

# Lymphoid Malignancies 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

### History of a known or suspected haematological or solid neoplasm and/or reactive disease condition

Information not provided

No

Yes, specify

### Known immune deficiency/dysregulation/cancer predisposition syndrome

Information not provided

No

Yes, specify

### Previous therapy

Information not provided

No

Yes (select all that apply)

Cancer therapy

Immune therapy

Other, specify

### Other clinical information, specify

## SAMPLING PROCEDURE (select all that apply) (Note 2)

Not specified

Core biopsy

Surgical biopsy (incisional/excisional)

Fine needle aspiration

Other, specify

## SPECIMEN(S) SUBMITTED (select all that apply) (Note 3)

Not specified

Lymph node(s), specify localisation

Extranodal site(s), specify

Bone marrow

Peripheral blood

## TUMOUR SITE (select all that apply) (Note 4)

Not specified

Peripheral blood

Lymph node(s), specify

Extranodal site(s), specify

Bone marrow

Percent involvement of neoplastic cells  %

Other, specify

## BLOCK IDENTIFICATION KEY (Note 5)

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

## FINAL INTEGRATED DIAGNOSIS<sup>a</sup> (select all that apply) (Note 6)

(Value list based on the World Health Organization Classification of Haematolymphoid Tumours, 5<sup>th</sup> Edition (2024))

B-cell lymphoid proliferations and lymphomas

B-cell lymphoma, not further classified

Indolent B-cell lymphoma, not further classified

Aggressive B-cell lymphoma, not further classified

B-lymphoblastic leukaemia/lymphoma

Entity, specify

<sup>a</sup> Refer to Table 1 for a listing of all Entities and Variants.

**FINAL INTEGRATED DIAGNOSIS (Note 6) continued**

Preneoplastic and neoplastic small lymphocytic proliferation

Entity/subtype, *specify*

Splenic B-cell lymphoma and leukaemia

Entity, *specify*

Lymphoplasmacytic lymphoma

Marginal zone lymphoma

Entity/subtype, *specify*

Follicular lymphoma

Entity/subtype, *specify*

Mantle cell lymphoma

Entity/subtype, *specify*

Diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS)

Subtype, *specify*

Large B-cell lymphoma (LBCL)

Entity/subtype, *specify*

Burkitt lymphoma

KSHV/HHV8-associated B-cell lymphoid proliferations and lymphoma

Entity/subtype, *specify*

Lymphoproliferative disorder and lymphoma associated with immune deficiency and dysregulation

Entity/subtype, *specify*

Plasma cell neoplasms<sup>b</sup>

Hodgkin lymphoma

Classic Hodgkin lymphoma

Subtype, *specify*

Nodular lymphocyte predominant Hodgkin lymphoma

Subtype, *specify*

<sup>b</sup> Refer to the ICCR Plasma cell neoplasms dataset.

T-cell and NK-cell lymphoid proliferations and lymphomas

T-cell and NK-cell lymphoma, not further classified

T-lymphoblastic leukaemia/lymphoma

Entity, *specify*

Mature T-cell and NK-cell leukaemia

Entity/subtype, *specify*

Primary cutaneous T-cell lymphoid proliferation and lymphoma

Entity/subtype, *specify*

Intestinal T-cell and NK-cell lymphoid proliferation and lymphoma

Entity, *specify*

Hepatosplenic T-cell lymphoma

Anaplastic large cell lymphoma

Entity, *specify*

Nodal T follicular helper cell lymphoma

Entity, *specify*

Peripheral T-cell lymphoma, NOS

Epstein-Barr virus (EBV)-positive T-cell and NK-cell lymphoma

Entity/subtype, *specify*

EBV-positive T-cell and NK-cell lymphoid proliferation and lymphoma of childhood

Entity/subtype, *specify*

Other, *specify*

Comments

  


**DISEASE STATUS (AFTER TREATMENT) (Note 7)**

Not known

Primary diagnosis

Relapsed disease

Date of initial diagnosis

DD - MM - YYYY

Refractory disease

Date of initial diagnosis

DD - MM - YYYY

**INDICATIONS FOR TRANSFORMED DISEASE (Note 8)**

- Transformed disease confirmed (with proof of clonal identity)
- Transformed disease suspected (clonal identity not known)

Transformed from, *specify*

Date of initial diagnosis of the low grade lymphoma

**IMMUNOPROFILING/PHENOTYPING STUDIES (Note 9)**

(select all that apply)

Markers to define lineage

- CD20
  - Not performed
  - Positive
  - Negative
- CD79A
  - Not performed
  - Positive
  - Negative
- CD3
  - Not performed
  - Positive
  - Negative
- CD2
  - Not performed
  - Positive
  - Negative

*If negative, other markers including:*

- PAX5
  - Not performed
  - Positive
  - Negative
- MPO
  - Not performed
  - Positive
  - Negative
- CD68
  - Not performed
  - Positive
  - Negative
- C163
  - Not performed
  - Positive
  - Negative
- CD34
  - Not performed
  - Positive
  - Negative
- TdT
  - Not performed
  - Positive
  - Negative

Additional T-cell markers, *specify*

Markers to define activation state

- CD30
  - Not performed
  - Positive
  - Negative

AND

Ki-67 proliferation index

 %

- Not performed

Markers representing essential diagnostic criteria in WHO HAEM5 to define entities (refer to Table 2), *specify*

*Comments*

**MOLECULAR GENETIC STUDIES (Note 10)**

(select all that apply)

Precursor B-cell neoplasms

BCR::ABL1

- Not performed
- Positive
- Negative



- Hyperdiploidy
- Hypodiploidy
- Other, *specify karyotype*

Other, *specify*

Mature B-cell neoplasms

MYC rearrangement

- Not performed
- Positive
- Negative

BCL2 rearrangement

- Not performed
- Positive
- Negative

BCL6 rearrangement

- Not performed
- Positive
- Negative

EBER if EBV association is suspected

- Not performed
- Positive
- Negative

Other (refer to Table 3), *specify*

Precursor T-cell neoplasms, *specify*

Mature T-cell and NK-cell neoplasms, *specify*

*Comments*

**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 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

The dataset has been developed for the pathology reporting of precursor and mature lymphoid malignancies involving bone marrow, blood, lymph node, extranodal lymphatic tissue or any other anatomic site.

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

Knowledge of history of a known or suspected haematological or solid neoplasm and/or any relevant non-malignant condition is a prerequisite for the pathologist to correctly interpret the histologic findings. The impact of morphological features of e.g., a large cell lymphoma may be entirely different if this is arising *de novo* or if, in case of a precedent/known indolent lymphoma, the question of high grade transformation arises. The former would implicate a different prognosis and the latter should prompt additional investigations regarding clonal identity or divergence of the two neoplasms, again influencing prognosis.<sup>1</sup> Knowledge of a pre-existing non-malignant disease may facilitate the interpretation of a lymphoid proliferation e.g., in extranodal marginal zone lymphoma arising in the background of Sjögren syndrome or Hashimoto thyroiditis.<sup>2</sup> History of a solid (non-haematological) neoplasm that was treated by chemotherapy or immune therapy may impact on the pathogenesis and classification of a lymphoid neoplasm by inferring an iatrogenic immune deficiency/dysregulation (IDD) context. Information to the pathologist of known IDD/cancer predisposition syndrome is a prerequisite to the correct taxonomic categorisation of the process. Whereas diffuse large B-cell lymphoma (DLBCL) arising *de novo* may be indistinguishable from a large cell lymphoid proliferation arising in the background of IDD, knowledge of the underlying condition will prompt additional investigations for virus associations (Epstein-Barr virus (EBV), HHV8, etc.) and result in a different diagnosis ('DLBCL arising in IDD (specify) with association to EBV').<sup>3</sup>

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## Note 2 – Specimen(s) submitted (Core)

The localisation of the submitted specimen must be clearly indicated. Although a resected lymph node infiltrated by lymphoma can usually be readily distinguished from an extranodal site specimen, this is not the case for core needle biopsies or fine needle aspiration biopsies. Morphologically identical tumours presenting in a lymph node or at an extranodal site may have an entirely different biological background and clinical behaviour, such as a nodal DLBCL – not otherwise specified (NOS) and a large B-cell lymphoma (LBCL) arising in an immune-privileged site, e.g., in the central nervous system.<sup>4</sup> Some lymphomas typically or by definition arise in defined locations, such as primary mediastinal LBCL and breast implant-associated anaplastic large cell lymphoma. Moreover, many lymphomas represent organ specific diseases not primarily arising in lymph nodes such as the different types of primary intestinal T-cell lymphomas and primary cutaneous lymphomas.<sup>5</sup>

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## Note 3 – Sampling procedure (Core)

It is important that the type and intent of the operative procedure is clearly stated by the clinician, as this impacts the diagnostic accuracy of the pathologic assessment.<sup>6,7</sup>

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## Note 4 – Tumour site (Core)

Knowledge on the extent of disease/involvement provides important prognostic information. Clinical staging (Stages I/II versus Stages III/IV) is prognostic in many types of lymphomas and may determine clinical decisions, including preference for localised versus systemic treatment. Organ-specific lymphomas such as duodenal-type follicular lymphoma (FL), extranodal marginal zone lymphoma or intestinal T-cell lymphoma are often diagnosed in localised/early clinical stage.

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## Note 5 – Block identification key (Non-core)

It is recommended to specify those blocks best representing tumour and/or normal tissue. 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, in which case a subsequent reviewer would need to know the anatomic sites from which samples were taken for proper assessment and staging purposes. If this information is not included in the final pathology report, it should be available on the laboratory computer system and relayed to the reviewing pathologist. It may be useful to have a digital image of the specimen and record of the origin of the tumour blocks.

Recording the origin/designation of tissue blocks also facilitates retrieval of the appropriate blocks for further immunohistochemical, molecular or research studies.

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## Note 6 – Final integrated diagnosis (Core and Non-core)

The final integrated diagnosis is based on the most recent World Health Organization (WHO) Classification of Haematolymphoid Tumours, 5<sup>th</sup> edition, 2025 (WHO-HAEM5) (refer to Table 1).<sup>8</sup> Determination of the lymphoma entity/type is based on routine histologic examination, immunohistochemistry and – in some of the entities – molecular studies such as EBER in-situ hybridisation (e.g., in EBV-positive DLBCL) or translocation testing in DLBCL/HGBCL-*MYC/BCL2* (e.g., by FISH). These tests may not be available in all parts of the world. Therefore, an approach is recommended that defines increasing layers of granularity of the diagnosis (see list). Using this approach, the minimum diagnostic requirement would be to define the category (B-cell or T-cell lymphoproliferation or lymphoma) followed by indicating the family/class (e.g., follicular lymphoma, mantle cell lymphoma). If this is not possible due to insufficient material or testing availability or for other technical reasons, the term ‘B-cell lymphoma, not further classified’ or ‘T-cell lymphoma, not further classified’ can be rendered. Within the family/class, the entity according to WHO-HAEM5 should be given (e.g., ‘in-situ follicular B-cell neoplasm’ or ‘classic follicular lymphoma’ within the follicular lymphoma family). Subtypes may be given as appropriate.<sup>8</sup> In some cases, more than one diagnosis applies, e.g., both classic follicular lymphoma and DLBCL within one lymph node or extranodal site. The WHO-HAEM5 also includes classification of tumour-like lesions with B-cell or T-cell predominance.<sup>8</sup> Since these are not lymphoid neoplasms, they are beyond the scope of the explanatory notes provided here.<sup>8</sup>

**Table 1: 5<sup>th</sup> edition of the World Health Organization Classification of lymphoid malignancies.<sup>8</sup>**

Descriptor	ICD-O codes <sup>a</sup>
<b>Precursor B-cell neoplasms</b>	
<b><i>B-lymphoblastic leukaemias/lymphomas</i></b>	
B-lymphoblastic leukaemia/lymphoma	9811/3
B-lymphoblastic leukaemia/lymphoma with high hyperdiploidy	9815/3
B-lymphoblastic leukaemia/lymphoma with hypodiploidy <sup>†</sup>	9816/3
B-lymphoblastic leukaemia/lymphoma with hypodiploidy, near-haploid	9816/3
B-lymphoblastic leukaemia/lymphoma with hypodiploidy, low hypodiploid	9816/3
B-lymphoblastic leukaemia/lymphoma with hypodiploidy, high hypodiploid	9816/3
B-lymphoblastic leukaemia/lymphoma with iAMP21	9811/3
B-lymphoblastic leukaemia/lymphoma with <i>BCR::ABL1</i> fusion	9812/3
B-lymphoblastic leukaemia/lymphoma with <i>BCR::ABL1</i> -like features	9819/3
B-lymphoblastic leukaemia/lymphoma with <i>KMT2A</i> rearrangement	9813/3
B-lymphoblastic leukaemia/lymphoma with <i>ETV6::RUNX1</i> fusion	9814/3
B-lymphoblastic leukaemia/lymphoma with <i>ETV6::RUNX1</i> -like features	9814/3
B-lymphoblastic leukaemia/lymphoma with <i>TCF3::PBX1</i> fusion	9818/3
B-lymphoblastic leukaemia/lymphoma with <i>IGH::IL3</i> fusion	9817/3
B-lymphoblastic leukaemia/lymphoma with <i>TCF3::HLF</i> fusion	9818/3
B-lymphoblastic leukaemia/lymphoma with other defined genetic alterations	9811/3
B-lymphoblastic leukaemia with <i>DUX4</i> rearrangement	9811/3
B-lymphoblastic leukaemia with <i>MEF2D</i> rearrangement	9811/3
B-lymphoblastic leukaemia with <i>ZNF384</i> rearrangement	9811/3
B-lymphoblastic leukaemia with <i>PAX5alt</i>	9811/3
B-lymphoblastic leukaemia with <i>PAX5</i> p.P80R	9811/3
B-lymphoblastic leukaemia with <i>NUTM1</i> rearrangement	9811/3
B-lymphoblastic leukaemia with <i>MYC</i> rearrangement <sup>†</sup>	9811/3
B-lymphoblastic leukaemia/lymphoma, not otherwise specified (NOS)	9811/3
<b>Mature B-cell neoplasms</b>	
<b><i>Preneoplastic and neoplastic small lymphocytic proliferations</i></b>	
Monoclonal B-cell lymphocytosis, chronic lymphocytic leukaemia type	9823/1
Monoclonal B-cell lymphocytosis, low count or clonal B-cell expansion (chronic lymphocytic leukaemia / small lymphocytic lymphoma type)	
Monoclonal B-cell lymphocytosis, non-chronic lymphocytic leukaemia type	9591/1
Chronic lymphocytic leukaemia / small lymphocytic lymphoma	9823/3
<b><i>Splenic B-cell lymphomas and leukaemias</i></b>	
Hairy cell leukaemia	9940/3

Descriptor	ICD-O codes <sup>a</sup>
Splenic marginal zone lymphoma	9689/3
Splenic diffuse red pulp small B-cell lymphoma	9591/3
Splenic B-cell lymphoma/leukaemia with prominent nucleoli†	9591/3
<b><i>Lymphoplasmacytic lymphoma</i></b>	
Lymphoplasmacytic lymphoma	9671/3
IgM-type lymphoplasmacytic lymphoma / Waldenström macroglobulinaemia†	9761/3
Non-IgM-type lymphoplasmacytic lymphoma / Waldenström macroglobulinaemia†	9761/3
<b><i>Marginal zone lymphoma</i></b>	
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue	9699/3
Immunoproliferative small intestinal disease (alpha heavy chain disease)	9762/3
Primary cutaneous marginal zone lymphoma†	9699/3
Primary cutaneous marginal zone lymphoma, heavy chain class-switched form (IgG+, IgA+, or IgE+)†	9699/3
Primary cutaneous marginal zone lymphoma, non-class-switched form (IgM+)†	9699/3
Nodal marginal zone lymphoma	9699/3
Paediatric nodal marginal zone lymphoma	9699/3
<b><i>Follicular lymphoma</i></b>	
In situ follicular B-cell neoplasm†	9695/1
Follicular lymphoma	9690/3
Follicular large B-cell lymphoma†	9698/3
Follicular lymphoma with uncommon features	9690/3
Paediatric-type follicular lymphoma	9690/3
Duodenal-type follicular lymphoma	9695/3
<b><i>Cutaneous follicle centre lymphoma</i></b>	
Primary cutaneous follicle centre lymphoma	9597/3
<b><i>Mantle cell lymphoma</i></b>	
In situ mantle cell neoplasm†	9673/1
Mantle cell lymphoma	9673/3
Cyclin D1-positive mantle cell lymphoma†	9673/3
Cyclin D1-negative mantle cell lymphoma†	9673/3
Leukaemic non-nodal mantle cell lymphoma†	9673/3
<b><i>Transformations of indolent B-cell lymphomas</i></b>	
See indolent lymphoma type	
<b><i>Large B-cell lymphomas</i></b>	

Descriptor	ICD-O codes <sup>a</sup>
Diffuse large B-cell lymphoma, NOS	9680/3
Diffuse large B-cell lymphoma, centroblastic subtype	9680/3
Diffuse large B-cell lymphoma, immunoblastic subtype	9684/3
Diffuse large B-cell lymphoma, anaplastic subtype	9680/3
Diffuse large B-cell lymphoma, germinal-centre B-cell subtype	9680/3
Diffuse large B-cell lymphoma, activated B-cell subtype	9680/3
Diffuse large B-cell lymphoma with <i>MYC</i> and <i>BCL6</i> rearrangements	9680/3
T-cell/histiocyte-rich large B-cell lymphoma	9688/3
T-cell/histiocyte-rich large B-cell lymphoma, de novo <sup>†</sup>	
T-cell/histiocyte-rich large B-cell lymphoma, progressed from nodular lymphocyte-predominant Hodgkin lymphoma <sup>†</sup>	
Diffuse large B-cell lymphoma / high-grade B-cell lymphoma with <i>MYC</i> and <i>BCL2</i> rearrangements (DLBCL/HGBL- <i>MYC</i> / <i>BCL2</i> )	9680/3
DLBCL/HGBL- <i>MYC</i> / <i>BCL2</i> without <i>BCL6</i> rearrangement	
DLBCL/HGBL- <i>MYC</i> / <i>BCL2</i> with <i>BCL6</i> rearrangement	
DLBCL/HGBL- <i>MYC</i> / <i>BCL2</i> (with or without <i>BCL6</i> rearrangement) with TdT expression	
ALK-positive large B-cell lymphoma	9737/3
Large B-cell lymphoma with <i>IRF4</i> rearrangement	9698/3
High-grade B-cell lymphoma with 11q aberration	9687/3
Lymphomatoid granulomatosis, NOS	9766/1
Lymphomatoid granulomatosis, grade 1	9766/1
Lymphomatoid granulomatosis, grade 2	9766/1
Lymphomatoid granulomatosis, grade 3	9766/3
EBV-positive diffuse large B-cell lymphoma	9680/3
Diffuse large B-cell lymphoma associated with chronic inflammation	9680/3
Fibrin-associated large B-cell lymphoma <sup>†</sup>	9678/3
Fluid overload-associated large B-cell lymphoma <sup>†</sup>	9678/3
Plasmablastic lymphoma	9735/3
Primary large B-cell lymphoma of immune-privileged sites <sup>†</sup>	9680/3
Primary large B-cell lymphoma of the CNS	9680/3
Primary large B-cell lymphoma of the vitreoretina	9680/3
Primary large B-cell lymphoma of the testis	9680/3
Primary cutaneous diffuse large B-cell lymphoma, leg type	9680/3
Intravascular large B-cell lymphoma	9712/3
Mediastinal large B-cell lymphoma	9679/3
Mediastinal grey zone lymphoma	9596/3

Descriptor	ICD-O codes <sup>a</sup>
High-grade B-cell lymphoma, NOS	9680/3
High-grade B-cell lymphoma, NOS, with <i>MYC</i> and <i>BCL6</i> rearrangements	9680/3
<b>Burkitt lymphoma</b>	
Burkitt lymphoma	9687/3
<i>Traditional subtypes:</i>	
Endemic Burkitt lymphoma	9687/3
Sporadic Burkitt lymphoma	9687/3
Immunodeficiency-associated Burkitt lymphoma	9687/3
<i>Recommended subtypes:</i>	
EBV-associated Burkitt lymphoma <sup>†</sup>	9687/3
EBV-negative Burkitt lymphoma <sup>†</sup>	9687/3
<b>KSHV/HHV8-associated B-cell lymphoid proliferations and lymphomas</b>	
Primary effusion lymphoma	9678/3
Extracavitary primary effusion lymphoma <sup>†</sup>	9678/3
KSHV/HHV8-positive diffuse large B-cell lymphoma <sup>†</sup>	9738/3
KSHV/HHV8-positive germinotropic lymphoproliferative disorder	
<b>Lymphoid proliferations and lymphomas associated with immune deficiency and dysregulation</b>	
Hyperplasias arising in immune deficiency/dysregulation	
Polymorphic lymphoproliferative disorders arising in immune deficiency/dysregulation	9971/1
EBV-positive mucocutaneous ulcer	9680/1
Lymphomas arising in immune deficiency/dysregulation (code as type of lymphoma)	
Inborn error of immunity-associated lymphoid proliferations and lymphomas (code as type of lymphoma)	
<b>Hodgkin lymphoma</b>	
Classic Hodgkin lymphoma	9650/3
Classic Hodgkin lymphoma, nodular sclerosis	9663/3
Classic Hodgkin lymphoma, mixed cellularity	9652/3
Classic Hodgkin lymphoma, lymphocyte-rich	9651/3
Classic Hodgkin lymphoma, lymphocyte-depleted	9653/3
Nodular lymphocyte-predominant Hodgkin lymphoma	9659/3
<b>Precursor T-cell neoplasms</b>	
<b>T-lymphoblastic leukaemia/lymphoma</b>	
T-lymphoblastic leukaemia/lymphoma, NOS	9837/3
Early T-precursor lymphoblastic leukaemia/lymphoma	9837/3

Descriptor	ICD-O codes <sup>a</sup>
<b>Mature T-cell and NK-cell neoplasms</b>	
<b><i>Mature T-cell and NK-cell leukaemias</i></b>	
T-prolymphocytic leukaemia	9834/3
T-large granular lymphocytic leukaemia	9831/3
NK-large granular lymphocytic leukaemia	9831/3
Adult T-cell leukaemia/lymphoma	9827/3
Smouldering adult T-cell leukaemia/lymphoma†	9827/3
Chronic adult T-cell leukaemia/lymphoma†	9827/3
Lymphoma adult T-cell leukaemia/lymphoma	9827/3
Acute adult T-cell leukaemia/lymphoma†	9827/3
Sézary syndrome	9701/3
Aggressive NK-cell leukaemia	9948/3
<b><i>Primary cutaneous T-cell lymphoid proliferations and lymphomas</i></b>	
Primary cutaneous CD4-positive small or medium T-cell lymphoproliferative disorder	9709/1
Primary cutaneous acral CD8-positive T-cell lymphoproliferative disorder†	9709/3
Mycosis fungoides	9700/3
Folliculotropic mycosis fungoides	9700/3
Pagetoid reticulosis	9700/3
Granulomatous slack skin disease	9700/3
Primary cutaneous CD30-positive T-cell lymphoproliferative disorder, lymphomatoid papulosis	9718/1
Primary mucosal CD30-positive T-cell lymphoproliferative disorder	9718/1
Lymphomatoid papulosis subtypes A, B, C, D, E	9718/1
Lymphomatoid papulosis with <i>DUSP22</i> locus rearrangement	9718/1
Primary cutaneous CD30-positive T-cell lymphoproliferative disorder, primary cutaneous anaplastic large cell lymphoma	9718/3
Subcutaneous panniculitis-like T-cell lymphoma	9708/3
Primary cutaneous gamma-delta T-cell lymphoma	9726/3
Primary cutaneous CD8-positive aggressive epidermotropic cytotoxic T-cell lymphoma	9709/3
Primary cutaneous peripheral T-cell lymphoma, NOS	9709/3
<b><i>Intestinal T-cell and NK-cell lymphoid proliferations and lymphomas</i></b>	
Indolent T-cell lymphoma of the gastrointestinal tract	9702/1
Indolent NK-cell lymphoproliferative disorder of the gastrointestinal tract†	9702/1
Enteropathy-associated T-cell lymphoma	9717/3
Monomorphic epitheliotropic intestinal T-cell lymphoma	9717/3

Descriptor	ICD-O codes <sup>a</sup>
Intestinal T-cell lymphoma, NOS	9717/3
<b>Hepatosplenic T-cell lymphoma</b>	
Hepatosplenic T-cell lymphoma	9716/3
<b>Anaplastic large cell lymphoma</b>	
ALK-positive anaplastic large cell lymphoma	9714/3
ALK-negative anaplastic large cell lymphoma	9715/3
Breast implant-associated anaplastic large cell lymphoma	9715/3
<b>Nodal T follicular helper cell lymphoma</b>	
Nodal T follicular helper cell lymphoma, angioimmunoblastic type <sup>†</sup>	9705/3
Nodal T follicular helper cell lymphoma, follicular type	9702/3
Nodal T follicular helper cell lymphoma, NOS	9702/3
<b>Other peripheral T-cell lymphomas</b>	
Peripheral T-cell lymphoma, NOS	9702/3
<b>EBV-positive T-cell and NK-cell lymphomas</b>	
EBV-positive nodal T- and NK-cell lymphoma <sup>†</sup>	9702/3
Extranodal NK/T-cell lymphoma <sup>†</sup>	9719/3
<b>EBV-positive T-cell and NK-cell lymphoid proliferations and lymphomas of childhood</b>	
Severe mosquito bite allergy	
Hydroa vacciniforme lymphoproliferative disorder	9725/1
Systemic chronic active EBV-positive disease <sup>†</sup>	9725/1
Systemic EBV-positive T-cell lymphoma of childhood	9724/3

<sup>a</sup> These morphology codes are from the International Classification of Diseases for Oncology, third edition, second revision (ICD-O-3.2). 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.

<sup>†</sup> Labels marked with a dagger have undergone a change in terminology of a previous code.

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## Note 7 – Disease status (after treatment) (Core)

The histological findings in lymphomas often do not allow a distinction between new (second) primary disease and relapsed/refractory disease. Since the latter situation in general heralds an inferior prognosis especially in aggressive lymphomas, and directs clinical decisions, this information is considered core and may prompt additional investigations, e.g., clonal identity of the relapsed tumour with the preceding tumour.<sup>9</sup>

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## Note 8 – Indications for transformed disease (Non-core)

High grade transformation in indolent lymphomas, e.g., Richter transformation in chronic lymphocytic leukaemia (CLL) or a diagnosis of DLBCL or high grade B-cell lymphoma (HGBCL) in the background of FL usually heralds a change in the disease course and more aggressive disease. However, transformed DLBCL or HGBCL cannot be distinguished by morphology from their *de novo* counterparts. If an aggressive lymphoma type is diagnosed in the setting of known indolent lymphoma, information on the clonal relationship with the preceding low grade lymphoma should be sought. Where necessary, investigation concerning the clonal evolution pattern - linear versus divergent - should be considered. Clonally unrelated secondary neoplasms in patients with indolent lymphomas may have different biological features and a different - usually better - prognosis than clonally related transformations.<sup>9-11</sup>

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## Note 9 – Immunoprofiling/phenotyping studies (Core and Non-core)

All immunostaining tests that contributed to the diagnosis should be documented. To this end, the committee discussed that immunohistochemical studies may be performed in several tiers, first using general/standard markers for cell lineage/category determination (B-cell, T-cell, myeloid, histiocytic/dendritic) then proceeding to more family/class- or entity-specific markers depending on local established procedures. The marker panels listed in Table 2 follow the criteria of essential and/or desirable diagnostic criteria as listed in WHO-HAEM5.<sup>8</sup> Staining for Ki-67 is a helpful adjunct in the assessment of indolent or aggressive disease, and the level of Ki-67 expression is listed as a prognostic and/or predictive marker in many entities as are various other immunohistochemical markers (mutant p53 over-expression or null-phenotype in many entities, or MYC/BCL2 double expression in DLBCL).

**Table 2: Immunohistochemistry markers**

<b>Suspect disease/disease category</b> (to which all pre-test information is in favour of)	<b>Recommended supporting immunohistochemical markers (non-core)</b>
Chronic lymphocytic leukaemia (CLL)	CD5, CD23
Splenic B-cell lymphoma/leukaemia	ANXA1, CD103, CyclinD1, CD25. CD200/CD80 (flow cytometry)
Lymphoplasmacytic lymphoma (LPL)	MUM1, kappa, lambda, IgM
Marginal zone lymphoma (MZL)	CD5, CD10, CD23, Cyclin D1, SOX11 (mainly to exclude other entities)
Follicular lymphoma (FL)	CD10, BCL6, BCL2
Mantle cell lymphoma (MCL)	CyclinD1, SOX11
Diffuse large B-cell lymphoma (DLBCL)	CD10, BCL6, MUM1 (Hans classifier) BCL2, MYC (double expresser status)
Specific entities of large B-cell lymphoma (LBCL)	CD10, BCL6, MUM1, TdT (HGBCL/DLBCL-MYC/BCL2) CD138, MUM1, ALK (ALK-positive LBCL) CD10, BCL6, IRF4/MUM1 (LBCL with <i>IRF4</i> rearrangement) CD10, BCL6, BCL2, MYC (HGBCL-11q) CD30, EBV-LMP1 (LYG) CD138, MUM1, EBV-LMP1, EBNA2 (Various LBCL entities associated with Epstein-Barr virus (EBV)) CD10, BCL6, MUM1 (IP-DLBCL) BCL2, MUM1, IgM (PCLBCL-LT) CD30, CD23, MAL, PDL1/2 (PMBCL)
Burkitt lymphoma	CD10, BCL6, BCL2, MYC, LMO2

High grade B-cell lymphoma (HGBCL), not otherwise specified (NOS)	CD10, BCL6, MUM1 (Hans classifier), TdT, CD34, CyclinD1
KSHV/HHV8-associated B-cell LPD/lymphomas	HHV8, CD30, CD138, MUM1, IgM (lambda)
Lymphoproliferative disorders (LPD)/lymphomas associated with immune deficiency/ dysregulation (IDD)	EBV-LMP1, EBNA2, Others according to subtype
Classic Hodgkin lymphoma	CD30, CD15, PAX5, CD20, EBV-LMP1, CD3, MUM1
Nodular lymphocyte predominant Hodgkin lymphoma	CD20, CD30, CD3, BCL6, OCT2, PD1, CD21
Plasma cell neoplasms	CD38, CD138, MUM1, kappa, lambda
T-cell and NK-cell LPDs and Lymphomas	Variable (as recommended by WHO-HAEM5 <sup>8</sup> ): TdT (T-LBL/ALL) TCL1 (T-PLL) CD4, CD5, CD7, CD8, TCR $\alpha\beta$ , TCR $\gamma\delta$ PD1, ICOS1, CXCL13, CD10, BCL6 (nTFHL) CD30, Perforin, TIA1, GranzymeB, ALK (ALCL) CD2, CD5, CD56, Perforin, Granzyme B, TIA1 (NK/T and NK LPDs/lymphomas)

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## Note 10 – Molecular genetic studies (Core and Non-core)

According to the essential diagnostic criteria listed in WHO-HAEM5, molecular genetic studies are mandatory for the diagnosis of certain entities defined by the presence of a molecular aberration (as examples *BCR::ABL1* fusion or ploidy assessment in precursor B-cell neoplasms, *IRF4* status in *IRF4*-rearranged large B-cell lymphoma (*IRF4r* LBCL), *MYC* and *BCL2* rearrangements in DLBCL/HGBCL-*MYC/BCL2*, or EBER assessment in EBV-positive DLBCL).<sup>8</sup> In some genetically defined entities, well-established surrogate immunohistochemical markers are available, such as ALK staining in ALK-positive anaplastic large cell lymphoma or ALK-positive large B-cell lymphoma; while in others, immunohistochemistry may be suggestive of the diagnosis if molecular testing is not

available, such as IRF4/MUM1 staining in *IRF4r* LBCL or MYC immunohistochemistry in Burkitt lymphoma. It should be noted that in case of absence of a molecular assay or a validated surrogate marker, a definite diagnosis at the entity level is not accepted. Table 3 lists molecular markers that either define the entity or that are helpful in characterising (molecular) subtypes. While the field of molecular markers in lymphoid disease is increasingly expanding,<sup>12</sup> the use of more sophisticated marker constellations to add more granularity to for example, the molecular classification of DLBCL<sup>13-15</sup> is currently not advised due to a lack of consensus regarding different algorithms and/or platforms.

**Table 3: Molecular analyses**

<b>Suspect disease/disease category</b> (to which all pre-test information is in favour of)	<b>Recommended supportive molecular investigations (non-core)</b>
Chronic lymphocytic leukaemia (CLL)	FISH 11q, 17p, <i>TP53</i> mutation
Splenic B-cell lymphoma/leukaemia	<i>BRAF</i> , <i>MAP2K1</i> , <i>KLF2</i> , <i>NOTCH2</i> mutations
Lymphoplasmacytic lymphoma (LPL)	<i>MYD88 L265P</i> , <i>CXCR4</i> mutations
Marginal zone lymphoma (MZL)	t(11;18)(q21;q21)/ <i>BIRC3::MALT1</i> fusion (in gastric MALT lymphoma)
Follicular lymphoma (FL)	<i>BCL2</i> rearrangement
Mantle cell lymphoma (MCL)	<i>CCND1</i> rearrangement
Diffuse large B-cell lymphoma (DLBCL)	Cell-of origin (COO) classification <i>MYC</i> , <i>BCL2</i> , <i>BCL6</i> rearrangement
DLBCL/high grade B-cell lymphoma (HGBCL), not otherwise specified (NOS)	<i>MYC</i> and <i>BCL2</i> rearrangement and 11q aberration negative
Primary mediastinal large B-cell lymphoma (PMBCL)	<i>CIITA</i> and <i>PDL1/2 (9p24.1)</i> <i>SOCS1</i> <i>JAK/STAT6</i> <i>CIITA</i> , <i>B2M</i> , <i>TNFAIP3</i>

Specific entities of large B-cell lymphoma (LBCL)	<i>MYC, IG::MYC, BCL2, BCL6</i> rearrangements (HGBCL/DLBCL- <i>MYC/BCL2</i> ) <i>IGH::IRF4</i> (LBCL with <i>IRF4</i> rearrangement) 11q FISH (HGBCL-11q) EBER (various EBV-associated LBCLs) <i>MYC</i> rearrangement, EBER (plasmablastic lymphoma (PBL))
Burkitt lymphoma	<i>IG::MYC fusion, BCL2, BCL6</i> rearrangements, EBER
KSHV/HHV8-associated B-cell lymphoproliferative disorders (LPD)/lymphomas	EBER
LPD/lymphomas associated with immune deficiency/dysregulation (IDD)	EBER
Hodgkin lymphoma	EBER
T-cell and NK-cell LPDs and lymphomas	Variable (as recommended by WHO-HAEM5 <sup>8</sup> ): t(14;14); inv14 (T-PLL) <i>DNMT3A, TET2, RHOA, IDH2</i> mutations (nTFHL) EBER (ENKTL, EBV-positive nodal T- and NK lymphoma) <i>SETD2; JAK/STAT (STAT5B, JAK3)</i> (MEITL) <i>JAK/STAT (JAK1, STAT3)</i> (EATL)

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