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Tumours of the Central Nervous System Integrated Final Diagnosis Reporting Guide

Family/Last name

Given name(s)

Date of birth DD – MM – YYYY

Patient identifiers

Date of request DD – MM – YYYY

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 SECTION

INTEGRATED FINAL DIAGNOSIS (Note 1)

◯ Diagnosis not classified elsewhere

TUMOUR GRADE (Note 2)

◯ Not applicable
◯ CNS World Health Organization (WHO) grade 1
◯ CNS WHO grade 2
◯ CNS WHO grade 3
◯ CNS WHO grade 4
◯ Cannot be determined, *specify*

INTEGRATED FINAL DIAGNOSIS BASED ON (select all that apply) (Note 3)

☐ CNS WHO Tumour Classification
☐ Histology
☐ CNS WHO grade - refer to **TUMOUR GRADE** (Note 2)
☐ Immunohistochemistry
☐ Molecular findings

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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 III-2 or above (based on prognostic factors in the National Health and Medical Research Council levels of evidence[1]). In rare circumstances, where level III-2 evidence is not available an element may be made a CORE element where there is unanimous agreement in the Dataset Authoring Committee (DAC).

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 III-2 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.

⬆ Back

Scope

This dataset section has been developed for the integrated final diagnosis of benign and malignant primary tumours of the central nervous system (CNS) and its coverings, as well as tumours from those structures of the peripheral nervous system immediately adjacent to the CNS. The CNS dataset applies to both biopsy and resection specimens of adult and paediatric CNS tumours. Haematological lesions involving the CNS and germ cell tumours are not covered in detail as these are not the primary focus of the CNS dataset. Most sarcomas are not included and are covered by separate ICCR datasets.[2,3] Secondary tumours of the CNS (for example metastatic tumours from carcinomas, sarcomas or melanomas in other organs) are not covered in this dataset. Tumours of the pituitary gland are included as the majority of these tumours are reported by neuropathologists worldwide.

This dataset section should be used in conjunction with the ICCR dataset sections on Histological assessment and Molecular information, where appropriate.

The 2nd edition of this dataset incorporates the World Health Organisation (WHO) Classification of Tumours of the CNS, 5th edition (CNS5), 2021.[4] The ICCR dataset includes 5th edition Corrigenda, July 2024.[5] Reports should incorporate these three dataset sections into a single layered report format (see **Note 1 – INTEGRATED FINAL DIAGNOSIS**).

A list of changes in this dataset edition can be accessed here.

The authors of this dataset can be accessed here.

Back

Note 1 – Integrated final diagnosis (Core)

All reports should strive to render a diagnosis from the WHO CNS5 Tumour Classification,[4] although it is recognised that this may not be possible in all instances (i.e., that more descriptive diagnoses may be needed for tumours that do not meet criteria for WHO CNS5 Tumour Classification entities).[4,6]

In many situations, CNS WHO[4] diagnoses 'integrate' histological and molecular information; for these entities, both histological and molecular information is needed. In this context, 'molecular' refers to the detection of molecular alterations in nucleic acids that can be detected at the nucleic acid or protein level. In some scenarios, there may be differences between histological appearance and the WHO CNS5[4] diagnosis (e.g., a diffuse glioma without overt oligodendroglial features but with IDH sequence variant and 1p/19q codeletion).

To capture this nosological heterogeneity and to provide as much clinically relevant information in each report, it is recommended that layered diagnostic formatting be utilised in reports, typically with four layers:

- Integrated diagnosis, ideally corresponding to a WHO CNS5 Tumour Classification diagnosis (as per this dataset section), and supplemented with CNS WHO grade;
- Histological appearance (as per 'Histological assessment of CNS specimens' dataset section);
- Molecular parameters (as per 'Molecular information for CNS specimens' dataset section);
- CNS WHO grade (as per 'Histological assessment of CNS specimens' and 'Molecular information for CNS specimens' dataset sections);

Increasingly, the CNS WHO grade is based on a combination of histological and molecular features. Therefore, CNS WHO grade is now more logically presented in the 4th layer (rather than in the 3rd layer as was initially proposed).[7] CNS WHO grade should also be included (or purposefully omitted) in the first layer in order to increase the visibility of this parameter.

For some entities, the WHO CNS5[4] diagnosis may be identical to the histological appearance (e.g., choroid plexus tumours), but for others there may be differences such as the following:

- WHO CNS5 Classification diagnosis: Astrocytoma, IDH-mutant, CNS WHO grade 4
- Histological appearance: Diffuse glioma, histologically grade 3
- Molecular parameters:
    - *IDH1* R132H alteration
    - *ATRX* alteration
    - *TP53* alteration
    - 1p/19q retention
    - *CDKN2A/B* homozygous deletion
- CNS WHO grade 4 (due to homozygous *CDKN2A/B* deletion)

Table 1. World Health Organization classification and grade of central nervous system tumours.[4]

Descriptor	ICD-O codes[a]	CNS WHO Grade
Gliomas, glioneuronal tumours and neuronal tumours		
Adult-type diffuse gliomas		
Astrocytoma, IDH-mutant	9400/3, 9401/3, 9445/3	2, 3, or 4
Oligodendroglioma, IDH-mutant and 1p/19q-codeleted	9450/3, 9451/3	2 or 3
Glioblastoma, IDH-wildtype	9440/3	4
Paediatric-type diffuse low grade gliomas		
Diffuse astrocytoma, *MYB*- or *MYBL1*-altered	9421/1	1
Angiocentric glioma	9431/1	1
Polymorphous low grade neuroepithelial tumour of the young	9413/0	1
Diffuse low grade glioma, MAPK pathway-altered	9421/1	n/a
Paediatric-type diffuse high grade gliomas		
Diffuse midline glioma, H3 K27-altered	9385/3	4
Diffuse hemispheric glioma, H3 G34-mutant	9385/3	4
Diffuse paediatric-type high grade glioma, H3-wildtype and IDH-wildtype	9385/3	4
Infant-type hemispheric glioma	9385/3	n/a
Circumscribed astrocytic gliomas		
Pilocytic astrocytoma	9421/1	1
High grade astrocytoma with piloid features	9421/3	n/a
Pleomorphic xanthoastrocytoma	9424/3	2 or 3
Subependymal giant cell astrocytoma	9384/1	1
Chordoid glioma	9444/1	2
Astroblastoma, *MN1*-altered	9430/3	n/a
Glioneuronal and neuronal tumours		
Ganglioglioma	9505/1	1
Gangliocytoma	9492/0	1
Desmoplastic infantile ganglioglioma/desmoplastic infantile astrocytoma	9412/1	1
Dysembryoplastic neuroepithelial tumour	9413/0	1
Diffuse glioneuronal tumour with oligodendroglioma-like features and nuclear clusters*		n/a
Papillary glioneuronal tumour	9509/1	1
Rosette-forming glioneuronal tumour	9509/1	1
Myxoid glioneuronal tumour	9509/1	1
Diffuse leptomeningeal glioneuronal tumour	9509/3	n/a
Multinodular and vacuolating neuronal tumour	9509/0	1
Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease)	9493/0	1

Descriptor	ICD-O codes[a]	CNS WHO Grade
Central neurocytoma	9506/1	2
Extraventricular neurocytoma	9506/1	2
Cerebellar liponeurocytoma	9506/1	2
Ependymal tumours		
Supratentorial ependymoma	9391/3	2 or 3
Supratentorial ependymoma, *ZFTA* fusion-positive	9396/3	2 or 3†
Supratentorial ependymoma, *YAP1* fusion-positive	9396/3	2 or 3†
Posterior fossa ependymoma	9391/3	2 or 3
Posterior fossa group A (PFA) ependymoma	9396/3	2 or 3†
Posterior fossa group B (PFB) ependymoma	9396/3	2 or 3†
Spinal ependymoma	9391/3	2 or 3†
Spinal ependymoma, *MYCN*-amplified	9396/3	n/a
Myxopapillary ependymoma	9394/1	2
Subependymoma	9383/1	1
Choroid plexus tumours		
Choroid plexus papilloma	9390/0	1
Atypical choroid plexus papilloma	9390/1	2
Choroid plexus carcinoma	9390/3	3
Embryonal tumours		
Medulloblastomas, molecularly defined		
Medulloblastoma, WNT-activated	9475/3	4†
Medulloblastoma, SHH-activated and *TP53*-wildtype	9471/3	4
Medulloblastoma, SHH-activated and *TP53*-mutant	9476/3	4
Medulloblastoma, non-WNT/non-SHH	9477/3	4†
Medulloblastomas, histologically defined		
Medulloblastomas, histologically defined	9470/3	4†
Other CNS embryonal tumours		
Atypical teratoid/rhabdoid tumour	9508/3	4
Cribriform neuroepithelial tumour*		n/a
Embryonal tumour with multilayered rosettes	9478/3	4
CNS Neuroblastoma, *FOXR2*-activated	9500/3	4
CNS tumour with *BCOR* internal tandem duplication	9500/3	n/a
CNS Embryonal tumour NEC/NOS	9473/3	n/a
Pineal tumours		
Pineocytoma	9361/1	1
Pineal parenchymal tumour of intermediate differentiation	9362/3	2 or 3
Pineoblastoma	9362/3	4

Descriptor	ICD-O codes[a]	CNS WHO Grade
Papillary tumour of the pineal region	9395/3	2 or 3
Desmoplastic myxoid tumour of the pineal region, *SMARCB1*-mutant*		n/a
Cranial and paraspinal nerve tumours		
Schwannoma	9560/0	1
Neurofibroma	9540/0	1
Perineurioma	9571/0	1
Hybrid nerve sheath tumour	9563/0	n/a
Malignant melanotic nerve sheath tumour	9540/3	n/a
Malignant peripheral nerve sheath tumour	9540/3	n/a
Cauda equina neuroendocrine tumour (previously paraganglioma)	8693/3	1†
Meningioma		
Meningioma	9530/0	1, 2 or 3
Mesenchymal, non-meningothelial tumours involving the CNS		
Fibroblastic and myofibroblastic tumours		
Solitary fibrous tumour	8815/1	1, 2 or 3†
Vascular tumours		
Hemangiomas and vascular malformations	9121/0, 9131/0, 9123/0	n/a
Haemangioblastoma	9161/1	1
Skeletal muscle tumours		
Rhabdomyosarcoma	8910/3	n/a
Tumours of uncertain differentiation		
Intracranial mesenchymal tumour, FET::CREB fusion-positive		n/a
CIC-rearranged sarcoma	9367/3	4†
Primary intracranial sarcoma, *DICER1*-mutant	9480/3	n/a
Ewing sarcoma	9364/3	4†
Chondrogenic tumours		
Mesenchymal chondrosarcoma	9240/3	n/a
Chondrosarcoma	9220/3	1, 2 or 3†
Notochordal tumours		
Chordoma	9370/3	n/a
Melanocytic tumours		
Diffuse meningeal melanocytic neoplasms		
Meningeal melanocytosis	8728/0	n/a
Meningeal melanomatosis	8728/3	n/a
Circumscribed meningeal melanocytic neoplasms		
Meningeal melanocytoma	8728/1	n/a

Descriptor	ICD-O codes[a]	CNS WHO Grade
Meningeal melanoma	8720/3	n/a
Tumours of the sellar region		
Adamantinomatous craniopharyngioma	9351/1	1†
Papillary craniopharyngioma	9352/1	1†
Pituicytoma, granular cell tumour of the sellar region, and spindle cell oncocytoma	9432/1, 9582/0, 8290/0	n/a
Pituitary adenoma/pituitary neuroendocrine tumour	8272/3	n/a
Pituitary blastoma	8273/3	n/a

[a] These morphology codes are from the International Classification of Diseases for Oncology, Third Edition, second revision (ICD-O-3.2).[6] Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours, primary site; and /6 for malignant tumours, metastatic site. Subtype labels are indented. Incorporates all relevant changes from the 5th edition Corrigenda, July 2024.[5]
CNS WHO grades marked 'n/a' do not have grade included in the tumour definition.
*Provisional entity.
† These CNS WHO grades are described in the section or chapter but not in the definition.

Table 2. World Health Organization classification of haematological tumours involving the central nervous system.[8]

Descriptor	ICD-O codes[a]
Lymphomas	
Lymphomas with predominant primary CNS presentation	
Primary large B-cell lymphoma of the CNS	9680/3
Lymphomas arising in immune deficiency/dysregulation	
Lymphomatoid granulomatosis	9766/1, 9766/3
Intravascular large B-cell lymphoma	9712/3
Extranodal NK/T-cell lymphoma	9712/3
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (EMZL) of the dura	9699/3
Lymphoplasmacytic lymphoma (Bing-Neel syndrome)	9671/3
Other rare lymphomas with predominant primary CNS presentation	
Other indolent B-cell lymphomas of the CNS	9690/3, 9823/3
Other aggressive B-cell lymphomas	9687/3
Peripheral T-cell lymphoma, NOS	9702/3
ALK-negative and ALK-positive anaplastic large cell lymphoma	9715/3, 9714/3
Histiocytic tumours	
Erdheim-Chester disease	9749/3
Rosai-Dorfman disease	9749/3
Juvenile xanthogranuloma	9749/1

Descriptor	ICD-O codes[a]
Langerhans cell histiocytosis	9751/1
Histiocytic sarcoma	9755/3
ALK-positive histiocytosis	9750/3

[a] These morphology codes are from the International Classification of Diseases for Oncology, Third Edition, second revision (ICD-O-3.2).[6] Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours, primary site; and /6 for malignant tumours, metastatic site. Subtype labels are indented.

In the event that all diagnostic information is present but the tumour still does not meet criteria for a tumour type defined by the 2021 WHO CNS5 Tumour Classification,[4] a 'descriptive' or 'not elsewhere classified' (NEC) diagnosis can be issued, which draws attention to the unusual nature of the lesion. Such designations are distinct from 'not otherwise specified' (NOS) diagnoses, which are cases in which necessary diagnostic information is not available (e.g., in the case of resource-limited settings, limited tissue volume that was exhausted before molecular testing could be performed, or unreliable results of molecular testing).[9]

⬆ Back

Note 2 –Tumour grade (Core)

In as many pathology reports of CNS neoplasms as possible, the diagnosis should include a grade based on the WHO CNS5 Classification (see Table 1).[4,10] As for other organ systems, different grades of a diagnostic entity do not have a separate entry in the WHO CNS5 Classification anymore but are grouped under the respective diagnostic tumour type.

The scale of CNS WHO grades from 1 to 4 reflects the natural histories of various tumour types, rather than their shifting prognoses with changes in therapeutic practice over time.[7]

- Generally speaking, a CNS WHO grade 1 tumour is considered benign and potentially curable by surgery, although in unfavourable locations, such tumours may still create significant morbidity. Note that this approach is different from that of many other tumour types in other parts of the body, for which a grade 1 designation would reflect a low grade malignancy. For this reason, CNS tumour grades are termed 'CNS WHO grades' rather than simply 'WHO grades'.
- CNS WHO grade 2 tumours typically are slowly growing tumours that often recur and are associated with significant mortality, albeit with survival times of many years in most cases.
- CNS WHO grade 3 tumours are rapidly growing malignancies with typically survival of only a few years if treated with surgery alone.
- CNS WHO grade 4 neoplasms are highly aggressive malignancies with rapid mortality (typically in less than two years after diagnosis) in the absence of therapies beyond surgery (e.g., glioblastomas and embryonal neoplasms).

Progression from lower grade malignancy to higher grade forms occurs in some CNS neoplasms, most commonly the IDH-mutant diffuse gliomas, and to a lesser extent in the meningiomas.

For some tumours, assigning a CNS WHO grade could cause more confusion than clarification for clinical colleagues (e.g., when the exact tumour subtype remains unclear or the when the prognostic impact of the grade is unclear); in such cases, it preferable to omit the CNS WHO grade from the final diagnosis. Also, for

some more recently defined tumour types, a CNS WHO grade has not been assigned because a definite understanding of that tumour's natural history is not yet available in the literature. Bone, soft tissue and haematological neoplasms occurring within the neural axis are mostly classified and graded using the same criteria as in other parts of the body, although the CNS grading scheme for solitary fibrous tumours differs from its soft tissue counterpart. For some tumours (especially adult-type diffuse gliomas, meningiomas) tumour grade is ideally based on a combination of morphological and molecular information. It should be reported if in such cases the grade is assigned based on morphology alone.

CNS tumour type and grade are strong predictors of clinical behaviour. Table 1 lists the grades for CNS tumour types as given in the WHO CNS5 Classification definition. In Table 1, 'n/a' means no specific information on the CNS WHO grade is provided in the definition of these tumours, and grade followed by the dagger symbol '†' means that information on grade is given in the chapter but not in the definition. For more information on malignancy grades of these tumours the reader is referred to the chapters in the WHO CNS5 Tumour Classification. Table 2 lists the haematological tumours involving the CNS as included in the (more recently published) 5th edition of the WHO Classification of Haematolymphoid Tumours.[8]

⬆ **Back**

Note 3 – Integrated diagnosis based on (Core)

The final integrated diagnosis is a core element and may be based on the following information:

- CNS WHO Tumour Classification
- Histology
- Immunohistochemistry
- Molecular findings
- CNS WHO grade (refer to **NOTE 2 – TUMOUR GRADE**).

Pathology reports optimally include an integrated assessment of all available information in a layered diagnostic format.

⬆ **Back**

References

1 Merlin T, Weston A and Tooher R (2009). Extending an evidence hierarchy to include topics other than treatment: revising the Australian 'levels of evidence'. *BMC Med Res Methodol* 9:34.

2 International Collaboration on Cancer Reporting (2021). *Soft Tissue Sarcoma Histopathology Reporting Guide – Biopsy Specimens. 1st edition*. Available from: https://www.iccr-cancer.org/datasets/published-datasets/soft-tissue-bone/soft-tissue-sarcoma-biopsy-specimens/ (Accessed 1st March 2024).

3 International Collaboration on Cancer Reporting (2021). *Soft Tissue Sarcoma Histopathology Reporting Guide – Resection Specimens. 1st edition*. Available from: https://www.iccr-cancer.org/datasets/published-datasets/soft-tissue-bone/soft-tissue-sarcoma-resection-specimens/ (Accessed 1st March 2024).

4 WHO Classification of Tumours Editorial Board (2021). *Central Nervous System Tumours, WHO Classification of Tumours, 5th Edition, Volume 6*. IARC Press, Lyon, France.

5 WHO Classification of Tumours Editorial Board (2024). *Central Nervous System Tumours, WHO Classification of Tumours, 5th Edition, Volume 6 - Corrigenda July 2024*. Available from: file:///C:/Users/tinas/Downloads/CNS5%20Corrigenda%20doc_2024-07-08-1.pdf (Accessed 1st August 2024).

6 Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM, Whelan S (eds) (2020). *International Classification of Diseases for Oncology, Third edition, Second revision ICD-O-3.2*. Available from: http://www.iacr.com.fr/index.php?option=com_content&view=category&layout=blog&id=100&Itemid=577 (Accessed 1st March 2024).

7 Louis DN, Perry A, Burger P, Ellison DW, Reifenberger G, von Deimling A, Aldape K, Brat D, Collins VP, Eberhart C, Figarella-Branger D, Fuller GN, Giangaspero F, Giannini C, Hawkins C, Kleihues P, Korshunov A, Kros JM, Beatriz Lopes M, Ng HK, Ohgaki H, Paulus W, Pietsch T, Rosenblum M, Rushing E, Soylemezoglu F, Wiestler O and Wesseling P (2014). International Society Of Neuropathology-Haarlem consensus guidelines for nervous system tumor classification and grading. *Brain Pathol* 24(5):429-435.

8 WHO Classification of Tumours Editorial Board (2022). *Haematolymphoid Tumours, WHO Classification of Tumours, 5th Edition, Volume 11*. IARC Press, Lyon, France.

9 Louis DN, Wesseling P, Paulus W, Giannini C, Batchelor TT, Cairncross JG, Capper D, Figarella-Branger D, Lopes MB, Wick W and van den Bent M (2018). cIMPACT-NOW update 1: Not Otherwise Specified (NOS) and Not Elsewhere Classified (NEC). *Acta Neuropathol.* 135(3):481-484.

10 Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, Hawkins C, Ng HK, Pfister SM, Reifenberger G, Soffietti R, von Deimling A and Ellison DW (2021). The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. *Neuro Oncol* 23(8):1231-1251.