CTRNet Standard Operating Procedure Assessing Quality of Tissue Specimens			
SOP Number:	05.001	Version:	e2.0
Supersedes:	5.1.001 e1.0	Category:	Quality Assurance

Approved By:	CTRNet Management Group (CMG)	01-May-2012
	Per: Brent Schacter	31-May-2012

1.0 PURPOSE

Quality assurance is fundamental to the successful operation of a tissue biobank offering tissue specimens for research purposes. A high standard of tissue quality is essential to avoid introducing inconsistencies and variables into research studies. CTRNet biobanks 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.

2.0 SCOPE

This standard operating procedure (SOP) outlines the minimum assessment required to evaluate the quality of tissue samples stored in the biobank in order to provide investigators with a product that is consistent with their needs. This SOP does not cover an assessment of molecular quality.

3.0 REFERENCE TO OTHER CTRNET SOPS OR POLICIES

Note: When adopting this SOP for local use please reference CTRNet.

3.1 *CTRNet Policy: POL 5 Records and Documentation*
3.2 *CTRNet Policy: POL 7 Material and Information Handling*
3.3 *CTRNet Standard Operating Procedure: SOP 05.002 Assessing Quality of Nucleic Acids*
3.4 *CTRNet Standard Operating Procedure: SOP 08.01.002 Biohazardous Material Waste Management*

4.0 ROLES AND RESPONSIBILITIES

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

Tumour Biobank Personnel	**Responsibility/Role**
Pathologist	Conduct histopathological characterization
Pathology Laboratory Technician/Technologist	Conducts and assists with quality assurance procedures. Records and documents outcomes.

5.0 MATERIALS, REAGENTS EQUIPMENT AND FORMS

The materials, reagents, 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

See the CTRNet Program Glossary: http://www.ctrnet.ca/glossary

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 calibre to meet the research needs of the investigators. An assessment of the quality of molecular elements is covered in *CTRNet SOP 05.002 - Assessing Quality of Nucleic Acids.*

7.1 General Considerations for Morphological Review

The biobank should ensure that morphological review to determine sample composition is conducted by the biobank or that the researcher knows that it has not been conducted.

7.1.1 At a minimum, assessment must consist of morphologic review of all collected tissue [frozen and formalin fixed paraffin embedded (FFPE)] samples (including archival material).

7.1.2 Use researcher feedback about sample quality to refine collection and storage practices and guide evolution of Quality Control procedures.

7.1.3 Use a defined scoring system that allows researchers to interpret whether the tissue is suitable for the proposed assay.

An empirical example of a scoring system for frozen tissue is as follows:

7.1.4 A Gold level specimen will be harvested directly from the participant, from either an intra-operative biopsy or as soon as possible (<15 min) following surgical resection.

7.1.5 A Silver level specimen will be harvested as soon as possible following specimen removal within a range of 15 - 30 minutes post resection.

7.1.6 A Bronze level specimen will be harvested within two hours of surgery (30 min to 120 min), either in the operating room or in the pathology specimen cutting room.

7.1.7 A Test Level specimen is one where the time from surgical resection to harvesting is unknown or longer than 2 hours.

7.2 Quality Assessment – Pathology Review

7.2.1 Basic quality control practice must include a morphologic review of Formalin fixed, Hematoxylin and Eosin (H&E) stained slide, representative (mirror-image, adjacent) of the snap frozen or formalin fixed paraffin embedded tissue sample (for each relevant FFPE block).

7.2.2 The review must be performed by a qualified individual.

7.2.3 It is suggested that the review 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

7.2.4 Ideally if digital imaging is available, a digital image of an area representative of the tissue sample should be stored in the biobank database.

7.2.5 Record Results of review in database. For sample review worksheets see Appendix.

8.0 APPLICABLE REFERENCES, REGULATIONS AND GUIDELINES

8.1 Declaration of Helsinki.
http://www.wma.net/en/30publications/10policies/b3/index.html

8.2 Tri-Council Policy Statement 2; 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, December 2010.
http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/Default/

8.3 Human Tissue and Biological Samples for use in Research. Operational and Ethical Guidelines. Medical Research Council Ethics
http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC002420

8.4 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/Search/search.asp?zoom_query=best+practices+for+repositories

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

8.6 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.

8.7 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.

8.8 Alberta Research Tumour Bank, Best Practices Guide, Version 2. 2006

8.9 RO, Parisien M, Murphy LC, Watson PH. Influence of Evolution in Tumour Biobanking on the Interpretation of Translational Research. Cancer Epidemiol Biomarkers Prev. 17(12): 3344-50. 2008. PMID: 19064549.
http://www.ncbi.nlm.nih.gov/pubmed/19064549

9.0 APPENDICES

9.1 Appendix A – Ovarian and Uterine Sample Worksheet
9.2 Appendix B – Breast Sample Worksheet
9.3 Appendix C – Colon Sample Worksheet
9.4 Appendix D – Generic Sample Worksheet

10.0 REVISION HISTORY

SOP Number	Date revised	Author	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)
5.1.001 e1.0	May 2012	CMG	• Grammatical and formatting throughout • Definitions removed • Revision History moved to bottom • Reference links updates • Updated SOP references • Section 1: Deleted second paragraph. • Section 2: Deleted second paragraph and inserted reference to SOP in Section 3. • Section 7.1 & 7.2: Procedures reviewed and revised. • Section 8 – Item 9 deleted. • Deleted Section 3, Generic QA SOP 001.001.

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.

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.

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.

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.