CM-Path Recommendations for Molecular Testing and Research.

### Best practice guidelines for labs within the CM-Path Network.

## Overview

The practice of molecular testing on pathological tissue samples is growing exponentially, but needs to be generalisable. The first step in this process is reducing variation introduced by processing of tissue from patient to Formalin Fixed Paraffin Embedded (FFPE) or Fresh Frozen (FF) sample. Low concordance rates of, for example, IHC are in part be due to variations in fixation media, time in fixation, processing protocols, and storage methods.

## Named Contact

CM-Path badged labs require at least one named individual within the lab who can be contacted regarding access to tissue, specimens available etc. The contact details of this person will be made available on the CM-Path website. It is advised that this person is a consultant histopathologist or senior lab manager.

## Fixation and processing

As a minimum standard the following data should be collected for all specimens:

* Time of procedure.
* Was the specimen transported refrigerated or vacuum packed?
* Was the specimen processed fresh for frozen tissue? If so:
  + Time of fresh tissue collection.
  + Number and type of specimens (tumour, background, etc)
  + How were the fresh specimens frozen? Snap frozen liquid nitrogen, cryospray.
* Time to addition of formalin.
* Time specimen opened if not processed fresh.
* Time spent in formalin before processing. 24 - 72 hrs is recommended.
* Fixative used - Neutral buffered formalin (NBF) or formal saline? NBF is recommended.
* Platform for processing. Program used - e.g. fatty tissue processing.

In larger tumours an additional block is recommended to be taken for research/immuno/molecular testing. This should be taken as either the first block or clearly labelled as a research block in the pathology report.

It is recommended that FF samples be snap frozen in liquid nitrogen and stored at -80C. Where these facilities are not available cryospray can be used, with the specimen clearly labelled as frozen in this way. Where possible any surplus tissue should be processed for biobanking. Please see biobanking guidelines [here](https://cmpath.ncri.org.uk/our-workstreams/discovery/cmpath-biobanking-overview/cm-path-biobanking-resources/).

## Judging quality

FF specimens for “-omic” testing should, as far as possible, comprise mostly of tumour (>60% of the tissue), with minimal necrosis/apoptosis (<5%), and high cellularity (50 thousand). This should be assessed as far as possible by trained individuals (e.g. Genomics England Limited (GEL) EQA) to avoid common errors resulting in overestimation of tumour content - e.g. hypocellular specimens (with low gDNA content) or specimens with high levels of lymphocytic infiltrate such that tumour gDNA is a low fraction of overall DNA.

GEL guidelines can be found [here](https://www.genomicsengland.co.uk/information-for-gmc-staff/sample-handling-guidance/). Ideally assessment of quality for “-omic” tests should be assessed by a named individual with GEL EQA competencies.

## Releasing tissue

Labs should have dedicated SOP for block release to research. Requirements for block release for research are evidence of: consent, ethical approval. Further guidance on Cellular Pathology procedures with regards to release of research tissue samples can be found [here](http://cmpath.ncri.org.uk/wp-content/uploads/2018/04/CM-Path-Cellular-Pathology-procedures-with-regards-to-release-of-research-tissue-samples.docx).

Labs should have a named contact to oversee block release.

An up-to-date database of stored samples should be maintained.

## Integrated reporting

Labs should adhere to the advice on integrated reporting set out in the document produced by the Royal College of Pathologists that can be found [here](https://www.rcpath.org/asset/442FCDC1-AF22-401F-8FCD1B4B65603810/).

## Diagnostic archive access

Guidelines for converting a diagnostic archive into a research archive can be found [here](http://www.npsa.nhs.uk/EasysiteWeb/getresource.axd?AssetID=62914&type=Full) and [here](https://www.mrc.ac.uk/publications/browse/human-tissue-and-biological-samples-for-use-in-research/).

## Fresh Tissue

For advice on fresh tissue handling and sampling, an SOP developed by CM-Path can be found [here](http://cmpath.ncri.org.uk/wp-content/uploads/2018/04/CM-Path-SOP-for-Fresh-Tissue-Sampling.docx).