renamed the *NCI Best Practices for Biospecimen Resources (NCI Best Practices)*, and released
23 on the OBBR Web site in June 2007.

24 This revised version of the *NCI Best Practices* is intended to both respond to comments received
25 from the biospecimen resource community and to provide more current and detailed
26 recommendations related to biospecimen and data quality. Major revisions include the addition
27 of new sections on [biospecimen resource management and operations](#) and [conflicts of interest](#)
28 (COIs), expansion of recommendations related to [custodianship](#) and [informed consent](#) based on
29 the consensus findings of the 2007 NCI-hosted Symposium-Workshop on Custodianship and
30 Ownership Issues in Biospecimen Research, addition of current references throughout the
31 document, and harmonization with current Federal guidance documents and recommendations
32 from international biospecimen organizations.

33 The *NCI Best Practices* identifies salient guiding principles that define state-of-the-science
34 biospecimen resource practices, promote biospecimen and data quality, and support adherence to
35 ethical and legal requirements. The current *NCI Best Practices* does not comprise detailed
36 laboratory procedures; rather, it consists of principles by which such procedures should be
37 developed by biospecimen resources. The recommendations contained within this document are
38 intended to be adapted, as appropriate, based on the mission and scientific needs of individual
39 biospecimen resources. While adoption of the *NCI Best Practices* is voluntary, the NCI believes
40 that the principles outlined in this document support the goal of optimizing biospecimens for
41 cancer research.

42 The *NCI Best Practices* will continue to evolve as the field of biospecimen biology advances;
43 novel scientific, technological, and clinical practices develop; and new ethical and legal policies
44 and regulations emerge. Results from biospecimen research initiatives will inform future
45 versions of the *NCI Best Practices* as the community moves toward the development of
46 evidence-based standard operating procedures (SOPs) that are both specimen type specific and
47 analysis platform specific. The NCI is committed to maintaining current and scientifically
48 accurate best practices for biospecimen resources and will continue to solicit input from
49 stakeholders in the cancer research community.

50

51 **NATIONAL CANCER INSTITUTE**
52 **BEST PRACTICES FOR BIOSPECIMEN RESOURCES**

53 **A. Scope, Applicability, and Implementation**

54 **A.1. Scope**

55 This document identifies technical; operational; and ethical, legal, and policy best practices in
56 order to ensure a level of consistency and standardization across biospecimen resources. A
57 biospecimen resource is defined as a collection of human specimens and associated data for
58 research purposes, the physical structure where the collection is stored, and all associated
59 processes and policies. Biospecimen resources vary considerably, ranging from formal
60 organizations to informal collections of materials in an individual researcher’s freezer.

61 **A.2. Applicability**

62 The implementation of the *NCI Best Practices* is voluntary, and several recommendations in the
63 *NCI Best Practices* can be broadly or narrowly applied depending on the mission of the
64 biospecimen resource and/or the study design.

65 **A.3. Implementation**

66 **A.3.1. Format of the NCI Best Practices**

67 The *NCI Best Practices* will be launched using an interactive Web format that will allow users
68 greater flexibility than hard copies in how they access and use the *NCI Best Practices*. In
69 addition, the online format will provide a mechanism for more frequent updates and include
70 additional resources and tools to assist the biospecimen resource community in implementation
71 of the *NCI Best Practices*. The interactive format will also encourage feedback from the
72 community about the *NCI Best Practices*.

73 **A.3.2. Biospecimen Resources**

74 Biospecimen resources are encouraged to consider the *NCI Best Practices* in their biospecimen
75 management plans.

76 **B. Technical and Operational Best Practices**

77 **B.1. Biospecimen Resource Management and Operations**

78 Daily and long-term responsibilities essential for efficient biospecimen resource management
79 and operations can be diverse and include organizational considerations, space planning and
80 functional design, resource development, evaluation and solidification of infrastructure
81 requirements, constant and consistent review of operational issues, and regular resource
82 evaluation. When executed and practiced in harmony, all of these factors can dramatically assist
83 success in managing and operating a high-quality, highly utilized, and valuable resource.

84 **B.1.1. Organizational Overview of the Biospecimen Resource**

85 An organizational overview can assist in defining the institutional structural components within
86 and around the biospecimen resource. An overview typically begins with description of the
87 organizational mandate; its associated goals, mission, and vision; operational scope; and core
88 areas of research support.

89 **B.1.1.1. Organizational Structure**

90 Organizational structures may vary according to the nature of the biospecimen resource.
91 Thoughtful documentation of the resource's organizational structure in relation to its parent
92 institution may help to predict needs, promote incorporation of existing resources, and
93 streamline workflow while increasing communication among stakeholders, management, and
94 end users.

- 95 • Biospecimen resources should seek to define and document their organizational
96 structure in advance of resource planning and/or development.

97 **B.1.1.2. Organizational Chart**

98 The organizational chart can be a significant tool in supporting existing governance
99 structures through elucidation of roles, responsibilities, chain of command, and requisite
100 reporting relationships.

- 101 • Biospecimen resources should develop and publicly display the current organizational
102 chart within the resource.
- 103 • Biospecimen resource management should provide a copy of the current
104 organizational chart and discuss with every new staff member as part of the orientation
105 process, reviewing the current [governance structure](#) of the institution.

106 **B.1.2. Biospecimen Resource Personnel**

107 Personnel involved in biospecimen resource management and use including researchers,
108 technicians, nurses, surgeons, pathologists, anesthesiologists, and assistants should be aware of
109 the purpose and goals of the biospecimen resource (see [Section B.1.2.1](#), Related Personnel
110 Descriptions and Roles). To ensure the collection of high-quality biospecimens for research,
111 personnel should be well qualified and trained to adhere to applicable SOPs. Updated training of
112 personnel ought to be conducted on a periodic basis, in accordance with applicable regulations
113 and position descriptions (ISBER 2008). A pathologist or his/her designee should be involved in
114 collecting and processing anatomical pathology biospecimens, including surgical and autopsy
115 tissue and body fluids. It is important that a pathologist determines which biospecimen, or
116 portion thereof, is necessary for complete evaluation and which is excess (remnant tissue) that
117 may be provided to the biospecimen resource for research purposes. The involvement of a
118 pathologist in this process is crucial in order to ensure that patient care is not compromised.

119 **B.1.2.1. Related Personnel Descriptions and Roles**

120 The following general personnel categories may be useful in biospecimen resource planning.
121 Note that these personnel and groupings may not be applicable to smaller biospecimen
122 resources.

- 123 • Stakeholders and Governance Team: Stakeholders may include leaders at institutional
124 cancer centers and pathology, surgery, and bioinformatics departments; leaders in
125 clinical research units, translational research, and epidemiology teams. Patient
126 advocates and research participants are also key stakeholders.
- 127 • Biospecimen Resource Management Team: Typically consists of a director, associate
128 director, and technical director.
- 129 • Adjunct Research Support Teams: May include clinical research coordinators and
130 study nurses, research assistants, laboratory technicians, bioinformatics professionals,
131 clinical residents and fellows, and statisticians.
- 132 • Internal Support System: May include space planning, financial administration,
133 comptroller, purchasing, environmental services/maintenance, telecommunications,
134 and marketing.
- 135 • External Support/Outsourced Roles: May include vendors, consultants, contractors,
136 architects, and engineers.

137 **B.1.2.2. Oversight Committees**

138 Oversight committees, often comprised of experts from outside the biospecimen resource,
139 serve to oversee the resource operations and activities, supporting transparent and
140 accountable operations. Care should be taken to define, evaluate, and document any potential
141 conflicts of interests ([COIs](#)) for any and all members. The type of oversight committee(s)
142 needed at each biospecimen resource will vary but may include the following:

- 143 • Scientific Advisory Committee: Provides guidance and scientific feedback concerning,
144 for example, the research functions of the resource and approaches to incorporating
145 new technologies, to the biospecimen resource management and stakeholders as well
146 as offers a sounding board for resource development to support quality research.
- 147 • Tissue Utilization Committee: Supports access to biospecimens for research by
148 confirming scientific rationale, ensuring validity of the scientific project, assessing
149 regulatory adherence, addressing potential conflicts of interest, and supporting fair
150 biospecimen/data allocation practices.

151 **B.1.2.3. Associated Institutional Offices and Adjunct Committees and Their Roles**

152 Institutional offices and committees play a supporting governance role for biospecimen
153 resources. Such offices can offer tremendous expertise along with essential support for the
154 internal resource and its collaborators.

155 Examples of associated offices include but may not be limited to the following:

- 156 • Office of Regulatory Affairs: Typically established to aid regulatory review and
157 oversight of research protocols.
- 158 • Office of Human Research: Typically performs an auditing function for clinical
159 research trials and related research support centers.
- 160 • Office of Research Services: Grant management support and assistance with contract
161 development.

- 162 • Technology and Materials Transfer Office: Assists with [material transfer agreement](#)
163 (MTA) development and management.
- 164 • Legal Affairs: Offers guidance on relevant case law, aids in contractual negotiations
165 and/or disputes.
- 166 • Office of Environmental Health and Radiation Safety: Offers advice on biosafety but
167 may also consult in regard to resource development and/or expansion.

168 Additional supporting adjunct committees may include Clinical Trials Scientific Review and
169 Monitoring Committee, which provides supplemental regulatory, data privacy, and safety
170 review in parallel with the institutional review board (IRB).

171 ***B.1.3. Considerations Related to Planning and Development***

172 Consideration of the biospecimen resource mission, operational scope, and objectives is crucial
173 in execution of all stages of the planning process. For startup resources, initial operational
174 planning and developmental considerations should aim to include establishment of a governance
175 structure as well as development of related policy, along with regulatory and procedural
176 standards. Once the foundation is set in place, the next step is to commence biobanking protocol,
177 procedural, and formal business development. For biospecimen resources that function as core
178 facilities and/or service providers, business planning may include financial and cost-recovery
179 modeling. Reconsideration of these issues may also be timely for established resources,
180 particularly to address any operational disparities in an effort to support best practices and
181 promote long-term sustainability.

182 **B.1.3.1 Oversight, Internal Policy, and Procedure Development**

183 Policy development can be crucial to provide a framework to guide operations.

- 184 • Biospecimen resources should define, document, and observe policies in alignment
185 with the resource mission, scope, and operational objectives.
- 186 • All resource policies should undergo a formal vetting and approval process.

187 **B.1.3.2. Determination of Procedural and Regulatory Standards**

188 During resource development it can be helpful to review current procedural and regulatory
189 standards and determine which are pertinent to the resource operations.

190 Biospecimen resource managers should aim to:

- 191 • Familiarize themselves with the current best practice documents to determine initial
192 base standards for resource development, operations, management, evaluation, and
193 expansion.
- 194 • Orient staff and adjunct teams to current best practice documents to promote practices
195 that follow best practice standards.
- 196 • Incorporate best practices and current relevant standards into resource policies, SOPs,
197 and procedures with an emphasis on supporting evidence-based practices.

198 **B.1.3.3. Business Planning**

199 Business planning can provide justification for financial and institutional commitment and
200 quantification of startup and sustainability costs.

- 201 • Business planning should be integrated into all aspects of operations, biospecimen
202 resource management, and evaluation.
- 203 • Resources should aim to establish a documented annual business plan developed with
204 department staff input and aligned with the vision and mission of the resource.
205 Business plan items should be specific, measurable, actionable, relevant, and time
206 bound.
- 207 • The resource business plan should also include a formal continuity plan that addresses
208 all possible operational disruptions, including disaster planning.
- 209 • If the resource functions as a service center, the business plan should address issues
210 related to service and revenue generation.

211 **B.1.4. Biospecimen Resource Infrastructure and Space Planning**

212 When planning, it is crucial to fully assess startup, operational, and maintenance costs for any
213 and all infrastructure. Some favor a centralized model in an attempt to promote harmonization to
214 achieve standardized, well-annotated, high-quality, robust biospecimen and data repositories. In
215 this regard, it can be helpful for each institution to perform evaluative exercises and cost-benefit
216 analyses in order to fully assess the inherent intrinsic and extrinsic value. In some cases, a
217 centralized resource model may reduce long-term cost.

218 Infrastructure requirements can vary based on the biospecimen resource scope and requirements.
219 Infrastructure requirements include but are not limited to the physical laboratory, office, and
220 adjunct and/or satellite space needs as well as requisite informatics, equipment, storage
221 platforms, telecommunications, and consumables needs.

222 In general, the baseline requirements should aim to include ample space for the following
223 functions, where appropriate, based on the nature and functions of the resource:

- 224 • Collection, receiving, tracking, and shipping as needed.
- 225 • Immediate and interim processing (i.e., fine and gross dissection benches).
- 226 • Areas to prepare and process blood products.
- 227 • Histological preparation.
- 228 • Stations for pathology case review.
- 229 • Storage for specimens, consumables, and related records.
- 230 • Office work areas to support data, operational, and end user management.

231 Note: More advanced models may include areas dedicated to nucleic acids purification,
232 tissue and cell culture, single-cell suspension, and other specialized laboratory space.

233 When possible, biospecimen resources should evaluate options and opportunities for
234 environmentally friendly and/or Leadership in Energy and Environmental Design–certified
235 infrastructure for any and all existing and/or future space.

236 **B.1.5. Overall Operational Considerations**

237 **B.1.5.1. Equipment Selection and Maintenance**

238 Equipment selection complements infrastructure planning and should be considered in
239 parallel with space planning and resource design.

240 Biospecimen resource management should:

- 241 • Consider the following factors when selecting equipment: Current resources and
242 budget, current and future services, need, frequency of use, vendor options,
243 manufacturing lead time, and cost—including maintenance, delivery, warranty,
244 service contracts, lifespan, eco-friendliness, performance, and efficiency cost savings,
245 along with current and future service provision options.
- 246 • Aim to factor depreciation for all capital equipment into the cost-recovery plan when
247 appropriate.
- 248 • Utilize resource sharing to defray financial investment in equipment.
- 249 • Determine if used/sale equipment is appropriate.
- 250 • Consider batching service contracts among neighboring resources to save money.
- 251 • Review calibration and validation instructions.
- 252 • Review preventive maintenance summaries and/or equipment log files after and prior
253 to scheduling all maintenance visits as part of the quality assurance program.

254 **B.1.5.2. Purchasing and Procurement from Vendors**

255 Familiarity with purchasing as well as the overall procurement process can help support best
256 practices; decrease errors in purchasing and product selection; streamline workflow; decrease
257 lags in ordering/purchasing; and increase awareness of institutional documentation
258 requirements, purchasing limitations, and rules.

259 **B.1.5.3. Project Management**

260 Proactive project management can ensure quality service provision and promote a smooth,
261 efficient operational workflow while avoiding duplication of effort and resources.

262 When possible, biospecimen resources should:

- 263 • Utilize a project management plan that includes but may not be limited to a statement
264 of work, deliverables document, and integrated project plan (as needed) for facility-
265 managed projects.

266 **B.1.5.4. Biospecimen Utilization**

267 Biospecimen utilization is the process of biospecimen management in an effort to promote
268 collaboration and timely research.

269 Biospecimen resources should aim to:

- 270 • Assess specimen utilization in a timely and efficient manner.

- 271 • Document and track utilization in conjunction with the resource inventory
272 management system.
- 273 • Share information about their biospecimens to the external community through a
274 biospecimen management information system or other means. One method to
275 publicize basic information about sharable biospecimens is via the Specimen Resource
276 Locator ([Section B.6.3](#), Interoperability).

277 **B.1.6. Biospecimen Resource Evaluation and Assessment**

278 The evaluation process can be a valuable exercise to aid executive decisionmaking with respect
279 to assessment of future funding needs, overall service quality and effectiveness, customer
280 satisfaction, program results, scientific and financial impact, opportunities for expansion, crucial
281 lessons learned, and program success.

282 Evaluation should include the following general topic areas:

283 **B.1.6.1. Self-Auditing, Audit Preparedness, and Clinical Research Monitoring**

284 Self-auditing and audit preparedness are cornerstones to support and/or evaluate areas of
285 poor performance as well as success in quality of operations. Audits may be conducted in
286 relation to monitoring of end-user support for clinical biobanking efforts.

287 **B.1.6.2. Strategic and Long-Range Planning, Setting Benchmarks**

288 Strategic and long-range planning can help to set a resource roadmap, provide opportunities
289 to fine tune and reset operational focus, offer proof of concept, provide analysis of resource
290 allocation, highlight crucial lessons learned, accelerate decisionmaking and resource growth,
291 and increase communication and understanding of resource benefits.

292 **B.1.6.3. Quantification of Performance, Utilization Review, and Assessment of 293 Continuing Research Needs of the Resource**

294 Formal quantification of performance justifies the benefit, utility, and overall need for the
295 stakeholder's financial investment in the biospecimen resource.

296 **B.1.6.4. Scientific Impact of the Resource**

297 Formal analysis of scientific impact can provide evidence of the inherent and extrinsic
298 scientific value and contribution of the resource.

299 **B.2. Biospecimen Collection, Processing, Storage, Retrieval, and 300 Dissemination**

301 The aim of every biospecimen resource should be to collect, maintain, and disseminate the
302 highest quality specimens for research. High-quality specimens are defined as those that most
303 closely resemble the specimen prior to its removal from the human research participant. Once the
304 specimen is collected (and sometimes prior to its removal) the specimen may begin to take on
305 new characteristics based on changes to the specimen's environment; e.g., changes in exposure
306 to certain nutritional, chemical, or other environmental factors that may occur during a surgical
307 or collection procedure. Such changes may result in incorrect determinations of the molecular

308 and physical characteristics of those components during subsequent analysis. Every attempt
309 should be made to minimize the effects of specimen handling on specimen integrity.

310 Note that this section assumes that specimens and data will be collected prospectively. In
311 addition, study design will dictate whether certain variables can be controlled and data collected
312 as described below.

313 ***B.2.1. Pre- and Post-Analytic Variables***

314 A variety of factors may affect biospecimen quality and research results; these may be divided
315 into two general categories designated “pre-analytic variables” and “post-analytic variables.”
316 Pre-analytic variables refer to factors that influence specimen integrity prior to its removal from
317 the human research participant and carry through to the point at which a biological specimen is
318 ready for testing. Post-analytic variables refer to those factors that affect performance of a
319 particular testing procedure.

320 **B.2.1.1. Pre-Analytic Variables**

321 Pre-analytic variables may be divided into three general areas:

- 322 • The physiology of the human research participant prior to specimen collection;
- 323 • Specimen collection practices; and
- 324 • Specimen handling practices prior to their inclusion in downstream testing.

325 ***B.2.1.1.1. Physiology of the Human Research Participant.*** Research now has
326 demonstrated that levels of analytes may be affected by a variety of factors such as the
327 overall general health of the human research participant, food and beverages consumed
328 prior to specimen collection, and the time of day at which the specimen is collected
329 (Taheri et al. 2004; Rosenkranz et al. 2007). Additional factors, such as phase of the
330 menstrual cycle in females, may affect some downstream analyses. Efforts should be
331 made to collect and record information pertaining to these variables to decrease or adjust
332 for the variability of these contributing factors.

333 ***B.2.1.1.2. Uniformity in Specimen Collection Practices.*** The methods used to remove
334 and collect specimens from human research participants may influence the quality of the
335 specimens collected. Significant research has indicated that during surgical removal of
336 specimens the amount of time following the cessation of blood flow to an organ can
337 affect both levels and molecular profiles of target analytes (Spruessel et al. 2004; Lin et
338 al. 2006). The specimen should be preserved as quickly as possible after removal from
339 the patient; e.g., appropriately sized tissue sections snap frozen and/or placed into 10
340 percent phosphate-buffered formalin, as appropriate. When biospecimens are collected
341 from participants, the site at which the specimen is removed (tumor or nontumor, as well
342 as location within the tumor), the medication status of the patient, the length of time
343 blood flow is blocked from the tissue, any stabilizing agents used to preserve the
344 specimen following its removal, the type of fixatives used and the length of time the
345 tissues are exposed to fixatives, and the temperature at which specimens are maintained
346 following collection may all affect molecular stability and degradation.

347 Prior to the collection or removal of biospecimens, a plan should be in place to allow for
348 the appropriate annotation of the biospecimens. This annotation should include
349 information about the human research participant and timing of collection and processing
350 activities; e.g., the type of clearing agent, the type and temperature of paraffin used to
351 process the biospecimen, etc. (ISBER 2008). These data should be maintained in a
352 database that can be linked to the specimen at all times (see [Section B.5](#), Collecting and
353 Managing Clinical Data, and [Section B.6](#), Biospecimen Resource Informatics).

354 ***B.2.1.1.3. Specimen Handling Procedures.*** Every attempt should be made to optimize
355 the handling of specimens to minimize resulting molecular changes that may result from
356 the processing activities. This includes not only the temperature and timing of specimen
357 processing but also such considerations as the size and volume of the specimen that will
358 be stored for future use. Smaller samples allow for minimal cycles of freezing and
359 thawing. When samples are stored in a frozen state, the rate at which they are cooled to
360 the storage temperature can influence the rate at which molecular degradation is allowed
361 to proceed.

362 **B.2.1.2. Post-Analytic Variables**

363 When these variables are introduced they lead to differences in the performance of a
364 particular assay. To minimize errors in assay reproducibility, the following considerations
365 should be made:

- 366 • Use of validated assays, where possible;
- 367 • Standardized training of technical staff in the performance of the assay;
- 368 • Lot uniformity of reagents;
- 369 • Inclusion of appropriate type and number of quality control (reference) samples; and
- 370 • Standardized methods for documenting and interpreting testing results.

371 ***B.2.2. Determining Which Biospecimens to Collect***

372 The specific mission and goals of a biospecimen resource will influence the type of
373 biospecimens collected. The specimens collected should be appropriate and feasible for the
374 clinical setting, as well as appropriate for the downstream applications anticipated for the
375 biospecimen.

376 ***B.2.3. Defining Reference Ranges***

377 Aside from pre- and post-analytic variables, research dictates that values for particular cellular
378 analytes are more accurately represented by a range of values, even among individuals
379 characterized as “normal” or “healthy.” Disease is defined as a distinct deviation from the range
380 of normal variation, and diagnosis of disease depends on knowing the scope of boundaries of
381 normal variation. Where possible, efforts should be made to characterize reference ranges for the
382 analyte of interest to ensure the likelihood of accurately detecting any deviation from the
383 reference range.

384 **B.2.4. Requirement for Evidence-Based Standard Operating Procedures**

385 To have confidence in research results, it is critical that all reagents included in the assay be of
386 the highest quality possible. SOPs should be reproducible with standard reference material
387 (where possible), and control biospecimens that provide a range of anticipated assay values
388 should be utilized. Specimens that have been poorly handled are likely to provide erroneous test
389 results due to the molecular changes resulting from the handling process.

390 It is impractical and currently not possible to consider the development of assays to measure
391 every cellular component within a biospecimen. To that effect, protocols that optimize the
392 general stability of biomolecules under certain environmental conditions are recommended
393 (ISBER 2008). Should a particular biomolecule be of interest, it is important to perform some
394 type of analysis to ensure that the storage and handling conditions implemented will allow for
395 accurate determinations of that biomolecule.

396 **B.2.5. Methods Research**

397 All research endeavors should be based on well-characterized and validated assays, where
398 possible. Even assays that are developmental in nature should be tested to ensure that they are
399 reproducible over time. “Proof of Performance” tests (ISBER 2008) allow for testing replicate
400 samples over time to allow for measurement of standard deviations in the assays performed.

401 Where possible, research should be performed to ensure that the storage and handling procedures
402 implemented are ones that will be conducive to stabilization of the molecular components within
403 the biospecimen.

404 **B.2.6. Biospecimen Storage**

405 The following general best practices apply to all types of biospecimens, such as wet tissue,
406 frozen tissue, paraffin-embedded tissue, glass slides, blood, serum, and urine. Individual types of
407 biospecimens should be handled according to SOPs specific to the biospecimen type and the
408 biomolecules to be analyzed; e.g., ribonucleic acid (RNA), deoxyribonucleic acid (DNA),
409 protein, and lipid.

410 **B.2.6.1.**

411 Standardized protocols should be applied consistently in preparing and storing biospecimens
412 to ensure quality and to avoid introducing variables into research studies. Biospecimen
413 resource personnel should record storage conditions along with any deviations from SOPs,
414 including information about temperature, thaw/refreeze episodes, and equipment failures
415 (ISBER 2008; Mager et al. 2004).

416 **B.2.6.2.**

417 Biospecimens should be stored in a stabilized state. Unnecessary thawing and refreezing of
418 frozen biospecimens or frozen samples of biomolecules extracted from the biospecimens
419 should be avoided, and appropriate size for aliquots and samples should be determined in
420 advance to avoid thawing and refreezing of biospecimens. When thawing/refreezing is
421 necessary, a biospecimen resource should follow consistent and validated protocols to ensure

422 continued stability of the analytes of interest. Methods such as inventory tracking should be
423 established to minimize disruption of the stable environment during sample retrieval.

424 In selecting biospecimen storage temperature, consideration should be given to the
425 biospecimen type, the anticipated length of storage, the biomolecules of interest, and whether
426 study goals include preserving viable cells (Hayes et al. 2002; Holland et al. 2003; Stevens et
427 al. 2007; ISBER 2008). *Paraffin blocks* should be stored at temperatures below 80 °F (27 °C)
428 in an area with pest and humidity control. In the case of *liquids*, such as blood and urine,
429 biospecimen components should be separated before storage to preserve each constituent
430 under its optimal condition. Whole blood (rather than fractional) cryopreservation may be an
431 efficient and cost-effective option for processing viable cells in large-scale studies (Hayes et
432 al. 2002; Stevens et al. 2007). When in doubt as to possible future uses, *tissues* should be
433 stored in the vapor phase of liquid nitrogen freezers to ensure long-term viability. Lower
434 storage temperatures and cryoprotectant (such as dimethyl sulfoxide) may be used to
435 maintain viable cells for long periods of time (ISBER 2008). The difference in temperature
436 between the bottom and top of a liquid nitrogen freezer should be measured and taken into
437 consideration in planned analyses; the temperature at the top of a liquid nitrogen freezer is
438 consistently below -140 °C.

439 **B.2.6.3.**

440 Storage vessels should be stable under planned storage conditions (Caporaso and Vaught
441 2002; Saylor et al. 2006; Bell et al. 2010). Biospecimen containers should be chosen with
442 analytical goals in mind. Vial size and number should be suitable for typical aliquots and
443 anticipated investigator uses. Optimal volume and type of containers may prevent sample
444 loss and minimize the costs of collection, storage, and retrieval. Screw-cap cryovials may be
445 used for long-term, low-temperature storage; glass vials or vials with popup tops are
446 unsuitable for long-term storage (Caporaso and Vaught 2002). Snap-frozen biospecimens
447 should be wrapped in aluminum foil or placed in commercial storage containers to minimize
448 desiccation (Bell et al. 2010). Labeling and printing systems should be chosen for stability
449 under the long-term storage conditions appropriate for the biospecimen. Face shields and
450 appropriate gloves should be worn for worker protection (see [Section B.4](#), Biosafety).

451 **B.2.6.4.**

452 Each biospecimen should have a unique identifier or combination of identifiers that are
453 firmly affixed to the container, clearly and legibly marked, and able to endure storage
454 conditions. All other relevant information should be tied to this identifier, bearing in mind
455 research participant confidentiality, security, and informed consent provisions. Inventory
456 systems should relate the presence of each aliquot to its position in a specific box, freezer,
457 refrigerator, or shelf. Consideration should be given to the location of specimens within
458 storage containers to allow for the most efficient strategies for subsequent retrieval; i.e., by
459 study and by material type within studies, as appropriate. Additional information related to
460 biospecimen resource informatics best practices can be found in [Section B.6](#), Biospecimen
461 Resource Informatics.

462 B.2.6.5.

463 Automated security systems should be in place to continuously monitor the function of
464 storage equipment and should have the capability to warn resource personnel when
465 equipment failure has occurred. Backup equipment, such as an alternative power source,
466 should be set to activate automatically when necessary. Alternate cooling sources may also
467 be available, as necessary. Written standard operating procedures (SOPs) that are tested on a
468 routine basis should be in place to respond to freezer failures, weather emergencies, and other
469 disaster recovery/emergency situations (Landi and Caporaso 1997; Caporaso and Vaught
470 2002; Eiseman et al. 2003; Friede et al. 2003; ISBER 2008).

471 B.2.6.6.

472 Specimens should be stored in a secure location with limited access only by authorized
473 personnel.

474 B.2.7. Specimen Retrieval

475 Samples should be retrieved from storage according to biospecimen resource SOPs that
476 safeguard sample quality.

477 B.2.8. Shipping Samples**478 B.2.8.1. Shipping Conditions**

479 **B.2.8.1.1.** When seeking to regulate sample temperature during shipping, the shipping time,
480 distance, climate, season, method of transportation, and regulations as well as the type of
481 samples and their intended use should be considered (Landi and Caporaso 1997; ISBER
482 2008). To maintain proper temperature during shipping, appropriate insulation, gel packs, dry
483 ice, or liquid nitrogen (dry shipper) may be used. To maintain refrigerated temperatures (2 °C
484 to 8 °C), gel packs conditioned at -15 °C or phase-change material rated for refrigerated
485 transport may be used. To maintain frozen temperatures, gel packs conditioned at or below -
486 20 °C should be used. For frozen temperatures at -70 °C, dry ice pellets or sheets should be
487 used; dry ice is considered a hazardous substance for shipping purposes. For maintaining
488 temperatures at or below -150 °C, a liquid nitrogen dry shipper should be used (ISBER
489 2008). Insulated packaging may be used to protect biospecimens from extremely hot or cold
490 ambient conditions. Whenever intending to maintain samples below ambient temperature,
491 enough refrigerant should be included to allow for a 24-hour delay in transport (ISBER
492 2008). Temperature-sensitive material should be handled by a courier with resources to
493 replenish the refrigerant in case of a shipping delay (ISBER 2008). A simple colorimetric or
494 other temperature-measuring device should be included with biospecimen shipments to
495 indicate the minimum and/or maximum temperature within the shipping container.

496 **B.2.8.1.2.** Paraffin blocks and slides may be shipped at room temperature in an insulated
497 package via overnight carrier. The use of insulated packages is considered important to
498 minimize the effect of temperature fluctuations and to protect the blocks from temperatures
499 higher than 80 °F (27 °C). Flat biospecimens, such as dried blood samples on absorbent pads
500 or cards, may be enclosed in watertight plastic bags and shipped in a sturdy outer package or
501 commercial envelope. Samples on glass or plastic slides should be cushioned and shipped
502 inside a sturdy (not flexible) outer package. Triple packaging should be used for liquid

503 samples. Inclusion of a simple maximum temperature indicator in each package and
504 documentation of the maximum temperature upon receipt are recommended.

505 **B.2.8.1.3.** The number of biospecimens per package also affects whether the appropriate
506 temperature can be maintained for all biospecimens in the shipment. A test shipment
507 (e.g., frozen water samples) should be made before shipping extremely valuable samples to
508 check the adequacy of coolants and any potential obstacles to a successful shipment. In
509 addition, conditions throughout a critical shipment should be monitored by enclosing a
510 device that records temperature during transport. Samples should be placed in sealed bags
511 with a desiccant to control humidity.

512 **B.2.8.2. Shipping Documentation**

513 **B.2.8.2.1.** Upon planned shipment of a package, documentation of the transfer in the form of
514 an MTA and requisition from the resource inventory is needed. An [MTA or similar](#)
515 [agreement](#) governs the transfer of research materials and any associated data between two
516 organizations. The MTA governs the rights and obligations of the provider and recipient with
517 respect to the materials, and it should be consistent with all applicable laws, regulations,
518 policies, and terms for transfer of those particular materials. The MTA also governs any
519 timelines, commercialization, or third-party transfer of the materials and data (ISBER 2008).

520 **B.2.8.2.2.** The biospecimen resource should notify the recipient before shipping to confirm
521 that someone will be present to accept the package and properly store the samples. Shipments
522 from and to the biospecimen resource should be tracked in a written or computerized
523 shipping log (ISBER 2008), which should include shipment/invoice number, recipient (or
524 source), date shipped (or received), courier name and package tracking number, sample
525 description, number of samples shipped (or received), condition on arrival, study name and
526 number (if available), key investigator's name, and signature of biospecimen recipient
527 (ISBER 2008).

528 Standardized paperwork should accompany shipments. Biospecimen resource personnel
529 should electronically send a shipping manifest, a list of sample identification numbers, and
530 descriptions of samples to the biospecimen recipient and should include a hard copy of the
531 manifest inside the shipment. Identifying data should be available for the use of shipping or
532 customs agents as well; some shipping agents require an itemized list of contents between the
533 inner and outer packaging of diagnostic biospecimens.

534 Upon receipt, biospecimen resource personnel should verify biospecimen labels and any
535 other documents or data shipped with the biospecimens against the packing list for
536 consistency and correctness. A feedback questionnaire requesting feedback about the quality
537 of samples received may be enclosed in each shipment for quality management purposes
538 (Eiseman et al. 2003).

539 **B.2.8.3. Regulatory Considerations**

540 **B.2.8.3.1.** All applicable laws and regulations for shipment should be satisfied. For example,
541 ISBER Best Practices and International Air Transport Association (IATA) regulations
542 (ISBER 2008; IATA 2009) should be consulted for information concerning international
543 transport regulations and classifying samples for shipment. Variation in national and regional

544 standards regarding biospecimen transport should be considered when shipping biospecimens
545 to or from an international location.

546 **B.2.8.3.2.** Additionally, Occupational Safety and Health Administration (OSHA) regulations
547 on toxic and hazardous substances ([29 CFR 1910 Subpart Z](#)) should be consulted to
548 determine whether a substance requires a biohazard label. Additional safety considerations
549 are enumerated in [Section B.4](#), Biosafety.

550 **B.2.8.4. Training**

551 Biospecimen resource personnel should be trained to ship samples appropriately. Periodic
552 retraining according to governing regulations should be conducted (ISBER 2008).

553 **B.3. Quality Management**

554 **B.3.1. Quality Management System**

555 Biospecimen collection, processing, management, and distribution should be carried out within a
556 quality management system (QMS) that contains formalized quality assurance/quality control
557 (QA/QC) policies and written SOPs. The QMS describes the biospecimen resource's QA/QC
558 policies and approaches for ensuring that program requirements are met. Each biospecimen
559 resource should either establish a written QMS or adhere to a QMS published by the
560 organization with which the biospecimen resource is associated. There are several common
561 quality management programs available upon which to pattern individual biospecimen resource
562 QMS policies. No particular approach is recommended, but several are mentioned below to help
563 design the appropriate QMS for the biospecimen resource. The following Web sites are relevant
564 to the development of a QMS:

- 565 • ISBER
566 <http://www.isber.org>
- 567 • Good Laboratory Practices
568 http://www.oecd.org/document/63/0,2340,en_2649_34381_2346175_1_1_1_1,00.htm
569 [1](#)
- 570 • Clinical Laboratory Improvement Amendment
571 <http://wwwn.cdc.gov/clia/>
- 572 • International Organization for Standardization (ISO9000)
573 <http://www.iso.org>
- 574 • U.S. Food and Drug Administration (FDA) Quality System Regulation, 21 CFR 820
575 <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?cfrpart=820>

576 **B.3.2. Quality Assurance/Quality Control**

577 Formalized QA/QC policies should be developed by biospecimen resources to minimize
578 circumstances that could adversely affect scientific results; to ensure the safety of personnel; to
579 aid in the efficient operation of the resource; and to increase the confidence of users that the
580 quality, quantity, and annotations of the specimens are as purported. QA/QC policies should be
581 customized for the intended and potential uses of the biospecimens in a given biospecimen

582 resource. QA/QC implementation should ensure that accurate data accompany specimens that are
583 to be analyzed for diagnostic as well as research purposes. The following are key issues for
584 QA/QC implementation and auditing:

- 585 • Staff proficiency
 - 586 ▪ Staff organization and responsibilities.
 - 587 ▪ Training and competency programs for personnel as appropriate; e.g., training in
 - 588 human subjects protections and privacy regulations such as the Health Insurance
 - 589 Portability and Accountability Act (HIPAA) training, safety training, or bloodborne
 - 590 pathogen training.
 - 591 ▪ Competency assessment as documentation of training.
 - 592 ▪ Documentation of staff compliance with policies and procedures.
 - 593 ▪ Risk mitigation, disaster response, and emergency preparedness.
- 594 • Facility infrastructure
 - 595 ▪ Equipment validation, calibration, maintenance, repair procedures, and
 - 596 environmental monitoring; e.g., temperature monitoring of freezers.
 - 597 ▪ Supplier management program, including inspection and validation of reagents and
 - 598 other supplies.
- 599 • Biospecimen control and documentation
 - 600 ▪ Control of biospecimen collection, processing, and tracking.
 - 601 ▪ Documentation of biospecimen collection, processing, and tracking, with detailed
 - 602 annotation of pre-analytical parameters (see [Section B.6](#), Informatics).
 - 603 ▪ Measurement and analysis of key process indicators to drive quality improvement.
 - 604 ▪ System security.
- 605 • Recordkeeping and document control
 - 606 ▪ Employment of a data quality management, assessment, and reporting system.
 - 607 ▪ Clinical data records.
 - 608 ▪ Accessibility of policies and procedures.
 - 609 ▪ Documentation records, including audit reports, deviation reports, and corrective
 - 610 action/preventive action reports.
 - 611 ▪ Staff training records, including record of staff adherence to training schedules.
 - 612 ▪ Data quality management (source documentation and electronic records),
 - 613 assessment of reporting system.
 - 614 ▪ Supply records.
- 615 • Internal audit of program and its policies, scheduled and unscheduled
 - 616 ▪ Audit for accuracy of all annotation data; e.g., the specimen is where it is purported
 - 617 to be, in the purported volume, with the appropriate labels/identifiers.
 - 618 ▪ Audit of compliance of biospecimen resource with institution policies; e.g., human
 - 619 subjects and privacy and confidentiality protections, prioritization of biospecimen
 - 620 use, etc.

- 621 ▪ Audit of SOPs for all activities and processes.
 622 o Each biospecimen resource ensures that SOPs are written, reviewed, and
 623 appropriately approved.
 624 o Process exists for review and updating at designated time intervals.

625 **B.3.3. Standard Operating Procedures Manual**

626 Each biospecimen resource should develop SOPs that state policies and describe relevant
 627 processes in detail. Additionally, a document control program and policies for governing,
 628 modifying, or revising SOPs should be at each biospecimen resource. All SOPs should be
 629 reviewed on a periodic basis or whenever significant changes in practices, procedures,
 630 technology, law, or regulation necessitate an update. The SOPs should be well structured and
 631 undergo a rigorous approval process. Upon implementation, all SOPs should be followed as
 632 written. Current copies of SOPs (SOPs manual) should be stored in designated locations and
 633 available to personnel at all times. Personnel should review new and revised SOPs prior to
 634 implementation; reviews and associated trainings should be recorded.

635 **B.3.3.1. Contents**

636 Specifically, the SOPs manual should minimally include the following information:

- 637 • *Informed Consent.* Each biospecimen resource should have documentation of the
 638 informed consent status for each biospecimen. In addition, procedures for obtaining
 639 informed consent and protecting the privacy of identifiable human research
 640 participants and confidentiality of data should be clearly described.
- 641 • *Equipment Monitoring, Calibration, Maintenance, and Repair.* Each biospecimen
 642 resource should have procedures to routinely monitor devices that are used for
 643 biospecimen storage or preparation. This includes ensuring that equipment is
 644 accurately calibrated, that operational settings are routinely recorded, and that
 645 scheduled maintenance and repairs are documented. Equipment SOPs and records
 646 should also cover associated backup and emergency notification systems.
- 647 • *Control of Biospecimen Collection Supplies (Disposables and Reagents).* Each
 648 biospecimen resource should have procedures to ensure that consumable supplies and
 649 reagents used for collection, processing, and storage conform to required standards.
 650 This includes ensuring purchased supplies are acquired from approved vendors, meet
 651 defined material specifications, and are in good condition for use.
- 652 • *Biospecimen Identification and Labeling Conventions.* Each biospecimen resource
 653 should define policies and procedures for labeling (coding) biospecimens and linking
 654 biospecimens to other data sets and patient informed consent.
- 655 • *Biospecimen Collection and Processing Methods.* Each biospecimen resource should
 656 define, in sufficient detail to allow replication, the procedures associated with
 657 biospecimen collection, handling, processing, and preservation for each biospecimen
 658 type. This includes detailed descriptions of supplies, equipment, methods, and
 659 processing for division of a biospecimen into multiple aliquots. Biospecimen
 660 collection and processing should always include the recording of personnel names,
 661 dates, and times to accurately record these potential sources of pre-analytic variation.

- 662 • *Storage and Retrieval.* Each biospecimen resource should define procedures for the
663 storage and retrieval of biospecimens from a biorepository, including processes for
664 adding new biospecimens, withdrawing biospecimens, responding to and filling
665 requests, and final disposition of biospecimens.
- 666 • *Shipping and Receiving.* Each biospecimen resource should have defined procedures
667 and policies for the packaging and transport of ambient temperature and frozen
668 biospecimens to ensure biospecimen integrity and safety. This includes packaging
669 specifications to maintain appropriate temperature conditions; wet ice, dry ice, and
670 liquid nitrogen handling; shipment temperature monitoring; shipment regulations for
671 hazardous materials; shipment logs; delivery notifications; confirmation of delivery;
672 shipment feedback mechanisms; and MTAs or other appropriate agreements to cover
673 transfers (see [Section B.2.8](#), Shipping Samples).
- 674 • *Laboratory Tests Performed In-House Including Biospecimen Quality Control*
675 *Testing.* Each biospecimen resource should have SOPs governing standardized in-
676 house testing procedures and should document the results in associated quality
677 records. This includes tests to assess and control biospecimen quality, such as
678 confirmation of histopathology diagnosis, nucleic acid integrity, or biomarker
679 expression.
- 680 • *Biospecimen Data Collection and Management (Informatics).* Each biospecimen
681 resource should have policies for managing records and procedures defining data
682 access, data collection methods, reporting, data QC, and standardized medical
683 terminology (see [Section B.6](#), Biospecimen Resource Informatics).
- 684 • *Biosafety.* Each biospecimen resource should have policies and procedures covering
685 biosafety, including reporting staff injuries, as well as standard precautions for
686 bloodborne pathogens, personal protection equipment, hazardous material handling,
687 and disposal of medical waste and other biohazardous materials (see [Section B.4](#),
688 Biosafety).
- 689 • *Training.* Each biospecimen resource should have policies and procedures for training
690 of all staff members. Such training should be documented and include policies and
691 procedures to manage corrective actions; to resolve inventory and shipment
692 discrepancies; to monitor all sample storage; and to manage power outages,
693 emergencies, and natural disasters.
- 694 • *Security.* Each biospecimen resource should have procedures for administrative,
695 technical, and physical security, including procedures for information systems security
696 (Stoneburner et al. 2002). Security SOPs and policies should include information on
697 points of contact and designated backup personnel, including names and emergency
698 contact numbers.

699 **B.3.3.2. Implementation**

700 The biospecimen resource director and/or the individual responsible for the QA/QC program
701 should review and approve all SOPs and associated process validation studies prior to
702 implementation. Upon implementation, all SOPs should be followed as written, and any
703 deviations from written SOPs should be clearly noted. Effectiveness of QA/QC measures
704 should be evaluated on a routine basis.

705 B.3.3.3. Modifications

706 Each biospecimen resource should have a document control program and policies for
707 governing, modifying, or revising SOPs. All SOPs should be reviewed at least every 2 years
708 and whenever significant changes in practices, procedures, technology, law, or regulation
709 necessitate an update.

710 B.3.3.4. Staff Access and Review

711 Current copies of the SOPs manual should be stored in designated locations and available to
712 the staff at all times. The staff should review new and revised policies and procedures prior
713 to implementation. Staff review and any associated training should be documented.

714 B.4. Biosafety

715 Laboratories and biospecimen resources that handle biospecimens expose their employees to
716 risks involving infectious agents and chemicals as well as the general dangers of a laboratory. A
717 predictable yet small percentage of biospecimens will pose a risk to biospecimen resource
718 personnel who process them. Consequently, all biospecimens should be treated as biohazards
719 (Grizzle and Fredenburgh 2001). In addition to taking biosafety precautions, biospecimen
720 resources should adhere to key principles of general laboratory safety.

721 B.4.1. Biohazard Precautions**722 B.4.1.1.**

723 Laboratories and biospecimen resources should assume that all human specimens are
724 potentially infective and biohazardous (Grizzle and Fredenburgh 2001). For example, OSHA
725 regulations ([29 CFR § 1910.1030\(f\)\(1\)\(i\)](#)), as applicable, require that employers “make
726 available the hepatitis B vaccine and vaccination series to all employees who have
727 occupational exposure, and post-exposure evaluation and follow-up to all employees who
728 have had an exposure incident.” Dried blood, tissue, urine, saliva, and other biospecimens
729 should be handled according to standard precautions and labeled according to applicable
730 OSHA requirements. Biospecimen resource work practices should be based on standard
731 precautions similar to those used in laboratories and clinical settings. Two basic safety
732 precautions should be followed in laboratories and biospecimen resources that handle
733 biospecimens: (1) Wash hands frequently, and (2) always wear face protection and gloves
734 when handling biospecimens or working within or around freezers. Additional good general
735 laboratory work practices are outlined by Grizzle and Fredenburgh (2001).

736 B.4.1.2.

737 A biospecimen resource should establish clear policies regarding the inclusion or exclusion
738 of high-risk biospecimens. For example, depending on the potential for exposure by splash or
739 aerosol, human specimens of unknown infectivity should be handled according to biosafety
740 level-2 (BSL-2) conditions, as outlined in the Centers for Disease Control and Prevention
741 (CDC)/National Institutes of Health (NIH) booklet “Biosafety in Microbiological and
742 Biomedical Laboratories” (BMBL) (CDC and NIH 2007). At BSL-2, when biospecimen
743 containers are opened for processing, they should be handled in a BSL-2 biological safety
744 cabinet (hood). All biospecimen resources that handle human specimens should operate

745 under the applicable [OSHA bloodborne pathogens standard](#) and develop an exposure control
746 plan ([29 CFR § 1910.1030](#)). Additional precautions should be applied, as outlined in the
747 BMBL. Some activities, such as droplet-based sorting procedures (Schmid et al. 2007), may
748 require higher containment, but in other cases, less stringent practices may be acceptable.
749 Therefore, biospecimen resource staff members should be trained to perform risk
750 assessments and determine appropriate levels of containment.

751 **B.4.1.3.**

752 Biospecimen resources should establish policies consistent with the CDC’s “Select Agents
753 and Toxins” regulation ([42 CFR Part 73](#)), as applicable. This regulation implements
754 provisions of the Public Health Security and Bioterrorism Preparedness and Response Act of
755 2002, setting forth the requirements for possession, use, and transfer of select agents and
756 toxins. The biological agents and toxins listed as Select Agents and Toxins (e.g., botulinum
757 neurotoxins, Ebola virus) have the potential to pose a severe threat to public health and
758 safety, to animal health, and to animal products.

759 **B.4.2. Biosafety Best Practices**

760 **B.4.2.1.**

761 Biospecimen resources should be familiar with governmental and accrediting agency
762 requirements regarding biohazards and sources of current information concerning laboratory
763 biosafety for use in developing an overall program in safety and associated training programs
764 (see CDC/NIH documents referenced in [Section B.4.1](#), Biohazard Precautions).

765 **B.4.2.2.**

766 Biospecimen resources should identify risks and other general issues of biosafety. Frequent
767 biospecimen resource activities should be identified, safety issues involved with each activity
768 analyzed, and suitable controls implemented.

769 **B.4.2.3.**

770 Written working guidelines that are based on Federal and State requirements, experience, and
771 published information should be developed to improve biosafety. These guidelines should be
772 reviewed and updated regularly and modified in response to problems or if they prove
773 ineffective.

774 **B.4.2.4.**

775 A training program should be developed and implemented. Each employee should receive
776 training in relevant areas of biosafety before beginning work, and the training should be
777 updated annually.

778 **B.4.2.5.**

779 Biospecimen resources should record and arrange for treatment in response to all incidents
780 where personnel are exposed to biohazards or are potentially infected.

781 **B.4.3. General Laboratory Safety**

782 In addition to biosafety, biospecimen resources should follow strict general safety regulations
783 and procedures regarding chemical, electrical, fire, physical, and radiological safety (ISBER
784 2008; [29 CFR 1910](#)).

785 **B.5. Collecting and Managing Clinical Data**

786 Appropriate annotation of biospecimens is crucial to the overall usefulness of the biospecimen
787 resource as a tool for scientific research (Eiseman et al. 2003). Biospecimen resources store
788 collected biospecimens using multiple methodologies and procedures. Researchers rely on
789 banked biospecimens for a wide variety of purposes, including target discovery and validation,
790 genetic studies, epidemiologic analyses, and research on prevention or early detection. The data
791 recorded by investigators and biospecimen resources depend on the types of biospecimens
792 collected and the studies' objectives.

793 **B.5.1. Regulatory Compliance**

794 **B.5.1.1.**

795 Data collection activities should conform to U.S. Food and Drug Administration (FDA)
796 requirements (see [21 CFR Part 11](#) or the FDA guidance document at
797 <http://tinyurl.com/21cfr11>), if and where applicable, so that the data may be cited and/or used
798 in Investigational New Drug and Investigational Device Exemption applications.

799 **B.5.2. Collecting Clinical Data**

800 **B.5.2.1.**

801 As appropriate for the purpose and nature of the biospecimen resource, relevant clinical data
802 associated with a biospecimen should be collected in accordance with relevant human subject
803 and privacy regulations. The NCI recognizes that data collection is not necessarily the
804 responsibility of the biospecimen resource.

805 **B.5.2.2.**

806 Biospecimen resources should employ a uniform, nonredundant vocabulary (e.g., Cancer
807 Biomedical Informatics Grid [[caBIG®](#)] common data elements [CDEs]) for clinical data.

808 **B.5.2.3.**

809 Biospecimen resources should comply with applicable privacy statutes and regulations and
810 human subjects protection regulations governing the acquisition of biospecimens and
811 associated clinical data (see [Sections C.2](#), Informed Consent, and [C.3](#), Privacy and
812 Confidentiality Protections, for additional information and references). Clinical data
813 associated with the biospecimens only should be used and disclosed for research in
814 compliance, as applicable, with HIPAA, with U.S. Department of Health and Human
815 Services (DHHS) and FDA human subjects protection regulations, and with applicable State
816 and local laws.

817 **B.5.2.4.**

818 Biospecimen resources should track researchers' requests for specimens with specific clinical
819 data to guide the refinement of clinical data collection, as appropriate, based on the intended
820 purpose of the resource and if the biospecimen resource is the point of access for specimens
821 and associated clinical data. Biospecimen resources should routinely summarize this
822 information and provide it to an entity that maintains and/or collects the clinical data in order
823 to improve the collection of clinical data.

824 ***B.5.3. Longitudinal Clinical Data***

825 **B.5.3.1**

826 If the study requirements dictate, biospecimen resources should collect and store longitudinal
827 data following applicable informed consent and authorization requirements.

828 **B.5.3.2.**

829 Depending on the purpose of the biospecimen resource, study design, and/or informed
830 consent/authorization, information linked to biospecimens may include demographic data,
831 lifestyle factors, environmental and occupational exposures, cancer history, structured
832 pathology data, additional diagnostic studies, information on initial staging procedure,
833 treatment data, and any other data relevant to tracking a research participant's clinical
834 outcome (see the Minimal Clinical Data Set, [Appendix 1](#) for a recommended set of CDEs
835 that may be included).

836 **B.5.3.3.**

837 Databases developed for longitudinal studies should use coded data associated with a
838 biospecimen but maintain a secure link to identify the research participant to allow additional
839 longitudinal data to be obtained, if permitted by law and by the research participant's
840 consent/authorization.

841 **B.5.3.4.**

842 Biospecimen resources should optimize their policies and protocols to facilitate access to
843 uniform longitudinal data (e.g., treatment and outcome information, as appropriate) while
844 protecting research participant privacy and confidentiality.

845 **B.5.3.5.**

846 To collect high-quality longitudinal information, biospecimen resources should ensure that
847 dedicated and trained personnel curate longitudinal clinical data with validation of the
848 collection process and QA/QC. These personnel may not necessarily be employed by the
849 biospecimen resource.

850 ***B.5.4. Informatics to Support the Tracking of Data***

851 **B.5.4.1.**

852 A biospecimen resource informatics system should track all aspects of biospecimen
853 collection, processing, and distribution to support high-quality annotation of the specimen, its

854 characteristics, and other associated data. Refer to [Section B.6](#), Biospecimen Resource
855 Informatics, for additional information.

856 **B.6. Biospecimen Resource Informatics: Data Management and Inventory** 857 **Control and Tracking**

858 Driven by the scale of data in genomics and proteomics, informatics systems have become
859 critical to the research enterprise. A minimum set of functional, operational, and legal
860 requirements should be considered best practices (as outlined in this document) and should be
861 incorporated when developing or selecting informatics systems to support biospecimen
862 resources. These informatics systems should be robust and operationally reliable to sustain day-
863 to-day operations of a biospecimen resource and offer the key requirements needed by those
864 using the biospecimen resource. Informatics systems should be able to adapt and meet changing
865 scientific needs. These needs may include ensuring the system can track new processing
866 methods, new biospecimen protocols, new equipment technology, or new container types.

867 An informatics system should support all aspects of biospecimen resource operations, including,
868 but not limited to, tracking of research participant enrollment and consent; biospecimen
869 collection, processing, storage, and dissemination; QA/QC processes and documentation;
870 collection of or electronic linkage to research participant (i.e., clinical) data; data security; and
871 management reporting functions (e.g., generating reports on inventory, collection, utilization,
872 QA, etc.). In addition, the system should store a minimum, common set of clinical and
873 experimental annotation data.

874 Biospecimen resource informatics systems are a key tool in providing accountability of
875 biospecimens (e.g., location) and related data uses to research participants. Biospecimen
876 resources should implement and operate their informatics systems with security mechanisms
877 such that this accountability demand is met (see [Section B.6.7](#), Regulatory Issues Pertaining to
878 Informatics Systems, and [Section C.1](#), Principles for Responsible Custodianship).

879 In addition, the informatics systems should ensure interoperability of systems (i.e., other
880 biospecimen resources or different data systems) because this is key to exchanging data and
881 biospecimens. This should include integrating with other systems where genomic, proteomic,
882 radiology imaging, pathology imaging, and other relevant data are captured or shared.

883 To address this need, the NCI Center for Bioinformatics developed caBIG®. caBIG® is a
884 voluntary network grid connecting individuals and institutions to enable the sharing of data and
885 tools across the NCI-supported research continuum, especially for clinical and translational
886 research.¹ Biospecimen resources are encouraged to draw upon caBIG® to implement the
887 informatics recommendations in this section. The caBIG® program and associated
888 tools/resources enable interoperability for all aspects of cancer research and are continually
889 evolving and growing in scope beyond cancer research. A subset of caBIG® tools is available to
890 support biospecimen management and biospecimen sharing.

¹ <https://cabig.nci.nih.gov/>.

891 **B.6.1. Functionality—General**

892 **B.6.1.1.**

893 At the biospecimen resource level, informatics systems should be focused on recording data
894 types as described in Section B.5. This includes inventory functions, tracking all phases of
895 biospecimen acquisition, processing, handling, QA/QC, and distribution from the collection
896 site (research participant) to utilization (researcher).

897 **B.6.1.2.**

898 The informatics system should have the capability of linking the labels on the physical
899 biospecimen container (e.g., paper labels or barcodes) to other information regarding that
900 biospecimen in the system.

901 **B.6.1.3.**

902 Informatics systems should track clinical data associated with a biospecimen and/or link
903 biospecimen data with external sources of clinical data, where applicable.

904 **B.6.1.4.**

905 Biospecimen resource informatics systems should monitor and report on biospecimen quality
906 2.

907 **B.6.1.5.**

908 Biospecimen resource informatics systems should provide vital system statistics and audit
909 logs of all access to protected health information (PHI) in the database.

910 **B.6.2. Functionality—Identification and Tracking of Biospecimens**

911 **B.6.2.1.**

912 For informatics purposes, a biospecimen refers to a physically distinct human specimen
913 usually stored in a single container. Multiple physical parts created by extraction, division
914 into aliquots, or other physical division of a biospecimen are considered new biospecimens
915 and are referred to in this document as samples, each requiring a new identifier. The origin of
916 each sample should be recorded.

917 **B.6.2.2.**

918 There is a functional need to employ a method to have global unique identification of
919 biospecimens since there are research needs to verify and trace back to the biospecimen
920 original source when associated aliquots/derivatives are used. In addition, as biospecimens
921 and derived samples are shared among biospecimen resources, QC questions rely on having a
922 global, unique identifier to ease traceability. Each biospecimen should be assigned a unique
923 identifier or combination of identifiers, such as a number and/or barcode. This
924 recommendation is most applicable to future biospecimen collections as implementation in
925 existing collections would be laborious. In this context, the scope within which identifiers are
926 unique applies to an individual system and the biospecimen resources it supports although it

927 is recommended that if a global identifier is able to be assigned, it should be used wherever
928 possible.

929 **B.6.2.3.**

930 The informatics system should be able to track a biospecimen from collection through
931 processing, storage, and distribution. Restocking of returned, unused samples from the
932 researcher should also be tracked. Tracking includes documenting multiple, preexisting,
933 and/or external physical biospecimen identifiers, such as barcodes with nonidentifying
934 information.

935 **B.6.2.4.**

936 The biospecimen resource database should be updated each time a biospecimen or sample is
937 moved within or out of the biospecimen resource, and the informatics system should be able
938 to track the location.

939 **B.6.3. Interoperability**

940 **B.6.3.1.**

941 Although biospecimen resources may have different informatics requirements based on
942 workflow that require different informatics systems, these systems should be interoperable to
943 integrate clinical and research data and establish distributed biospecimen resources. This
944 interoperability should enable integration with local systems and with other cross-site
945 systems.

946 **B.6.3.2.**

947 The informatics system at each biospecimen resource should be capable of integrating with
948 other clinical data systems, including the anatomic pathology laboratory information system,
949 the clinical pathology laboratory information system, and cancer registries. Integration with
950 clinical data systems should conform to HIPAA regulations and human subjects protection
951 regulations, as applicable.

952 **B.6.3.3.**

953 Informatics systems of biospecimen resources should support a minimum set of common
954 queries that can be submitted to all systems using CDEs.

955 **B.6.3.4.**

956 The informatics systems selected or developed for new biospecimen resources should be
957 caBIG® compatible, with the goal of interoperability with other systems.² This will be
958 accomplished by implementing one or more caBIG® standard service specifications. The
959 latest information on [caBIG® compatibility](#) may be found on the caBIG® Web site. Where
960 systems for existing biospecimen resources are being replaced or upgraded, they should be
961 caBIG® compatible at a level to ensure maximum available interoperability. For existing
962 software, migration paths to caBIG® compatibility should be identified.

² https://cabig.nci.nih.gov/guidelines_documentation.

963 **B.6.3.5.**

964 The informatics systems should utilize data elements from a common metadata repository,
965 such as the [Cancer Data Standards Repository](#).

966 **B.6.3.6.**

967 Biospecimen resource informatics management systems should be capable of sharing
968 appropriate, deidentified biospecimen data to users at remote locations for multiple purposes
969 including satisfying reporting and regulatory requirements as well as searching for potential
970 biospecimens for a proposed scientific study. The NCI is developing tools for interoperability
971 that aid biospecimen resources in reporting and locating specimens, including OBBR and
972 caBIG® efforts in the [Specimen Resource Locator](#) and a [caBIG® Common Biorepository
973 Model](#) that enables sharing of deidentified biospecimen information via [caGrid](#), an open-
974 source software platform.

975 ***B.6.4. Development of Biospecimen Resource Informatics Management Systems***

976 There are a large number of mature, open-source, and commercial informatics system tools that
977 should fulfill the needs of most biospecimen resources. However, these best practices should be
978 considered when opting to develop an informatics management system from scratch.

979 **B.6.4.1.**

980 Biospecimen resource informatics management systems should be based on use cases and
981 other techniques (e.g., data or object models) that capture needs for managing biospecimen
982 resources. SOPs for the activities carried out in a biospecimen resource should largely drive
983 the design of informatics systems.

984 **B.6.4.2.**

985 Software and system development methodology should be followed for initial development
986 and subsequent revisions.

987 **B.6.4.3.**

988 Software and system engineering organizations should be encouraged to meet at least
989 Capability Maturity Model Integration ([CMMI](#)) Level 3.

990 ***B.6.5. Selection of Biospecimen Resource Informatics Management Systems***

991 **B.6.5.1.**

992 Biospecimen resources should identify the minimum set of requirements for software needs
993 and storage needs to address the current and estimated future needs of the resource. The
994 requirements should incorporate the best practices described in this document.

995 **B.6.5.2.**

996 Biospecimen resources should use criteria identified above to judge mature open-source and
997 commercially available systems, taking into account other factors including ease of
998 implementation, infrastructure needs, support needs, and cost for purchase and maintenance.

999 **B.6.6. Validation and Operation of Biospecimen Resource Informatics Systems**

1000 **B.6.6.1.**

1001 Biospecimen resource informatics management systems should have an operational
1002 infrastructure to support operation 24 hours a day, 7 days a week.

1003 **B.6.6.2.**

1004 Biospecimen resource informatics management systems should have processes defined and
1005 in place to cope with system downtimes and disaster recovery.

1006 **B.6.6.3.**

1007 Biospecimen resource informatics management systems should be periodically evaluated to
1008 ensure that the system is fulfilling the criteria advised in best practices and the latest needs of
1009 the biospecimen resource.

1010 **B.6.6.4.**

1011 Tools used to extract structured information from free-text data, such as surgical pathology
1012 reports, should be validated to ensure their accuracy in performing that task. Biospecimen
1013 resources should have processes in place to routinely monitor the performance of such tools.

1014 **B.6.6.5.**

1015 All biospecimen resource databases at an individual institution should be in a secure site
1016 monitored by the institution. Plans should be in place for data storage and retrieval in
1017 response to a wide variety of conditions that could affect the performance of an informatics
1018 system. Biospecimen resources should eliminate unsecured, ad hoc databases and manage
1019 data through the central informatics system. Resources without the capabilities to provide
1020 such infrastructure should seek external hosting arrangements for their informatics system.

1021 **B.6.7. Regulatory Issues Pertaining to Informatics Systems**

1022 Besides those issue identified in the Ethical, Legal, and Policy section in these guidelines, the
1023 following regulatory issues should be addressed as applicable.

1024 **B.6.7.1.**

1025 Biospecimen resources should meet relevant State and Federal requirements that encourage
1026 the use of electronic signatures where appropriate and information technology accessibility
1027 standards for handicapped persons.

1028 **B.6.7.2.**

1029 Biospecimen resources should refer to the National Institute of Standards and Technology
1030 Special Publication 800-30 “[Risk Management Guide for Information Technology Systems](#),”
1031 as applicable, to determine the appropriate level of security for informatics systems.

1032 **C. Ethical, Legal, and Policy Best Practices**

1033 In addition to technical issues relating to the physical integrity and quality of biospecimens,
1034 multiple ethical, legal, and policy issues should be considered in biospecimen research activities.
1035 Key ethical issues include respecting the autonomy of human research participants (human
1036 subjects³), protecting human research participants from breaches of privacy and confidentiality,
1037 and minimizing individual and group harms. Legal and policy issues include adhering to relevant
1038 Federal, State, and local laws and regulations surrounding the collection, storage, dissemination,
1039 and use of biospecimens; developing appropriate guidelines for biospecimen access; ensuring
1040 that biospecimens are used in scientifically meritorious research; and establishing biospecimen
1041 resource governance. (Refer to [Sections C1](#) through [C6](#) for specific details about relevant
1042 regulations and policies.)

1043 In 2005, the NCI hosted a workshop that assembled diverse representatives from the cancer
1044 research community as well as ethics, legal, and policy experts to discuss and propose
1045 approaches that could help unify, integrate, and improve NCI-supported biospecimen resources
1046 and biospecimen research in general. The recommendations that resulted from this workshop as
1047 well as additional NCI-sponsored meetings and work conducted between 2002 and 2005 formed
1048 the basis of the *NCI Best Practices*. This first (2009) revision to the *NCI Best Practices* provides
1049 additional recommendations formulated during the 2007 NCI-hosted Symposium-Workshop on
1050 [Custodianship and Ownership Issues in Biospecimen Research](#). Featuring leaders from the
1051 academic community, private sector, patient advocacy groups, and Government agencies, this
1052 landmark symposium-workshop was convened to develop recommendations for best practices
1053 concerning the custodianship of biospecimens and associated data at NCI-supported resources
1054 and to expand upon the original *NCI Best Practices* in four key areas: (1) Considerations for
1055 human research participants, investigators, and institutions; (2) financial conflicts of COIs;
1056 (3) intellectual property (IP); and (4) access to products and benefits. Recommendations
1057 generated during this symposium-workshop comprise the revisions to Section C of the *NCI Best*
1058 *Practices*.

1059 The ethical, legal, and policy best practices outlined in this document identify key regulations
1060 and recommendations relevant to biospecimen collection, storage, dissemination, and use in
1061 research. These best practices are more detailed and extensive than, for example, a grant policy
1062 statement; however, not every element outlined in the *NCI Best Practices* would apply to every
1063 biospecimen research activity. Investigators and biospecimen resource directors should consider
1064 these principles carefully in conjunction with the objective of the research project and the
1065 mission of the biospecimen resource to determine the most appropriate operational policies.
1066 Furthermore, investigators and biospecimen resources should consult their IRBs, as needed, and
1067 appropriate institutional officials to determine how Federal and State regulations and policies
1068 would apply to their resource and how to implement recommendations in the *NCI Best Practices*
1069 related to human subjects research, as defined in [45 CFR Part 46](#).

³ The NCI views the terms “human research participant” and “human subject” as equivalent. The former term is used throughout this document in order to recognize the important and active role of patients and volunteers in research. “Human research participant” is intended to have the same meaning as human subject, as defined in [45 CFR Part 46](#).

1070 The regulations and proposed standards discussed in this document are for research using
1071 biospecimens in the United States. Many countries have their own ethical and policy standards
1072 for human subjects research including, in some cases, specific provisions for the use of
1073 biospecimens. Investigators and biospecimen resources should be aware of international
1074 standards that may be applicable and address any differences between international and U.S.
1075 regulatory requirements prior to the initiation of a new collaboration or collection.

1076 **C.1. Principles for Responsible Custodianship**

1077 Custodianship is the caretaking responsibility for biospecimens that extends from collection
1078 through research use. Responsible custodianship requires careful planning and transparent
1079 policies to ensure the long-term physical quality of the biospecimens, the privacy of human
1080 research participants, the confidentiality of associated data, and the appropriate use of
1081 biospecimens and data. In the interest of transparency, biospecimen resource policies should be
1082 made available to the public either electronically or for onsite inspection.

1083 The custodian is the trusted intermediary and caretaker of biospecimens and associated data, and
1084 the custodian's caretaking responsibilities should align with applicable ethical and policy
1085 standards. The custodian should be clearly designated and, ideally, be someone other than the
1086 research investigator or sponsor(s) of the biospecimen resource; e.g., a biospecimen resource
1087 manager, to eliminate any potential conflicts of interest. When the research investigator is the
1088 primary holder of the biospecimens and data, he or she should have the same duties of
1089 custodianship and abide by the same ethics that apply to research use. Thus, principles
1090 concerning oversight and QC mechanisms that apply to traditional biospecimen resources could
1091 also be relevant to the collection, storage, distribution, and use of biospecimens in small
1092 collections held by individual investigators; e.g., [protection of the privacy of human research](#)
1093 [participants](#) and confidentiality of their data, well-documented [QA/QC procedures](#), etc.
1094 Alternatively, research investigators with small biospecimen collections that will be stored for
1095 future studies could consider joining an institutional IRB-approved biospecimen resource. This
1096 consolidation would help ensure baseline quality standards for smaller biospecimen collections.

1097 In their role as trusted intermediaries, custodians and managers of biospecimen resources should
1098 establish a governance plan consisting of the set of authorities, processes, and procedures
1099 guiding key operational decisions made within the resource. Governance affects access to
1100 biospecimens as well as custodial relationships and responsibilities and should be part of the
1101 resource's general custodianship plan. In addition, biospecimen resources should demonstrate
1102 their accountability to promote public trust by accepting all of the custodial responsibilities listed
1103 below and, as appropriate, establishing advisory boards—with human research participants
1104 among the active members—to accomplish them.

- 1105 • Implementing overall operational, ethical, and legal policies based on feedback from
1106 individuals and the community, where practicable and appropriate.
- 1107 • Ensuring appropriate scientific assessment of access requests and proposed research
1108 use as well as management of COIs.
- 1109 • Providing advice regarding publications and dissemination of research data that are
1110 potentially stigmatizing or discriminating to groups.

- 1111 • Educating the public and obtaining their feedback, where practicable, through the
1112 biospecimen resource’s public Web site or alternate mechanism.

1113 More specific recommendations by topic area are provided throughout this section.

1114 **C.1.1.**

1115 Biospecimen resources should address formal and continuing responsibility for custodianship of
1116 collected biospecimens and associated data as part of their protocols. The following issues
1117 should be addressed in the governance plan: (1) How does the biospecimen resource propose to
1118 ensure the physical integrity of biospecimens? (2) How does the biospecimen resource propose
1119 to ensure the integrity of the human research participant data that accompany the biospecimens?
1120 (3) What plans and protocols are in place for the distribution of samples to investigators? and (4)
1121 What are the roles and responsibilities of the biospecimen resource director and his or her
1122 institution? (Also see [Section C.4](#), Access to Biospecimens and Data.)

1123 **C.1.2.**

1124 Biospecimen resources’ legacy or contingency plans should be part of the overall governance
1125 plan and should address the handling and disposition of biospecimens and associated data at one
1126 or more of the following points: (1) End of the budget period of the grant, (2) loss of
1127 management or termination of funding, (3) accomplishment of the specific research objectives of
1128 the study, (4) depletion of biospecimens, (5) achievement of critical data end points, and/or
1129 (6) discontinuation of participation by human research participants. At any of these points, an
1130 assessment of whether the stored biospecimens still have value for research should be conducted.
1131 If the stored biospecimens still have research value, the resource should consider whether to
1132 become financially self-sustaining. Alternatively, the resource should consider announcing the
1133 availability of the biospecimens for transfer to suitable research facilities by means appropriate
1134 for reaching a wide audience, if permitted by the informed consent document and the relevant
1135 IRB. Biospecimen resources should use the same decisionmaking criteria for allowing transfer of
1136 biospecimens to other biospecimen resources as they do when allowing transfer of biospecimens
1137 to investigators. The transfer of such biospecimens should be consistent with human subjects
1138 regulations, the informed consent under which the specimens and data were initially collected,
1139 and any other prior agreements and institutional policies that may apply. (Also see [Section C.2](#),
1140 Informed Consent.)

1141 **C.1.3.**

1142 Biospecimen resources should establish and document transparent policies governing the
1143 retention of biospecimens and data. In addition, usage agreements, such as MTAs, should specify
1144 the retention policies of the recipient investigator. Other considerations related to specimen
1145 retention include the following:

- 1146 • The retention of clinical biospecimens may be governed by Federal and/or State laws.
1147 • For research biospecimens, permanent storage is generally preferred, subject to
1148 sufficient resources and storage space and foreseeable research utility; i.e., poor-
1149 quality biospecimens as determined via QA/QC processes should not be stored
1150 indefinitely.

- 1151 • Biospecimen availability should be reviewed periodically (e.g., at the time of funding
1152 renewal) to determine the utility of the retained biospecimens and the need for new
1153 biospecimens.

1154 **C.1.4.**

1155 Biospecimen resources, as responsible custodians, should manage existing or potential COIs and
1156 adhere to regulations regarding COIs at [42 CFR Part 50 Subpart F](#) as well as other applicable
1157 regulations and policies. (Also see [Section C.6](#), Conflicts of Interest.)

1158 **C.1.5.**

1159 Biospecimen resources should implement transparent policies for maintaining the confidentiality
1160 and security of the biospecimens and associated clinical data, if applicable. Specifically,
1161 biospecimen resources that store coded samples and data should establish policies regarding how
1162 the link or code that allows identification of human research participants will be secured.

1163 **C.1.6.**

1164 Where practicable, biospecimen resources should share the following general information with
1165 human research participants via their Web site or alternate mechanism:

- 1166 • Whether biospecimens are shared with other researchers;
1167 • How access decisions are made and what privacy protections are in place; and
1168 • What general types of research studies are performed using biospecimens.

1169 This information, or the corresponding Web link, should be included in the informed consent
1170 supplementary material; e.g., a brochure.

1171 **C.1.7.**

1172 A biospecimen resource should make public (e.g., on a Web site) a summary of its governance
1173 plan and/or an accompanying graphic of its organization.

1174 **C.2. Informed Consent**

1175 Informed consent (pursuant to the human subjects regulations at [45 CFR Part 46 Subpart A](#)) is
1176 designed to present potential human research participants with sufficient information—including
1177 anticipated procedures, risks, and benefits—to make an informed decision about whether to
1178 participate in research studies. Obtaining informed consent for the collection, storage, and future
1179 research use of biospecimens can be challenging since the specifics of the future research often
1180 are not known at the time of biospecimen collection. In addition, under DHHS regulations at [45](#)
1181 [CFR Part 46 Subpart A](#), informed consent may not be required even if the research is considered
1182 human subjects research if (1) the human subjects research is exempt from the regulations at [45](#)
1183 [CFR § 46.101\(b\)](#) or (2) the research is nonexempt human subjects research that has been granted
1184 a waiver of the requirements for informed consent by an IRB under [45 CFR § 46.116\(c\) or \(d\)](#).

1185 **C.2.1. Federal Regulations and Guidelines Pertaining to Informed Consent**

1186 **C.2.1.1.**

1187 DHHS-conducted or -supported research on human research participants is regulated by [45](#)
1188 [CFR Part 46](#). The DHHS regulations describe both when informed consent is required and
1189 what elements must be in an informed consent process and document. The biospecimen
1190 resource should track whether appropriate informed consent is present (if required) or the
1191 reason why informed consent is not necessary. (See the Office for Human Research
1192 Protections [OHRP] Web site for guidance on informed consent:
1193 <http://www.hhs.gov/ohrp/policy/index.html#informed>.)

1194 **C.2.1.2.**

1195 The OHRP has issued guidance on regulatory requirements that must be satisfied by
1196 biospecimen resources (available at
1197 <http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm> and
1198 <http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.htm>). The OHRP recommends
1199 that the following be included in informed consent documents for biospecimen collection:

- 1200 • A clear description of the operation of the biospecimen resource. This description
1201 could include details that may be of interest to human research participants, such as
1202 whether identifiable information will be maintained by the biospecimen resource
1203 and/or whether research results will be linked to the biospecimen. (See [Section C.1](#),
1204 Principles for Responsible Custodianship, for NCI recommendations.)
- 1205 • The conditions under which samples and data will be released to recipient
1206 investigators. (See [Section C.4](#), Access to Biospecimens and Data, for NCI
1207 recommendations.)
- 1208 • Procedures for protecting the privacy of human research participants and
1209 confidentiality of data. (See [Section C.3](#), Privacy and Confidentiality Protections, for
1210 NCI recommendations.)
- 1211 • Specific descriptions of the nature and purpose of the research.
- 1212 • Information about the consequences of DNA typing if human genetic research is
1213 anticipated.

1214 **C.2.1.3.**

1215 FDA regulations regarding informed consent should be considered when applicable,
1216 particularly when human specimens are used for *in vitro* diagnostic device studies. (See [21](#)
1217 [CFR Part 812](#), [21 CFR Part 50](#), and [21 CFR Part 56](#).) The FDA may exercise enforcement
1218 discretion as to the requirement for informed consent for *in vitro* diagnostic device studies
1219 that utilize “leftover” specimens (e.g., remnants of specimens collected for routine clinical

1220 care or analysis of specimens previously collected for another research purpose) that are not
1221 individually identifiable if certain conditions have been met.⁴

1222 **C.2.2. General NCI Recommendations Pertaining to Informed Consent**

1223 The extent to which a biospecimen resource is involved in the informed consent process varies
1224 widely and depends on the mission of the resource. Many biospecimen resources collect
1225 biospecimens and participate in the informed consent process whereas others store biospecimens
1226 originally collected for alternate purposes or by researchers not affiliated with the resource.
1227 Regardless of the level of involvement in the informed consent process, biospecimen resources
1228 should ensure that the research uses of biospecimens are consistent with the informed consent of
1229 the human research participant.

1230 **C.2.2.1.**

1231 The NCI recommends informed consent whenever practicable, consistent with applicable
1232 regulations. Respect for individuals who have provided data and/or biospecimens for
1233 research is of paramount importance; therefore, their preferences should be considered when
1234 deciding whether informed consent should be sought. Some individuals may prefer to
1235 provide anonymous samples and/or may be opposed to being recontacted to consent for
1236 additional research or future uses. The biospecimen resource should have transparent policies
1237 concerning the informed consent process, including when consent is sought from human
1238 research participants.

1239 **C.2.2.2.**

1240 Personal, religious, and culturally held beliefs and traditions should be respected in
1241 biomedical research using biospecimens. For example, some cultures believe that the body is
1242 sacred and should not be disturbed (Andrews 2005; Burhansstipanov et al., 2005).
1243 Investigators should consider the beliefs and traditions of the community when planning a
1244 research study that will include collection of biospecimens and whether any of the following
1245 issues should be addressed for the population under study during the informed consent
1246 process:

- 1247 • Whether there are any religious, cultural, or personal restrictions regarding the
1248 biospecimen;
- 1249 • What are the instructions for disposal or return, if practicable, of the biospecimen; and
- 1250 • What is the participant's primary language and whether the consent is explained in
1251 that language.

1252 **C.2.2.3.**

1253 For biospecimens collected during the course of medical care, the timing of consent (e.g.,
1254 before or after a medical procedure) to use biospecimens for research purposes should not be

⁴ Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens That Are Not Individually Identifiable. Available at: <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm078384.htm>.

1255 imposed rigidly but instead informed by a number of important considerations, including
1256 ethical guidelines and logistical constraints.

1257 Generally, consent should be obtained prior to the medical procedure, but post-medical
1258 procedure consent may be appropriate in some circumstances. These decisions should be
1259 made on a case-by-case basis with sensitivity to the situation a patient faces when undergoing
1260 a medical procedure or a test for a serious disease. For example, post-medical procedure
1261 consent may be acceptable for the use of remnant biospecimens beyond what is needed for
1262 diagnostic purposes if it was not practicable to previously consent the patient due to
1263 considerations about illness, undue stress, or the ability of the patient to fully comprehend
1264 what was being asked. However, prior informed consent would be required in cases where
1265 biospecimens are collected from human research participants for research purposes or when
1266 the procedure for collecting biospecimens for clinical purposes is changed to meet a research
1267 need unless an IRB grants a waiver of the requirements for obtaining informed consent.

1268 **C.2.2.4.**

1269 Information about policies governing the retention of biospecimens, records pertaining to
1270 informed consent, and protections for the privacy of human research participants and the
1271 confidentiality of their data should be provided to participants either in the informed consent
1272 document or in supporting materials. (Also see [Section C.1](#), Principles for Responsible
1273 Custodianship.)

1274 **C.2.2.5.**

1275 The informed consent document should disclose whether biospecimens may at some point be
1276 anonymized and subsequently used for secondary research purposes beyond those described
1277 in the original informed consent. Human research participants deciding whether to contribute
1278 biospecimens for research should understand how their tissue may be used in the future,
1279 including any potential anonymous use.

1280 **C.2.3. NCI Recommendations on Key Informed Consent Elements and**
1281 **Supplementary Materials**

1282 The list of elements in this section is provided to guide and inform biospecimen resources about
1283 important ethical and policy issues relevant to the informed consent document. The informed
1284 consent document for the collection and future research use of biospecimens should balance the
1285 requirement to provide sufficient information to human research participants to make an
1286 informed decision with the need to ensure that the document is comprehensible and reasonable in
1287 length. The elements listed below may be adapted depending on the nature of the resource and its
1288 mission.

1289 **C.2.3.1.**

1290 For the benefit of human research participants, an informed consent document outlining
1291 important issues and risks in straightforward language should be developed and
1292 implemented. The informed consent document should specify the following:

- 1293
 - Why particular biospecimens are being sought and why human research participants
1294 are being asked to participate.

- 1295 • The source of the biospecimens that will be collected for research; for example,
1296 whether the biospecimen will come from leftover tissue from a surgical procedure or
1297 from tissue excised for research purposes during a special procedure.
- 1298 • Who will be the custodian of the biospecimens and what role the custodian will have.
- 1299 • How the obtained biospecimens will be used and whether biospecimens will be used
1300 in secondary research.⁵
- 1301 • Whether biospecimens will continue to be stored and shared as long as they are
1302 potentially useful for research, respectfully destroyed when no longer useful for
1303 research, or transferred to another established resource in accordance with the terms of
1304 the informed consent.

1305 **C.2.3.2.**

1306 The informed consent document should describe what types of data will be collected and
1307 how the data will be used and stored. Where applicable, the informed consent document
1308 should state whether identifiable or coded information will be maintained in the biospecimen
1309 resource and if research results will be linked to other data about the human research
1310 participant, such as clinical data obtained from anatomic pathology and clinical pathology
1311 laboratory information systems and cancer registries. (Refer to [Section B.5.3](#), Longitudinal
1312 Clinical Data, for further recommendations on the integration of informatics systems.) If
1313 longitudinal data will be collected by accessing the participant’s medical records, the
1314 informed consent document should clearly state this. The informed consent document also
1315 should describe whether the biospecimens and/or the data associated with or derived from
1316 biospecimens will be shared with other investigators and, if so, the oversight mechanisms for
1317 such sharing.

1318 **C.2.3.3.**

1319 If appropriate, the informed consent document may include an option that allows human
1320 research participants to select whether they would be willing to be recontacted about the use
1321 of their biospecimens and/or data in future research studies.

1322 **C.2.3.4.**

1323 The informed consent document should state whether research participation could benefit or
1324 potentially negatively impact participants’ families and communities; e.g., if there is a risk of
1325 stigmatization and discrimination based on research results.

1326 **C.2.3.5.**

1327 If a study involves genetic sequencing or analysis, the informed consent document should
1328 include information about the types of genetic sequencing or analysis that will be conducted
1329 (e.g., somatic, familial, or whole genome analysis) and the potential risks to the human
1330 research participant posed by such research, if applicable. The Genetic Information
1331 Nondiscrimination Act ([GINA](#)) of 2008 may reduce some of these risks by prohibiting
1332 employment and health insurance discrimination on the basis of genetic information. GINA

⁵ “Secondary research” is defined as any other research use beyond the scope of the primary study.

1333 does not protect against potential discrimination on the basis of genetic information for
1334 disability or long-term care insurance. For more information on GINA, please refer to the
1335 guidance from the [OHRP](#) and the fact sheet produced by the [National Human Genome](#)
1336 [Research Institute](#).

1337 **C.2.3.6.**

1338 The informed consent document should address the use of biospecimens and/or data by
1339 private or for-profit entities and the possibility of research leading to future development of
1340 commercial products, as appropriate. The document should describe whether human research
1341 participants, their families, or communities will receive any financial or nonfinancial benefits
1342 from the products, tests, or discoveries resulting from the research.

1343 **C.2.3.7.**

1344 The informed consent document should state whether individual or aggregate research results
1345 will be released to the human research participant, the participant's healthcare provider, or
1346 the participant's family and, if so, the mechanism for communicating such results; e.g., e-
1347 mail, newsletter, telephone call, etc. The procedure for opting out of all communications
1348 should be clearly indicated. The [HIPAA Privacy Rule](#) may affect the release of research
1349 results and should be considered.

1350 **C.2.3.8.**

1351 General information about COIs, institutional policies for sharing samples with other
1352 investigators or companies, the financial implications of sharing, and any known or likely
1353 benefit to the institution or investigator should be easily found online at the resource's or
1354 institution's Web site or provided in a brochure that accompanies the informed consent
1355 document. (Also see [Section C.6](#), Conflicts of Interest.)

1356 **C.2.3.9.**

1357 A tiered system of consent may be considered where human research participants could
1358 specify the types of research for which their contributed biospecimens will be used.

1359 While a tiered system of consent will provide the human research participant with greater
1360 specificity about secondary research, it also can lead to ambiguities in terms of how to
1361 classify certain types of interdisciplinary or multidisciplinary research. If the purpose of the
1362 biospecimen resource is to provide biospecimens for a broad range of research, tiered consent
1363 may be burdensome and uninformative. Tiered consent may be used if consent categories are
1364 well defined and relatively constant over time and if an informatics system capable of
1365 tracking the levels of consent for each human research participant is already in place.
1366 Whenever tiered consent is utilized, biospecimen resources should adhere to the human
1367 research participant's choices in order to ensure that his or her wishes are honored.

1368 Examples of tiered consent categories are as follows:

- 1369
- My tissue may be kept for use in research to learn about, prevent, or treat cancer.
 - My tissue may be kept for use in secondary research to learn about, prevent, or treat other health problems; e.g., diabetes, Alzheimer's disease, or heart disease.
- 1370
- 1371

- 1372 • My tissue may be associated with my medical record and history.
1373 • I am willing to be contacted about future research studies.

1374 **C.2.3.10.**

1375 Biospecimen resources should consider whether, in addition to the informed consent
1376 document, more detailed supplementary materials should be made available to interested
1377 human research participants. If supplementary materials are provided, protocols should be in
1378 place to ensure that such materials are consistently offered to human research participants
1379 and that the content does not conflict with the informed consent document. These materials
1380 may include the following:

- 1381 • A one-page graphic or written summary outlining the biospecimen resource’s
1382 governance, with an emphasis on oversight and access protocols.
1383 • An accompanying brochure that provides more detailed information about the
1384 biospecimen resource, either directly or by referencing the resource’s Web site, and
1385 covers any other issues that could not be addressed in the informed consent document.

1386 **C.2.4. Issues Pertaining to Discontinuation of Participation in Research**

1387 Biospecimen resources should develop policies for responding to requests for discontinuation of
1388 participation in research, consistent with [OHRP draft guidance](#)⁶ and [FDA guidance](#). Participation
1389 in research includes the collection of individually identifiable private information or
1390 biospecimens from human research participants (even if the investigator does not interact or
1391 intervene with the participant) and the use or testing of individually identifiable biospecimens
1392 already collected. The informed consent document should highlight the human research
1393 participant’s ability to discontinue participation in research and describe what will take place
1394 should this occur. In turn, biospecimen resources should develop procedures to track
1395 biospecimens and associated data for human research participants who discontinue participation
1396 in research.

- 1397 • In the event that a human research participant discontinues participation in research,
1398 collection of individually identifiable biospecimens or data and use or testing of
1399 individually identifiable biospecimens already collected from that individual should
1400 cease. In addition, any remaining identifiable biospecimens and associated clinical
1401 data from the human research participant should be withdrawn from the biospecimen
1402 resource and not distributed for further research. However, anonymous or coded
1403 samples and/or clinical data that have been transferred from the biospecimen resource
1404 to investigators need not be withdrawn.
1405 • Following discontinuation of participation, analysis of data that include identifiable,
1406 private information generated from individually identifiable biospecimens obtained

⁶ Section C.2.4 is based in part on the draft OHRP document titled [Guidance on Important Considerations for When Participation of Human Subjects in Research is Discontinued](#) released November 7, 2008. This section will be revised as needed once the final OHRP guidance on this topic is released.

1407 prior to the date of discontinuation of participation may continue, provided that such
1408 analysis falls within the scope of the analysis described in the IRB-approved protocol.

- 1409 • Upon a human research participant’s discontinuation of participation in research,
1410 custodians and directors of the biospecimen resource (and recipient investigator, if
1411 applicable) should respectfully destroy identifiable specimens from that participant.
1412 Any exceptions should be in accordance with the original consent framework and the
1413 participant’s indicated preferences or a demonstrated clinical need for continued
1414 storage of the biospecimen.
- 1415 • Discontinuation of participation in research may be complete or partial. In some cases,
1416 the human research participant may wish to discontinue some elements of the research
1417 project, such as activities involving interaction or intervention, but may be willing to
1418 allow other activities to continue, such as analysis of biospecimens already collected.
1419 When a human research participant seeks to discontinue participation in research, the
1420 custodian or resource’s director should determine whether the human research
1421 participant intends to discontinue all types of participation or just certain types of
1422 participation.
- 1423 • Biospecimen resources should be sensitive to cultural issues and work with affected
1424 groups to develop mechanisms for the proper destruction of biospecimens or, as
1425 appropriate and practicable, the return of biospecimens to the individual or affected
1426 group (see [Section C.2.2](#)).

1427 ***C.2.5. Considerations for Use of Pediatric Biospecimens***

1428 Biospecimen resources that store identifiable biospecimens and/or identifiable data from children
1429 for future research use should consider the need for obtaining informed consent when the
1430 formerly pediatric human research participant reaches the legal age to consent for a research
1431 study. Under [45 CFR 46](#), activities that involve the use of identifiable biospecimens and/or
1432 associated identifiable medical data constitute human subjects research and would therefore
1433 require investigators to seek and obtain the legally effective informed consent of the now-adult
1434 participants.⁷ However, the IRB may consider whether a waiver of informed consent under [45](#)
1435 [CFR 46.116\(d\)](#) is appropriate. In addition, the following operational best practices related to this
1436 issue should be considered when developing a biospecimen resource:

- 1437 • Biospecimen resources that plan to store identifiable biospecimens from children
1438 should consult with their IRB during planning and development of the resource to
1439 determine whether future research uses of stored biospecimens are likely to constitute
1440 no more than minimal risk. If future uses of identifiable stored biospecimens are likely
1441 to constitute greater than minimal risk, biospecimen resources should develop
1442 procedures for recontacting human research participants to obtain consent at the age of
1443 majority and ensuring that accurate contact information is maintained. Where
1444 practicable, human research participants should be recontacted for consent by an
1445 individual or institution with which they have an ongoing relationship.

⁷ See the OHRP frequently asked questions related to this topic at: <http://www.dhhs.gov/ohrp/informedconsfaq.pdf>.

- 1446
- 1447
- 1448
- Permission and/or assent documents for contribution of pediatric biospecimens for research should state whether recontact and consent will be attempted once the child reaches the age of majority.
- 1449
- Community engagement should be considered when planning a biospecimen resource that will store identifiable biospecimens and/or data from children, if appropriate. Community engagement may range from public forums to inclusion of patient advocates or community representatives on access or governance committees. As part of biospecimen resource planning activities, input from the affected community may be sought in regard to the perceived risk-benefit ratio of the proposed research and whether a waiver of consent or consent at age of majority would be preferable. Community engagement may be unnecessary or inappropriate in some cases, such as for the use of archived biospecimens or for minimal-risk research.
- 1450
- 1451
- 1452
- 1453
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- 1455
- 1456
- 1457

1458 **C.3. Privacy and Confidentiality Protections**

1459 Biospecimen research depends on protecting the privacy of individuals who contribute
1460 biospecimens and on maintaining the confidentiality of associated clinical data and information
1461 (Eiseman et al. 2003). Applying the highest possible ethical standards is necessary to ensure the
1462 support and participation of human research participants, physicians, researchers, and others in
1463 biospecimen resource activities (Friede et al. 2003). With the recent advances in genomic and
1464 proteomic technology, the sequencing of the human genome, and the increasing reliance of
1465 biospecimen resources on electronic and Web-based databases for data tracking, it is even more
1466 crucial to address the risk of breaches in privacy. The unintended release or disclosure of
1467 sensitive information can place individuals at risk for discrimination and related groups at risk
1468 for stigmatization although the frequency of these types of harms is unknown.

1469 ***C.3.1. Federal Regulations Pertaining to Privacy***

1470 The DHHS-issued regulation titled “Standards for Privacy of Individually Identifiable Health
1471 Information,” commonly known as the HIPAA Privacy Rule (see [45 CFR Part 160](#) and Subparts
1472 [A](#) and [E](#) of Part 164), was created to protect the privacy of health information that identifies an
1473 individual while still allowing other activities of benefit to society, such as research. While the
1474 HIPAA Privacy Rule does not apply to biospecimens directly, it may affect biospecimen
1475 resources that are considered covered entities in that human specimens often are accompanied by
1476 identifiable protected health information.

1477 If the biospecimen resource is considered a covered entity under HIPAA, compliance with the
1478 regulation titled “Security Standards for the Protection of Electronic Protected Health
1479 Information,” commonly known as the Security Rule, is required to ensure appropriate security
1480 of electronic protected health information (PHI) (see [45 CFR Part 160](#) and [Part 164](#) Subparts [A](#)
1481 and [C](#)). Detailed information on the HIPAA Security Rule is available at
1482 <http://www.hhs.gov/ocr/privacy/hipaa/administrative/securityrule/index.html>.

1483 The Health Information Technology for Economic and Clinical Health (HITECH) Act was
1484 enacted on February 17, 2009, as Title XIII of Division A and Title IV of Division B of the
1485 American Recovery and Reinvestment Act of 2009. Portions of the HITECH Act will impact the
1486 provisions and implementation of the HIPAA Privacy Rule and Security Rule. For current

1487 information about the HITECH Act as well as detailed information on the HIPAA Privacy Rule,
1488 see <http://www.hhs.gov/ocr/privacy>.

1489 **C.3.2. NCI Recommendations Pertaining to Privacy and Confidentiality**

1490 **C.3.2.1.**

1491 Biospecimen resources should establish clear policies for protecting the confidentiality of
1492 identifiable information. These policies may include data encryption, coding, establishing
1493 limited access or varying levels of access to data by biospecimen resource employees, and
1494 use of nondisclosure agreements. An honest broker–guided procedure, if appropriate, should
1495 be considered for sharing of samples and data to protect research participants’ privacy (Merz
1496 et al. 1997). The informatics system and not necessarily an individual can function as the
1497 honest broker.

1498 **C.3.2.2.**

1499 Biospecimen resources may apply for “certificates of confidentiality” to protect identifiable
1500 research information from forced disclosure. Under section 301(d) of the Public Health
1501 Service Act ([42 USC 241\(d\)](#)), the NIH may issue certificates of confidentiality to authorize
1502 persons engaged in biomedical, behavioral, clinical, or other research to refuse to disclose
1503 identifying information about human research participants in any Federal, State, or local
1504 civil, criminal, administrative, legislative, or other proceeding. Certificates of confidentiality
1505 should be considered by the biospecimen resource and/or the recipient investigator
1506 depending on the nature and sensitivity of the identifiable data associated with the specimen.
1507 Certificates of confidentiality may not be appropriate for all biospecimen resources. If a
1508 certificate of confidentiality is obtained, this should be explicitly stated in the informed
1509 consent document. Further information about certificates of confidentiality may be found at
1510 <http://grants2.nih.gov/grants/policy/coc/index.htm>.

1511 **C.3.2.3.**

1512 Biospecimen resources should document their policies for maintaining the privacy of human
1513 research participants and the confidentiality of associated clinical data, including descriptions
1514 of mechanisms for auditing effectiveness, enforcement measures, and required training for
1515 employees. The level of security should be appropriate to the type of biospecimen resource
1516 and the sensitivity of the data it houses.

1517 **C.3.2.4.**

1518 Biospecimen resources should comply with all applicable State and local statutes and
1519 regulations pertaining to privacy.

1520 **C.3.2.5.**

1521 Biospecimen resources should use a system of data access with defined levels of access
1522 privileges for biospecimen resource staff in order to protect the confidentiality of human
1523 research participants’ data, if necessitated by data type and sensitivity.

- 1524 • Access levels for biospecimen resource staff should be described in the protocol for
1525 operation of the biospecimen resource and approved by an IRB and/or a
1526 bioethics/scientific advisory board, as appropriate.
- 1527 • Access to human research participants' identities and medical, genetic, social, and
1528 personal histories should be restricted to only those biospecimen resource staff
1529 members who need to access such records as part of their assigned duties or to those
1530 persons permitted access by law.
- 1531 • The number of personnel allowed to access links and reidentify information should be
1532 kept to a minimum, and access should be appropriately monitored to ensure
1533 compliance.

1534 **C.4. Access to Biospecimens and Data**

1535 Timely access to human specimens and data is crucial for research fields such as genomics,
1536 proteomics, metabolomics, molecular imaging, and nanotechnology. Researchers in these areas
1537 often rely on federally funded biospecimen resources for high-quality biospecimens and
1538 associated data. To best serve the needs of the research community, biospecimen resources
1539 should establish guidelines for sample distribution and clinical data sharing consistent with
1540 ethical principles; governing statutes and regulations; and, if applicable, informed consent
1541 language. These guidelines should have the following characteristics:

- 1542 • *Clear* to ensure their comprehension and adoption;
- 1543 • *Flexible* to allow application to diverse and evolving scientific needs; and
- 1544 • *Amendable* to facilitate their adaptability over time.

1545 In addition, the guidelines established by biospecimen resources should delineate when
1546 biospecimens and clinical data are narrowly or broadly accessible and what justifications should
1547 be provided in the access requests to the biospecimen resources. These guidelines should apply
1548 to all new collections and, whenever practicable, to existing collections.

1549 **C.4.1.**

1550 Access decisions should be guided by the following general principles, as appropriate:

- 1551 • Timely, equitable, and appropriate access to human specimens without undue
1552 administrative burden.
- 1553 • Scientific merit and institutional research qualifications, proven investigator
1554 experience with the proposed method, and a research plan appropriate to answer the
1555 study question.
- 1556 • Community attitudes and ethical/legal considerations as primary factors.
- 1557 • Fair, transparent, and clearly communicated access procedures.
- 1558 • Appropriate allocation of specimens based on the nature of the scientific investigation
1559 (e.g., discovery, prevalence, initial validation, and hypothesis testing) and the need for
1560 annotation. The level of identifiability of the biospecimen and related transfer
1561 documents should be appropriate for the proposed research.

- 1562
- A mechanism for addressing disputes over allocation decisions.
- 1563
- An investigator agreement covering confidentiality, use, disposition, and security of
- 1564
- data.
- 1565
- The parties' written agreement in an MTA or other appropriate document that is
- 1566
- consistent, as applicable, with the [NIH Research Tools Policy](#) and other applicable
- 1567
- [NIH sharing policies](#).

1568 **C.4.2.**

1569 A scientifically sound and appropriate research plan should be included in access requests. If
1570 applicable to the study design and biospecimen resource purpose, the following specific issues
1571 are among those to be considered by the biospecimen resource in access decisions:

- 1572
- Use of standardized, validated research biomarker assay methodology.
- 1573
- Statistical evaluation that shows that the study question can be addressed with the
- 1574
- samples available and, if applicable, a negotiated arrangement with a clinical protocol
- 1575
- coordinating group to provide timely statistical analysis of study results.
- 1576
- Compliance with protocol-specific requirements needed to achieve study goals before
- 1577
- other access is considered.
- 1578
- Confirmation that an investigator has defined funding and IRB approval for the
- 1579
- project, if applicable (for information on application for and exemption from IRB
- 1580
- approval, see OHRP guidance at <http://www.hhs.gov/ohrp/policy/index.html#human>).
- 1581
- Agreement that the investigator will publish or provide public information about the
- 1582
- project outcome according to applicable NIH policies, which may include the
- 1583
- Research Tools Policy, and the [Revised Policy on Enhancing Public Access to](#)
- 1584
- [Archived Publications Resulting from NIH-Funded Research](#). Of note, the NIH
- 1585
- Research Tools Policy permits reasonable short-term publication delays; e.g., to file a
- 1586
- patent or allow a collaborator to review a manuscript.

1587 **C.4.3.**

1588 Appropriate policies should be developed to ensure that researchers' access to biospecimens and
1589 associated clinical data is appropriate and in compliance with all applicable Federal and State
1590 privacy and human subjects regulations and statutes as well as the human research participant's
1591 informed consent. The following issues should be considered when developing access policies:

- 1592
- Inclusion of appropriate provisions for the security of biospecimens and
- 1593
- confidentiality of associated data in the usage agreement between the biospecimen
- 1594
- resource and the researcher. For OHRP guidance on the use of coded biospecimens
- 1595
- and data, see <http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.htm>.
- 1596
- Consistency of the MTA or other appropriate document, as applicable, with the [NIH](#)
- 1597
- [Research Tools Policy](#) and other applicable [NIH sharing policies](#).
- 1598
- Development of an informatics system to facilitate use or disclosure of biospecimens
- 1599
- consistent with the research participant's permission for the use of his/her

1600 biospecimens, including procedures to identify if and when that research participant
1601 has revoked consent for future research use.

1602 **C.4.4.**

1603 Appropriate models of biospecimen resource sustainability should emphasize accessibility to
1604 biospecimens and data and sustainability of the biospecimen resource within a framework that
1605 maintains public trust. These models should account for potential loss of funding; i.e., a legacy
1606 plan should be in place. (Also see [Section C.1.2.](#)) For example, in a cost-recovery model, charges
1607 for samples, if any, are used only to recover reasonable costs associated with operation of the
1608 biospecimen resource and not to generate undue profit for the biospecimen resource.
1609 Biospecimen resource sustainability models other than cost recovery (e.g., a collaborative
1610 agreement model involving more than one approved funding partner) may also be considered to
1611 support a biospecimen resource over the long term. Note that receipt of Government funding,
1612 regardless of other financial sources, results in the expectation that biospecimens and resulting
1613 research resources and data will be available, consistent with applicable NIH sharing policies
1614 (for example, see <http://sharing.nih.gov>).

1615 **C.4.5.**

1616 The existence of biospecimens may be made public through the resource's Web site itself and/or
1617 through well-known resources such as the [NCI Specimen Resource Locator](#), which serves as a
1618 directory of biospecimen resources. Restrictions on accessibility to stored biospecimens should
1619 be indicated in these tools. In addition, biospecimen resources should encourage investigators to
1620 indicate the source of the biospecimens when research data resulting from the use of
1621 biospecimens are published.

1622 **C.5. Intellectual Property and Resource Sharing**

1623 Inventions and data arising from research using annotated biospecimens may have commercial
1624 value. As researchers and industry sponsors have sharply increased their demand for properly
1625 prepared and clinically annotated biospecimens, some institutions have begun to assert control
1626 over biospecimens, associated data, and research findings. The current variability in intellectual
1627 property (IP) policies at institutions hosting research and biospecimen resources may ultimately
1628 lead to problems in biospecimen and data access, timely and open publication, sharing of
1629 research findings, and establishment of new biospecimen resources. Sharing of research data
1630 obtained through use of biospecimens and associated research materials (e.g., derivatives) is
1631 essential for the advancement of science. Accordingly, research data and tools generated through
1632 the use of biospecimens should be shared in a timely manner and, to the greatest extent possible,
1633 in a manner consistent with applicable NIH sharing policies (for example, see
1634 <http://sharing.nih.gov>).

1635 **C.5.1.**

1636 An agreement (e.g., MTA or contract) with terms consistent, as applicable, with the [NIH](#)
1637 [Research Tools Policy](#), the [NIH Data Sharing Policy](#), and other applicable [NIH sharing policies](#)
1638 should be used for the transfer of materials among academic, nonprofit, and/or industrial
1639 organizations (see [Appendix 4](#) for a sample MTA). Clinical protocols are not designed to

1640 document material transfers and are usually inappropriate for this purpose. Examples of
1641 agreements that capture the basic principles of the NIH policies above are the NIH Simple Letter
1642 of Agreement and the Uniform Biological Material Transfer Agreement. However, these
1643 agreements are insufficient for the transfer of human specimens without appropriate
1644 modification. Desirable terms in an MTA for the transfer of biospecimens include the following:

- 1645 • Clear descriptions of the biospecimens and/or unmodified functional derivatives
1646 thereof (e.g., DNA and RNA) and identification of the institutions involved;
- 1647 • Clear identification of the human subjects status of the biospecimens and associated
1648 obligations;
- 1649 • Agreement to abide by appropriate laws, rules, and regulations associated with human
1650 subjects research and private information;
- 1651 • Acknowledgement of the recipient’s right, or lack thereof, to further distribute the
1652 biospecimens;
- 1653 • Assurances of the end user’s academic freedom and the right to publish research
1654 results will not be hindered by the biospecimen resource; IP terms consistent with, as
1655 applicable and permissible, the basic principles of the [NIH Research Tools Policy](#) and
1656 other applicable [NIH sharing policies](#), such as no reach-through by the biospecimen
1657 resource to end users’ IP and the sharing of research resources and data by the end-
1658 user with the research community;
- 1659 • Description of any expectations regarding the dissemination of research data; and
1660 • Conditions, or limitations, on commercial use, if any.

1661 The following Web pages are relevant to this issue:

- 1662 • <http://sharing.nih.gov>
- 1663 • http://ott.od.nih.gov/policy/research_tool.html
- 1664 • <http://tinyurl.com/AUTM-UMBTA>
- 1665 • http://grants.nih.gov/grants/policy/data_sharing/
- 1666 • http://cabig-ut.nci.nih.gov/working_groups/DSIC_SLWG

1667 **C.5.2.**

1668 Generally, biospecimen resource staff, as custodians of biospecimens, will not be considered a
1669 priori inventors under patent law for inventions made using materials distributed by the
1670 biospecimen resource. In general, one whose sole contribution to an invention consists of the
1671 routine collection, handling, storage, and disbursement of biospecimens might not rise to the
1672 level of “inventor.” Inventorship is determined by patent law and is considered on a case-by-case
1673 basis by legal personnel.

1674 **C.5.3.**

1675 Generally, biospecimen resources have no inherent rights to future IP of end-users, such as
1676 reach-through rights to inventions made by investigators using samples obtained from the
1677 biospecimen resource.

1678 **C.5.4.**

1679 When IP resulting from biospecimen research is exclusively licensed, a research use license
 1680 should be retained that allows nonprofit and Government research use and ensures access to
 1681 resources and data for research and educational purposes.

1682 **C.5.5.**

1683 Through MTAs or other appropriate documents, research data and research resources obtained
 1684 using biospecimens should be made available to the research community to the greatest extent
 1685 possible, consistent with, as applicable, the [NIH Data Sharing Policy](#), other applicable [NIH](#)
 1686 [sharing policies](#), and the [NIH Research Tools Policy](#). Consistent with the applicable NIH
 1687 policies, completed data sets and resources should be released in a timely fashion; i.e., no later
 1688 than acceptance for publication of the main findings from the final data set. To promote future
 1689 biomedical research, data and resources developed with biospecimens would be retained only as
 1690 long as necessary for legitimate and imminent research purposes. Information that is identifiable
 1691 or linked to a specific individual should be shared under an agreement with appropriate privacy
 1692 safeguards and adherence to applicable legal requirements. A reasonable delay to ensure an
 1693 investigator's publication priority or to secure IP protection is acceptable.

1694 **C.6. Conflicts of Interest**

1695 A financial COI exists, according to Public Health Service (PHS) regulations, when a designated
 1696 institutional official(s) reasonably determines that an extramural Investigator's significant
 1697 financial interest could directly and significantly affect the design, conduct, or reporting of PHS-
 1698 funded research (42 CFR § 50, Part F and 45 CFR § 94).⁸ An Investigator is defined by these
 1699 regulations as the principal investigator and any other person who is responsible for the design,
 1700 conduct, or reporting of research funded by PHS or proposed for such funding. For purposes of
 1701 the requirements of the regulations, the term Investigator includes the Investigator's spouse and
 1702 dependent children. Generally, it is the awardee institution that is responsible for maintaining
 1703 compliance with the requirements of the regulations, identifying and managing Investigator
 1704 Financial Conflicts of Interest and reporting them to the PHS-awarding component. Investigators
 1705 disclose their Significant Financial Interests, as defined in 42 CFR § 50.63 and 45 CFR § 94.3, to
 1706 their institutions. Extramural investigators conducting biospecimen research activities supported
 1707 by PHS grants, cooperative agreements, or research contracts are subject to the requirements of
 1708 these regulations (see the [NIH Office of Extramural Research](#) Web site for more information on
 1709 COIs). Federal employees are subject to different regulations related to COI, as described in 18
 1710 USC 208, the Standards of Ethical Conduct for Employees of the Executive Branch and agency-
 1711 specific regulations (see the [NIH Conflict of Interest](#) Web site for more information related to
 1712 federal employees).

⁸ NIH is currently in the process of proposed rule-making related to Responsibility of Applicants for Promoting Objectivity in Research for Which Public Health Service Funding Is Sought and Responsible Prospective Contractors. The *NCI Best Practices* will be updated as needed once these regulations are finalized.

1713 **C.6.1.**

1714 The regulations governing extramural research contain examples of conditions or restrictions that
1715 might be imposed by an awardee institution to manage Investigator financial conflicts of interest,
1716 which includes public disclosure of a significant financial interest. The responsibility of COI
1717 management rests with the awardee institution as described in the regulations. Awardee
1718 institutions and Investigators should adhere to institutional and PHS regulations governing COIs.

1719 **C.6.2.**

1720 Institutional financial COIs should be considered and managed as appropriate. Any known or
1721 likely financial benefit to the institution or biospecimen resource should be disclosed
1722 accordingly, for example on the biospecimen resource Web site or in a clear and concise manner
1723 in a brochure that accompanies the informed consent document. (Also see [Section C.2.3](#), NCI
1724 Recommendations on Key Informed Consent Elements and Supplementary Materials.)

1725 **C.6.3.**

1726 Nonfinancial COIs should be identified and managed to the extent practicable. An example of a
1727 nonfinancial COI includes situations in which the individual managing the biospecimen resource
1728 is also a researcher seeking access to biospecimens. In cases where nonfinancial COIs are
1729 unavoidable (e.g., small biospecimen collections), biospecimen resources should manage the
1730 COIs by adhering to NIH policies and, if deemed necessary, publicly disclosing the COIs; e.g.,
1731 via the resource's Web site or written materials.

1732

1733 **References**

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 1758 [molecular epidemiological studies. *Mutation Res*. 2003;543:217-34.](#)
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 1764 [Practices for Repositories: Collection, Storage, Retrieval and Distribution of Biological](#)
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1798

1799 **Web Resources⁹**

1800 **Code of Federal Regulations**

1801 Government Printing Office Access

1802 <http://www.gpoaccess.gov/cfr/index.html>

1803 **Conflict of Interest**

1804 Conflict of Interest

1805 NIH Office of Extramural Research

1806 <http://grants.nih.gov/grants/policy/coi/>

1807

1808 Conflict of Interest Information and Resources, NIH

1809 http://www.nih.gov/about/ethics_COI.htm

1810

1811 **Electronic Records and Electronic Signatures**

1812 Electronic Records; Electronic Signatures

1813 Office of Regulatory Affairs, U.S. Food and Drug Administration

1814 <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=11&showFR=1>

1815 **Health Information Portability and Accountability Act of 1996**

1816 HIPAA Security Rule

1817 Centers for Medicare and Medicaid Services

1818 Department of Health and Human Services

1819 <http://www.cms.gov/HIPAAGenInfo/>

1820

1821 Medical Privacy–National Standards to Protect the Privacy of Personal Health Information

1822 Office for Civil Rights–HIPAA

1823 Office for Civil Rights

1824 Department of Health and Human Services

1825 <http://www.hhs.gov/ocr/hipaa/>

1826 **Human Subjects Regulations**

1827 Application for and exemption from IRB approval

1828 Office for Human Research Protections

1829 Department of Health and Human Services

1830 <http://www.hhs.gov/ohrp/policy/index.html#human>

1831 Frequently asked questions

1832 Office for Human Research Protections

1833 Department of Health and Human Services

⁹ All listed Web sites were accessed on June 23, 2010.

- 1834 <http://www.dhhs.gov/ohrp/informedconsfaq.pdf>
- 1835 Genetic Discrimination Fact Sheet
- 1836 <http://www.genome.gov/10002328>
- 1837 Genetic Information Nondiscrimination Act of 2008
- 1838 <http://thomas.loc.gov/cgi-bin/bdquery/z?d110:h.r.00493:>
- 1839 Guidance on the Genetic Information Nondiscrimination Act: Implications for Investigators and
- 1840 Institutional Review Boards
- 1841 <http://www.hhs.gov/ohrp/humansubjects/guidance/gina.html>
- 1842 Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human
- 1843 Specimens That are Not Individually Identifiable
- 1844 Food and Drug Administration
- 1845 <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm078384.htm>
- 1846 Guidance on Research Involving Coded Private Information or Biological Specimens
- 1847 Office for Human Research Protections
- 1848 Department of Health and Human Services
- 1849 <http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.htm>
- 1850 <http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm>
- 1851 Human Subjects Policy Guidance
- 1852 Office for Human Research Protections
- 1853 Department of Health and Human Services
- 1854 <http://www.hhs.gov/ohrp/policy/index.html#human>
- 1855 Office for Human Research Protections
- 1856 Department of Health and Human Services
- 1857 <http://www.hhs.gov/ohrp/>
- 1858 **Informed Consent Policy Guidance**
- 1859 Issues to Consider in the Research Use of Stored Data or Tissues
- 1860 Office for Human Research Protections
- 1861 Department of Health and Human Services
- 1862 <http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm>
- 1863 Office for Human Research Protections
- 1864 Department of Health and Human Services
- 1865 <http://www.hhs.gov/ohrp/policy/index.html#informed>
- 1866 Policies for responding to requests for discontinuation of participation in research
- 1867 Office for Human Research Protections
- 1868

- 1869 Department of Health and Human Services
1870 <http://www.hhs.gov/ohrp/requests/200811guidance.pdf>
1871 <http://edocket.access.gpo.gov/2008/pdf/E8-28387.pdf>
- 1872 **Informatics Interoperability**
- 1873 caGrid
1874 <http://cagrid.org/display/cagridhome/Home>
- 1875 Cancer Data Standards Repository
1876 <https://cabig.nci.nih.gov/concepts/caDSR/>
- 1877 Specimen Resource Locator
1878 <http://biospecimens.cancer.gov/locator>
- 1879 **Informatics System Development**
- 1880 Capability Maturity Model Integration
1881 Carnegie Mellon[®] Software Engineering Institute
1882 <http://www.sei.cmu.edu/cmml/>
- 1883 **Informatics System Security**
- 1884 Risk Management Guide for Information Technology Systems
1885 National Institute of Standards and Technology
1886 <http://csrc.nist.gov/publications/nistpubs/>
- 1887 **Laboratory Practices**
- 1888 Clinical Laboratory Improvement Amendment
1889 <http://wwwn.cdc.gov/clia/regs/toc.aspx>
- 1890 Good Laboratory Practices
1891 http://www.oecd.org/document/63/0,2340,en_2649_34381_2346175_1_1_1_1,00.html
- 1892 International Organization for Standardization (ISO9000)
1893 <http://www.iso.org/iso/home.htm>
- 1894 ISBER
1895 <http://www.isber.org>
- 1896 U.S. Food and Drug Administration (FDA) Quality System Regulation, 21 CFR 820
1897 <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm>
- 1898 **National Cancer Institute**
- 1899 Biospecimen Research Network
1900 <http://biospecimens.cancer.gov/researchnetwork/>

- 1901 cancer Biomedical Informatics Grid®
1902 <https://cabig.nci.nih.gov/>
- 1903 cancer Biomedical Informatics Grid® Enterprise Support Network
1904 <http://cabig.nci.nih.gov/esn/>
- 1905 Data Sharing and Intellectual Capital Workspace
1906 http://cabig-ut.nci.nih.gov/working_groups/DSIC_SLWG
- 1907 National Biospecimen Network Blueprint
1908 <http://biospecimens.cancer.gov/archive/resources/reports/nbn.asp>
- 1909 *NCI Best Practices* Frequently Asked Questions
1910 <http://biospecimens.cancer.gov/practices/faq.asp>
- 1911 Office of Biorepositories and Biospecimen Research
1912 <http://biospecimens.cancer.gov/>
- 1913 Symposium-Workshop on Custodianship and Ownership Issues in Biospecimen Research
1914 <http://biospecimens.cancer.gov/archive/resources/workshop/cow.asp>
- 1915 **National Institutes of Health Policies and Guidelines**
- 1916 Certificates of Confidentiality Kiosk
1917 Office of Extramural Research
1918 National Institutes of Health
1919 <http://grants2.nih.gov/grants/policy/coc/index.htm>
- 1920 Conflict of Interest
1921 Office of Extramural Research
1922 National Institutes of Health
1923 <http://grants.nih.gov/grants/policy/coi/>
- 1924 Guidelines for Research Involving Recombinant DNA Molecules
1925 Office of Biotechnology Activities
1926 National Institutes of Health
1927 <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-052.html>
- 1928 NIH Data Sharing Policy
1929 Office of Extramural Research
1930 National Institutes of Health
1931 http://grants.nih.gov/grants/policy/data_sharing/
- 1932 NIH Research Tools Policy
1933 Sharing Biomedical Research Resources: Principles and Guidelines for Recipients of NIH
1934 Research Grants and Contracts

- 1935 Office of Technology Transfer
1936 National Institutes of Health
1937 http://ott.od.nih.gov/policy/research_tool.html

1938 **Other Biospecimen Resource References**

- 1939 Case Studies of Existing Human Tissue Repositories—“Best Practices” for a Biospecimen
1940 Resource for the Genomic and Proteomic Era
1941 <http://biospecimens.cancer.gov/archive/resources/reports/csehtr.asp>
1942 <http://www.rand.org/pubs/monographs/MG120/index.html>

- 1943 Handbook of Human Tissue Sources—A National Resource of Human Tissue Samples
1944 http://www.rand.org/pubs/monograph_reports/MR954/

1945 **Uniform Biological Material Transfer Agreement**

- 1946 UBMTA Federal Register
1947 <http://www.nhlbi.nih.gov/resources/tt/docs/ubmta.pdf>

1948

1949 **Glossary of Terms**

1950 This glossary is included to provide instruction as to how terms used in the *NCI Best Practices*
1951 *for Biospecimen Resources* should be interpreted. Wherever possible, standardized definitions
1952 from Federal documents and/or the NCI Thesaurus were used.¹⁰ Where such sources were not
1953 available or appropriate, definitions were selected from widely used texts, such as *Black's Law*
1954 *Dictionary* (8th ed.), *Taber's Cyclopedic Medical Dictionary* (20th ed.), Merriam-Webster's
1955 Online Dictionary; reports specific to biospecimen resources, such as ISBER *Best Practices for*
1956 *Repositories, Second Edition* (2008), and RAND Corporation's *Case Studies of Existing Human*
1957 *Tissue Repositories* (2003); or relevant Web sites such as the CDC Web site. The citation "*NCI*
1958 *Best Practices working definition*" refers to definitions drafted specifically for this document by
1959 the NCI in consultation with appropriate experts. In some cases, two definitions may be listed for
1960 a single term to convey both a general and a biospecimen resource-specific meaning or to
1961 provide definitions from two Federal regulations. Where two definitions are listed, the first
1962 definition contains the meaning most relevant to the *NCI Best Practices*.

1963 **Access.** The right to obtain or make use of or take advantage of something (as services or
1964 membership); the right to enter. (NCI Thesaurus).

1965 **Aerosol.** A fine mist or spray that contains minute particles (Centers for Disease Control and
1966 Prevention Special Pathogens Branch, Glossary of Terms,
1967 <http://www.cdc.gov/ncidod/dvrd/spb/mnpages/glossary.htm>).

1968 **Age of majority.** The age—usually 18 or 21 years—at which a person achieves full legal rights
1969 to make one's own decisions, enter into contracts, and be held personally accountable for the
1970 consequences of one's actions (Taber's Medical Dictionary).

1971 **Aliquot.** 1. Pertaining to a portion of the whole; any one of two or more samples of something,
1972 of the same volume or weight (NCI Thesaurus). 2. A process wherein a specimen is divided into
1973 separate parts which are typically stored in separate containers as individual samples (ISBER
1974 2008).

1975 **Analyte.** A substance or chemical constituent that is determined in an analytical procedure
1976 (ISBER 2008).

1977 **Annotation.** Explanatory information associated with a biospecimen (*NCI Best Practices*
1978 working definition).

1979 **Assay.** A qualitative or quantitative analysis performed to determine the amount of a particular
1980 constituent in a biospecimen (adapted from NCI Thesaurus).

¹⁰ A collaborative effort of the NCI Office of Communications and the NCI Center for Bioinformatics to standardize terminology within the NCI, available at <http://ncit.nci.nih.gov/>.

- 1981 **Associated data.** Any factual information affiliated with a biospecimen, including but not
1982 limited to research, phenotypic, clinical, epidemiologic, and biospecimen-resource procedural
1983 data (*NCI Best Practices* working definition).
- 1984 **Audit.** 1. A documented review of procedures, records, personnel functions, equipment
1985 materials, facilities, and/or vendors to evaluate adherence to written standard operating
1986 procedures or government laws and regulations (ISBER 2008). 2. To perform an audit (Merriam-
1987 Webster's Online Dictionary).
- 1988 **Barcode.** A machine-readable representation of information in a visual format on a surface (NCI
1989 Thesaurus).
- 1990 **Best practice.** A technique, process, or protocol that has been shown or is otherwise believed to
1991 be state-of-the-science in that it provides superior results to those achieved by any other
1992 technique, process, or protocol. Best practices may evolve as new evidence emerges. While best
1993 practices are consistent with all applicable ethical, legal, and policy statutes, regulations, and
1994 guidelines, they differ from guidance, policy, or law in that they are recommendations and are
1995 neither enforced nor required (*NCI Best Practices* working definition).
- 1996 **Biohazard.** A biological or chemical substance that exerts toxic or pathologic effects on living
1997 entities (NCI Thesaurus).
- 1998 **Biomarker.** A biological molecule found in blood, other body fluids, or tissues that is a sign of a
1999 normal or abnormal process, or of a condition or disease. A biomarker may be used to see how
2000 well the body responds to a treatment for a disease or condition. Also called molecular marker
2001 and signature molecule (NCI Online Cancer Dictionary).
- 2002 **Biomolecule.** An organic molecule and especially a macromolecule (as a protein or nucleic acid)
2003 in living organisms (Merriam-Webster's Online Dictionary).
- 2004 **Biorepository.** An organization, place, room, or container (a physical entity) where
2005 biospecimens are stored. In the context of the *NCI Best Practices*, only biorepositories
2006 containing human specimens intended for research purposes (research biorepositories) are
2007 addressed. The physical structure, policies, biospecimens, and data contained within it are
2008 defined collectively as a biospecimen resource, defined below (*NCI Best Practices* working
2009 definition).
- 2010 **Biosafety.** Safety with respect to the effects of biological research on humans and the
2011 environment (Merriam-Webster's Online Dictionary).
- 2012 **Biosafety level.** Specific combinations of work practices, safety equipment, and facilities, which
2013 are designed to minimize the exposure of workers and the environment to infectious agents.
2014 Biosafety level 1 applies to agents that do not ordinarily cause human disease. Biosafety level 2
2015 is appropriate for agents that can cause human disease, but whose potential for transmission is
2016 limited. Biosafety level 3 applies to agents that may be transmitted by the respiratory route which
2017 can cause serious infection. Biosafety level 4 is used for the diagnosis of exotic agents that pose
2018 a high risk of life-threatening disease, which may be transmitted by the aerosol route and for
2019 which there is no vaccine or therapy (Centers for Disease Control and Prevention Special

- 2020 Pathogens Branch, Glossary of Terms,
2021 <http://www.cdc.gov/ncidod/dvrd/spb/mnpages/glossary.htm>).
- 2022 **Biospecimen.** A quantity of tissue, blood, urine, or other human-derived material. A single
2023 biopsy may generate several biospecimens, including multiple paraffin blocks or frozen
2024 biospecimens. A biospecimen can comprise subcellular structures, cells, tissue (e.g. bone,
2025 muscle, connective tissue, and skin), organs (e.g., liver, bladder, heart, and kidney), blood,
2026 gametes (sperm and ova), embryos, fetal tissue, and waste (urine, feces, sweat, hair and nail
2027 clippings, shed epithelial cells, and placenta). Portions or aliquots of a biospecimen are referred
2028 to as samples (*NCI Best Practices* working definition).
- 2029 **Biospecimen resource.** A collection of human specimens and associated data for research
2030 purposes, the physical entity in which the collection is stored, and all associated processes and
2031 policies. Biospecimen resources vary considerably, ranging from formal institutions to informal
2032 collections in a researcher’s freezer (*NCI Best Practices* working definition).
- 2033 **Biospecimen resource governance.** The set of authorities, processes, and procedures guiding
2034 key operational decisions made within the resource. Governance affects access to biospecimens
2035 as well as custodial relationships and responsibilities and should be part of the resource’s general
2036 custodianship plan (*NCI Best Practices* working definition).
- 2037 **Biospecimen resource informatics system.** The software, hardware, documentation, support,
2038 operating procedures, and training necessary to annotate, track, and distribute biospecimens
2039 within a biospecimen resource or resources (*NCI Best Practices* working definition).
- 2040 **Bloodborne pathogen.** Pathogenic microorganisms that are present in human blood and can
2041 cause disease in humans. These pathogens include, but are not limited to, hepatitis B virus and
2042 human immunodeficiency virus (Occupational Safety and Health Administration Bloodborne
2043 Pathogen Standards, [29 CFR § 1910.1030](#)).
- 2044 **cancer Biomedical Informatics Grid (caBIG®).** A voluntary network or grid connecting
2045 individuals and institutions to enable the sharing of data and tools, creating a World Wide Web
2046 of cancer research. The goal is to speed the delivery of innovative approaches for the prevention
2047 and treatment of cancer. The infrastructure and tools created by caBIG® also have broad utility
2048 outside the cancer community. caBIG® is being developed under the leadership of the National
2049 Cancer Institute’s Center for Bioinformatics (NCI Thesaurus). For more information, visit
2050 <https://cabig.nci.nih.gov>.
- 2051 **cancer Biomedical Informatics Grid (caBIG®) compatibility.** Refers to meeting caBIG®
2052 requirements. To aid in the creation of software that will be able to interoperate within the
2053 caBIG® program, a set of compatibility guidelines was developed that spells out requirements
2054 for interoperability in areas of Interface Integration, Vocabularies/Terminologies and Ontologies,
2055 Information Models and Data Elements. Systems that meet the requirements are said to be
2056 “caBIG® compatible.”
- 2057 **cancer Data Standards Repository (caDSR).** The database that hosts common data elements
2058 and information models developed by various NCI-sponsored organizations. caDSR tools
2059 facilitate the search and retrieval of common data elements and models. caDSR is the single,

2060 authoritative source of common data (*NCI Best Practices* working definition). For more
2061 information, visit http://ncicb.nci.nih.gov/NCICB/infrastructure/cacore_overview/cadsr.

2062 **Capability Maturity Model Integration (CMMI).** A process improvement approach that
2063 provides organizations with the essential elements of effective processes. It can be used to guide
2064 process improvement across a project, a division, or an entire organization. CMMI helps
2065 integrate traditionally separate organizational functions, set process improvement goals and
2066 priorities, provide guidance for quality processes, and provide a point of reference for appraising
2067 current processes (Carnegie Mellon[®] Software Engineering Institute CMMI Web site,
2068 <http://www.sei.cmu.edu/cmmi/>).

2069 **Certificate of Confidentiality.** Issued by the National Institutes of Health (NIH) to protect
2070 identifiable research information from forced disclosure. It allows the Investigator and others
2071 who have access to research records to refuse to disclose identifying information on research
2072 participants in any civil, criminal, administrative, legislative, or other proceeding, whether at the
2073 Federal, State, or local level. Certificates of Confidentiality may be granted for studies collecting
2074 information that, if disclosed, could have adverse consequences for subjects or damage their
2075 financial standing, employability, insurability, or reputation (Certificates of Confidentiality
2076 Kiosk Web site, <http://grants.nih.gov/grants/policy/coc/>).

2077 **Clinical data.** 1. Factual information (as measurements or statistics) or observations relating to
2078 the patient used as a basis for reasoning, discussion, or calculation pertaining to clinical trials,
2079 diagnosis, or treatment (*NCI Best Practices* working definition). 2. Data obtained through patient
2080 examination or treatment (NCI Thesaurus).

2081 **Clinical research.** Research conducted with human subjects or on material of human origin in
2082 which an investigator directly interacts with human subjects; includes development of new
2083 technologies, study of mechanisms of human diseases, therapy, clinical trials, epidemiology,
2084 behavior and health services research (NCI Thesaurus).

2085 **Code of Federal Regulations (CFR).** The annual collection of executive-agency regulations
2086 published in the daily *Federal Register*, combined with previously issued regulations that are still
2087 in effect (Black's Law Dictionary). See <http://www.gpoaccess.gov/cfr/index.html> for more
2088 information.

2089 **Coded.** Having (1) identifying information (such as name or Social Security number) that would
2090 enable the investigator to readily ascertain the identity of the individual to whom the private
2091 information or specimens pertain has been replaced with a number, letter, symbol, or
2092 combination thereof (i.e., the code); and (2) a key to decipher the code exists, enabling linkage of
2093 the identifying information to the private information or specimens (Office for Human Research
2094 Protections, Guidance on Research Involving Coded Private Information or Biological
2095 Specimens, <http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.htm>).

2096 **Common data elements.** Annotations collected in a uniform manner across multiple institutions
2097 to allow sharing of data in a standardized format (caBIG[®] Glossary,
2098 <https://cabig.nci.nih.gov/glossary>).

2099 **Confidentiality.** Treatment of information so that it is not divulged in ways that are inconsistent
2100 with the understanding of the original disclosure. Particularly, the ethical principle or legal right
2101 that a physician or other health professional will hold secret all information relating to a patient,
2102 unless the patient gives consent permitting disclosure (NCI Thesaurus).

2103 **Conflict of interest.** 1. Exists when the designated official(s) reasonably determines that a
2104 Significant Financial Interest could directly and significantly affect the design, conduct, or
2105 reporting of the Public Health Service–funded research. Examples of conditions or restrictions
2106 that might be imposed to manage conflicts of interest include, but are not limited to: (1) Public
2107 disclosure of significant financial interests; (2) Monitoring of research by independent reviewers;
2108 (3) Modification of the research plan; (4) Disqualification from participation in all or a portion of
2109 the research funded by the Public Health Service; (5) Divestiture of significant financial
2110 interests; or (6) Severance of relationships that create actual or potential conflicts ([42 CFR §](#)
2111 [50.605](#)). 2. Prejudice or bias that may occur when one’s impartiality is compromised by
2112 opportunities for personal gain or occupational advancement, or by the chance that one’s work
2113 may support a favored point of view or social agenda (Taber’s Medical Dictionary).

2114 **Consumables (a.k.a. disposables).** Items that are liable to be used up or exhausted (*NCI Best*
2115 *Practices* working definition).

2116 **Cost recovery.** Charging a sufficient amount for products and services such as biospecimen
2117 collection, processing, storage, and shipping to recover or partially recover operational fees
2118 incurred by a biospecimen resource (*NCI Best Practices* working definition).

2119 **Custodianship.** The caretaking responsibility for biospecimens that extends from collection
2120 through research use. Responsible custodianship requires careful planning and transparent
2121 policies to ensure the long-term physical quality of the biospecimens, the privacy of human
2122 research participants, the confidentiality of associated data, and the appropriate use of
2123 biospecimens and data (*NCI Best Practices* working definition).

2124 **Data.** A collection or single item of factual information, derived from measurement or research,
2125 from which conclusions may be drawn (NCI Thesaurus).

2126 **Demographic data.** Information pertaining to the statistical characterization of human
2127 populations or segments of human populations; e.g., characterization by age, sex, race, or income
2128 (adapted from NCI Thesaurus).

2129 **Deviation.** An intentional or unintentional event that is a departure from a procedure or a normal
2130 practice (ISBER 2008).

2131 **Discontinuation of participation.** Discontinuation of a subject’s participation in research means
2132 discontinuation of one or more of the following activities described in the IRB-approved
2133 protocol: (1) interacting or intervening with the subject; (2) collecting individually identifiable
2134 private information about the subject without the investigator interacting or intervening with the
2135 subject; (3) collecting individually identifiable biological specimens originating from the subject
2136 without the investigator interacting or intervening with the subject; or (4) using or testing
2137 individually identifiable biological specimens already collected by the Investigator (Office for
2138 Human Research Protections, Guidance on Important Considerations for When Participation of

2139 Human Subjects in Research Is Discontinued,
2140 <http://www.hhs.gov/ohrp/requests/200811guidance.html>).

2141 **Disposition.** Final destination of specimens (ISBER 2008).

2142 **Distribution.** A process that includes receipt of request for samples, selection of appropriate
2143 samples, and final inspection, in conjunction with subsequent shipment and delivery of samples
2144 to another biospecimen resource, biospecimen collection center, or laboratory (*NCI Best
2145 Practices* working definition).

2146 **End user.** 1. A health care practitioner, scientist, or laboratory staff member who performs an
2147 appropriate procedure, test, or archival function (ISBER 2008). 2. The ultimate consumer of a
2148 finished product (Merriam-Webster’s Online Dictionary).

2149 **Epidemiologic.** Of or relating to epidemiology, the study of the causes, incidence, and
2150 distribution of disease in the population and its application for prevention or control (NCI
2151 Thesaurus).

2152 **Evaluation.** Systematic, objective appraisal of the significance, effectiveness, and impact of
2153 activities or condition according to specified objectives and criteria (NCI Thesaurus).

2154 **Extramural.** External to the National Institutes of Health (*NCI Best Practices* working
2155 definition).

2156 **Genomics.** The study of the complete genetic complement of an organism or organ (Taber’s
2157 Medical Dictionary).

2158 **Honest broker.** An individual, organization, or system acting for, or on behalf of, a covered
2159 entity to collect and provide health information to research investigators in such a manner
2160 whereby it would not be reasonably possible for the investigators or others to identify the
2161 corresponding patients-subjects directly or indirectly. The honest broker cannot be one of the
2162 investigators. The information provided to the investigators by the honest broker may
2163 incorporate linkage codes to permit information collation and/or subsequent inquiries (i.e., a “re-
2164 identification code”), however, the information linking this reidentification code to the patient’s
2165 identity must be retained by the honest broker and subsequent inquiries are conducted through
2166 the honest broker (NCI Thesaurus).

2167 **Human research participant.** See Human subject.

2168 **Human subject.** A living individual about whom an investigator (whether professional or
2169 student) conducting research obtains (1) data through intervention or interaction with the
2170 individual or (2) identifiable private information ([45 CFR § 46.102\(f\)](#)).

2171 **Identifiable.** The identity of the subject is or may readily be ascertained by the investigator or
2172 associated with the information ([45 CFR § 46.102\(f\)](#)).

- 2173 **Informatics.** An occupational discipline which unites information science with computer
2174 science. It is concerned with the development of techniques for the collection and manipulation
2175 of data, and the use of such data (NCI Thesaurus).
- 2176 **Infrastructure.** The basic facilities, equipment, or underlying framework that are necessary for a
2177 system or organization to function (NCI Thesaurus).
- 2178 **Informed consent.** A decision to participate in research, taken by a competent individual who
2179 has received the necessary information; who has adequately understood the information; and
2180 who, after considering the information, has arrived at a decision without having been subjected
2181 to coercion, undue influence or inducement, or intimidation (Council for International
2182 Organizations of Medical Sciences [CIOMS]. International Ethical Guidelines for Biomedical
2183 Research Involving Human Subjects. “Guideline 4: Individual Informed Consent” [2002]).
- 2184 **Institutional review board (IRB).** A specially constituted review body established or
2185 designated by an entity to protect the rights and welfare of human subjects recruited to
2186 participate in biomedical or behavioral research. The relevant regulatory requirements for an IRB
2187 are provided at 45 CFR Part 46.107 -109, and 21 CFR 56 (Trans-NIH Bioethics Committee
2188 Framework Guidelines).
- 2189 **Intellectual property.** A commercially valuable product of the human intellect, in a concrete or
2190 abstract form, such as a copyrightable work, a protectable trademark, a patentable invention or a
2191 trade secret (Black’s Law Dictionary).
- 2192 **Interoperability.** The ability of systems or tools to both access and use data from a remote data
2193 resource (caBIG® Glossary, <https://cabig.nci.nih.gov/glossary>).
- 2194 **Invention.** Any art or process (way of doing or making things), machine, manufacture, design,
2195 or composition of matter, or any new and useful improvement thereof, or any variety of plant,
2196 which is or may be patentable under the patent laws of the United States (U.S. Patent and
2197 Trademark Office, Glossary of Terms, <http://www.uspto.gov/main/glossary/index.html#i>).
- 2198 **Inventory.** 1. A detailed, itemized list, report, or record of samples in a biospecimen resource,
2199 especially a periodic survey of all stored biospecimens (*NCI Best Practices* working definition).
2200 2. The act or process of taking an inventory (Merriam-Webster’s Online Dictionary).
- 2201 **Label.** Any written, printed, or graphic material on or affixed to a specimen container or package
2202 (ISBER 2008).
- 2203 **Longitudinal data.** Data in which the same units are observed over multiple time periods (U.S.
2204 Department of Labor, Bureau of Labor Statistics, Glossary, <http://stats.bls.gov/bls/glossary.htm>).
- 2205 **Material transfer agreement.** An agreement that governs the transfer of tangible research
2206 materials and data between two organizations, when the recipient intends to use it for his or her
2207 own research purposes. It defines the rights and obligations of the provider and the recipient with
2208 respect to the use of the materials (ISBER 2008).

- 2209 **Package.** A product container with any accompanying materials or components (NCI
2210 Thesaurus).
- 2211 **Paraffin embedded.** A method of preserving biospecimens where they are chemically or
2212 otherwise fixed and then infiltrated with molten wax, which later solidifies (*NCI Best Practices*
2213 working definition).
- 2214 **Patent.** A property right granted by the U.S. Government to an inventor “to exclude others from
2215 making, using, offering for sale, or selling the invention throughout the United States or
2216 importing the invention into the United States” for a limited time in exchange for public
2217 disclosure of the invention when the patent is granted (U.S. Patent and Trademark Office,
2218 Glossary of Terms, <http://www.uspto.gov/main/glossary/index.html#ip>).
- 2219 **Preservation.** Use of chemical agents, alterations in environmental conditions, or other means
2220 during processing to prevent or retard biological or physical deterioration of a specimen (ISBER
2221 2008).
- 2222 **Prevalence.** The total number of cases of a given disease in a specified population at a
2223 designated time. It is differentiated from “incidence,” which refers to the number of new cases in
2224 the population at a given time (NCI Thesaurus).
- 2225 **Privacy.** 1. The condition or state of being free from public attention to intrusion into or
2226 interference with one’s acts or decisions (Black’s Law Dictionary). 2. The ability of a person to
2227 control the availability of information about and exposure of him- or herself (adapted from NCI
2228 Thesaurus).
- 2229 **Private information.** Information about behavior that occurs in a context in which an individual
2230 can reasonably expect that no observation or recording is taking place, and information which
2231 has been provided for specific purposes by an individual and which the individual can reasonably
2232 expect will not be made public (for example, a medical record) ([45 CFR § 46.102\(f\)](#)).
- 2233 **Procedure.** A series of steps designed to result in a specific outcome when followed in order
2234 (ISBER 2008).
- 2235 **Process validation studies.** The process of demonstrating that a specific procedure will
2236 consistently produce expected results within predetermined specifications (ISBER 2008).
- 2237 **Processing.** Any procedure employed after specimen collection but prior to its distribution,
2238 including preparation, testing, and releasing the specimen to inventory and labeling (ISBER
2239 2008).
- 2240 **Project management.** The application of knowledge, skills, tools and techniques to a broad
2241 range of activities to meet the requirements of the particular project ([Babylon Business](#)
2242 [Dictionary](#)).
- 2243 **Proteomics.** The global analysis of cellular proteins. Proteomics uses a combination of
2244 sophisticated techniques including two-dimensional (2D) gel electrophoresis, image analysis,
2245 mass spectrometry, amino acid sequencing, and bio-informatics to resolve comprehensively, to

2246 quantify, and to characterize proteins. The application of proteomics provides major
2247 opportunities to elucidate disease mechanisms and to identify new diagnostic markers and
2248 therapeutic targets (NCI Thesaurus).

2249 **Quality.** Conformance of a specimen or process with pre-established specifications or standards
2250 (ISBER 2008).

2251 **Quality assurance.** An integrated system of management activities involving planning,
2252 implementation, documentation, assessment, and improvement to ensure that a process or item is
2253 of the type and quality needed for the project. Same as quality management system (ISBER
2254 2008).

2255 **Quality control.** Specific tests defined by the QA or QMS Program to be performed to monitor
2256 procurement, processing, preservation and storage; specimen quality; and test accuracy. These
2257 may include but are not limited to performance evaluations, testing, and controls used to
2258 determine accuracy and reliability of the biospecimen resource's equipment and operational
2259 procedures as well as monitoring of the supplies, reagents, equipment, and facilities (ISBER
2260 2008).

2261 **Quality management system.** See Quality assurance.

2262 **Reach-through rights.** Rights claimed by the provider of materials to the recipient's
2263 downstream discoveries to which the provider would not otherwise be entitled through its
2264 ownership or patent coverage of the material alone.. Examples of reach-through rights required
2265 by providers in exchange for use of their material by the recipient might include ownership of
2266 recipient's discoveries, license exclusivity, or payments upon the sale of the discovery. Reach-
2267 through rights may give the provider an unfairly high level of compensation for the research use
2268 of the material by the recipient (*NCI Best Practices* working definition).

2269 **Research.** 1. Systematic investigation, including research development, testing, and evaluation,
2270 designed to develop or contribute to generalizable knowledge ([CFR 45 § 46.102\(d\)](#)).
2271 2. Systematic investigation into a subject in order to discover facts, establish or revise a theory,
2272 or develop a plan of action based on the facts discovered (NCI Thesaurus).

2273 **Resource sharing.** The sharing of materials and data in a timely manner (NCI Thesaurus).

2274 **Retrieval.** The removal, acquisition, recovery, harvesting, or collection of specimens (ISBER
2275 2008).

2276 **Sample.** 1. A portion of a biospecimen (*NCI Best Practices* working definition). 2. A single unit
2277 containing material derived from one specimen (ISBER 2008). 3. Serving as an illustration or
2278 example (Merriam-Webster's Online Dictionary).

2279 **Secondary research.** Any research use beyond the scope of the primary study. See Primary
2280 research (*NCI Best Practices* working definition).

2281 **Silver-level compatibility.** A level of caBIG® compatibility requiring use of the architectures
2282 and vocabularies specified for the caBIG® system. Use of these architectures and vocabularies

2283 will ensure a high level of compatibility between systems enabling interchange of scientific
2284 information (*NCI Best Practices* working definition). For full details, see caBIG® Compatibility
2285 Guidelines, https://cabig.nci.nih.gov/guidelines_documentation/.

2286 **Simple letter agreement (SLA).** Streamlined form of material transfer agreement approved for
2287 use at the NIH. The NIH encourages the use of the SLA to facilitate exchanges between
2288 academic institutions (NCI Technology Transfer Branch glossary,
2289 <http://ttb.nci.nih.gov/glossary.php>).

2290 **Space planning.** The process of designing the layout of a building, suite, or laboratory for
2291 optimal efficiency in the intended purpose (*NCI Best Practices* working definition).

2292 **Specimen.** See Biospecimen.

2293 **Stakeholder.** One that has a stake or an interest in an enterprise. In the context of the *NCI Best*
2294 *Practices*, the term stakeholder embraces research participants, patient advocates, researchers,
2295 clinicians, and biospecimen resource operational/managerial personnel (*NCI Best Practices*
2296 working definition).

2297 **Standard operating procedure.** An established procedure to be followed in carrying out a given
2298 operation or in a given situation (NCI Thesaurus).

2299 **Standard operating procedures (SOPs) manual.** A group of SOPs detailing specific policies
2300 of a repository and the procedures required to be used by the staff/personnel (ISBER 2008).

2301 **Standard precautions.** The CDC publication titled “Guideline for Isolation Precautions:
2302 Preventing Transmission of Infectious Agents in Healthcare Settings 2007” is also known as
2303 “Standard Precautions.” Standard precautions are based on the principle that all blood, body
2304 fluids, secretions, excretions except sweat, nonintact skin, and mucous membranes may contain
2305 transmissible infectious agents, and include a group of infection-prevention practices. These
2306 include: hand hygiene; use of gloves, gown, mask, eye protection, or face shield, depending on
2307 the anticipated exposure; and safe injection practices. Also, equipment or items in the patient
2308 environment likely to have been contaminated with infectious body fluids must be handled in a
2309 manner to prevent transmission of infectious agents (“Guideline for Isolation Precautions:
2310 Preventing Transmission of Infectious Agents in Healthcare Settings 2007,”
2311 <http://www.cdc.gov/ncidod/dhqp/pdf/guidelines/Isolation2007.pdf>).

2312 **Storage.** 1. Maintenance of specimens under specified conditions for future use (ISBER 2008).

2313 **Sustainable.** Of, relating to, or being a method of using a resource so that the resource is not
2314 depleted (adapted from Merriam-Webster’s Online Dictionary).

2315 **Tissue.** An aggregate of cells with different specialized characteristics that are organized
2316 anatomically, usually in the fixed framework of an organic matrix. The architectural organization
2317 that is maintained contributes to the performance of a specific collective function. Tissues are
2318 parts of organs. The term tissue is most often referred to in the context of solid tissue, as
2319 originating from a solid organ; however, tissue also can be defined broadly to include collections

2320 of cells and the extracellular matrix and/or intercellular substances from bodily fluids such as
2321 blood (*NCI Best Practices* working definition).

2322 **Uniform Biological Material Transfer Agreement (UBMTA).** A Master Agreement among
2323 the NIH, universities, and other nonprofit research facilities used to expedite transfer of research
2324 materials among noncommercial entities (NCI Technology Transfer Branch glossary,
2325 <http://ttb.nci.nih.gov/glossary.php>). More information about the terms of the UBMTA and its
2326 signatories is available at (<http://www.bioinfo.com/ubmta.html>).

2327 **Unique identifier.** A set of characters used as a code that is unique in the context or the system
2328 for which it is created. It serves as a means of identification and reference (often instead of a
2329 name) for an entity, person, thing, function, procedure, activity, variable, or body of data (NCI
2330 Thesaurus).

2331 **Use case.** A document that describes the interaction between a user (or other initiator of the
2332 interaction) and a system, represented as a sequence of simple steps leading to a particular goal
2333 (NCI Thesaurus).

2334 **Validation (of procedures or equipment).** 1. The act of confirming a product or service meets
2335 the requirements for which it was intended (Babylon Business Dictionary). 2. A statistical
2336 method of partitioning a sample of data into subsets such that the analysis is initially performed
2337 on a single subset, while the other subsets are retained for subsequent use in confirming and
2338 validating the initial analysis (NCI Thesaurus).

2339

2340 **Acronym List**

BMBL	Biosafety in Microbiological and Biomedical Laboratories
BSL	biosafety level
caBIG®	Cancer Biomedical Informatics Grid
CDC	Centers for Disease Control and Prevention
CDE	common data element
CMMI	Capability Maturity Model Integration
COI	conflict of interest
DHHS	U.S. Department of Health and Human Services
DNA	deoxyribonucleic acid
FDA	U.S. Food and Drug Administration
GINA	Genetic Information Nondiscrimination Act
HIPAA	Health Insurance Portability and Accountability Act
HITECH	Health Information Technology for Economic and Clinical Health
IATA	International Air Transport Association
IP	intellectual property
IRB	institutional review board
MTA	material transfer agreement
NCI	National Cancer Institute
OBRR	Office of Biorepositories and Biospecimen Research
OHRP	Office for Human Research Protections
OSHA	Occupational Safety and Health Administration
PHI	protected health information
PHS	Public Health Service
QA/QC	quality assurance/quality control
QMS	quality management system
RNA	ribonucleic acid
SOP	standard operating procedure

2341

2342 **Appendices**

2343 **Appendix 1. Minimal Clinical Data Set**

2344 The Minimal Clinical Data Set in this appendix is the minimal clinical data that are
 2345 recommended for annotation of disease state or risk of cancer in biospecimen resources. The
 2346 items in this recommended data set are not meant to be inclusive and are only suggested
 2347 examples. Different biospecimen resources may require more or less detailed annotations that
 2348 focus on the primary use of the clinical specimens. Good practice suggests that the data set for
 2349 clinical annotation be tailored to the needs of the users of the biospecimen resource. Also this
 2350 Minimal Clinical Data Set is not to be confused with other data sets such as that used by CMS to
 2351 evaluate nursing home patients (<http://www.cms.hhs.gov/MDSPubQIandResRep/>).

Item		Notes
Age		or ≥ 90, at collection
Exposures (where age > 18)	Smoking	
	Drinking	
	Occupation	
Gender		
Race		
Ethnicity		
Disease diagnosis/Normal		
Source/Method of diagnosis		
Treatment type/None		
Height		
Weight		
Family history of cancer		
For tissue specimens only,	Histologic type	Also record for blood specimens in bloodborne cancers
	Grade	
	Size	
	Nodal status (pos/neg, # pos/total nodes, etc)	
	TNM stage	
	Procedure	Procedure by which specimen was obtained

Biomarkers		Biomarkers used in routine care; e.g. Estrogen and Progesterone receptor sensitivity
Outcome—or will it be possible to get these data when outcome is known	Death	Year only
	Date of last cancer follow-up	Year only
	Recurrence (local, distant, unknown)	
Collection method		
Comorbidity		

2352

2353 **Appendix 2. Additional Resources Related to Ethical, Legal, and Policy**
2354 **Issues in Biospecimen Research**

2355 The resources listed below are not intended to be exhaustive but rather to provide useful
2356 examples and references for biospecimen resources. All Web links were last accessed on July 12,
2357 2010.

2358 **I. General Resources Related to Ethical, Legal, and Policy Issues in Biospecimen**
2359 **Research**

2360 The reports and resources listed below provide an overview of ethical, legal, and policy
2361 challenges in biospecimen research. Topics include State and international regulations related to
2362 biospecimens and tools for institutional review boards (IRBs) and biospecimen resource
2363 managers.

2364
2365 **A. *NCI Documents***

2366 National Cancer Institute (NCI) 50-State Survey of Laws Regulating the Collection,
2367 Storage, and Use of Human Tissue Specimens and Associated Data for Research

2368 This survey reflects the status of state laws as of November 2004 that affect the use of
2369 biospecimens and associated data in research. The report includes a chart with the
2370 requirements for the conduct of biospecimen research State by State and a table compiling
2371 State statutes.

2372
2373 <http://www.cancerdiagnosis.nci.nih.gov/humanSpecimens/survey/50-state-survey.pdf>
2374

2375 **B. *Documents from Other Sources***

2376 Public Responsibility in Medicine & Research (PRIM&R) Human Tissue/Specimen
2377 Banking White Paper

2378 The PRIM&R White Paper includes a discussion of the challenges and recommendations to
2379 the Federal regulatory and funding agencies as well as tools for IRBs, repository managers,
2380 and researchers in the form of educational materials, discussions of relevant issues, and
2381 points to consider.

2382
2383 <http://www.primr.org/PublicPolicy.aspx?id=68>
2384

2385 Research Involving Human Biological Materials: Ethical Issues and Policy Guidance—
2386 Volume I: Report and Recommendations of the National Bioethics Advisory Commission

2387 This 1999 report from the National Bioethics Advisory Commission (NBAC) addresses the
2388 question of whether the Common Rule is effective in protecting human subjects from harm
2389 in research involving biospecimens. The NBAC report also provides recommendations
2390 related to biospecimen research, including interpretations of several key terms and concepts
2391 in the Common Rule.

2392
2393 <http://bioethics.georgetown.edu/nbac/hbm.pdf>
2394

2395 International Compilation of Human Research Protections
2396 This compilation was developed by the Office for Human Research Protections (OHRP)
2397 for IRBs/ethics committees, researchers, sponsors, and others who are involved in
2398 international research. The report includes a table for each country that lists the key
2399 organizations, legislation, regulations, and guidelines related to human biological materials.

2400
2401 <http://www.hhs.gov/ohrp/international/HSPCompilation.pdf>
2402

2403 **II. Sample Informed Consent Documents**

2404 The following list of sample informed consent documents is provided to guide and inform
2405 biospecimen resources about possible approaches to the informed consent process. These
2406 documents may be adapted depending on the nature of the resource and its mission.

2407 **A. NCI Documents**

2408 The Cancer Genome Atlas (TCGA)

2409 The NCI and the National Human Genome Research Institute have developed informed
2410 consent documents that are consistent with the goals and activities of TCGA, a
2411 comprehensive and coordinated effort to accelerate the understanding of the molecular
2412 basis of cancer through the application of genome analysis technologies. Both documents,
2413 one for retrospective biospecimen collections and another for prospective collections,
2414 specifically address genetic research, broad sharing of biospecimens and clinical data, the
2415 possibility of future research use, the deposition of genomics data into electronic database
2416 with partial public access, and the risk of loss of privacy.

2417
2418
2419 http://cancergenome.nih.gov/about/policies/informed_consent.asp
2420

2421 cancer Biomedical Informatics Grid (caBIG®)

2422 Members of the caBIG® Data Sharing and Intellectual Capital (DSIC) workspace have
2423 developed this combined informed consent and Health Insurance Portability and
2424 Accountability Act authorization template to facilitate specimen and data collection and
2425 sharing for research. This is a living document and will be further developed and revised
2426 over time.

2427
2428 https://cabig-kc.nci.nih.gov/DSIC/KC/index.php/Model_Informed_Consent
2429

2430 **B. Documents from Other Sources**

2431 Public Project in Population Genetics (P3G)

2432 P3G designed an informed consent template for use in prospective, longitudinal population
2433 genomics studies based on approaches used by P3G members.

2434
2435 *General information:*

2436 <http://www.p3gobservatory.org/repository/ethics.htm>
2437

2438 *Sample consent form:*

2439 http://www.p3gobservatory.org/download/Modelconsentform_Finalnov6.doc
2440

2441 *Sample patient information pamphlet:*
2442 http://www.p3gobservatory.org/download/Modelinfosheet_Finalnov6.doc

2443
2444 **III. Patient Information Documents**

2445 The following list of sample patient information documents is provided to guide and inform
2446 biospecimen resources about additional resources that may be useful during the informed consent
2447 process. These documents are intended to explain the informed consent process and/or the
2448 importance of biospecimens in research to a general audience and may be adapted depending on
2449 the nature and mission of the resource.

2450
2451 **A. *NCI Documents***

2452 Providing Your Tissue for Research

2453 This three-page booklet is meant to complement the face-to-face education that occurs
2454 between clinicians and potential clinical trial participants. It provides a balanced discussion
2455 of questions and answers on how biospecimens are collected and used in research.

2456
2457 <http://biospecimens.cancer.gov/global/pdfs/ProvidingYourTissueforResearch.pdf>

2458
2459 Guide to Understanding Informed Consent

2460 This guide explains what a human research participant should expect during the informed
2461 consent process, explains the importance of the informed consent process to clinical human
2462 research participants, and describes how informed consent fits into a larger system that
2463 protects the welfare of people who take part in clinical trials.

2464
2465 <http://www.cancer.gov/clinicaltrials/conducting/informed-consent-guide>

2466
2467 **B. *Documents from Other Sources***

2468 Research Advocacy Network

2469 The Research Advocacy Network (RAN) is a nonprofit organization working to bring
2470 together all participants in the medical research process. The RAN has developed booklets
2471 about the importance of biospecimens in research directed toward human research
2472 participants and IRB members. Documents are available in English or Spanish.

2473
2474 <http://www.researchadvocacy.org/publications/posters.php>

2475
2476 **IV. Resources for Simplifying Informed Consent Documents**

2477 Several groups have been established to provide recommendations on simplifying and improving
2478 the readability of informed consent documents. The following resources are not specific to
2479 biospecimen resources but instead provide general information on how to improve the informed
2480 consent process to meet the needs of human research participants.

2481
2482 **A. *NCI Documents***

2483 NCI-OHRP-FDA Initiative

2484 The NCI, along with the OHRP and the U.S. Food and Drug Administration, formed an
2485 Informed Consent Working Group to address concerns that informed consent documents

2486 for clinical trials were becoming too long, complicated, and difficult to understand. In
2487 1998, the group issued “Recommendations for the Development of Informed Consent
2488 Documents for Cancer Clinical Trials.” The recommendations may be used by
2489 investigators developing consent documents and by IRBs reviewing such documents.

2490
2491 [http://www.cancer.gov/clinicaltrials/understanding/simplification-of-informed-consent-](http://www.cancer.gov/clinicaltrials/understanding/simplification-of-informed-consent-docs/)
2492 [docs/](http://www.cancer.gov/clinicaltrials/understanding/simplification-of-informed-consent-docs/)

2494 **B. *Documents from Others Sources***

2495 Group Health Center for Health Studies

2496 The Project to Review and Improve Study Materials (PRISM) is a Group Health Center for
2497 Health Studies initiative to improve the readability of print materials used in
2498 communication with study participants. The PRISM Readability Toolkit is a
2499 comprehensive resource that includes sample informed consent language, editing
2500 checklists, a reference guide for improving readability, and examples of how to improve
2501 readability.

2502
2503 http://www.centerforhealthstudies.org/capabilities/readability/readability_home.html

2504
2505 Association of American Medical Colleges

2506 The summary from a May 2007 strategic planning meeting titled “Universal Use of Short
2507 and Readable Informed Consent Documents: How Do We Get There?” includes a review
2508 of informed consent literature, potential approaches for improving informed consent, and
2509 success stories from the field.

2510
2511 <http://www.aamc.org/research/clinicalresearch/hdickler-mtgsumrpt53007.pdf>

2512

2513 **Appendix 3. Governance Plan**

2514 This governance plan is provided as an example to biospecimen resources to help with planning
 2515 the resource and defining the authorities, processes, and procedures that are needed to guide key
 2516 operational decisions. The governance plan should become part of the resource's documents and
 2517 available if requested. (Please see [Section C.1](#) of the *NCI Best Practices* for more information
 2518 and additional recommendations related to custodianship.)

2519

2520 Principal Investigator:

2521 Grant Number:

2522 Project Title:

2523 Project Period:

2524 Name of the Biospecimen Resource (if different than the project):

2525

2526 **A. *Name of the Custodian:***

2527 **B. *Summary of the Project:***

2528 **C. *Governance Structure of the Project (See [Section C.1.](#)):***

2529 1. Outline the resource's management structure and discuss the roles and responsibilities of
 2530 each management or oversight body.

2531 2. Outline the resource's protocols and procedures that guide its operations and discuss
 2532 whether the protocols are documented and approved by the institutional review board
 2533 and/or a project oversight committee.

2534 **D. *Integrity of Biospecimens and Data (See [Sections C.1.5.](#) and [C.3.](#)):***

2535 1. Describe the resource's protocols to ensure the physical integrity of collected
 2536 biospecimens.

2537 2. Describe the resource's protocols to ensure the integrity of the human research
 2538 participants' data that accompany the biospecimens.

2539 **E. *Access to Biospecimens and Data (See [Sections C.3.](#) and [C.4.](#)):***

2540 1. Outline the resource's protocols and procedures for the distribution of samples to
 2541 investigators. Describe how the scientific merit, prioritization of access requests, and
 2542 proposed research use are assessed and by what review group.

2543 2. Describe whether samples will be accompanied by data and the type of data. Outline the
 2544 safeguards that are in place to ensure that confidentiality of the data is not compromised.

2545 **F. *Release of Research Results (See [Section C.2.3.7.](#)):***

2546 1. Outline the protocols that are in place for publication and dissemination of research
 2547 results from biospecimen research. Describe the process for handling results that are
 2548 potentially stigmatizing to groups.

2549 2. Outline any process to provide educational materials to the public such as brochures,
 2550 literature, meetings, or public Web sites.

- 2551 **G. Legacy and Contingency Plans (See [Section C.1.2.](#)):**
- 2552 1. Outline the resource’s plans for the handling and disposition of biospecimens and
- 2553 associated data when reaching any of the following points: (a) End of the budget period
- 2554 of the grant, (b) loss of management or termination of funding, (c) accomplishment of the
- 2555 specific research objectives of the study, (d) depletion of biospecimens, or
- 2556 (e) achievement of critical data end points.
- 2557 **H. Retention of Biospecimens, Data, and Records (See Sections [C.1.3.](#) and [C.2.3.1.](#)):**
- 2558 1. Outline the resource’s protocols for the handling and disposition of biospecimens and
- 2559 associated data sets following the discontinuation of participation by a human research
- 2560 participant.
- 2561 2. Outline the resource’s protocols for the retention of biospecimens, data, and records
- 2562 pertaining to informed consent and the identity of human research participants.
- 2563 **I. Sharing of Resources (See Sections [C.1.6.](#) and [C.5.](#)):**
- 2564 1. Outline the resource’s protocols and procedures for the sharing of research data and tools
- 2565 generated from biospecimen research consistent with the NIH Data Sharing Policy
- 2566 (http://grants.nih.gov/grants/policy/data_sharing/) and the NIH Research Tools Policy
- 2567 (http://ott.od.nih.gov/policy/research_tool.html).
- 2568 2. Outline the resource’s protocols for communicating information to human research
- 2569 participants regarding the general type of research performed on biospecimens and the
- 2570 sharing of biospecimens with other researchers, when practicable.
- 2571 **J. Conflict of Interests (COIs) (See Sections [C.1.4.](#) and [C.6.](#)):**
- 2572 1. Describe the protocols for managing and limiting any potential COIs for the resource’s
- 2573 staff consistent with [42 CFR Part 50 Subpart F](#), as well as applicable [NIH COI policies](#).
- 2574

2575 **Appendix 4. Sample Material Transfer Agreement**

2576 The following Material Transfer Agreement (MTA) is intended to serve as a sample agreement for
2577 use between biospecimen resources and approved end-users receiving biospecimens and/or data.
2578 This sample MTA may need to be modified depending on the material and data that are being
2579 transferred and the specific requirements of the research project. Please note, this MTA is intended
2580 for transfer of deidentified biospecimens and data. (Please see [Section C.5](#) of the *NCI Best*
2581 *Practices* for more information and additional recommendations related to MTAs.)

2582

2583 **Sample Material Transfer Agreement**
2584 **For Transfers from Biospecimen Resources to Approved Third-Party End Users**
2585

2586 This Material Transfer Agreement (the “Agreement”) is by and between *<insert name of*
2587 *biospecimen resource>* (“Provider”) and *<insert name of third-party institution>* (“Recipient”)
2588 regarding the transfer of human specimens, with or without associated data, from the *<insert name of*
2589 *biospecimen resource>* to approved third-party end users for research purposes as further defined
2590 below. Throughout this Agreement, Provider and Recipient are collectively referred to as the “Parties.”
2591 This Agreement will become effective upon the date of the last signature affixed below.

2592
2593 The Provider and Recipient agree as follows:

2594 **1. DEFINITIONS.** Within this Agreement, the following terms will have the same meaning and effect as
2595 those used in the Standards for Privacy of Individually Identifiable Health Information set forth in 45
2596 CFR Parts 160 and 164 (“HIPAA Privacy Rule”). These terms are repeated here for convenience:

2597 (a) “De-identified” information is information that formerly contained individually identifiable health
2598 information but which has had all unique identifying information, numbers, characteristics, and codes
2599 removed such that the information a record contains cannot be used alone or in combination with other
2600 information to identify the individual who is the subject of the information (45 CFR 164.514). Identifying
2601 information includes, but is not limited to, the 18 categories of identifiers described in 45 CFR
2602 164.514(b)(2).

2603 (b) “Protected Health Information” or “PHI” means any information, whether oral or recorded in any
2604 form or medium: (i) that relates to the past, present, or future physical or mental condition of an
2605 individual; the provision of health care to an individual; or the past, present, or future payment for the
2606 provision of health care to an individual, and (ii) that identifies the individual or with respect to which
2607 there is a reasonable basis to believe the information can be used to identify the individual (45 CFR
2608 164.103).

2609 **2. DESCRIPTION OF MATERIAL AND DATA.** The Provider will transfer to the Recipient the
2610 following biospecimens and/or derivatives (“MATERIAL”): *<insert description of specific samples to*
2611 *be transferred>* with the following data (“DATA”): *<insert description of specific data to be*
2612 *transferred, if applicable>*.

2613 **3. COLLECTION OF MATERIAL AND DATA.** The MATERIAL and DATA were collected
2614 and/or processed from human biospecimens as part of *<insert name of biospecimen resource>* in
2615 accordance with appropriate Federal and local laws, Assurances, and Institutional Review Board
2616 approvals related to human subjects research, as appropriate.

2617 **4. TRANSFER OF MATERIAL AND DATA.** The MATERIAL and DATA provided by Provider
2618 will be de-identified and all Protected Health Information (PHI), as defined by the Federal Health
2619 Insurance Portability and Accountability Act (HIPAA, 45 C.F.R. 164) will have been removed.

2620 **5. RESPONSIBILITIES AND AUTHORIZATIONS OF RECIPIENT**

2621 (a) Recipient agrees to use the MATERIAL and DATA for the approved research project only (see
2622 Appendix 1 “Research Project”) and will not use the MATERIAL and DATA for any unapproved
2623 commercial purposes, including selling or transferring to a third party for commercial purposes.

2624 (b) Recipient is responsible for obtaining any necessary Human Subjects research approvals or
2625 exemptions required to use the MATERIAL and DATA at the respective institution. The

2626 MATERIAL and DATA will be used by the Recipient in compliance with all applicable Federal,
2627 state, and local statutes and regulations.

2628 (c) Recipient will allow the use of MATERIAL and DATA only by *<insert name of third party P.I.>*
2629 (“Recipient Investigator”) and Recipient Investigator’s research team that are under the direct
2630 supervision of Recipient Investigator, and only after they have been informed of and agreed to the
2631 provisions and restrictions stated herein. Any transfer of MATERIAL and DATA to other than
2632 Recipient Investigator’s research team requires the advanced written approval of the Provider.

2633 (d) It is acknowledged that the Recipient may already have in its possession or will obtain from
2634 another source, PHI related to the MATERIAL and DATA, and to which the Recipient may be
2635 subject to additional restrictions or obligations under separate agreements. Recipient shall notify
2636 Provider in writing within five (5) working days of its discovery of any unauthorized use or
2637 disclosure of PHI related to the MATERIAL and DATA of which Recipient, its officers, employees,
2638 or agents become aware. Recipient shall take (i) prompt corrective action to cure any deficiencies or
2639 (ii) any action pertaining to such unauthorized disclosure required by applicable federal law.

2640 (e) Recipient agrees to not identify or contact any donor, or living relative of a donor, who may have
2641 provided the MATERIAL or any DATA received by Recipient under this Agreement from Provider.

2642 (f) Recipient agrees to report data, inventions, and publications resulting from the use of the MATERIAL
2643 and/or DATA to Provider.

2644 **6. THE MATERIAL AND DATA ARE NOT FOR USE IN HUMAN SUBJECTS OR FOR THE**
2645 **TREATMENT OR DIAGNOSIS OF HUMAN SUBJECTS.**

2646 **7. DISCLAIMER.** Any MATERIAL delivered pursuant to this Agreement is understood to be
2647 experimental in nature and may have hazardous properties. THE PROVIDER MAKES NO
2648 REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER
2649 EXPRESSED OR IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF
2650 MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF
2651 THE HUMAN MATERIAL WILL NOT INFRINGE ANY PATENT, COPYRIGHT,
2652 TRADEMARK, OR OTHER PROPRIETARY RIGHTS. To the extent allowed by law, Recipient
2653 assumes liability for claims for damages against it by third parties which may arise from its use, storage,
2654 processing, distribution, or disposal of the MATERIAL except that, to the extent permitted by law,
2655 Provider shall be liable to Recipient when the damage is caused by the gross negligence or willful
2656 misconduct of Provider.

2657 **8. TERMINATION AND DISPOSAL.** Either Party may terminate this Agreement with sixty (60)
2658 days written notice to the other Party. When the Research Project is completed or this Agreement is
2659 terminated, whichever comes first, any unused MATERIAL and DATA will either be destroyed in
2660 compliance with all applicable statutes and regulations or will be returned to the Provider as
2661 requested by the Provider.

2662 **9. ACKNOWLEDGEMENT.** In all oral presentations or written publications resulting from the use
2663 of the MATERIAL and DATA, the Recipient will acknowledge the *<insert name of biospecimen*
2664 *resource>* as the source of the MATERIAL and DATA, unless requested otherwise by Provider, as
2665 follows:

2666 “Biospecimens {and/or Derivatives} and associated data were provided by the *<insert name of*
2667 *biospecimen resource>*, an initiative developed through funding from the *<insert funding source, if*
2668 *applicable>*.”

2669 **10. COST AND SHIPPING.** The MATERIAL and DATA are provided at no cost to Recipient. Provider
2670 will notify Recipient when the MATERIAL and DATA are ready for shipment. Recipient will be
2671 responsible for the pick-up and shipment, including shipping costs, of the MATERIAL and DATA.

2672

2673 The Parties have executed this Agreement by their respective duly authorized officers on the day and
2674 year hereinafter written. Any communication or notice to be given shall be forwarded in writing to
2675 the respective addresses listed below.

2676

2677

SIGNATURES APPEAR ON THE FOLLOWING PAGE

2678

2679 **Signatures for Provider**

2680

2681 Provider Scientist:

2682 Provider Organization:

2683 Address:

2684

2685

2686 Name of Authorized Official:

2687 Title of Authorized Official:

2688

2689

2690

2691 _____
Signature of Authorized Official Date

2692

2693 Certification of Provider Authorized Official: This Agreement ___has / ___has not been modified. If
2694 modified, the modifications are attached.

2695

2696

2697 **Signatures for Recipient**

2698

2699 Recipient Scientist:

2700 Recipient Organization:

2701 Address:

2702

2703

2704 Name of Authorized Official:

2705 Title of Authorized Official:

2706

2707

2708

2709 _____
Signature of Authorized Official Date

2710

2711 Certification of Recipient Scientist: I have read and understood the conditions outlined in this
2712 Agreement and I agree to abide by them in the receipt and use of the MATERIAL and DATA.

2713

2714

2715

2716 _____
Scientist Receiving Material Date