

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

 Presurgical therapy, *specify* Other clinical information, *specify* Lymph node(s), *specify site(s)* Excision Other, *specify***SPECIMEN ORIENTATION***(Per information received from the clinician on orientation of specimen by marking sutures, clips or other techniques)***TUMOUR SITE** (Note 2) Not specified *Specify site***MACROSCOPIC PRIMARY LESION DESCRIPTION***(Including descriptive features, dimensions and proximity to resection margin)***SPECIMEN LATERALITY** (Note 3) Not specified Left Midline Right**OTHER LESION(S)** (Note 5)*(Macroscopic description of other lesion(s))***SPECIMEN(S) SUBMITTED** (Note 4) Not specified *Punch, specify* *Shave, specify***BLOCK IDENTIFICATION KEY** (Note 6)*(List overleaf or separately with an indication of the nature and origin of all tissue blocks)*

**HISTOLOGICAL TUMOUR TYPE** (Note 7)

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

- Invasive melanoma<sup>a</sup> (select all that apply)
  - Melanoma, not otherwise specified (NOS)
  - Low-cumulative sun damage (CSD) melanoma (superficial spreading melanoma)
  - High-CSD melanoma (Lentigo maligna melanoma)
  - Desmoplastic melanoma
    - Pure (>90% desmoplastic melanoma)
    - Mixed desmoplastic/non-desmoplastic melanoma
  - Spitz melanoma
  - Acral melanoma
  - Mucosal melanomas (genital)<sup>b</sup>
  - Melanoma arising in blue naevus
  - Melanoma arising in giant congenital naevus
  - Nodular melanoma
  - Naevoid melanoma
  - Other, specify
- Indeterminate

<sup>a</sup> Reporting the melanoma tumour subtype is only a core element when clinically relevant and if the subclassification can be made confidentially. Otherwise, it is sufficient to report the diagnosis of melanoma.

<sup>b</sup> For mucosal melanomas arising in the head and neck, refer to the ICCR Mucosal melanomas of the head and neck dataset.

**BRESLOW THICKNESS** (Note 8)

(Measurement should be to the nearest 0.1 mm)

- Specify 

mm
- At least 

mm
- Indeterminate, describe

**ULCERATION** (Note 9)

- Not identified
- Indeterminate
- Present
  - Extent of ulceration 

mm

**MITOTIC COUNT** (Note 10)

- /mm<sup>2</sup>
- Indeterminate

**NON-NODAL LOCOREGIONAL CUTANEOUS METASTASES** (Note 11)

- Not identified
- Indeterminate
- Present, specify

**Metastases at margins**

- Cannot be assessed
- Not involved
- Involved

**CLARK LEVEL** (Note 12)

- Confined to epidermis (Level 1)
- Infiltrates but does not fill papillary dermis (Level 2)
- Fills/expands papillary dermis (Level 3)
- Infiltrates into reticular dermis (Level 4)
- Infiltrates into subcutaneous fat (Level 5)

**LYMPHOVASCULAR INVASION** (Note 13)

- Not identified
- Indeterminate
- Present
  - Immunohistochemistry, specify results if used

**TUMOUR-INFILTRATING LYMPHOCYTES** (Note 14)

- Brisk
- Non brisk

**TUMOUR REGRESSION** (Note 15)

- Not identified
- Present
  - Tumour regression: Margins**
    - Not involved by regression
    - Involved by regression
      - Extent of regression 

%

**PERINEURAL INVASION** (Note 16)

- Not identified
- Indeterminate
- Present

**ASSOCIATED MELANOCYTIC NAEVUS OR OTHER LESION** (Note 17)

**SURGICAL MARGIN/TISSUE EDGES** (Note 18)

- Cannot be assessed
  - Not involved by melanoma in situ or invasive melanoma
- Distance of melanoma in situ or invasive tumour from closest margin
- ≤1 mm    >1 mm

Specify closest location(s), if possible

- Involved by melanoma in situ
  - Involved by melanoma in situ
- Specify location(s), if possible

- Involved by invasive melanoma
  - Involved by invasive melanoma
- Specify location(s), if possible

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

**LYMPH NODES STATUS** (Note 19)

(Applicable only if lymph nodes submitted)

**Sentinel lymph nodes**

Number of sentinel lymph nodes examined

Number cannot be determined

Number of involved sentinel lymph nodes (i.e., clinically occult)

Number cannot be determined

Extranodal extension<sup>c</sup>

- Not identified
- Indeterminate
- Present

Maximum dimension of largest metastasis in sentinel node<sup>c</sup>  mm

Location of largest sentinel node metastases<sup>c</sup> (select all that apply)

- Subcapsular
- Intraparenchymal

NODAL NAEVUS

- Not identified
- Present

<sup>c</sup> Required only in the presence of involved nodes.

**Non-sentinel lymph nodes (clinically negative)**

Number of non-sentinel lymph nodes examined

- Number cannot be determined

Number of involved non-sentinel lymph nodes (i.e., clinically occult)

- Number cannot be determined

Extranodal extension<sup>c</sup>

- Not identified
- Indeterminate
- Present

Maximum dimension of largest metastasis in non-sentinel node<sup>c</sup>  mm

NODAL NAEVUS

- Not identified
- Present

**Clinically apparent lymph nodes**

Number of non-sentinel lymph nodes examined

- Number cannot be determined

Number of involved non-sentinel lymph nodes

- Number cannot be determined

Extranodal extension<sup>c</sup>

- Not identified
- Indeterminate
- Present

Maximum dimension of largest metastasis in non-sentinel node<sup>c</sup>  mm

NODAL NAEVUS

- Not identified
- Present

**ANCILLARY STUDIES** (Note 20)

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

Test	Result

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

**PATHOLOGICAL STAGING (UICC TNM 9<sup>th</sup> edition)<sup>d</sup> (Note 21)****TNM Descriptors** (only if applicable) (select all that apply)

- m - multiple primary tumours  
 sn - sentinel node biopsy

**Primary tumour (pT)<sup>e</sup>**

- TX<sup>f</sup> Primary tumour cannot be assessed<sup>g</sup>  
 T0 No evidence of primary tumour or regressed melanomas  
 Tis Melanoma in situ (Clark level I)  
 T1 Tumour 1 mm or less in thickness  
 T1a less than 0.8 mm in thickness without ulceration  
 T1b less than 0.8 mm in thickness with ulceration or 0.8 mm or more but no more than 1 mm in thickness, with or without ulceration  
 T2 Tumour more than 1 mm but not more than 2 mm in thickness  
 T2a Without ulceration  
 T2b With ulceration  
 T3 Tumour more than 2 mm but not more than 4 mm in thickness  
 T3a Without ulceration  
 T3b With ulceration  
 T4 Tumour more than 4 mm in thickness  
 T4a Without ulceration  
 T4b With ulceration

**Regional lymph nodes (pN)**

- No nodes submitted or found  
 NX<sup>f</sup> Regional lymph nodes cannot be assessed  
 N0<sup>h</sup> No regional lymph node metastases  
 N1 Metastasis in one regional lymph node or intralymphatic regional metastasis *without* nodal metastases  
 N1a Only microscopic metastasis (clinically occult)  
 N1b Macroscopic metastasis (clinically apparent)  
 N1c Satellite or in-transit metastasis *without* regional nodal metastasis  
 N2 Metastasis in two or three regional lymph nodes or in-transit metastasis *with* lymph node metastases  
 N2a Metastasis in two or three regional lymph nodes, with only microscopic nodal metastasis  
 N2b Metastasis in two or three regional lymph nodes, clinically detected in at least one node  
 N2c Satellite or in-transit metastasis *with* only one regional nodal metastasis, (microscopic or clinical)  
 N3 Metastasis in four or more regional lymph nodes, or matted metastatic regional lymph nodes, or satellite(s) or in-transit metastasis *with* metastasis in two or more regional lymph node(s)  
 N3a Metastasis in four or more regional lymph nodes with only microscopic nodal metastasis  
 N3b Metastasis in four or more regional lymph nodes clinically detected in at least one node, or two or more matted nodes  
 N3c Satellite(s) or in-transit metastasis either with two or more regional nodal metastasis (microscopic or clinical) or two or more matted nodes

<sup>d</sup> Reproduced with permission. Source: UICC TNM Classification of Malignant Tumours, 9th Edition, eds by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, Elizabeth Van Eycken. 2025, Publisher Wiley (incorporating errata published 12th October 2025).

<sup>e</sup> Tumour thickness measurements are rounded to the nearest 0.1 mm before the T category is assigned.

<sup>f</sup> TX and NX should be used only if absolutely necessary.

<sup>g</sup> TX includes shave biopsies and curettage that do not fully assess the thickness of the primary.

<sup>h</sup> Histological examination of a regional lymphadenectomy specimen will ordinarily include six or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0. Classification based solely on sentinel node biopsy without subsequent axillary lymph node dissection is designated (sn) for sentinel nodes, e.g., (p)N1(sn).

## 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 above (based on the Hierarchy of Research Evidence for Tumour Pathology<sup>1</sup>). 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 pathology reporting of primary cutaneous invasive melanoma. Separate ICCR datasets are also available for reporting mucosal melanomas of the head and neck and Merkel cell carcinomas.<sup>2,3</sup>

The third edition of this dataset includes changes to align the dataset with the World Health Organization (WHO) Classification of Skin Tumours, 5<sup>th</sup> edition, 2025.<sup>4</sup> In development of this dataset, the DAC considered evidence up until November 2025.

A list of changes in this dataset edition can be accessed [here](#).

The authors of this dataset can be accessed [here](#).

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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. 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 including any family history. For re-excision or prior biopsy specimens, if known include earlier diagnoses, Breslow thickness measurements, and any past molecular test results for melanoma, if available. If there is uncertainty as to whether a melanoma is a new primary or a recurrence, this should be documented.

### **Clinical intent of procedure**

When interpreting a pigmented lesion, 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 (incomplete removal) of the lesion. This may influence the diagnostic interpretation of the biopsy and informs about the need for a reporting on the margin status.

Incomplete biopsies of melanomas may also preclude accurate assessment of critical prognostic features for staging, such as Breslow thickness, ulceration or microsatellitosis.

### **Presurgical therapy**

Clinical details of any presurgical therapy, including the status of post neoadjuvant therapy, should be provided.

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## **Note 2 – Tumour site (Core)**

Sufficient information is required to localise the lesion for subsequent therapy. A diagram or photograph can facilitate this.

It is important that the site of the biopsy be recorded as specifically as possible to reduce the risk of a re-excision occurring at the incorrect site. Anatomic site is also a data element relevant for prognosis.<sup>5</sup> It may also affect the pathologic interpretation of the histologic features observed.<sup>6</sup>

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## **Note 3 – Specimen laterality (Core)**

Specimen laterality information is needed for identification purposes and to localise the lesion for subsequent therapy.

The term ‘midline’ is 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)**

Although clinical considerations are important in determining the most appropriate biopsy technique for a melanocytic tumour, a partial biopsy may impair an optimal diagnostic interpretation and staging.<sup>7</sup> Specifying the type of procedure is also important for quality assurance. Correlation of the type of procedure with the material received can on rare occasion be helpful to recognise a misidentification of the specimen.

If appropriate, document if the report reflects findings from the excision alone or combined histologic parameters of the melanoma from both excision and prior biopsy.

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## **Note 5 – Other lesion(s) (Non-core)**

Other lesions are often naevi or other benign lesions. However, it is particularly important to identify the presence of satellite metastases because these portend a worse prognosis and impact classification and staging.<sup>8,9</sup>

The description of the lesion includes such features as shape, colour, border, contour, evidence of surface crusting or ulceration and its proximity to the primary lesion and the resection margins.

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## **Note 6 – 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 tumour and normal tissue block(s) for future ancillary studies.

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## **Note 7 – Histological tumour type (Core)**

The diagnosis of melanoma is a core element. A number of melanoma subtypes have been adopted by the WHO Classification of Skin Tumours, 5<sup>th</sup> edition, 2025 (Table 1) which correspond to the nine pathways of melanoma.<sup>4</sup> While the DAC encourage using this classification in pathology reports, the subtype designation is non-core when it cannot be made with confidence – for example, on a small or partial biopsy or is clinically irrelevant

In rare scenarios when the tumour shows unusual features, such as undifferentiated melanoma or melanoma with osteocartilaginous differentiation, the DAC recommend commenting on such findings.

Since some historically recognised histopathologic subtypes of melanoma (superficial spreading melanoma or lentigo maligna melanoma) have little prognostic significance independent of tumour thickness.<sup>6,10</sup> Therefore, reporting these sub-values is also considered non-core.

On the other hand, certain melanoma subtypes do influence prognosis and clinical management and should be reported whenever possible. Examples include:

- Pure desmoplastic melanoma – which is less frequently associated with sentinel node positivity<sup>11,12</sup>
- Desmoplastic neurotropic melanoma – may be managed with post operative radiotherapy<sup>13</sup>
- Blue naevus-related melanomas or deep soft tissue melanomas arising in a large congenital naevus for which current pathological staging systems are of limited prognostic value.<sup>6</sup>

In these situations, documenting the specific subtype adds meaningful information for treatment planning.

**Table 1: 5<sup>th</sup> edition of the World Health Organization classification of tumours of the skin.<sup>4</sup>**

<b>Descriptor</b>	<b>ICD-O codes<sup>a</sup></b>
<b>Melanoma in intermittently sun-exposed skin</b>	
Low-cumulative sun damaged melanoma (including superficial spreading melanoma)	8743/3
Low-cumulative sun damaged melanoma in situ	8743/2
<b>Melanoma in chronically sun-exposed skin</b>	
High-cumulative sun damaged melanoma (lentigo maligna melanoma)	8742/3
Desmoplastic melanoma	8745/3
<b>Spitz tumours</b>	
Spitz naevi	
Spitz melanocytoma (Atypical Spitz tumour)	8770/1
Spitz melanoma	8770/3
<b>Melanocytic tumours in acral skin</b>	
Acral naevus	8744/0
Acral melanoma	8744/3
<b>Genital and mucosal melanocytic tumours</b>	
Mucosal and genital naevi	8720/0
Mucosal melanoma	8720/3
Mucosal lentiginous melanoma	8746/3
Nodular melanoma	8721/3
Melanoma, not otherwise specified (NOS)	8720/3
<b>Blue naevus and related tumours</b>	
Melanoma arising in blue naevus	8780/3
<b>Congenital melanocytic tumours</b>	
Melanoma arising in giant congenital naevus	8761/3
<b>Nodular, naevoid and metastatic melanomas</b>	
Nodular melanoma	8721/3
Naevoid melanoma	8720/3
Dermal melanoma	8750/3

<sup>a</sup> The morphology codes are from the International Classification of Diseases for Oncology (ICD-O).<sup>14</sup> Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; /3 for malignant tumours, primary site; and /6 for malignant tumours, metastatic site. Behaviour code /6 is not generally used by cancer registries. Subtype labels are indented.

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## **Note 8 – Breslow thickness (Core)**

Breslow thickness is the single most important prognostic factor for clinically localised primary melanoma.<sup>6,9,15</sup> Breslow thickness is measured from the top of the granular layer of the epidermis (or, if the surface is ulcerated, from the base of the ulcer) to the deepest invasive cell across the broad base of the tumour (dermal/subcutaneous) as described by Breslow.<sup>6,16</sup>

Deep, vertical extensions of the tumour, perpendicular to the base should be assumed to be periannexal and should not be included in the Breslow thickness. Similarly, satellite lesions or areas of vascular invasion should not be included.

Tumour thickness measurements only need to be recorded to the nearest 0.1 millimetres (mm). For tumours measuring  $\leq 1$  mm in thickness one may attempt to record to the nearest 0.01 mm, if possible. For tumours  $> 1$  mm, the DAC recommend recording thickness to the nearest 0.1 mm.<sup>9,17</sup>

To promote consistency in the evaluation of the Breslow thickness the following points are worthy of note:

1. The Breslow thickness can only be evaluated accurately in sections cut perpendicular to the epidermal surface. Otherwise, a note should be included indicating that 'the section is cut tangentially and an accurate Breslow thickness cannot be provided'. Nevertheless, an attempt should be made to provide at least an approximate tumour thickness.
2. When the measured thickness on initial sections is at or near a staging threshold level, consideration should be given to obtaining deeper levels to minimise staging errors related to histopathologic sampling.<sup>18,19</sup>
3. The Breslow thickness should be measured in the standard way when there is dermal regression (i.e., dermal regression extending to a greater thickness than the melanoma should not be included in the measurement of Breslow thickness).
4. When invasive melanoma is only or predominantly seen in the stroma surrounding hair follicles or sweat glands, it can on occasion be difficult to precisely measure tumour thickness. In that circumstance, Breslow thickness may be measured, if possible, from the centre of the hair follicle (from the inner layer of the outer root sheath epithelium, if visible) or sweat gland (best from the inner luminal surface of eccrine units), to the furthest extent of infiltration into the periannexal dermis. The measured distance of periannexal invasive melanoma from the granular layer of the epidermis may also be reported, but it should then be stated how this measurement was obtained and acknowledged that the measurement is an approximate estimate and may not accurately reflect 'true' tumour thickness. Melanoma within adnexal epithelium is in situ disease and should not be included in measurements of tumour thickness.

5. Microsatellites, as discussed in detail below, are foci of tumour discontinuous from the primary melanoma (probably representing local metastases) and should not be included in the measurement of tumour thickness.
6. The Breslow thickness cannot be determined if a superficial biopsy transects a melanoma and includes only its superficial portion at the deep edge/margin. In such instances, the pathologist can only report the melanoma to be 'at least' a certain thickness. Correlation with the re-excision specimen is necessary.
7. In some instances, particularly when a melanoma arises in association with a naevus, it may be difficult to distinguish small 'nevoid' melanoma cells from naevus cells, and this may have implications for measuring tumour thickness. Careful assessment of architectural and especially cytologic features as well as immunohistochemical stains could assist in distinction, but at times this remains difficult, subjective, and prone to interobserver variability. The uncertainty involved in such distinctions should be communicated.
8. In very rare occasions a clinician may perform a shave biopsy of a melanocytic tumour and then another additional deeper biopsy, because pigment is seen at the base of the biopsy site. Upon histopathologic examination of the superficial biopsy, the tumour is typically transected and residual tumour is present in the second biopsy. In the case of an invasive melanoma an attempt may be made to reconcile the findings in the two separate biopsies by adding the depth of invasion from the second biopsy to the measured thickness of the first. However, such an attempt should only be made, if the tissue pieces are well oriented, non tangential, and there are clear histopathologic landmarks for measurements. It is generally best to refrain from attempts to add thickness values and report only what can be measured reliably. If tumour is transected at the base of the tissue used for measurement, the thickness value should be preceded by 'at least' to acknowledge that the depth of invasion is likely higher than what was measured.
9. When invasive melanoma is present in an excision, the DAC also recommend reconciling the findings with those of the prior biopsy. If the thickness value of the residual invasive melanoma is greater than the thickness value reported in the prior biopsy, the DAC recommend using the value obtained from the examination of the excision based on the distance between granular cell layer and deepest portion of the invasive tumour. In the scenario when the thickness value of the initial biopsy (e.g., 0.8 mm) was greater than the value measured in the excision (e.g., 0.5 mm tumour thickness), the DAC recommend using the greater value of tumour thickness determined from the biopsy.

The presence of any of the above attributes may warrant the inclusion of an explanatory note in the report to ensure that any uncertainty or nuance is clearly communicated.

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## **Note 9 – Ulceration (Core and Non-core)**

Ulceration is an integral component of the Union for International Cancer Control (UICC) 9<sup>th</sup> edition/American Joint Committee on Cancer (AJCC) 8<sup>th</sup> edition Cancer Staging Manuals,<sup>20,21</sup> and an independent predictor of outcome in patients with clinically localised primary cutaneous melanoma.<sup>8,9</sup>

Assessing the presence of ulceration may be difficult in recently biopsied lesions and in cases in which there is only a focal loss of the epidermis; in the latter case, it is difficult to determine whether the epidermal deficiency is due to ulceration or to sectioning artefact. Absence of reactive changes such as fibrin or

granulation tissue from putative areas of ulceration would be clues that the apparent ulceration is actually due to sectioning artefact of only part of the epidermis.<sup>6</sup>

Extent of ulceration measured microscopically as a diameter in mm (or as a percentage of the dermal invasive tumour width), provides more accurate prognostic information than the mere presence of ulceration.<sup>22</sup> Extent of ulceration is optional (non-core) to report.

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## **Note 10 – Mitotic count (Core)**

Multiple studies indicate that mitotic count in the invasive portion is an important prognostic factor for localised primary melanomas (including very large studies utilising the methodology for mitotic count determination described below).<sup>23-28</sup>

The number of mitotic figures can vary greatly between different parts of a tumour. For consistency and reproducibility, a standardised method must be used to assess mitotic count. It is recommended that the field diameter of a microscope be formally calibrated using a stage micrometre to determine the number of high-power fields that equates to a 1 mm<sup>2</sup> area.

In the UICC 9<sup>th</sup> edition/AJCC 8<sup>th</sup> edition Cancer Staging Manuals,<sup>20,21</sup> the recommended method to enumerate mitotic figures is to find an area in the dermis with obvious mitotic activity (the ‘hot spot’), and begin the count in this area, then extending the area counted to immediately adjacent non-overlapping high-power fields in a 1 mm<sup>2</sup> area. If no hot spot is identified and the mitotic figures are sparse and randomly scattered, then the count should begin in a field containing a mitosis, then extended to immediately adjacent non-overlapping high-power fields until a 1 mm<sup>2</sup> area of tissue containing melanoma is assessed. When the invasive component of the tumour involves an area <1 mm<sup>2</sup>, a 1 mm<sup>2</sup> area of dermal tissue that includes the tumour should be assessed and recorded as a number per mm<sup>2</sup>. The number of mitotic figures should be listed as a whole number/mm<sup>2</sup>. If no mitotic figures are identified, the mitotic count may be recorded ‘none identified’ or ‘0/mm<sup>2</sup>’. The mitotic count may be recorded as <1/mm<sup>2</sup>. However, practically for data purposes this would be coded as ‘0’. This methodology for determining the mitotic count of a melanoma has been shown to have excellent interobserver reproducibility including amongst pathologists with widely differing experiences in the assessment of melanocytic tumours.<sup>29</sup>

It is also recommended that the mitotic count should be assessed in all primary melanomas (as whole number/mm<sup>2</sup>) for prognostic purposes.

The data that demonstrated the strong prognostic significance of mitotic count were obtained from the melanoma pathology reports of routinely assessed haematoxylin and eosin-stained sections. It is therefore not recommended that any additional sections be cut and examined (or immunohistochemical analysis be performed), in excess of those that would normally be used to report and diagnose the melanoma, to determine the mitotic count (i.e., no additional sections should be cut and examined for the purpose of determining the mitotic count; this includes the situation when no mitotic figures are identified on the initial, routinely examined sections).

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## Note 11 – Non-nodal locoregional cutaneous metastases (Core)

Non-nodal locoregional cutaneous metastases are often referred to as satellites or in-transit metastases. The terms ‘microsatellites’, ‘satellites’ and ‘in-transit metastases’ represent biologically identical processes with identical adverse prognostic implications.<sup>30</sup> The presence or absence of microsatellite, satellite, or in-transit metastases, regardless of the number of such lesions, represents an N-category criterion. They are included in the same prognostic group in the UICC 9<sup>th</sup> edition/AJCC 8<sup>th</sup> edition Cancer Staging Manuals and are classified as Stage III melanoma.<sup>8,9,20,21</sup>

Satellites may be clinically detected (macroscopic satellites) or only microscopically seen (microsatellites). Only after histopathologic confirmation can a suspected satellite be characterised as unequivocal metastasis. Satellite metastases are classically defined as any foci of clinically evident cutaneous and/or subcutaneous metastases occurring within 20 mm of but discontinuous from the primary melanoma. In-transit metastases are clinically evident cutaneous and/or subcutaneous metastases occurring >20 mm from the primary melanoma in the region between the primary and the regional lymph node basin.

Locoregional cutaneous or subcutaneous microscopic metastases are recognised as metastatic tumour cells discontinuous from the primary tumour (but not separated only by fibrosis or inflammation). There is no longer a minimum size threshold or distance from the primary tumour that defines a microsatellite. Fibrous scarring and/or inflammation between an apparently separate nodule and the primary tumour (rather than normal stroma) may represent regression of the intervening tumour; if these findings are present, the nodule is considered to be an extension of the primary tumour and not a satellite.

### Metastases at margins

The presence of a melanoma satellite metastasis or microsatellite at a peripheral excision margin, if present, is core to document. When identified, this may be an indication for re-excision, because it can serve as a source of recurrence and may imply the presence of further melanoma in the skin beyond the visible margins.

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## Note 12 – Clark level (Non-core)

Evidence suggests that the Breslow thickness of a melanoma is a more accurate prognostic indicator than the Clark level.<sup>23</sup> In the UICC 9<sup>th</sup> edition/AJCC 8<sup>th</sup> edition Cancer Staging Manuals,<sup>20,21</sup> Clark level is not used as a primary criterion for the definition of T1b tumours, which is why it is a non-core element. Clark level may on rare occasion provide useful prognostic information if an accurate Breslow thickness cannot be determined, for example where the specimen has been tangentially sectioned. If Clark level is reported, it is recommended that alphanumeric numbers be used to specify each of the Clark levels, rather than using the traditional Roman numerals to avoid confusion of Clark level with tumour stage.

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## Note 13 – Lymphovascular invasion (Core and Non-core)

Lymphovascular invasion refers to the presence of melanoma cells within the lumina of blood vessels (termed vascular invasion) or lymphatics (termed lymphatic invasion), or both. It is an uncommon finding in the excision specimens of primary cutaneous melanoma, but it correlates with microsatellite formation<sup>30,31</sup> and is generally regarded as a marker of poor prognosis.

There is a possible role for immunohistochemistry to highlight the presence of vascular invasion in selected cases.<sup>27</sup> At times it may be difficult to distinguish whether invasive tumour is present within a lymphatic channel or represents a microsatellite. In this instance, the use of immunohistochemistry for a specific lymphatic marker such as D2-40 may assist in distinction.<sup>32</sup> Invasion of tumour into the wall of a blood vessel but without tumour within the lumen of the blood vessel, should not be recorded as lymphovascular invasion.

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## Note 14 – Tumour-infiltrating lymphocytes (Non-core)

To be regarded as tumour-infiltrating lymphocytes (TILs), lymphocytes must infiltrate and disrupt tumour nests and/or directly oppose tumour cells. The degree of infiltration can be described by both the extent and the intensity of the TIL infiltrate.

The most commonly applied grading scheme for quantitating the presence of TILs is the system described by Clark et al (1989),<sup>33</sup> which contains the three categories of ‘absent’, ‘non-brisk’ and ‘brisk’.

Other systems for grading TIL infiltrates based on the density and distribution of them have also been proposed,<sup>34-36</sup> but these have not been independently validated.

Reports on the prognostic effect of TILs vary, but most suggest the presence of ‘brisk’ or dense TILs is associated with lower probability of sentinel lymph node (SLN) metastasis and a more favourable prognosis.<sup>37,38</sup>

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## Note 15 – Tumour regression (Non-core)

A host immunologic response may be directed against melanoma and may result in elimination of part or all of the melanoma; this is termed regression. Regression may result in partial or complete loss of melanoma. It is characterised by immature and mature dermal fibrosis, often accompanied by the presence of melanophages and telangiectasia and effacement of the rete architecture, with absence of melanoma in the region of regression.

The prognostic significance of tumour regression is controversial.<sup>39-42</sup>

### **Tumour regression: Margins**

Regression at a peripheral excision margin may be an indication for re-excision because it implies that there may be further melanoma in the skin beyond the visible margins.

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### **Note 16 – Perineural invasion (Core)**

Perineural invasion (PNI) is identified by the presence of melanoma cells around nerve sheaths. On occasion tumour cells may also be found within nerves (intra-neural invasion).

Infiltration along nerve sheaths (or occasionally within the endoneurium) may be associated with an increased local recurrence rate (local persistence).<sup>27</sup> PNI is common in desmoplastic melanoma (desmoplastic neurotropic melanoma), but may occur in other forms of melanoma. One large study reported that the presence of PNI was not associated with increased risk of local recurrence compared with other non-neurotropic melanomas if adequate surgical margins were obtained.<sup>13</sup> However, adjuvant radiotherapy reduced the risk of recurrence if adequate surgical margins could not be achieved. It may be helpful for the clinician if the pathologist reports whether the PNI is 'extensive' or 'focal' (i.e., involving only a single or multiple nerves) and/or size of involved nerves, but evidence for this is lacking. There is also limited data on the reproducibility of assessing PNI.

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### **Note 17 – Associated melanocytic naevus or other lesion (Non-core)**

Although of no known prognostic value, the recognition of an associated benign melanocytic lesion is relevant to the pathogenesis of melanoma, and may be important for clinicopathological correlation and epidemiological, clinical and genetic studies.<sup>6</sup> It is helpful for staging in the case of a nodular melanoma associated with a nevus remnant to provide evidence in support of the primary nature of the melanoma. Documentation of associated benign melanocytic tumour is also of relevance where there may be residual melanocytic tumour in the re-excision specimen, and when knowledge of this may assist in the interpretation of the residual tumour overlying a scar as persistent/recurrent naevus, rather than melanoma.

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### **Note 18 – Surgical margin/Tissue edges (Core and Non-core)**

When the clinical intention of surgical procedure (excisional biopsy or wide local excision with residual tumour) is to completely remove a melanoma, it is important to document when the surgical margins are microscopically involved (positive) by in situ or invasive melanoma and to specify the precise location of the positive margin, if possible. If the margins are microscopically clear, for clinical management purposes, it is usually sufficient to simply state this in the pathology report, unless the microscopic margin is narrow (where there is a risk that limited routine pathological sampling may fail to detect a positive margin, especially in the case of a tumour with ill-defined growth).

When the deep margin is microscopically positive with invasive melanoma, it may be helpful to specify whether the margin involvement is focal or more extensive.<sup>20,21</sup>

The standard treatment for primary melanoma is wide excision of the skin and subcutaneous tissues around the melanoma. Such definitive treatment is not usually performed until after a pathological diagnosis of melanoma has been established. The aim is complete surgical excision of all in situ and invasive melanoma components. Involvement of the surgical margin may result in regrowth or metastasis from residual melanoma and may adversely affect patient outcome. Guidelines from multiple societies of several countries have recommended clinical measurements for re-excision based on the tumour thickness (and at times subtype) of the primary melanoma.<sup>43-46</sup> The main purpose of these guidelines<sup>43-46</sup> is to ensure a high likelihood of a histopathologically negative final margin in most cases. In some instances, a margin may still be positive, in which case a re-excision can be performed as clinically judged appropriate.

When a margin is negative for melanoma, but a naevus is transected at a surgical margin, the DAC recommend documenting such a finding, since it may be relevant to explain subsequent repigmentation at the site of a scar.

If an excision of a melanoma contains additional tumours (e.g., squamous cell or basal cell carcinomas), the margin status of such additional tumours also needs to be recorded.

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## **Note 19 – Lymph node status (Core and Non-core)**

Regional lymph nodes are the most common site of initial metastasis in patients with cutaneous melanoma. Among patients with regional lymph node metastasis, the majority have clinically occult disease that is detected by the technique of lymphatic mapping and SLN biopsy. Patients without clinical or radiographic evidence of regional lymph node metastases but who have microscopically documented nodal metastases (usually detected by lymphatic mapping and sentinel node biopsy) are defined as 'clinically occult' whereas nodal metastases detected by palpation or radiological imaging are defined as 'clinically detected'.<sup>20,21,47</sup> If a node is clinically detected it is not, strictly speaking, a sentinel node.

If a lymph node is received but it is not specifically stated that it is a sentinel node then it should be reported as a non-sentinel node. Any additional relevant microscopic comments should be recorded.

Extranodal extension (ENE) is an adverse prognostic factor in melanoma patients. It is defined as the presence of a nodal metastasis extending through the lymph node capsule and into adjacent tissue, which may be apparent macroscopically but must be confirmed microscopically. Matted nodes (defined as two or more nodes adherent to one another through involvement by metastatic disease, identified at the time the specimen is examined macroscopically in the pathology laboratory) often suggest the presence of ENE, but the latter must be confirmed microscopically.

### **Sentinel lymph nodes**

Tumour-harboring status of the SLN is a strong predictor of outcome for clinically localised primary cutaneous melanoma patients.<sup>47,48</sup>

There are a number of potential pitfalls in the microscopic examination of SLNs.<sup>6</sup> The most common diagnostic problem is distinguishing nodal naevus cells or non-melanocytic cells with cross-reacting antigenic determinants from a melanoma metastasis. This can usually be resolved by careful assessment of the

location, morphologic features, and immunohistochemical staining characteristics of the cells and, in some instances, comparing the cytology of the nodal melanocytes with the cells of the primary invasive melanoma.

Histologic parameters of melanoma deposits in SLNs have been shown to be predictive of the presence or absence of tumour in non-SLNs and clinical outcome.<sup>49-51</sup>

Sentinel lymph node (SLN) parameters shown to be predictive of clinical outcome include the size of metastases, tumour penetrative depth (also known as maximal subcapsular depth and centripetal thickness and defined as the maximum distance of melanoma cells from the nearest inner margin of the lymph node capsule), the location of tumour deposits in the SLN, the percentage cross-sectional area of the SLN that is involved, and the presence of extranodal spread. However, individual features of melanoma metastases in SLNs are not always reliable for predicting tumour involvement in non-SLNs. Tumour deposits are often irregularly shaped, making the limits of tumour deposits difficult to discern. Measurements of tumour burden show suboptimal reproducibility<sup>52,53</sup> and to some degree are dependent on the sectioning protocol used. More extensive sectioning may reveal additional tumour deposits or demonstrate a greater dimension of deposit(s) in the deeper sections.

It is recommended that guidelines provided for the measurement of the maximum dimension of the largest sentinel node metastasis in the UICC 9<sup>th</sup> edition/AJCC 8<sup>th</sup> edition Cancer Staging Manuals be used.<sup>20,21,52</sup> The single largest maximum dimension (measured in mm to the nearest 0.1 mm using an ocular micrometre) of the largest discrete metastatic melanoma deposit measured in a straight line in sentinel nodes should be measured and recorded. "To be considered a discrete deposit, the tumour cells must be in direct continuity with adjacent tumour cells. In some instances, multiple small tumour aggregates may be dispersed within a lymph node and separated by lymphoid cells. In this circumstance, the size of the largest discrete single deposit (not the nodal area over which the multiple deposits are contained) should be recorded."<sup>8</sup>

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## **Note 20 – 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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## **Note 21 – Pathological staging (Core)**

Staging data should be assessed according to the 9<sup>th</sup> edition UICC/8<sup>th</sup> edition AJCC Cancer Staging Manuals.<sup>20,21</sup>

### **Primary tumour (pT)**

In the current TNM Staging Manuals,<sup>20,21</sup> tumour thickness and ulceration continue to define T1, T2, T3 and T4 categories, which is why a pathology report must contain these data elements.

## Regional lymph nodes (pN)

To determine the number of nodes involved for pathological staging, the number of tumour-positive sentinel nodes should be added to the number of tumour-positive non-sentinel nodes, if any, identified after completion lymph node dissection (CLND), if performed. Few patients with a positive SLN biopsy undergo CLND. If a patient undergoes SLN biopsy (sn) that is positive for a single sentinel node metastasis, and does not undergo CLND, the designation of pN1 (sn) is recommended. In the context of patients who undergo completion lymphadenectomy after SLN biopsy, the pN1a, pN1b, or pN1c subcategory (without the suffix '(sn)') implies that a CLND has been performed and the (sn) description is not used.

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