

Invasive Melanoma in the Setting of Neoadjuvant Therapy Histopathology Reporting Guide

Family/Last name Date of birth

Given name(s)

Patient identifiers Date of request Accession/Laboratory number

Elements in **black text** are **CORE**. Elements in **grey text** are **NON-CORE**.

indicates multi-select values indicates single select values

SCOPE OF THIS DATASET

CLINICAL INFORMATION (Note 1)

- Information not provided
- Information provided (select all that apply)
- Previous history of melanoma, *specify*
- Clinical intent of procedure
- Excisional/complete diagnostic biopsy
- Incisional/incomplete (partial) diagnostic biopsy
- Wide excision
- Other, *specify*

TUMOUR SITE (Note 2)

- Not specified
- Specify site*

SPECIMEN LATERALITY (Note 3)

- Left
- Midline
- Right

SPECIMEN(S) SUBMITTED (select all that apply) (Note 4)

- Not specified
- Biopsy, *specify*
- Excision, *specify*
- Other, *specify*

MACROSCOPIC PRIMARY LESION DESCRIPTION

(Including descriptive features, dimensions and proximity to resection margins)

BLOCK IDENTIFICATION KEY (Note 5)

(List overleaf or separately with an indication of the nature and origin of all tissue blocks)

HISTOLOGICAL TUMOUR TYPE (Note 6)

(Value list based on the World Health Organization Classification of Skin Tumours, 5th Edition (2025))

- Invasive melanoma
- Metastatic melanoma
- Primary melanoma^a
- Other, *specify*
- Indeterminate

^a Refer to ICCR Invasive melanoma dataset.

TUMOUR REGRESSION/PATHOLOGICAL RESPONSE^b (Note 7)

Residual viable tumour (RVT)^c

Percentage of treated tumour bed surface area with viable tumour %

OR

Pathological response score

- 0% viable tumour
- 1-≤10% viable tumour
- Regions of both 0% and ≤10% of viable tumour in the treated tumour bed
- >10% but ≤50% viable tumour
- >50% viable tumour

Necrosis

%

Regression^d

%

Comments (e.g., observations regarding tumoural melanosis)

^b The values represent an estimated percentage of the surface area across the examined slides of the tissue. The percentage of each of the three components should equal 100%. This element can be repeated for distinct separate tumours

^c In situ disease is not included in the RVT surface area calculation.

^d Regression refers to fibrovascular and inflammatory stromal changes presumed to have replaced the tumour.

COEXISTENT PATHOLOGY (Note 8)

- None identified
- Present, *specify*

▼

SURGICAL MARGIN/TISSUE EDGES^e (Note 9)

- Cannot be assessed
- Not involved by invasive melanoma

▼

Distance of melanoma from closest margin

≤1 mm >1 mm

Specify closest location(s), if possible

--

Involved by invasive melanoma^f

Specify location(s), if possible

--

Other observations at the margin (e.g., regression, satellite, perineural invasion), *specify*

--

^e Core for excision specimens only.

^f Refer to ICCR Invasive melanoma dataset for primary excisions.

ANCILLARY STUDIES (Note 10)

- Not performed
- Performed (e.g., BRAFV600E immunohistochemistry performed - tumour cells are positive), *record type of test(s) and result(s)*

▼

Representative blocks for ancillary studies, *specify those blocks best representing tumour and/or normal tissue for further study*

Definitions

CORE elements

CORE elements are those which are essential for the clinical management, staging or prognosis of the cancer. These elements will either have evidentiary support at Level P2 or higher (based on the Hierarchy of Research Evidence for Tumour Pathology¹). In rare circumstances, where level P2 evidence is not available an element may be made a CORE element where there is unanimous agreement in the Dataset Authoring Committee (DAC). An appropriate staging system e.g., Pathological TNM staging would normally be included as a CORE element.

Molecular and immunohistochemical testing is a growing feature of cancer reporting. However, in many parts of the world this type of testing is limited by the available resources. In order to encourage the global adoption of ancillary tests for patient benefit, International Collaboration on Cancer Reporting (ICCR) includes the most relevant ancillary testing in ICCR Datasets as CORE elements, especially when they are necessary for the diagnosis. Where the technical capability does not yet exist, laboratories may consider temporarily using these data elements as NON-CORE items.

The summation of all CORE elements is considered to be the minimum reporting standard for a specific cancer.

NON-CORE elements

NON-CORE elements are those which are unanimously agreed should be included in the dataset but are not supported by level P2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.

Key information other than that which is essential for clinical management, staging or prognosis of the cancer such as macroscopic observations and interpretation, which are fundamental to the histological diagnosis and conclusion e.g., macroscopic tumour details, may be included as either CORE or NON-CORE elements by consensus of the DAC.

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Scope

This dataset has been developed for the pathology reporting of biopsy or resection specimens of metastatic or primary invasive melanoma at cutaneous sites following neoadjuvant treatment.

Separate ICCR datasets are available for reporting invasive cutaneous melanoma without neoadjuvant therapy, mucosal melanomas of the head and neck and Merkel cell carcinomas.²⁻⁴

This dataset overlaps with the ICCR dataset for reporting invasive melanoma.² Reporting of resection specimens after neoadjuvant therapy from patients with invasive melanoma requires multidisciplinary collaboration and specialised handling of the resection specimen. This dataset contains both the standard elements that remain applicable after neoadjuvant therapy and the elements specific for the neoadjuvant setting and can be used in conjunction with the ICCR Invasive melanoma dataset,² as appropriate.

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Note 1 – Clinical information (Core and Non-core)

For optimal tissue diagnosis and patient treatment, it is important that pathologists receive key clinical information with the specimen.^{5,6} Therefore, if relevant clinical information is received with the specimen, this should be documented and is a core element for reporting. However, in acknowledging that the pathologist is only capable of documenting the clinical information that they receive, the clinical information sub-values (e.g., previous history of melanoma, presurgical therapy) are non-core.

Previous history of melanoma

If received, any previous history of melanoma should be documented and it should be indicated whether the current specimen represents metastatic or primary melanoma. If there is uncertainty as to whether a melanoma is primary or metastatic, this should be documented.

Clinical intent of procedure

It is helpful for the pathologist to be advised by the clinician on whether the specimen was taken with the intent of its complete removal or as a partial sample of the lesion. This informs about the need for a reporting on the margin status.

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Note 2 – Tumour site (Core)

Information on tumour site is required to localise the lesion and procedure site anatomically.^{7,8}

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Note 3 – Specimen laterality (Non-core)

Specimen laterality is part of the information needed to localise a lesion and procedure site correctly.^{7,8}

The term ‘midline’ would be used in instances where the tumour is not specifically on the left or right hand side of the anatomical location.

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Note 4 – Specimen(s) submitted (Core)

The type of procedure (e.g., biopsy or excision) should be specified.⁹ This is important for quality assurance and for the need for margin assessment.

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Note 5 – Block identification key (Non-core)

The origin/designation of all tissue blocks should be recorded. This information should ideally be documented in the final pathology report and is particularly important should the need for internal or external review arise.

Recording the origin/designation of tissue blocks also facilitates retrieval of blocks for further immunohistochemical or molecular analysis, research studies or clinical trials. Indicate the most suitable block(s) for future ancillary studies and refer to best practice guidelines.^{10,11}

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Note 6 – Histological tumour type (Core)

The histological diagnosis of invasive melanoma is a core element. Further subclassification as per the WHO Classification of Skin Tumours, 5th edition, 2025,¹² is only indicated in the case of a primary melanoma, for which the ICCR Invasive melanoma dataset is to be followed.²

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Note 7 – Tumour regression/pathological response (Core and Non-core)

Components of pathological response

The minimum essential reporting elements for pathologic response include:¹³⁻¹⁶

- Percentage residual viable tumour (RVT)
- Percentage necrosis
- Percentage regression (fibrovascular and inflammatory changes including melanosis).

The values represent an estimated percentage of the surface area across the examined slides of the tissue. To simplify reporting, percentages can be rounded to the nearest 10%. The sum of each component should equal 100%.

Residual viable tumour (RVT)

Viable tumour cells are characterised by the presence of a nucleus that stains blue/blueish on haematoxylin and eosin (H&E) stained sections surrounded by cytoplasm.

Pathologists should report either the basic percentage of viable tumour or the tumour response score at their discretion.¹⁰ In situ disease is not included in the RVT surface area calculation. Note that in cases involving multiple tumours from distinct organ sites, reporting a basic percentage for each tumour separately may help avoid confusion.

Pathological response score captures the extent of residual viable melanoma following neoadjuvant treatment and serves as an early surrogate endpoint for clinical outcome. It is defined by the International Neoadjuvant Melanoma Consortium (INMC) and aligns with the emerging consensus for standardised histopathologic assessment of resected melanoma specimens.¹⁴ This may be used at the discretion of the pathologist, or a basic percentage may be given.

When reporting the percentage of viable tumour, the numerator is the surface area of RVT. The denominator is the 'tumour bed' – defined as the area occupied by residual tumour together with the area presumed to have been previously occupied by tumour cells. The surface area of the tumour bed is estimated on a biopsy or across representative sections of a resected specimen.

Necrosis

While dying tumour cells, as the first histologically visible sign of cell necrosis, may show faint nuclear labelling and poorly defined nuclei; in contrast, dead cells lack nuclear staining on H&E sections. Groups of dead tumour cells typically appear as amorphous eosinophilic material on H&E-stained sections. Chronic inflammatory infiltrates are often present at the periphery of necrotic tumour.

Regression

A spontaneous or treatment-induced host immune response may be directed against melanoma and can result in partial or complete elimination of the melanoma – a process termed regression. This is characterised by immature and mature dermal fibrosis, often accompanied by inflammation (with variable proportions of lymphocytes, plasma cells, and macrophages) and stromal hypervascularity. In pigmented melanomas the macrophages may contain melanin pigment (melanophages).¹⁷

Tumoural melanosis (TM) is defined as nodular or sheetlike aggregates of melanophages devoid of melanocytes or neoplastic cells with various prognostic implications as follows:^{15,18}

- Spontaneous regression – TM signals tumour regression and is linked to a favourable prognosis.
- Post-treatment regression – When TM is found within a tumour bed after systemic therapy, it provides an indicator of therapeutic response and guides further management.
- Treatment-naïve disease – In patients who have not received prior therapy, the presence of TM is associated with better melanoma-specific survival, adding prognostic information beyond conventional staging.¹⁸

Documenting TM informs clinicians about melanoma risk, treatment effectiveness, and overall prognosis. Observations regarding TM can be recorded in the comments field where appropriate.

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Note 8 – Coexistent pathology (Non-core)

Reporting coexistent pathology can be useful for clinicopathological correlation or patient management. Examples are haemorrhage, cystic transformation, tattoo pigment, or incidental findings such as lymphoma.

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Note 9 – Surgical margin/Tissue edges (Core and Non-core)

When metastatic tumours are removed after treatment, margin assessment is only needed for tumour resection specimens (not applicable for biopsies). A designation of 'involved' or 'not involved' is sufficient for the margin status of a resected melanoma metastasis.^{5,6,19-22}

Invasive melanoma, at or close to the margin, refers specifically to viable tumour and does not include treated tumour bed. Pathologists may wish to report tumour bed involvement at the margins at their

discretion; however, the clinical impact is still under investigation. Reporting the distance of melanoma to the margin is a non-core component of surgical margin status.

When a primary melanoma is excised after treatment, the DAC recommend using the ICCR Invasive melanoma dataset.²

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Note 10 – Ancillary studies (Non-core)

Various ancillary studies may be used to assist in establishing a diagnosis of melanoma, for margin assessment, staging and for evaluating treatment options. They include immunohistochemical, cytogenetic and molecular methods. When such methods are used for clinical purposes, this should be documented in the pathology report.

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