Sample Submission Instructions

Purpose

To provide instructions for submission of samples by Users of the OICR Genomics platform.

Scope

OICR Genomics receives fresh frozen (FF) tissue, formalin-fixed paraffin embedded (FFPE) tissue, whole blood, blood components, cells collected using laser-capture microdissection (LCM), and nucleic acids (DNA, RNA) for use in downstream molecular assays.. This Standard Operating Procedure (SOP) provides instructions for Users to guide their submission of samples to OICR, ensuring that all materials are appropriate for testing. The SOP applies to all staff who receive samples, and all Users who ship samples.

Responsibilities

Management:
Define acceptable sample submission criteria
Review criteria at least annually to ensure that they are appropriate

Laboratory Staff:
Inspect samples, submission forms and other required documents to ensure criteria are met

User:
Review and follow Sample Submission Instructions

Sample Submission Procedure

1. Project details are determined and documented by the Production Manager, Genomics Program Manager and the User.
    a. The Project Information Form is completed by the User. This form must describe:
        i. The type of specimens to be submitted by the Users
        ii. The laboratory assays and sequencing device configuration to be applied for each specimen type
        iii. Metadata fields to be provided with each sample, including the minimum data elements necessary for laboratory and bioinformatic analysis
        iv. Desired bioinformatic analysis and any custom analysis required
        v. How samples and data are handled at project closure. At the request of the User, specimens or data will either be destroyed, returned, or retained for a specified period of time.

   b. The Genomics Production Manager creates a project on the LIMS (MISO) and on the wiki.
2. A project cost estimate is created by the Genomics Program Manager via FreshBooks and approved by the User.
3. Once the estimate is approved, the User will document the specimens for submission in one of two ways:
   a. For RUO projects, they will complete the TW. OICR Genomics Sample Submission Form and email it to the Genomics Production Manager and the Tissue Portal Project Coordinator. This is done for delivery of each batch of samples.
   b. For clinically reported assays, they will submit a single requisition per patient through the OICR Genomics Requisition System, as described in QM. Requisition and Reporting System.
   c. If human derived samples or animal samples are being submitted, the User must forward their REB approval letter for verification before samples will be accepted. This is not required for commercially-available cell lines.
4. After reviewing submission documents to ensure they are complete, Tissue Portal will contact the User via email to coordinate the material transfer. The samples will either be mailed to Tissue Portal, or a drop-off will be scheduled at a mutually convenient time.
5. Samples will be received by Tissue Portal in accordance with TM. Genomics Sample Receipt.

Sample Submission Requirements

Nucleic Acids

1. Sample Volume
   a. DNA should be suspended in 1X TE buffer to a total volume of at least 12ul.
   b. RNA should be suspended in RNAse-free water to a total volume of at least 12ul.
2. Containers
   a. Low-bind (low-retention) plastic tubes or plates should be used to contain the samples.
   b. Containers must not be leaking or broken in any way.
3. Labeling
   a. The User must de-identify samples prior to submission and ensure that **no PHI** is sent to OICR.
   b. Tubes and plates must be clearly labeled with sample IDs matching those listed on the Sample Submission Form or Requisition form.
   c. Sample IDs must be unique within the batch submitted.
4. Shipping Conditions
   a. Samples must be shipped on dry ice.
   b. Avoid sending samples on holidays or over weekends, where delays may occur, leading to temperature fluctuations.

FFPE Tissue

1. Amount of Tissue
    a. 10x 10um sections mounted on slides (uncharged preferred).
        i. These must be air dried for validated clinical assays.
    b. 5x 10um sections mounted on slides (uncharged prefered).
        i. These must be air dried for validated clinical assays.
    c. Tissue block
2. Tumour Content
    a. For validated clinical assays, a tumour content $\geq$30% is required within marked regions of interest.
3. Corresponding H&E
    a. If macrodissection is needed, a corresponding H&E section reviewed and marked by a pathologist must be submitted with the tissue, unless prior agreement has been made for an H&E to be cut at Tissue Portal (RUO) and reviewed by a pathologist (clinical).
    b. Marked region of interest must be $\geq$15 mm^2.
    c. The following information (when applicable) must be listed for all validated assays:
        - % Necrosis of the tumor area.
        - % Tumor cellularity of the tumor area
4. Labeling
    a. The User must de-identify samples prior to submission and ensure that **no PHI** is sent to OICR.
    b. Blocks and/or slides must be clearly labeled with sample IDs matching those listed on the Sample Submission Form or Requisition Form.
    c. Sample IDs must be unique within the batch submitted and for validated clinical assays, two identifiers must be used.
5. Shipping Conditions
    a. Slides and FFPE blocks must be shipped at ambient temperature, with an ice pack during warm weather.
    b. Slides must be packaged in such a way that they do not break in transit.
    c. Avoid sending samples on holidays or over weekends, where delays may occur, leading to temperature fluctuations.

Fresh Frozen Tissue

1. Amount of Tissue
    a. Tissue pieces >5mm^3 should be submitted and may be mounted in OCT.
        i. For validated clinical assays, a fresh frozen tissue block must be submitted.
    b. If LCM tissue is being accepted, a pilot project must be completed to determine the amount of material that is required to be submitted, as this is highly variable across tissue types and regions of interest.

2. Tumour Content
    a. For validated clinical assays, a tumour content ≥30% is required.
3. Corresponding H&E
    a. The following information (when applicable) must be listed for all validated assays:
        - % Necrosis of the tumor area.
        - % Tumor cellularity of the tumor area
4. Labeling
    a. The User must de-identify samples prior to submission and ensure that **no PHI** is sent to OICR.
    b. Frozen tissue blocks and/or slides must be clearly labeled with sample IDs matching those listed on the Sample Submission Form or Requisition Form.
    c. Sample IDs must be unique within the batch submitted and for validated clinical assays, two identifiers must be used.
5. Containers
    a. Tubes should be used to contain the samples if not embedded. If embedded, a mold wrapped with aluminum foil is acceptable.
    b. Containers must not be leaking or broken in any way.
6. Shipping Conditions
    a. Tissue must be shipped on dry ice.
    b. Slides must be shipped at ambient temperature.
    c. Slides must be packaged in such a way that they do not break in transit.
    d. Avoid sending samples on holidays or over weekends, where delays may occur, leading to temperature fluctuations.

Blood for Reference DNA

1. Sample Volume
    a. A minimum of 250uL of buffy coat or whole blood is suggested.
        i. 250uL of buffy coat is suggested for validated clinical assays, but is not an absolute requirement. The sample will be accepted as long as it produces a sufficient amount of nucleic acid for processing.
2. Containers
    a. Well-sealed cryovials or microcentrifuge tubes of any volume may be submitted.
    b. Containers must not be leaking or broken in any way.
3. Labeling
    a. The User must de-identify samples prior to submission and ensure that **no PHI** is sent to OICR.
    b. Tubes must be clearly labeled with sample IDs matching those listed on the Sample Submission Form or Requisition Form.
    c. Sample IDs must be unique within the batch submitted and for validated clinical assays, two identifiers must be used.
4. Shipping Conditions

a. Samples must be shipped on dry ice. STRECK or EDTA tubes must be shipped with an ice pack within the shipping container. These tubes must NOT be frozen or shipped with dry ice.
b. Avoid sending samples on holidays or over weekends, or when delays may occur leading to temperature fluctuations.

Blood Plasma for cfDNA Extraction

1. Sample Volume
    a. A minimum of 1mL of plasma is required for RUO assays.
    b. A minimum of 6mL of plasma is required for clinically reported assays, this must have been obtained using a double spin protocol from an EDTA or STRECK tube.
2. Containers
    a. Well-sealed cryovials, conicals or microcentrifuge tubes should be submitted.
    b. Containers must not be leaking or broken in any way.
3. Labeling
    a. The User must de-identify samples prior to submission and ensure that **no PHI** is sent to OICR.
    b. Tubes must be clearly labeled with sample IDs matching those listed on the Sample Submission Form or Requisition Form.
    c. Sample IDs must be unique within the batch submitted and for validated clinical assays, two identifiers must be used.
4. Shipping Conditions
    a. Samples must be shipped on dry ice.
    b. Avoid sending samples on holidays or over weekends, or when delays may occur leading to temperature fluctuations.

Quality Indicators

1. Quality indicators will be used to assess whether samples may enter library preparation.
2. The full list of Quality indicators can be found in the QM. Quality Control and Calibration Procedures SOP, located on the Genomics Quality SharePoint.

Rejected Samples

1. If samples do not meet the requirements for testing, the following procedure should be followed:
    a. A note of the issue will be made in TW. Genomics Q-Notes Log.
    b. The User will be notified that their samples do not meet minimum requirements for testing.
    c. The User will authorize sample return/destruction sample re-submission or one of the options in the table below depending on failed criteria.

Criteria Not Met	Action (other than sample return or destruction)
Volume	DNA and RNA ▪ Prior to User notification, Tissue Portal to dilute sample to appropriate volume with diluent as specified in the TM. Nucleic Acid Aliquotting Procedure SOP provided concentration meets or exceeds requirements. ▪ User to provide additional sample to be pooled with original. Plasma ▪ User to provide additional sample to be pooled with original.
Containers: Tubes or plates leaking or broken	▪ Sample destruction and request for re-submission.
Labeling: Sample labels not clear or unique	▪ Tissue Portal to relabel samples following clarification from User or Genomics Program Manager.
Shipping: Frozen samples arrive thawed	▪ User to authorize sample to proceed for DNA only. Accredited assay may not proceed. ▪ User to provide additional sample to be processed.
Amount of tissue: Insufficient sample volume, material or number of sections	▪ User to provide additional material or authorize sample to proceed.
H&E: Not received.	▪ User to provide H&E or User to authorize the use of 1 unstained slide for H&E at OICR and provide guidance on which pathologist should be contacted for mark-up.
H&E: Not marked.	▪ If pathologist review data indicated 100% tumour, proceed ▪ Return H&E to User for mark-up

2. If the sample will not be tested, this will be marked in MISO by changing the QC status to “Failed: QC” and a QC note will be entered describing the reason for rejection.
3. If the sample is considered sub-optimal, but has been authorized for testing in a Research Use Only (RUO) capacity, communication of this authorization and the action

to be taken will be documented via email and noted in MISO by changing the QC status to: “OKd by User”.

   a. Specimens **MUST** meet submission requirements to be tested using a validated assay.

4. Clients or sites that frequently submit samples improperly will be contacted by the Production Manager or Genomics Program Manager to correct the situation.
   a. A non-conformance will be filed, and corrective actions may result, depending on the nature of the non-conformance.