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.

<table>
<thead>
<tr>
<th>Tumour Biobank Personnel</th>
<th>Responsibility/Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathologist</td>
<td>Conduct histopathological characterization</td>
</tr>
<tr>
<td>Pathology Laboratory Technician/Technologist</td>
<td>Conducts and assists with quality assurance procedures. Records and documents outcomes.</td>
</tr>
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</table>
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.

<table>
<thead>
<tr>
<th>Materials and Equipment</th>
<th>Materials and Equipment (Site Specific)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Markers, ink and pens</td>
<td></td>
</tr>
<tr>
<td>Eosin</td>
<td></td>
</tr>
<tr>
<td>Harris Haematoxylin (filtered)</td>
<td></td>
</tr>
<tr>
<td>Microscope</td>
<td></td>
</tr>
<tr>
<td>Slides</td>
<td></td>
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</table>

6.0 DEFINITIONS

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

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.  

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


8.5 US National Biospecimen Network Blueprint  


Assessing Quality of Tissue Specimens


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

<table>
<thead>
<tr>
<th>SOP Number</th>
<th>Date revised</th>
<th>Author</th>
<th>Summary of Revisions</th>
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<tr>
<td>QA 001.001</td>
<td>JdSH 2005</td>
<td></td>
<td></td>
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<tr>
<td>5.1.001 e1.0</td>
<td>JdSH 2008</td>
<td></td>
<td>Modified to cover quality assessment of tissue specimens only (pathology review)</td>
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<td>5.1.001 e1.0</td>
<td>May 2012 CMG</td>
<td></td>
<td>• Grammatical and formatting throughout</td>
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<td>• Definitions removed</td>
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<td>• Section 2: Deleted second paragraph and inserted reference to SOP in Section 3.</td>
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<td>• Section 7.1 &amp; 7.2: Procedures reviewed and revised.</td>
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<td>• Section 8 – Item 9 deleted.</td>
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<td>• Deleted Section 3, Generic QA SOP 001.001.</td>
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</table>
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, \textit{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 \textit{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. 
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