AIDS and Cancer Specimen Resource (ACSR)	Effective Date: August 2018
Technical: RBR Biospecimen Quality Assurance SOP	Version 2.0
ACSR SOP ID# Tech014	Page 1 of 15
Approved by ACSR Executive Committee	July 2018

1.0 PURPOSE

The purpose of this document is to establish the procedure to monitor and assess the quality of the biorepositories and affiliate sites, data and biospecimens stored in the AIDS and Cancer Specimen Resource (ACSR).

2.0 SCOPE

This standard operating procedure (SOP) describes the minimum assessment required to evaluate the quality of the biorepositories, data and biospecimens stored in the ACSR in order to provide investigators with a product that is consistent with their needs. This SOP applies to all personnel from ACSR Regional Biospecimen Repositories (RBRs) and affiliates that are responsible for performing quality assurance. The ACSR RBRs and affiliates process and bank biospecimens under site specific approved Human Subjects Protocols. Biospecimens, Samples, Aliquots and Derivatives are entered into the ACSR database when consent for banking and research use have been verified by the Protocol PI or ACSR designee. Each RBR and affiliate site is responsible for Human Subjects compliance as per their institutional guidelines and their local approved Human Subjects Protocol. The SOP does not cover detailed procedures for handling biohazardous material and it is recommended that personnel follow institutional biosafety guidelines.

3.0 REFERENCE TO OTHER ACSR SOPS OR POLICIES

ACSR SOP Tech002 Solid Tissue Collection

ACSR SOP Tech003 Oral Biospecimen Processing and Storage

ACSR SOP Tech004 HPV Biospecimen Processing

ACSR SOP Tech005 Blood Products Body Fluids Collection

ACSR SOP Tech006 Live Tissue Collection

ACSR SOP Tech007 DNA and RNA Quality Assessment

ACSR SOP Tech008 Hematoxylin Eosin Stain

ACSR SOP Tech009 Biospecimen Handling

ACSR SOP Tech010 Biospecimen Labeling

ACSR SOP Tech011 Tissue Microarray Construction Protocol

4.0 DEFINITIONS

Term/Acronym	Definition
ACSR	AIDS and Cancer Specimen Resource
ACSR Management	ACSR staff designated by their official job title and descriptions as a Principal Investigator, Manager or Director.
Aliquot	The sample has the original characteristics of the original or parent specimen but in smaller quantities (FFPE block vs unstained sections from the FFPE block)
Assessment	The gathering of information on the condition of a process or activity for evaluation of such.
ATLAS	Annotation of a Tissue Library and Searching Platform
Biospecimen	Human material such as urine, blood, tissue stored in a biorepository for use in laboratory research. For the ACSR this is considered the original or parent biospecimen.
BSL2	Bio Safety Level 2
Calibration	Set of operations that establish, under specified conditions, the relationship between values of quantities indicated by a measuring instrument or measuring system, or values represented by a material measure or a reference material, and the corresponding values realized by standards (Values Indicated by Measuring).
Competence	An individual's demonstration of knowledge of key concepts, ability to apply knowledge and skills, or adequately perform a task.
Conformity	Fulfillment of a requirement, or compliance with a set standard.
Corrective action	Action to eliminate the cause of a detected nonconformity or other undesirable situation; **NOTE 1:** There can be more than one cause for a nonconformity; **NOTE 2:** Corrective action is taken to prevent recurrence whereas preventive action is taken to prevent occurrence.
Customer	Organization or person that receives a product; EXAMPLES: Consumer, researcher, client, or end user.; **NOTE 1:** A

	customer can be internal or external to the organization; **NOTE 2:** Employees may be regarded as internal customers.
Cytology	Cytology is the diagnostic branch of pathology medicine which is based on the microscopic examination of cells to recognize physiological conditions and to diagnose benign, pre-malignant and malignant processes
Derivative	The original characteristics of the specimen are changed (FFPE vs DNA derived from FFPE).
Deviation	A change from what is usual or expected. Deviations can apply to any documented policy, process or procedure as well as behavior.
Document	Information and its supporting medium; **NOTE:** This may be paper-based or electronic. Examples include Standard Operating Procedures and Pathology Reports.
Error	A deviation from truth, accuracy, or correctness; a mistake.
EC	Executive Committee
Failure	In the broadest sense, a case when the system does not meet user or customer expectations; **NOTE:** This includes the inability to perform its intended functions satisfactorily or within specified performance limits.
FFPE	Formalin Fixed Paraffin Embedded
Form	A paper or electronic document on which information or results are captured; **NOTE:** Once completed, a form becomes a record.
H&E	Hematoxylin & Eosin
HIIRS	Hub for Integrated Informatics and Research Support
HPV	Human Papilloma Virus
Objective	Planning element that delineates in detail how to accomplish a specific goal at the process level.
OC	Office of the Chairs
OCT	Optimal Cutting Temperature Compound
PBS	Phosphate Buffered Saline
PCR	Polymerase Chain Reaction
Policy	A documented statement of overall intentions and directions defined by those in the organization and endorsed by management.
PPE	Personal Protective Equipment such as gloves, lab coat, face shield.
Preventative	Action to prevent the cause of a potential **nonconformity** or

Action	other undesirable potential situation.
PI	Principal Investigator
Procedure	Specified way to carry out an activity of a process. A procedure is a set of instructions that describes the stepwise actions taken to complete activities identified in processes.
Process	Set of interrelated or interacting activities that transform input into outputs.
Quality System Essentials	Management foundation of interrelated processes that support the laboratory's path of workflow for quality management.
QWG	Quality Working Group
RBR	Regional Biorepository
Record	Document stating results achieved or providing evidence of activities performed. Some examples include freezer logs, incident reports, the master equipment file, etc.
RNA	Ribonucleic acid
Sample	This is an aliquot, derivative or if the Parent Specimen received is stored as a whole specimen, it is referred to as a sample, as per ACSR database definition.
SOP	Standard Operating Procedure. A set of written instructions that document a routine or repetitive activity followed by an organization.
Specimen	The same as Biospecimen. Human material such as urine, blood, tissue stored in a biorepository for use in laboratory research. For the ACSR this is considered the original or parent biospecimen/ specimen.
TMA	Tissue Microarray
Tissue Transport Vessels	A sterile container used to transport biospecimens such as: urine cup, draw tube, conical tube or capped vessel.
Universal Precautions	This is an approach to infection control to treat all human blood and certain human body fluids as if they were known to be infectious for HIV, HBV and other bloodborne pathogens,
Validation	Confirmation through the provision of objective evidence that the requirements for a specific intended use or application have been fulfilled; **NOTE:** Examples include validation of the process to use a new diagnostic tool, such as an automated laboratory test system or information system; or evidence-based medicine.
WG	Working Group

5.0 ROLES AND RESPONSIBILITIES

This SOP applies to all personnel from ACSR member RBRs and affiliate sites that are responsible for collecting and processing biospecimens, entering data into databases or who perform quality metrics on biospecimens.

ACSR Personnel	Responsibility/Role
ACSR Staff	Inventory control, quality assessment, and report of findings
Quality Working Group	Biospecimen selection, receipt of report of findings

6.0 MATERIALS, EQUIPMENT AND FORMS

RBR Self-audit Checklist

7.0 PROCEDURES

The quality procedures covered are the RBR self-assessment, random data quality testing, biospecimen quality testing and researcher feedback.

7.1 SPECIAL SAFETY PRECAUTIONS

7.1.1 Comply with “Universal Precautions” when handling all specimens

7.1.2 Use PPE in accordance with the institution’s guidelines.

7.1.3 Standard best-practice working procedures include careful manipulation of the patient samples, disinfection of countertops and equipment used during testing, and disposal of biohazardous waste into appropriate receptacles.

7.2 Self-Assessment

7.2.1 At the end of the first quarter of the grant year, the QWG will initiate the RBR and affiliates self-audit.

7.2.2 Each RBR and affiliate site performs the self-audit and submits the report to the QWG by the specified date.

7.2.3 The QWG will compile and summarize the data for presentation at the

next EC meeting.

7.2.4 Determined by the EC and collaborating with the QWG, the RBRs and affiliates will produce a plan and timeline for resolving non-conformities.

7.3 Data Quality Testing

Data Quality Testing is carried out to ensure that database records a) correspond to genuine physical biospecimens, b) are consistent with the original documentation generated by clinicians and pathologists at the time of biospecimen collection.

7.3.1 Annually, at the end of the first quarter of the grant year, the HIIRS will generate a list of biospecimens for each ACSR RBR and affilate to audit. The list will contain randomly selected biospecimens in the Annotation of a Tissue Library and Searching (ATLAS) database (See also exceptions, below). The following will be determined:

7.3.1.1 The biospecimen is actually stored in the location given in the database.

7.3.1.2 The biospecimen has the number of units and/or volume given in the database.

7.3.1.3 The biospecimen's processing type (i.e. paraffin block, red-top tube) corresponds to that noted in the database.

7.3.1.4 The database records (for patient, biospecimen batch, and biospecimen) agree with the corresponding processing and original documentation.

7.3.2 If there are any discrepancies between the database and the data review form, the site must resolve this discrepancy on a case-by- case basis and document and list of cases being audited.

7.3.3 Biospecimens will not be randomly selected for a Data Quality Test if they have already been tested within the previous three years.

7.3.4 HIIRS will routinely generate a data query and submit to RBRs and affiliates for data cleanup. A specific data query will be sent for the annual review.

7.3.5 When Data Quality testing is completed for each biospecimen, the site notes the completion date and a brief description of the test findings either electronically or on paper and data is entered into the ACSR database as appropriate

7.4 Biospecimen Quality

Biospecimen quality assessments should include key performance indicators and/or measurements as recorded when processing, quality checks before distribution or survey feedback from researchers. When Biospecimen Quality information is obtained from investigators, the RBR receives a copy of this information for the RBR records. Biospecimen quality assessments are found in the Technical SOPS mentioned in section 3.0

7.5 Preferred Data Standards for Acquiring Biospecimen Collections

7.5.1 Cold chain management information, key performance indicators, collection date, unit type, number of units, volume, processing type, and diagnosis of biospecimen are preferred.

7.5.2 SOPs, submission and processing documentation, data from research which utilized the biospecimens for Quality purposes are also preferred.

7.6 Researcher Feedback

An informal but essential part of Quality Assurance for ACSR is feedback from customers, the researchers, that use ACSR specimens. After disbursement of specimens, an ACSR point of contact sends researchers a Specimen Survey that solicits feedback on the quality of the specimens.The ACSR point of contact will follow up with the researcher whenever possible and ascertain the quality of the specimens received. In many cases, researchers may perform tests on a specimen that can be linked to additional remaining units of that specimen. In addition, these data can be added to processing information for the speciemens. See Appendix - ACSR Biospecimen Survey Form to be filled out by Investigator receiving Specimens

7.7 Quality Assurance Reporting

7.7.1 ACSR RBRs and Affiliates will provide the Quality Working Group a Quality Assurance Summary Report as follows:

7.7.1.1 Results of RBR audit and, if available, feedback from researchers are reported in time for ACSR third quarter EC meeting.

7.7.1.2 The QWG will summarize and provide a recommended plan for improvement for any ACSR component found in need of improvement and this plan will be presented to the EC.

7.7.1.3 The EC will provide guidance for improvement based on the QWG recommendations.

7.7.1.4 The QWG or EC may request additional auditing to resolve any questions or problems regarding key performance indicators.

7.7.2 In general, all procedures should be carried out in a timely manner to facilitate reporting for the annual grant submission.

8.0 APPLICABLE REFERENCES, REGULATIONS AND GUIDELINES

8.1 NCI Best Practices for Biospecimen Resources
http://biospecimens.cancer.gov/practices/default.asp

8.2 US National Biospecimen Network Blueprint
http://biospecimens.cancer.gov/resources/publications/reports/nbn.asp

8.3 National Bioethics Advisory Commission: Research involving human biological materials: Ethical issues and policy guidance, Vol. I: Report and recommendations of the National Bioethics Advisory Committee. August 1999.
http://bioethics.georgetown.edu/nbac/hbm.pdf

8.4 Best Practices for Repositories IV. Collection, Storage, and Retrieval of Biological Materials for Research. International Society for Biological and Environmental Repositories (ISBER). Feb 2018 http://www.isber.org/?page=BPR

9.0 APPENDICES

9.1 ACSR Biospecimen Survey

ACSR Biospecimen Survey

To be filled in by ACSR:

Investigators Name	
LOI#:	
Name of ACSR PI for LOI	
Date Shipped	
Date Received	
Requested Biospecimens	
Data requested	

1. Were all biospecimens listed on the shipping manifest received?
   a. Yes No

2. Did the biospecimens arrive in acceptable condition (proper temperature, tubes/slides intact, etc)?
   a. Yes No
   b. If No, please explain:

9.2 RBR checklist

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Annual RBR Self Assessment Tool

	A	B	C	D	E
1				**ACSR RBR Audit Checklist**	
2	**RBR name**				
3	**Audit Year**				
4	**Responsible person/s**				
5	**Date audit completed**				
6	**Date sent for review**				
7					
8	**I. Facilities**				
9	**Yes**	**No**	**N/A**		**Comments**
10				Is adequate space available at the RBR to carry out the functions assigned by the NCI award?	
11				Do RBR personnel, individually, have sufficient and appropriate work space to accomplish their tasks?	
12				Are computer systems and other electronic systems protected by uninterruptible power supplies (e.g. generators, surge protectors, battery back-up units)?	
13				Are emergency power systems tested periodically to ensure automatic starting and load capacity?	
14				Does the RBR keep a log of the names to whom keys, codes, or access cards have been issued?	
15				Does the RBR have a plan for responding to all emergencies appropriate to its geographic location?	
16				Are emergency contact numbers posted in obvious places?	
17	**II. Personnel**				
18	**Yes**	**No**	**N/A**	**1. General**	**Comments**
19				Is current staffing sufficient to meet the award objectives of the RBR?	
20				Does the RBR have a documented organizational chart that clearly defines reporting relationships available for inspection?	
21				Are written position descriptions available for all ACSR-supported personnel and consultants working for the RBR?	
22				If yes, are there clearly delineated scopes of work for each?	
23				Are CVs available for key personnel for inspection?	
24				Does the RBR require personnel to sign Confidentiality Agreements?	
25				If yes, are the signed agreements available for inspection?	
26				Have there been any changes in key personnel from the previous Site Visit?	
27				Have any job descriptions changed from the previous Site Visit?	
28				Does the RBR have a documented personnel absence notification procedure?	
29				Does the RBR have a plan of action in place to cover key personnel activities during the absence of staff?	
30	**Yes**	**No**	**N/A**	**2. Training**	**Comments**
31				Are any of the following education and/or training programs required for the employee:	
32				Ethics certification?	
33				HIPAA certification?	
34				Shipping Certification?	
35				Blood borne pathogens?	
36				Safety?	
37				IRB/Human Research Training?	
38				Other? (list in comments)	
39				Are records of required personnel activities reviewed annually to ensure that all required training and education programs are completed?	

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	A	B	C	D	E
34	**III. Internal Guidelines – Policies and Procedures**				
35	**Yes**	**No**	**N/A**	**1. General**	**Comments**
36				Is there a mechanism in place that the RBR uses to evaluate its interactions with the HIIRS?	
37				Is there a mechanism in place that the HIIRS uses to evaluate its interactions with the RBR?	
38				Are policies and procedures that outline the roles and functions within the ACSR enterprise in place?	
39				Are current hard-copies of the MOO and SOP available for personnel?	
40				Are electronic copies of the current MOO and SOPs available for personnel?	
41				Are RBR personnel required to review the ACSR's MOO and SOPs relevant to their positions and the internal operation of the ACSR at time of hire, annually and after updates are posted?	
42				Is there a mechanism in place for documenting personnel's review and comprehension of the MOO and SOPs?	
43				Is there a mechanism in place to document non-compliance to the MOO or SOPs?	
44				If yes, are incidences of non-compliance reported to the Executive Committee for review and resolution?	
45	**Yes**	**No**	**N/A**	**2. Administrative**	**Comments**
46				Has the RBR had any issues/incidents related to regulations on human subjects, handling of specimens and/or data, workplace safety, or any other aspect of ACSR operations?	
47				If yes, is there documentation that the incident has been resolved?	
48				Are current SOPs available to provide guidelines for all major internal functions?	
49				Does the RBR utilize a "trouble log" to document problems, errors, or accidents that personnel bring to the attention of the PI and/or the Executive Committee?	
50	**IV. External Guidelines**				
51	**Yes**	**No**	**N/A**		**Comments**
52				Does the RBR interface with entities providing external guidance and feedback (e.g. host institution)?	
53				If yes, are these events documented so that the activity can be reviewed?	
54				Are letters/certificates of IRB current approval kept in a central location and/or available for review?	
55				When specimen data is shared, are mechanisms in place that ensure proposed uses are consistent with the informed consent and authorization?	

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	A	B	C	D	E
56	**V. Bioinformatics Management**				
57	**Yes**	**No**	**N/A**	**1. General**	**Comments**
58				Is the computer facility and computer hardware (server) in a dust free, well-maintained and adequately ventilated environment?	
59				Is there a point of contact person at the RBR for all computer and database issues including malfunctions?	
60				Does the RBR track the identity of all persons who have access to ACSR computers and software?	
61				Are there defined permissions for access into the informatics system?	
62				Is there documentation showing that all users of the ACSR database received adequate training initially, after system modifications, and/or after installation of a new or updated version?	
63				Does the RBR test revised or new software when first installed and after any modifications?	
64				Is there a current user's manual for data entry?	
65				If the facility uses a public network, such as the internet as a data exchange medium (e.g. quarterly exports), are there adequate network security measures in place to ensure confidentiality of ACSR biorepository data?	
66	**Yes**	**No**	**N/A**	**2. Maintenance**	**Comments**
67				Is there a process to monitor computer system performances, to ensure that data storage capacity and performance of the ACSR database system is sufficient to meet Site needs?	
68				Does the RBR have a site-specific SOP for the preservation of data and equipment in case of an unexpected destructive event (e.g. earthquake, flood), software failure and/or hardware failure?	
69				Do these procedures allow for the timely restoration of data?	
70				Is there a documented mechanism in place to verify the integrity of the system (operating system, applications and database) after restoration of data files?	
71				Is there a documented schedule and procedure for regular maintenance of hardware and software either by maintenance contracts or documented in-house procedures?	
72				Has the RBR used an interface to populate the ACSR Database with data from another source?	
73				If yes, did the Site work with the HIIRS to ensure that the interface was compatible with the current ACSR Database and was properly encrypted?	
74				Is there documentation for each instance of custom interface use with data transfer?	

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	A	B	C	D	E
75	**VI. Biospecimen Management**				
76	**Yes**	**No**	**N/A**	**1. Policies, Procedures and Protocols**	**Comments**
77				Are the following SOPs utilized?	
78				Biospecimen collection SOPs?	
79				Biospecimen processing SOPs?	
80				Biospecimen storage SOPs?	
81				Biospecimen distribution SOPs?	
82				Biosafety SOPs?	
83				Are plans in place to protect biospecimens in the event of a natural disaster or other conditions?	
84				Are specimens labeled following ACSR accepted procedures?	
85				Does the RBR review and maintain Patient and Clinical Forms?	
86				Are adequate QA/QC measures in place to verify the Biospecimen inventory?	
87				Is the percent of the current inventory subject to QA/QC measures:	
88				1 - 25%	
89				26 - 50%	
90				51 - 75%	
91				76 - 100%	
92				Are adequate QA/QC measure in place to ensure Biospecimen quality?	
93				Is the percent of the current inventory subject to QA/QC measures:	
94				1 - 25%	
95				26 - 50%	
96				51 - 75%	
97				76 - 100%	
98				Are biospecimens examined and confirmed by pathologists on entering the biorepository?	
99				Are biospecimens examined and confirmed by pathologists upon disbursement from the biorepository?	
100				Are biomolecular derivatives (e.g. DNA, RNA, and protein) analyzed to ensure molecular integrity?	
101				Are the Biospecimen inventory QA/QC measures compliant with the ACSR Best Practices?	
102	**Yes**	**No**	**N/A**	**2. Custodianship**	**Comments**
103				Does the RBR house anonymized specimens?	
104				Does the RBR have a formal plan for custodianship of biospecimens?	
105				Does the RBR have a formal plan for custodianship of related data?	
106				Does the RBR track the following:	
107				Movement of biospecimens within the RBR?	
108				Movement of biospecimens between RBRs?	
109				Results of QA/QC tests on biospecimens?	
110				Dissemination of specimens and associated data within the ACSR?	
111				Dissemination of specimens and associated data outside the ACSR?	
112				Current Biospecimen availability?	
113				Events which affect the integrity of the specimens (e.g. thawing events)?	
114				The receipt of approved MTAs?	

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	A	B	C	D	E
121	**VI. Biospecimen Management continued**				
122	**Yes**	**No**	**N/A**	**3. Privacy Protection**	**Comments**
123				Does the RBR adequately protect the privacy and confidentiality of research participants?	
124				Is the transfer of data done in a manner that complies with HIPAA and other regulations?	
125				Is there a data access policy to control access to PHI by Site personnel?	
126	**VII. ACSR Interface**				
127	**Yes**	**No**	**N/A**	**1. HIIRS**	**Comments**
128				Does the RBR work with the HIIRS to confirm site inventory and activities (publications, presentations, conference attendance) to post to the quarterly dossier report and web Site?	
129				Does the RBR work with the HIIRS to confirm activities (publications, presentations, conference attendance) to post to the quarterly dossier report and web Site?	
130				Does the RBR respond to inquiries from the HIIRS in a timely manner ensuring that site inventory matches information in the database?	
131				Does the RBR work with the HIIRS to confirm receipt of MTAs prior to shipping specimen to approved investigators?	
132				Does the RBR communicate to the HIIRS when specimens have been shipped to approved investigators?	
133				Has the RBR identified all personnel who should have access to the member's tab on the ACSR web site?	
134	**Yes**	**No**	**N/A**	**2. ACSR Working Groups**	**Comments**
135				Does the RBR have representation on each of the following working groups?	
136				Marketing	
137				Science and Technology	
138				Informatics	
139				Quality	

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10.0 REVISION HISTORY

SOP Number	Date revised	Author	Summary of Revisions
Tech014	4-3-218	AL/BGG/TY/ MS/MC	Revise Section 7.4, 7.5, 7.6 and add checklist, format, and definitions, edit checklist