MOHCCN GOLD COHORT STANDARDS POLICY V1.3

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1. Introduction

The Marathon of Hope Cancer Centres Network (MOHCCN) aims to create a "gold-standard" cohort of clinical cancer specimens with a well-annotated, uniformly generated, and consistently quality-controlled dataset (clinical and genomic) from 15,000 (15k) cases collected from across Canada over 5 years. Not only does the MOHCCN aim to build a pan-Canadian Cancer Network and to produce immediate clinical impact by identifying actionable targets through molecular profiling, but it also proposes to generate in-depth molecular profiling data from cancer patient cohorts to address important scientific questions. This richly clinically annotated molecular dataset, starting with standardized clinical information, treatment response data, and whole-genome and transcriptome profiles (WGTS), will serve as an invaluable resource for cancer biology discovery (Figure 1).

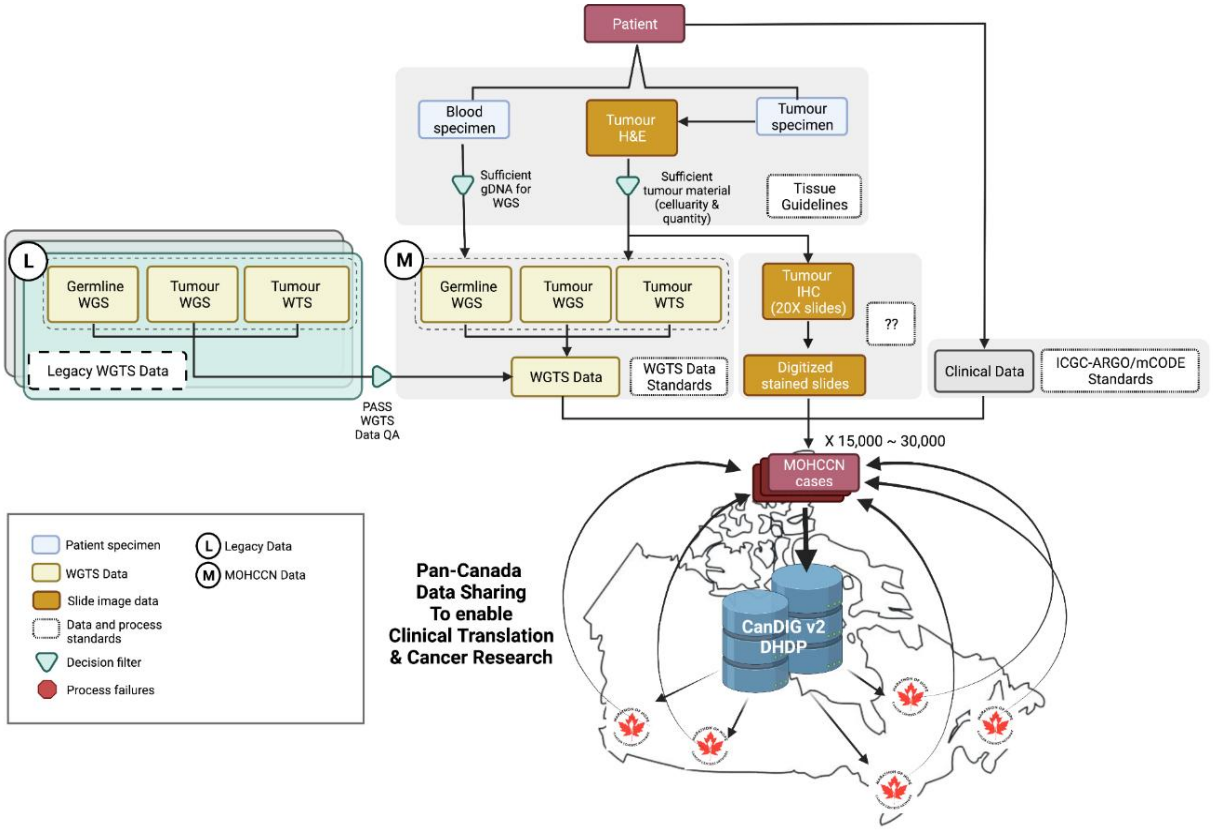

Figure 1. MOHCCN data roadmap to 15k gold standard cases.

2. MOHCCN Case Definition and Data Requirements for the 15k Gold Cohort

A MOHCCN case is defined as a unique patient. The table below provides the patient specimen requirements (tumour samples and non-tumour samples, like blood or non-neoplastic tissue) to meet the minimum (Gold Standard) data standards. Guidelines to support collections of samples will be developed through the following MOHCCN Working Groups:

Complete Case Components	MOHCCN Working Group
Clinical data	Clinical Data Standards Subcommittee
Specimen/non-neoplastic materials (whole blood, buffy-coat, PBMC, extracted genomic DNA)	Biospecimens Working Group
Tumor materials (FFPE, FF, viably frozen, extracted genomic DNA and RNA). Digitized image of the pathology reviewed H&E	Biospecimens Working Group
WGTS data	Technology Working Group

Data Requirements for the 15k Gold Standard Case

	Required* (MOHCCN standards available)	Preferred** (MOHCCN standards needed)
Clinical data		
Cross-sectional imaging (CT/MRI/PET)		✓
MOHCCN Clinical Fields	✓	✓
Health technology assessment		✓
Disease-specific		✓
Tumor Tissue		
Pathology-reviewed cellularity (Digital H&E slide or clinical flow-cytometry)	✓	✓
Whole Genome (FFPE & frozen)	✓	✓
Whole Transcriptome (FFPE & frozen)	✓	✓
Multiplexed IHC (FFPE & frozen) [*Solid tumors only*]		✓
ATAC-seq (frozen)		✓
ChIP-seq (frozen)		✓
Bisulphite Whole Genome (frozen)		✓
Proteomic Assay (FFPE & frozen)		✓
Flow cytometry or CyTOF (frozen)		✓
Single cell RNAseq (viable/frozen)		✓
Spatial transcriptomics/proteomics profiling (FFPE/frozen)		✓

Blood	
PBMC Flow Cytometry (viable)	✓
Plasma cell-free whole genome	✓
Plasma cytokines/metabolites	✓
Others (stool, urine, pleural fluid, etc.)	
Microbiome analysis (stool)	✓

*Required: MOHCCN standards are available to support data collection.
**Preferred: MOHCCN standards to support data collection are in development.

Case Collection: Prospective and/or Retrospective

Patient specimens for WGTS and molecular profiling can be obtained via one of or a mixture of two methods: Prospective and/or Retrospective.

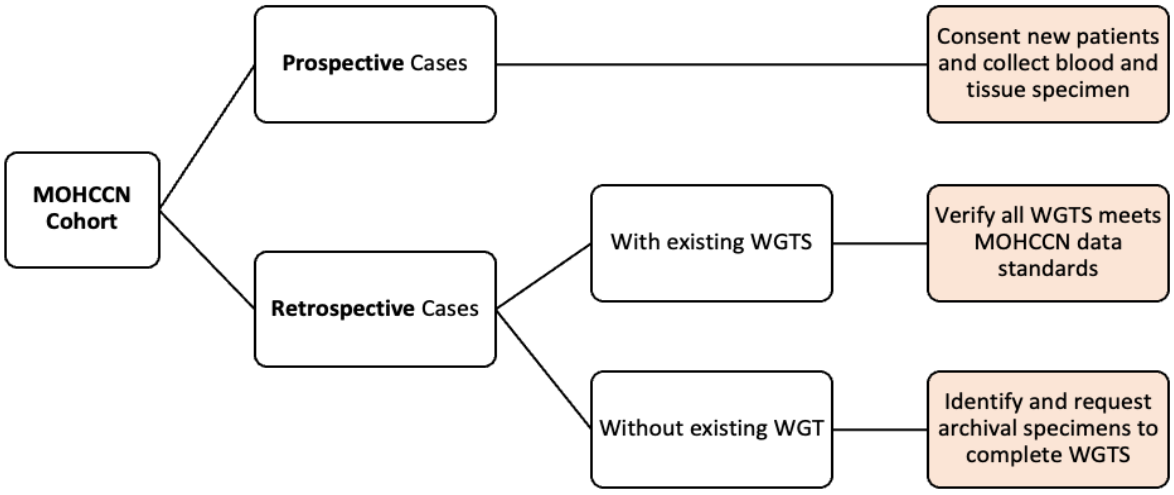

Figure 2. Prospective/retrospective cases.

Prospective specimen procurement is the set of procedures to collect and store new (since the time of study approval) patient specimens for WGTS. Solid tumor tissues can be collected via surgical resection or biopsies at baseline. If possible, prospective specimen handling protocols should be followed to ensure quality of specimens for WGTS success. By adhering to best-practices guidelines for specimen collection and processing for WGTS, prospective cases have the highest probability of success in meeting MOHCCN case standards. We recommend focusing the majority of efforts towards acquiring and enrolling patients/cases prospectively for the MOHCCN 15k gold cohort in Years 3 to 5.

Retrospective specimen procurement is the set of procedures to identify the most optimal available/archival (previously collected) patient specimen for WGTS. This procedure may also involve identifying and obtaining available partial germline WGS and or tumor WGTS data. As

the specimens may originate from multiple biobanks and storage facilities, this is a labor-intensive and nuanced process. Cohorts relying on retrospective specimen procurement encounter many unique challenges prohibiting successful WGTS data generation. To complete the MOHCCN 15k gold cohort, we recommend minimizing the number of retrospectively procured specimens or cases where possible.

3. MOHCCN Case Data Requirements and Quality Tiers

To find a more linear and straightforward operational process in the generation of the molecular data for MOHCCN cases, a Tier B of data has been defined as part of the standards to be approved as a "Gold Cohort" case given their scientific value.

While all projects will do their best efforts and aim for the coverages outlined in the WGTS guideline, data that does not meet the outlined thresholds will fall under Tier B and still be considered a MOHCCN case. Any data that falls below Tier B will not be considered a MOHCCN "Gold Cohort" case. Please refer to the chart below for threshold details.

The BAM files delivered should be considered "lossless". That is, the BAM should contain all the reads generated by the instrument. This should include mapped and unmapped reads and reads flagged as PCR or optical duplicates. In the absence of a lossless bam file, raw fastq files should be provided.

A. Molecular Requirements

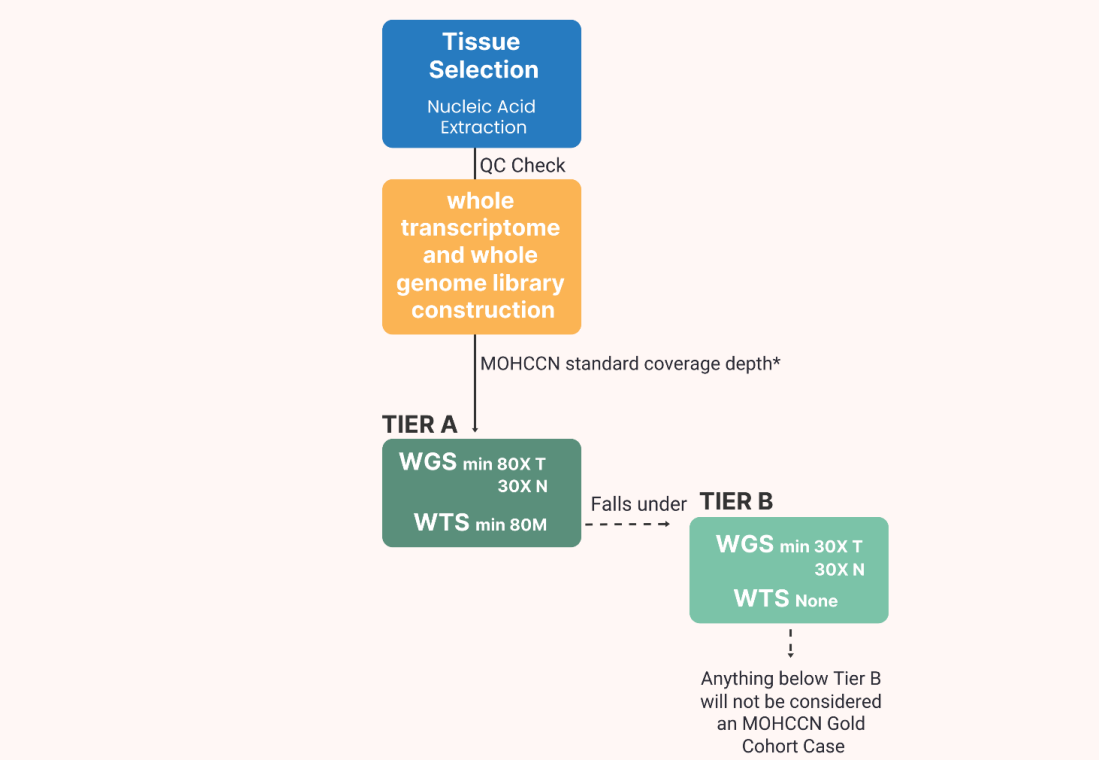

Figure 3. WGTS General Workflow for generation of a MOHCCN Gold Cohort Case.
*It is recommended to overshoot the MOHCCN standards coverage to ensure a higher probability of achieving Tier A. This policy will be revised to include more details on best practices to achieve the gold standards once that information is collected and harmonized across centres.

Tier A

Case Technology	Standards
Whole Genome Sequencing (WGS)	Minimum 30X normal and 80X tumour coverage (WGTS Guideline)
Whole Transcriptome Sequencing (WTS)	Minimum 80M pairs (WGTS Guideline)

Tier B

Case Technology	Standards
Whole Genome Sequencing (WGS)	Minimum 30X normal and 30X tumour coverage
Whole Transcriptome Sequencing (WTS)	No RNA

B. Sequencing Metadata Requirements

Upon successful completion of sequencing of a case, the cohort or the sequencing centre shall submit to CanDIG the information outlined in the MOHCCN Sequencing Metadata Policy. The MOHCCN will follow the standards used by the International Nucleotide Sequence Database Collaboration (INSDC).

C. Clinical Requirements

Upon successful completion of sequencing of a case, the cohort shall submit to CanDIG the complete clinical data within six months. The complete clinical data shall consist of the mandatory and conditional/optional fields described in the most current MOHCCN Clinical Data Model (CDM). The complete clinical data may be submitted in a staggered fashion if desired, provided that submissions are completed within six months. If a good faith effort has been made to obtain a mandatory clinical field and has failed, the field may be submitted as “Not Available.”

Subsequent to submission of "complete" clinical data, clinical follow-up information, including but not limited to a patient's vital and disease status, shall be submitted on an annual basis for a minimum of five years subject to available funding.

D. H&E Requirements

In Progress – Biospecimens Working Group

Document Revision History

Developed by	Reviewed by	Endorsed by	Effective Date	Policy Version	Summary of revisions
TWG & DPSC	Steering Committee	Network Council	August 1, 2025	V1.3	n/a
DPSC	Steering Committee	Network Council	October 3, 2024	V1.2	n/a
TWG	Network Council and Exec Ad hoc	Network Council	February 1, 2024	V1.1	n/a
TWG	Steering Committee	Network Council	October 6, 2022	V1	n/a

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