

CTRNet Standard Operating Procedure Assesing Quality of Tissue Specimens			
SOP Number:	5.1.001	Version	e1.0
Supersedes:	SR 001.001	Effective Date	09 Jan 08
Subject:	Assesing Quality of Tissue Specimens	Category	Quality Assurance

Prepared By:		Jean de Sousa-Hitzler		
	Signature	Name	Title	ddMmmyy
Approved By:		Peter Geary	CEO	09 Jan 08
	Signature	Name	Title	ddMmmyy
Approved By:				
	Signature	Name	Title	ddMmmyy

REVISION HISTORY

SOP Number	Author (initials)	Date Issued	Summary of Revisions
QA 001.001	JdSH	2005	
5.1.001 e1.0	JdSH	2008	Modified to cover quality assessment of tissue specimens only (pathology review)

1.0 PURPOSE

Quality control is fundamental to the successful operation to a tissue bank offering tissue specimens for research purposes. High level of tissue quality is essential to avoid introducing inconsistencies and variables into research studies. CTRNet repositories should be confident that they are providing tissue samples with the appropriate quality to meet the research needs of investigators. Testing procedures should be in place to monitor and assess the quality of the samples.

The purpose of this procedure is to outline a minimum of testing and assessment that should be carried on tissue to maintain standardization of tissue quality.

2.0 SCOPE

This standard operating procedure (SOP) outlines minimum assessment and testing of morphological features that that should be in place to evaluate the quality of tissue samples stored in the repository; in order to provide investigators with a product that is consistent with their needs. This SOP does not cover an assessment of molecular quality.

The SOP does not cover detailed safety procedures for handling Human Biological Materials (HBMs) or hazardous chemicals and it is recommended that personnel follow institutional safety guidelines.

3.0 REFERENCE TO OTHER POLICIES AND SOPS

1. CTRNet Policy: POL 005.001 Records and Documentation
2. CTRNet Policy: POL 007.001 Material and Information Handling Policy
3. CTRNet Generic SOP # QA 001.001 Assessing Quality of Tissue Samples
4. CTRNet SOP: 5.1.003 Assessing Quality/Purity of Extracted Nucleic Acids.

4.0 ROLES AND RESPONSIBILITY

The policy applies to all personnel from CTRNet member repositories that are responsible for assessing the quality of tissue specimens.

Tumour Bank Personnel	Responsibility/Role	Site Specific Personnel and Contact Information
Pathologist	Conduct Histopathological characterization	
Pathology Lab Technician	Conducts and assists with quality assurance procedures. Records and documents outcomes.	

5.0 MATERIALS, REAGENTS EQUIPMENT AND FORMS

The materials, equipment and forms listed in the following list are recommendations only and may be substituted by alternative/equivalent products more suitable for the site-specific task or procedure.

Materials and Equipment	Materials and Equipment (Site- Specific)
Markers, ink and pens	
Eosin	
Harris Haematoxylin (filtered)	
Microscope	
Slides	

6.0 DEFINITIONS

Quality: Conformance of a specimen or process with pre-established specifications or standards.

Quality Assurance (QA): All those planned and systematic actions that are established to ensure that the Tumour Repository Program is performed and the data are generated, documented (recorded), and reported in compliance with applicable regulatory requirement(s).

Quality Control: Quality control is the system of technical activities that measures the attributes and performance of a process, or item, against defined standards, to verify that the stated requirements are fully met.

QMS: Same as QA above

7.0 PROCEDURES

The research and scientific utility of the data obtained from the analysis of tissue depends on the quality of the tissue sample. These procedures outline minimum steps that should be followed to ensure that tissue samples collected stored and distributed are of sufficient morphological caliber to meet the research needs of the investigators. An assessment of the quality of molecular elements (nucleic acids) is covered in CTRNet SOP # 5.1.003.

7.1 General Considerations for morphological review.

1. At a minimum, assessment must consist of morphologic review of all collected tissue [FROZEN and FORMALIN FIXED PARAFFIN EMBEDDED (FFPE)] samples (including archival material).
2. Use researcher feedback about sample quality to refine collection and storage practices and guide evolution of Quality Control procedures.
3. Develop a defined scoring system that allows a 'quality score' to be assigned to a tissue or molecular sample that has undergone assessment at a designated quality control laboratory. The score (assigned levels) will help in the interpretation of the quality assessment results and correlate to the suitability of the tested sample for specified research applications.

7.2 Levels of frozen tissue specimen.

CTRNet will recognizes four levels of specimens based on time to freezing (for FROZEN TISSUE samples only) and these levels will determine the particular research application for which they may be utilized. This system does not assess quality but serves as a prediction

that certain molecular elements may be conserved. The choice of banking Test Level specimens is left to the discretion of the member repositories.

1. A Gold level specimen will be harvested directly from the participant, from either an intra-operative biopsy or as soon as possible following surgical resection.
2. A Silver level specimen will be harvested as soon as possible following specimen removal within a range of 15 - 30 minutes post resection.
3. A Bronze level specimen will be harvested within two hours of surgery, either in the operating room or in the pathology specimen cutting room.
4. A Test Level specimen is one where the time from surgical resection to harvesting is unknown or longer than 2 hours.
5. Record level of specimen quality based on harvesting times recorded during specimen collection, harvesting and freezing.
6. In the event of any deviation from normal procedure, the quality of samples may be compromised. In this case, assess any adverse change in quality and adjust the quality level assigned to reflect this.
7. Record adjustments to the assigned quality level.

7.3 Quality Assessment - Pathology Review

1. Basic quality control practice must include a morphologic review of Formalin fixed, H&E stained slide, representative (mirror-image, adjacent) of the SNAP FROZEN or FORMALIN FIXED PARAFFIN EMBEDDED tissue sample (for each relevant FFPE block).
2. The review must be performed by an independent individual, qualified by experience and training to do so.
3. The review must confirm and assess:
 - Tissue type and assessment of diagnosis
 - Tumour type
 - Tumour grade
 - Presence of tumour
 - Percent cellularity of tumour and stroma
 - Percent necrosis or signs of degradation
 - Presence of inflammatory cells
4. Upon microscopic examination of the slide a digital image of an area representative of the tissue sample must be stored in the bank database.
5. Record results of review in database. For sample review worksheets see Appendix 1.

8.0 APPLICABLE REFERENCES, REGULATONS AND GUIDELINES

1. Declaration of Helsinki. <http://ohsr.od.nih.gov/helsinki.php3>
<http://www.wma.net/e/policy/b3.htm>
2. Tri-Council Policy Statement; Ethical Conduct for Research Involving Humans; Medical Research Council of Canada; Natural Sciences and Engineering Council of Canada; Social Sciences and Humanities Research Council of Canada, August 1998. <http://www.pre.ethics.gc.ca/english/policystatement/policystatement.cfm>
3. Human Tissue and Biological Samples for use in Research. Operational and Ethical Guidelines. Medical Research Council Ethics Series. http://www.mrc.ac.uk/pdf-tissue_guide_fin.pdf
4. Best Practices for Repositories I. Collection, Storage and Retrieval of Human Biological Materials for Research. International Society for Biological and Environmental Repositories (ISBER). <http://www.isber.org>
5. US National Biospecimen Network Blueprint http://www.ndoc.org/about_ndc/reports/NBN_comment.asp
6. Jewell, S. et al. 2002, Analysis of the Molecular Quality of Human Tissues, an experience from the Cooperative Human Tissue Network. Am. J. Clin. Pathol. 118:733-741.
7. Snell L. and P. H. Watson. 2006, Breast Tissue Banking: Collection, Handling, Storage, and Release of Tissue for Breast Cancer Research. Methods Mol Med. 120:3-24.
8. Alberta Research Tumour Bank, Best Practices Guide, Version 2. 2006
9. Pathology Review Worksheets. British Columbia Cancer Agency - Tumour Tissue Repository.

Appendix A. Ovarian and Uterine Sample Worksheet

Sample ID:

Pathologist:

Date Reviewed:

Type: Serous Mucinous Endometriod Other:_____

Grade:

Score: Nuclei= Mitosis= Architecture= Total=

Category: Well diff Mod diff Poor diff

Epithelial Components: INV%_____ N%_____

Stroma: STR%_____

Nec% : _____

Inf (0-3): _____

Qc (1-3): _____

Additional Comments:

Type, Grade Score, Grade Category: Standard clinical definitions

INV%, N%, STR%: estimated % of cross sectional area in each section occupied by invasive and normal epithelial components and muscle/fat/stroma components. INV, N, are estimated and STR% is a database calculated field, such that the total of all three components =100%.

Nec%: estimated % of cross sectional area of invasive tumour component in each section occupied by necrosis.

Inf: estimated intensity of inflammatory infiltrates within each section on a scale of 0 (absent), 1 (sparse), 2 intermediate, 3 (extensive, high).

Qc: estimated quality of nuclear morphological preservation. 1=poor preservation of chromatin, nuclear shape and distinction of mitotic figures such that accurate grading is not possible, 2=moderate preservation such that some nuclear detail and mitotic figures can only be distinguished with difficulty, 3= good to excellent preservation of nuclear features.

Appendix B. Breast Sample Worksheet

Sample ID:

Pathologist:

Date Reviewed:

Type: Ductal Lobular D-L Mix Tubular Mucinous DCIS
Other: _____

Grade:

Score: Tubules= Nuclear= Mitosis= Total=

Category: Well diff Mod diff Poor diff

Epithelial Components: INV% _____ N% _____ IS%

Stroma: STR% _____

Nec% INV: _____

NEC% IS: _____

Inf (0-3): _____

Qc (1-3): _____

Additional Comments:

Type, Grade Score, Grade Category: Standard clinical definitions by Nottingham criteria

INV%, IS%, N%, STR%: estimated % of cross sectional area in each section occupied by invasive, *in situ* and normal epithelial components and muscle/fat/stroma components. INV, IS, N, are estimated and STR% is a database calculated field, such that the total of all three components =100%.

Nec%: estimated % of cross sectional area of invasive and *in situ* tumour component in each section occupied by necrosis.

Inf: estimated intensity of inflammatory infiltrates within each section on a scale of 0 (absent), 1 (sparse), 2 intermediate, 3 (extensive, high).

Qc: estimated quality of nuclear morphological preservation. 1=poor preservation of chromatin, nuclear shape and distinction of mitotic figures such that accurate grading is not possible, 2=moderate preservation such that some nuclear detail and mitotic figures can only be distinguished with difficulty, 3= good to excellent preservation of nuclear features.

Appendix C. Colon Sample Worksheet

Sample ID:

Pathologist:

Date Reviewed:

Type: Adenocarcinoma Adenocarcinoma(mucinous)
 Adenocarcinoma (signet ring) Adenoma Other: _____

Grade:

Score: Tubules= Nuclear= Mitosis= Total=

Category: Well diff Mod diff Poor diff

Epithelial Components: INV% _____ N% _____ IS%

Stroma: STR% _____

Nec% INV: _____

Inf (0-3): _____

Qc (1-3): _____

Additional Comments:

Type, Grade Score, Grade Category: Standard clinical definitions by Nottingham criteria

INV%, IS%, N%, STR%: estimated % of cross sectional area in each section occupied by invasive, *in situ* and normal epithelial components and muscle/fat/stroma components. INV, IS, N, are estimated and STR% is a database calculated field, such that the total of all three components =100%.

Nec%: estimated % of cross sectional area of invasive and *in situ* tumour component in each section occupied by necrosis.

Inf: estimated intensity of inflammatory infiltrates within each section on a scale of 0 (absent), 1 (sparse), 2 intermediate, 3 (extensive, high).

Qc: estimated quality of nuclear morphological preservation. 1=poor preservation of chromatin, nuclear shape and distinction of mitotic figures such that accurate grading is not possible, 2=moderate preservation such that some nuclear detail and mitotic figures can only be distinguished with difficulty, 3= good to excellent preservation of nuclear features.

Appendix D. Generic Sample Worksheet

Sample ID:

Pathologist:

Date Reviewed:

Type: Adenocarcinoma Squamous carcinoma Transitional carcinoma
 Carcinoma, NOS Other_____

Grade:

Score: Tubules= Nuclear= Mitosis= Total=

Category: Well diff Mod diff Poor diff

Epithelial Components: INV%_____ N%_____ IS%

Stroma: STR%_____

Nec% INV: _____

Inf (0-3): _____

Qc (1-3): _____

Additional Comments:

Type, Grade Score, Grade Category: Standard clinical definitions by Nottingham criteria

INV%, IS%, N%, STR%: estimated % of cross sectional area in each section occupied by invasive, *in situ* and normal epithelial components and muscle/fat/stroma components. INV, IS, N, are estimated and STR% is a database calculated field, such that the total of all three components =100%.

Nec%: estimated % of cross sectional area of invasive and *in situ* tumour component in each section occupied by necrosis.

Inf: estimated intensity of inflammatory infiltrates within each section on a scale of 0 (absent), 1 (sparse), 2 intermediate, 3 (extensive, high).

Qc: estimated quality of nuclear morphological preservation. 1=poor preservation of chromatin, nuclear shape and distinction of mitotic figures such that accurate grading is not possible, 2=moderate preservation such that some nuclear detail and mitotic figures can only be distinguished with difficulty, 3= good to excellent preservation of nuclear features.