Data quality checks for validation of the ECIS database

ECIS Technical report

April 2026, Version 1.1

Working document updating the publication Martos, C., Giusti, F., Van Eycken, E., Visser, O., *A common data quality check procedure for European cancer registries*, European Commission, Ispra, Italy, 2023, JRC132486.

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Abstract

The aims of population-based cancer registries (CRs) are: a) to collect information from all new cases in a well-defined geographic area in order to assess the magnitude of the cancer burden and its evolution, and b) to provide a basis for research on cancer causes and outcome (incidence, prevalence and survival).

The reliability and utility of the information provided by CRs depends on the quality of the data collected. The JRC Technical report "A common data quality check procedure for European cancer registries" is the reference document reporting rules to harmonize cancer registry data, including recommendations for checking its internal consistency. It describes checks for validating internal consistency within and between cancer registry variables; allowed values for each variable are based on the ECIS data protocol.

To ensure consistency across variables, several checks are proposed: 1) verification of date coherence; 2) assessment of consistency between tumour data and demographic information; 3) evaluation of consistency among tumour variables; 4) validation of consistency between follow-up variables, basis of diagnosis and stage; and 5) consistency checks between stage, treatment variables and other tumour characteristics. In addition to intra-record checks, inter-record checks are proposed for validating multiple primary tumours.

The report is the reference document that guided development of the JRC-ENCR Quality Check Software, and as such, it is continually revised and updated.

Contributors

Changes introduced in the current document

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Acknowledgement

This report was prepared with the support and input of several collaborators. The authors gratefully acknowledge the contributions of Steering Committee members of the European Network of Cancer Registries (ENCR).

1. Introduction

The aims of population-based cancer registries (CRs) are: a) to collect information from all new cases in a well-defined geographic area in order to assess the magnitude of the cancer burden and its evolution, and b) to provide a basis for research on cancer causes and outcome (incidence, prevalence and survival). Registries are a key actors in providing information for planning and evaluation of cancer control activities (1-3).

The reliability and utility of the information provided by CRs depends on the quality of the data collected. Dimensions considered when evaluating CRs data quality are comparability, completeness and validity. An additional quality indicator - timeliness - is also very relevant (4, 5).

Historically, a variety of methods and tools were used to check CRs data (6-9). To address this diversity, the European Network of Cancer Registries (ENCR) in collaboration with the European Commission's Joint Research Centre (JRC) undertook the development of a comprehensive and standardised framework of data quality checks. This framework was intended for adoption by European CRs and projects, thereby harmonising data validation practices that had previously been fragmented.

The adoption of a common list of variables, formats and standard data quality checks is essential to enhance the harmonisation of European cancer data and to enable CRs to more easily participate easily in international projects.

In 2014 the JRC Technical report "A proposal on cancer data quality checks: one common procedure for European cancer registries" was published as the outcome of the Working Group on Cancer Data Quality Check (10). The document was the result of a collaborative project between the JRC, the ENCR and the European Experts. Since then, updated versions of the report were published in 2018 (11) and 2023 (31). This current version is aligned with the latest version of the ECIS data protocol.

2. Case definition and variables included in the quality checklist

2.1. Case definition

- All primary malignant tumours (behaviour=3), including all malignant skin tumours (e.g. basal cell carcinoma, squamous cell carcinoma, Merkel cell carcinoma).
- In situ tumours (behaviour=2): breast (ICD-O C50), urothelial tumours (C65-C68), ovary (C56) and skin melanoma.
- Uncertain behaviour tumours (behaviour=1): thymoma (8580/1-8585/1), urothelial tumours (C65-C68), ovary (C56) and central nervous system (CNS) (C70-C72, C75.1-C75.3), gastrointestinal stromal tumours (GIST) (8936/1) and gastro-entero-pancreatic neuroendocrine tumours (GEP-NET)(C15-C26, C48, C76.2, C80 and morphology codes 8150/1, 8152/1, 8153/1, 8155/1, 8156/1, 8158/1, 8240/1, 8242/1, 8248/1).
- Benign tumours (behaviour=0) of the CNS (C70-C72 and C75.1-C75.3) and gastrointestinal stromal tumours (GIST) (8936/0).

2.2. Variables and valid values

Table *1* shows the list of the variables considered: description, missing/ unknown values and the allowed values on which quality checks are based.

Some variables included in this report are not listed in the current Call for Data Protocol. Nevertheless, they are considered in the report to provide a standard coding and checking system to improve the data harmonisation in the European cancer registries. For example, laterality is not included in the protocol, but it is important for recording multiple primary tumours according to the current international rules for multiple primary cancers (16).

Table 1. Variable description, missing/unknown and allowed values.

Variable description	Missing/unknown values	Coding and allowed values
Patient variables		
Patient identification number	Not allowed	According to registry coding system[1]
Month of birth	99	Range of allowed values: from 1 to 12 **Warning for value = 99**
Year of birth	9999	Range of allowed values: >1842 and ≤the current year **Warning for value = 9999**
Sex	9	Allowed values: 1, 2, 3 1→Male 2→Female 3→Other **Warning for value=9**
Tumour variables		
Tumour identification code	Not allowed	According to registry coding system[1] **Not allowed** to have **duplicate** combination of the two variables: **Patient identification code + tumour identification code** in the same dataset
Geographical area of residence at diagnosis code	XX99	NUTS2 when available or the highest level of administrative sub-division that can be provided [1] Blank→ not applicable
Geographical area of residence at diagnosis name	9	Blank→ not applicable
Age at diagnosis in years	999	Range of allowed values: ≥ 0 and < 121 **Warning for value=999** if complete date of birth and/or date of incidence are missing or unknown
Month: date of incidence[2]	99	Range of allowed values: from 1 to 12 **Warning for value=99**

Table 1. *Continued*

Variable description	Missing/unknown values	Coding and allowed values
Year: date of incidence[2]	Not allowed	Range of allowed values: > 1941 and ≤ the current year
Basis of diagnosis[3]	9	Allowed values: 0, 1, 2, 4, 5, 7, 8 0 → Death certificate only (DCO) 1 → Clinical 2 → Clinical investigation 4 → Specific tumour markers 5 → Cytology 7 → Histology 8 → Cytogenetic and/or molecular testing **Warning for value=9**
ICD-O-3 topography (topography of the metastasis is not admitted)	Not allowed	Valid code in ICD-O-3 The code for unknown primary site is C809
ICD-O-3 morphology	Not allowed	Valid code in any ICD-O-3 version The code for unknown morphology is 8000 for solid tumours, 9590 for lymphoma NOS and 9800 for Leukaemia NOS
ICD-O-3 behaviour	Not allowed	Allowed values: from 0 to 3 Behaviour 6 (malignant, metastatic) and behavior 9 (Malignant, uncertain whether primary or metastatic) should be coded in the cancer registry as behaviour 3
ICD-O-3 grade[4]	9	Allowed values: 0-8 1 → Well differentiated 2 → Moderately differentiated 3 → Poorly differentiated 4 → Undifferentiated, anaplastic 5 → T-cell; T-precursor 6 → B-Cell; Pre-B; B-precursor 7 → Null cell; Non T-non B 8 → NK cell (natural killer cell) Non-applicable = 0
Variables related to the follow-up		
Incidental finding of cancer at autopsy	9	Allowed values: 0, 1 0→No 1→Yes
Last known vital status	9	Allowed values: 1, 2 1 → Alive 2 → Dead **Warning for value=9**
Month of the last known vital status	99	Range of allowed values: from 1 to 12 **Warning for value=99**

Table 1. *Continued*

Variable description	Missing/unknown values	Coding and allowed values
Year of the last known vital status	9999	Range of allowed values: >1941 and ≤ the current year **Warning for value=9999**
Duration of survival in days	99999	≥0 **Warning for value=99999** if complete date of incidence and/or date of last known vital status are missing or unknown
International Classification of Diseases (ICD) edition used for coding cause of death	99	Range of allowed values: > 0 and < 12 Blank → not applicable
Official underlying cause of death	R99 (ICD-10), 7999 (ICD-9)	Valid code in ICD according to ICD edition Blank → not applicable
Stage variables		
TNM edition	99	Allowed values: > 0 and ≤ 8 It has to be periodically updated
TNM: clinical T-category (cT)	9	Valid values according to TNM Classification and edition (references 13, 22-25) Blank → not applicable
TNM: clinical N-category (cN)	9	Valid values according to TNM Classification and edition (references 13, 22-25) Blank → not applicable
TNM: clinical M-category (cM)	9	Valid values according to TNM Classification and edition (references 13, 22-25) Blank → not applicable
TNM: pathological T-category (pT)	9	Valid values according to TNM Classification and edition (references 13, 22-25) Blank → not applicable
TNM, pathological N-category (pN)	9	Valid values according to TNM Classification and edition (references 13, 22-25) Blank → not applicable
TNM, pathological M-category (pM)	9	Valid values according to TNM Classification and edition (references 13, 22-25) Blank → not applicable
ToS	9	A → Ann Arbor/ Lugano stage D → Dukes' stage E → Extent of disease F → FIGO stage S → TNM stage, unknown whether clinical or pathological clS → clinical TNM stage paS → pathological TNM stage ypS -> pathological TNM stage after neoadjuvant therapy cpS → combination of clinical & pathological TNM stage coS → condensed TNM stage

		esS → essential TNM stage Ti1 → Tier 1 stage for paediatric tumours Ti2 → Tier 2 stage for paediatric tumours COG → COG Tier 2 stage for Wilms tumours, findings at surgery when NO chemotherapy prior to surgery SIO → SIOP Tier 2 stage for Wilms tumours: findings at surgery when chemotherapy prior to surgery 8 → Other staging system
Stage	9	0 →Stage 0, stage 0a, stage 0is, carcinoma in situ, non-invasive 1 →Stage I, FIGO I, localized, localized limited (L), limited, Dukes A 1A -> Stage IA, FIGO IA, Ann Arbor 1B -> Stage IB, FIGO IB 1B1 -> FIGO IB1 ... 2 →Stage II, FIGO II, localized advanced (A), locally advanced, advanced, direct extension, Dukes B 2A -> Sage IIA, FIGO IIA 2B -> Stage IIB, FIGO IIB ... 3 →Stage III, FIGO III, regional (with or without direct extension), R+, N+, Dukes C ... 4 →Stage IV, FIGO IV, metastatic, distant, M+, Dukes D ... See also Annex 4 for Toronto childhood cancer stage in the ECIS data call protocol
First course of Treatment variables (coding and allowed values are based on the current Call for Data Protocol (reference 15). These checks will be updated according to the ENCR recommendations on treatment data harmonisation when they are published)		
Surgery[6, 7] (Resection of the primary tumour)	9	Allowed values: 0, 1, 2, 3 0 -> No 1 -> Yes, without specification 2 -> Yes, local surgery only[8] 3 -> Yes, 'operative' surgery[9]
Radiotherapy	9	Allowed values: 0, 1, 2, 3 0 -> No 1 ->Yes, without specification 2 ->Yes, neoadjuvant (pre-operative) radiotherapy 3->Yes, adjuvant (post-operative) radiotherapy
Chemotherapy	9	Allowed values: 0, 1, 2, 3, 4 0 -> No 1 -> Yes, without other specification 2 -> Yes, neoadjuvant (pre-operative) 3 -> Yes, adjuvant (post-operative) 4 -> Yes, both neoadjuvant and adjuvant
Targeted therapy[10] (including monoclonal antibodies)	9	Allowed values: 0, 1 0 -> No 1 -> Yes
Immunotherapy (excl. monoclonal antibodies)	9	Allowed values: 0, 1 0 -> No 1 -> Yes

Hormone therapy	9	Allowed values: 0, 1 0 -> No 1 -> Yes
Other or unspecified systemic therapy	9	Allowed values: 0, 1, 2, 3 0 -> No 1 -> Yes, without other specification 2 -> Yes, neoadjuvant (pre-operative) 3 -> Yes, adjuvant (post-operative)
Stem cell transplantation	9	Allowed values: 0, 1 0 -> No 1 ->Yes

([1]) Depending on the registry coding

([2]) According to ENCR recommendation for incidence date (18)

([3]) According to ENCR recommendation for basis of diagnosis (19)

([4]) Except for central nervous system tumours (these tumours should be coded according to the ENCR Recommendation for Central Nervous System Tumours (2024) (20) and urothelial tumours (these tumours should be coded according to the "ENCR Recommendations for Recording and Reporting of Urothelial Tumours of the Urinary Tract (22))

([5]) Obsolete classification, mentioned because of historical series

([6]) If available, type of surgery (local surgery [2] versus operative surgery [3]) should be coded for solid cancers of the following cancer sites: C01-C06, C16-C20, C30-C34, C53-C55, C61 and C65-C68. For other cancers, code 1 (surgery without specification) suffices.

([7]) If both local surgery and operative surgery were performed for the same tumour, operative surgery should be coded.

([8]) The following procedures should be coded as local surgery: polypectomy (mainly gastro-intestinal tract), transurethral resection (TUR; bladder & other urinary tract), cone biopsy/loop excision (cervix), as well as all other procedures which leave the organ in situ, such as cryosurgery, laser coagulation, thermos ablation, radiofrequency ablation (RFA), etc.

([9]) This includes all resections of the tumour which require the removal of an organ or a major part of that organ, such as a lobectomy, hemicolectomy, hysterectomy, cystectomy, prostatectomy, etc.

([10]) Targeted therapy comprises all drugs that block the growth of cancer cells by inhibition of certain pathways in the cancer cell.
Traditional chemotherapy also affects other cells in the body that divide quickly. The main categories of targeted therapy are small molecules (mostly tyrosine kinase inhibitors such as imatinib and many other -nibs) and monoclonal antibodies (such as rituximab and many other -mabs). Monoclonal antibodies are considered a form of immunotherapy but should be coded as targeted therapy.

([a]) A: asymptomatic;
B: presence of B symptoms (including fever, night sweats and weight loss of ≥10% of body weight over 6 months);
E: involvement of a single, extranodal site, contiguous or proximal to a known nodal site (stages I to III only; additional extranodal involvement is stage IV);
S: splenic involvement;
X: bulky nodal disease: nodal mass >1/3 of intrathoracic diameter or 10 cm in dimension.

([b]) A: asymptomatic;
B: presence of systemic symptoms (fever/night sweats/unexplained weight loss);
E: refers to extranodal contiguous extension that can still be encompassed within a irradiation field appropriate for nodal disease of the same anatomic extent;
Bulky: if a single nodal mass >10 cm or >1/3 of transthoracic diameter.

3. List of quality checks: internal consistency

3.1 Consistency within variables

Most of the quality checks for single variables concern allowed values are detailed in **Table *1***. Nevertheless, other specific quality checks detailed below are required for dates.

Age at diagnosis: measured as the age in years at the patient's last birthday. Age could be calculated if both incidence and birth dates are registered (or at least the incidence year and birth year). It is recommended using algorithms to impute the dates before calculating the age, when possible. The range of values must be between 0 and 120.

This variable could be computed if at least both incidence and birth years are available:

- If only year of diagnosis and birth are available, then age at diagnosis is computed as a difference:

Age at diagnosis = year of incidence – year o birth

- If the month and year of both dates are known, then age at diagnosis is computed as:

Age at diagnosis (integer) = [(year of incidence*12 + month of incidence) - (year of birth*12 + month of birth)]/12

- If the month of diagnosis and birth are known and equal, and the day of diagnosis is earlier than the day of birth, then 1 is subtracted from the calculated age.

Once computed, the age at diagnosis should be compared with what was provided by the CRs, and be consistent according to the following rule:

Age at diagnosis computed = registered age at diagnosis ± 1

TNM and stage grouping values depend on the cancer topography, morphology and edition of the TNM classification. The clinical (cT, cN, cM) and pathological (pT, pN, pM) categories and stage should be coded according to the corresponding version of the TNM classification (13, 22-25).

3.1 Consistency between variables

3.1.1 Coherence between dates

The proposed rules below check for coherence between variables: *date of birth*, *date of incidence* and *date of the last known vital status*:

- Date of birth ≤ Date of incidence.
- This rule is valid unless the case was diagnosed in utero. If the diagnosis is in utero, the difference in months between dates should be no more than nine.
- Date of birth ≤ Date of the last known vital status.
- Date of incidence ≤ Date of the last known vital status.

For each comparison between dates, if years are known but at least one of the months is unknown/missing, then the years are only compared.

3.1.2 Consistency between tumour data and demographic information

- Consistency between age/ topography / morphology

Some cancers occur almost exclusively in certain age groups such as retinoblastoma (tumour of young children) or prostate cancer in older men; therefore, some combinations age/topography/morphology are unlikely and should result in a warning.

Nevertheless, there are other age and tumour type combinations that are not unlikely *but* rare. A warning for these combinations improves the precision of these rare tumours.

***Table* 2** shows unlikely and rare combinations by age group and tumour type. The updated morphologies included in the ICD-O-3.2 (12) and frequencies of warnings found in the data submitted through the 2015 ENCR-JRC data call by the European CRs have been taken into account for updating this table.

Table 2. Unlikely and rare combinations of age and tumour type.

Age group [years]	Morphology	Topography
0-2	Hodgkin lymphoma: 9650-9667	–
> 9	Retinoblastoma: 9510-9514	–
> 8	rhabdoid tumour: 8963	C64.9
0-8	Renal carcinoma: 8010-8041, 8050-8075, 8082, 8120-8122, 8130-8141, 8143, 8155, 8190-8201, 8210, 8211, 8221-8231, 8240, 8241, 8244-8246, 8260-8263, 8290, 8310, 8320, 8323, 8401, 8430, 8440, 8480-8490, 8504, 8510, 8550, 8560-8573	C64.9
	8312	–
> 19	Hepatoblastoma: 8970	–

Table 2. *Continued*

Age group [years]	Morphology	Topography
0-8	Hepatic carcinoma: 8010-8041, 8050-8075, 8082, 8120-8122, 8140, 8141, 8143, 8155, 8190-8201, 8210, 8211, 8230, 8231, 8240, 8241, 8244-8246, 8260-8263, 8310, 8320, 8323, 8401, 8430, 8440, 8480-8490, 8504, 8510, 8550, 8560-8573	C22.0, C22.1
< 20	Cholangiocarcinoma: 8160/3 Combined hepatocellular carcinoma and cholangiocarcinoma: 8180/3	
0-5	Osteosarcomas: 9192-9195	–
0-5	Chondrosarcoma: 9220-9230	
> 7	Malignant extra-cranial and extra-gonadal germ cell: 9060-9065, 9070-9072, 9080-9085, 9100-9105	C00-C37, C40-C47, C50, C60-C61, C63-C69, C73-C75.0, C75.4-C76.8, C80
0-14	Gonadal carcinoma: 8010-8041, 8050-8075, 8082, 8120-8122, 8130-8141, 8143, 8190-8201, 8210, 8211, 8221-8241, 8244-8246, 8260-8263, 8290, 8310, 8320, 8323, 8380-8384, 8430, 8440, 8480-8490, 8504, 8510, 8550, 8560-8573, 9014, 9015	C56,C62
	Gonadal carcinoma: 8313, 8441, 8450, 8460-8471, 9000	–
0-5	Thyroid carcinoma: 8010-8041, 8050-8075, 8082, 8120-8122, 8130-8141, 8155, 8190, 8200, 8201, 8211, 8230, 8231, 8244-8246, 8260-8263, 8290, 8310, 8320, 8323, 8430, 8440, 8480, 8481, 8510, 8560-8573	C73
	Thyroid carcinoma: 8330-8347, 8350	-
0-5	Nasopharyngeal carcinoma: 8010-8041, 8050-8075, 8082, 8083, 8120-8122, 8130-8141, 8190, 8200, 8201, 8211, 8230, 8231, 8244-8246, 8260-8263, 8290, 8310, 8320, 8323, 8430, 8440, 8480, 8481, 8500-8576	C11
0-4	Skin carcinoma: 8010-8041, 8050-8075, 8078, 8082, 8090-8110, 8140, 8143, 8147, 8190, 8200, 8240, 8246, 8247, 8260, 8310, 8320, 8323, 8390-8420, 8430, 8480, 8542, 8560, 8570-8573, 8940, 8941	C44

Table 2. *Continued*

Age group [years]	Morphology	Topography
0-4	8010-8084, 8120-8158, 8190-8264, 8290, 8310, 8314-8315, 8320-8325, 8380-8384, 8430-8440, 8452-8454, 8480-8586, 8588-8589, 8940-8941, 9010-9016, 9020, 9030	C00-C10, C12-C21, C23-C39, C48, C50-C55, C57-C61, C63, C65-C72, C75-C76, C80
0-14	Mesothelial neoplasms: 9050-9053	Any
0-14	8085-8110, 8161-8175, 8265-8281, 8300, 8311, 8316-8319, 8348-8349, 8360-8375, 8390-8420, 8442-8443, 8451, 8472-8474, 8587	C15, C19, C20, 21, C23, C24, C38.4, C50-C55
5-14	8010-8084, 8120-8158, 8190-8264, 8290, 8310, 8314-8315, 8320-8325, 8330-8347, 8350, 8380-8384, 8430-8440, 8452-8454, 8480-8586, 8588	
< 25	Multiple myeloma: 9732 Chronic lymphocytic leukaemia: 9823 Chronic myeloid leukaemia: 9876, 9945	Any
0-19	8085-8110, 8161-8175, 8265-8281, 8300, 8311, 8316-8319, 8348-8349, 8360 -8375, 8390-8420, 8442-8443, 8451, 8472-8474, 8587	C60
5-19	8010-8084, 8120-8158, 8190-8264, 8290, 8310, 8314-8315, 8320-8325, 8330-8347, 8350, 8380-8384, 8430-8440, 8452-8454, 8480-8486, 8588	
15-19	8313, 8441, 8450, 8460-8471, 9000	
< 35	Adenocarcinoma: 8140	C61
> 55	Choriocarcinoma: 9100	C58
>14	8910, 8960, 8981, 8991, 9470, 9687/9826	Any
>14	Juvenile myelomonocytic leukaemia: 9946	Any

Consistency between sex/ topography

Some sex/topography combinations are impossible. Invalid combinations are presented in ***Table 3***.

Table 3. Invalid sex and topography combinations.

Sex=1 (male)	Sex=2 (female)
C51 Vulva	C60 Penis
C52 Vagina	C61 Prostate gland
C53 Cervix uteri	C62 Testis
C54 Corpus uteri	C63 Other and unspecified male genital organs
C55 Uterus, NOS	
C56 Ovary	
C57 Other and unspecified female genital organs	
C58 Placenta	

3.1.3 Consistency between tumour variables

- Consistency between basis of diagnosis/ morphology/ behaviour

It is unlikely for specific morphologies not to have undergone a histological/ cytological examination. Nevertheless, some combinations are considered as exceptions. ENCR recommendations have been followed for 'specific' morphology codes in absence of microscopic verification (19).

Morphology codes for cases with 'death certificate only' (DCO) are allowed when they can be identified from the underlying cause of death code (International Classification of Diseases10th Revision). ***Table 4*** shows the accepted combinations between basis of diagnosis (BoD) and morphology. Combinations not included in ***Table 4*** need to be verified.

Table 4. Valid combinations for basis of diagnosis, morphology and behaviour by topography.

Basis of diagnosis	Morphology and behaviour code allowed	Comments
0 (Death Certificate Only)	8000/3 8170/3 (C22.0 ICD-10) 81603 (C22.1 ICD-10) 8970/3 (C22.2 ICD-10) 9120/3 (C22.3 ICD-10) 8800/3 (C22.4 ICD-10) 8010/3 (C22.7 ICD-10) 8720/3 (C43 ICD-10) 9050/3 (C45 ICD-10) 9140/3 (C46 ICD-10) 9590/3-9993/3 (C81-C96/D45-D47 ICD-10)	Any morphology code could be included in cases with DCO if the morphology text is included in the death certificate. Nevertheless, for checking purposes only morphology codes included in the ICD-O-10 codes are accepted.
1 (Clinical)	8000/3 (*), 8720/3 (C44, C69.0, C69.3, C69.4), 9120/3 (C44.5[a]), 9140/3 (C44), 9510/3 (C69.2)	(*) Any topography [a]Angiosarcoma of the skin of the breast following radiotherapy of the breast
2 (Clinical investigation)	8000/3 (*), 8000/0 (C70-C72, C75.1-C75.3), 8000/1 (C70-C72, C75.1-C75.3), 8720/3 (C69.0, C69.3, C69.4), 8960/3 (C64), 8970/3 (C22), 9510/3 (C69.2), 8170/3 (C22.0), 8150/3 (C25.4), 8160/3 (C22.1, C24.0, C24.9), 8240/3 (C17), 8453/2 (C25), 8453/3 (C25), 8800/3 (*), 8850/3(*), 8890/3(*), 9120/3 (*), 9180/3 (C40, C41), 9220/3 (C40, C41), 9370/3 (C41.0), 8272/0 (C75.1), 9080/0 (C71, C75.1, C75.3), 9080/1 (C71, C75.1, C75.3), 9080/3 (C71, C75.1, C75.3), 9161/1 (C71, C72.0), 9350/1 (C75.2), 9360/1 (C75.3), 9361/1 (C75.3), 9362/3 (C75.3), 9380/3 (C71, C72.0), 9380/3 (C71, C72.0), 9380/3 (C71, C72.0), 9380/3 (C71, C72.0), 9383/1 (C71.5, C71.7), 9384/1 (C71.5, C71.7), 9390/0 (C71.5, C71.7), 9390/1 (C71.5, C71.7), 9390/3 (C71.5, C71.7), 9391/3 (C71.5, C71.7, C72.0), 9392/3 (C71.5, C71.7, C72.0), 9394/1 (C72.0, C72.1), 9395/3 (C75.3), 9400/3 (C71, C72.0), 9400/3 (C71, C72.0), 9401/3 (C71, C72.0), 9412/1 (C71), 9413/0 (C71), 9421/1 (C71, C72.0, C72.3), 9440/3 (C71, C72.0), 9450/3 (C71), 9450/3 (C71), 9451/3 (C71), 9470/3 (C71.6), 9473/3 (C71, C72.0), 9492/0 (C71, C72.0, C75.1), 9493/0 (C71.6), 9505/1 (C71, C72.0), 9506/1 (C71), 9509/0 (C71), 9509/1 (C71, C72.0), 9530/0 (C70), 9539/1 (C70), 9530/3 (C70), 9560/0 (C72.4, C72.5), 9590/3 (C71), 9751/3 (C34, C41, C71**)	(*) Any topography (**) Other topographies are possible

Table 4. *Continued*

Basis of diagnosis	Morphology and behaviour code allowed	Comments
4 (Specific tumour markers)	8000/3 (C18-C20)	Carcinoembryonic antigen (CEA)
	8170/3 (C22.0)	Alfa-fetoprotein (AFP)
	8000/3 (C23- C25)	Cancer antigen 19-9 (CA 19-9)
	8000/3 (C56)	Cancer antigen 125 (CA-125)
	8000/3 (C61)	Prostate-specific antigen (PSA)
	9100/3 (C58)	Human chorionic gonadotropin (HCG)
	9064/3 (C56, C62)	HCG
	9065/3 (C62)	AFP (+/- HCG)
	8240/3	Chromogranin A
	8151/3 (C25)	Insulin
	8152/3 (C25)	Glucagon
	8153/3 (C16, C17.0, C25)	Gastrin
	8155/3 (C25)	Vasoactive intestinal peptide (VIP)
	8156/3 (C17.0, C25)	Somatostatin
	8241/3	Serotonin
	8158/3	Adrenocorticotropic hormone (ACTH) and other hormones
	8345/3 (C73)	Calcitonin
	9500/3	Catecholamine degradation products (homovanilic acid [HVA], vanillylmandelic acid [VMA])
	8271/0 (C75.1)	Prolactin
	8272/0 (C75.1)	Growth hormone, follicle-stimulating hormone (FSH), luteinizing hormone (LH), ACTH, thyroid stimulating hormone (TSH)
	8700/3 (C74.1)	Catecholamines, chromogranin A
	9732/3 (C42.1)	M-protein (IgG, IgM, IgA) >30g/L
	9761/3 (C42.0)	IgM

Table 4. *Continued*

Basis of diagnosis	Morphology and behaviour code allowed	Comments
5 (Cytology)	All morphologies **except** any in situ carcinoma and 8023/3, 9385/3, 9396/3, 9445/3, 9475/3-9478/3, 9806/3, 9807/3, 9812/3-9819/3, 9865/3, 9866/3, 9869/3, 9875/3-9879/3, 9896/3, 9897/3, 9911/3, 9912/3, 9965/3-9968/3, 9986/3	
7 (Histology)	All morphologies **except** 8001/3, 8023/3, 9385/3, 9396/3, 9445/3, 9475/3-9478/3, 9806/3, 9807/3, 9812/3-9819/3, 9865/3, 9869/3, 9876/3-9879/3, 9896/3, 9897/3, 9911/3, 9912/3, 9965/3- 9968/3, 9986/3	
8 (Cytogenetic and/or molecular testing)	8023, 9385, 9396, 9400, 9401, 9440, 9445, 9450, 9451, 9475-9478, 9806, 9807, 9812-9819, 9865, 9866, 9869, 9875-9879, 9896, 9897, 9911, 9912, 9965-9968, 9986	
9 (Unknown)	All morphologies	

- Consistency between morphology/grade

Only malignant tumours (behaviour=3) should be graded, except CNS, urothelial tumours and ductal carcinoma in situ of breast.

CNS tumour grade should be coded according to the ENCR Recommendations for coding tumours of the CNS (21).

Urothelial tumour grade should be coded according to the ENCR Recommendations for Recording and Reporting of Urothelial Tumours of the Urinary Tract (22).

The combination between a 'behaviour' code less than 3 and a 'grade' code less than 9 and different from 0 or blank will be considered as an error, except for CNS, urothelial tumours and ductal carcinoma in situ of breast.

Grade and morphology values for urothelial tumours and ductal carcinoma in situ of breast with behaviour less than 3 are included in ***Table 5***.

Table 5. Valid morphology and grade combinations for urothelial tumours and ductal carcinoma in situ of breast with behaviour less than 3.

Morphology/behaviour	Grade values
Urothelial tumours: 8120/2 8130/2	 1, 3 1, 3
Ductal carcinoma in situ of breast : 8500/2 Low grade or grade I Moderate grade or grade II High grade or grade III	 1 2 3

Grade values and the allowed corresponding morphology codes for haematological malignancies are shown in ***Table 6***.

Table 6. Valid morphology and grade combinations for haematological malignancies.

Grade→	5	6	8
Morphology	9700-9702, 9705, 9708, 9709, 9714-9719, 9724-9726, 9729, 9805-9807, 9809, 9820, 9827, 9831, 9834, 9837	9591, 9596, 9597, 9650-9667, 9670, 9671, 9673, 9678-9680,9684, 9687-9691, 9695, 9698, 9699, 9712, 9728, 9731-9735, 9737, 9738, 9761, 9762, 9805-9808, 9811, 9812-9818, 9820, 9823, 9826, 9833, 9836, 9940	9719, 9727, 9831, 9948

The combination between **grades 5-8** and **morphology out of the range 9590-9993** is **impossible**.

Grade values from 1 to 4 are not allowed for morphology range 9590-9993 **except for** 9801/34.

Some terms in ICD-O-3 carry an implied statement of grade; therefore, an appropriate grade code could be associated. These combinations are specified in the following ***Table 7***.

Table 7. Morphology code and description, and correct associated grade for ICD-O-3 terms with implied statement of grade.

Morphology code	Morphology description	Grade
8020/3	Carcinoma, undifferentiated, NOS	3, 4
8021/3	Carcinoma, anaplastic, NOS	4
8240/3	Neuroendocrine carcinoma, well-differentiated Neuroendocrine tumour, grade 1 Neuroendocrine carcinoma, low grade	1
8246/3	Poorly differentiated neuroendocrine neoplasm	3
8249/3	Neuroendocrine carcinoma, moderately differentiated Neuroendocrine tumour, grade 2 Neuroendocrine tumour, grade 3	2, 3
8331/3	Follicular adenocarcinoma, well-differentiated	1
8332/3	Follicular adenocarcinoma, moderately differentiated Follicular carcinoma, moderately differentiated	2
8337/3	Poorly differentiated thyroid carcinoma	3
8585/3	Well-differentiated thymic carcinoma	1
8631/3	Sertoli-Leydig cell tumour, poorly differentiated	3
8634/3	Sertoli-Leydig cell tumour, poorly differentiated, with heterologous elements	3
8830/3	Undifferentiated high grade pleomorphic sarcoma of bone	4
8851/3	Liposarcoma, well-differentiated, NOS	1
9062/3	Seminoma, anaplastic	4
9082/3	Malignant teratoma, undifferentiated Malignant teratoma, anaplastic	4
9187/3	Low grade central osteosarcoma	1
9511/3	Retinoblastoma, differentiated	1
9512/3	Retinoblastoma, undifferentiated	4

- Consistency between topography/ morphology

The topography / morphology combinations include those morphologies **commonly** identified in specific primary topography (**allowed topography** codes) as well as the ones occurring only rarely or never in some specific primary topographies (**not allowed topography** codes).

Table 8 reports allowed/ not allowed combinations.

Table 8. Morphology codes and allowed/refused topography codes.

Morphology code	Allowed topography codes	Not allowed topography codes
8000-8005		C42.0, C42.1, C77 The combinations of these topographies with morphologies 8000-8005 should be reviewed and changed. If the primary site cannot be identified, topography should be C809.
8010-8589		C38, C40-C42, C47, C48.0, C49, C70-C72, C77 These combinations should be reviewed and changed. If the primary site cannot be identified, topography should be C809.
8015	C53 Any other topographies should be reviewed and changed.	
8077	C00-C15, C21, C30-C32, C44, C51-C53, C60	
8080	C60	
8081	C00, C30.0, C44, C51, C60, C63.2, C69.0, C69.1	
8082	C00-C14, C16, C30-C34, C44, C53, C65-C68, C80	
8085, 8086	C01, C05.1, C05.2, C09, C10, C21, C51, C52, C53, C60, C80	
8090-8095, 8097, 8100-8103, 8110	C30.0, C44, C51, C60, C63.2 These morphology codes in lip (skin) the topography should be coded as C44.0, in breast (skin) or anus (skin) the topography should be coded as C44.5. Topographies C80 and C76 with these topographies should be reviewed and consider to code them as C44.9	
8098	C53 The combination of the morphology 8098 with another topography such as C44 should be reviewed and changed.	
8120, 8122, 8130, 8131	C56, C65-C68, C80 The combination of these morphologies with other topographies such as C64 or C61 should be reviewed and changed topography or morphology codes.	
8121	C30.0, C31, C65-C68	
8124	C212	
8142	C16	

Table 8. *Continued*

Morphology code	Allowed topography codes	Not allowed topography codes
8144	C15-C26, C30, C31, C52, C53, C56, C67, C80	
8145	C15-C20, C25, C34, C61, C80	
8147	C00-C14, C30-C32, C50, C61 If the topography is C44 morphology should be reviewed and a possible code could be 8090.	
8148	C15-C25, C61 If the topography is C53 morphology should be reviewed, and a possible code could be 8077.	
8150-8152, 8154, 8155	C25	
8153	C16, C17.0, C25, C80	
8156	C17.0, C25, C80	
8160, 8161	C22.1, C23.9, C24.0 Other topographies such as C25 should be reviewed and changed.	
8162	C240	
8163	C22-C25	
8170-8175	C22.0	
8180	C22.1, C22.0	
8201	C15-C26, C34, C50, C54, C61, C80	
8210	C15-C26, C54	
8211	C15-C26, C34, C50, C53, C54, C56, C61, C64, C80	
8213	C18	
8214	C16	
8215	C21.1	
8220, 8221	C18-C20, C26	
8243	C18, C56, C80	
8247	C30.0, C44, C51, C60, C63.2, C80	
8250-8254	C34, C50, C61	
8256, 8257	C34, C80	

Table 8. *Continued*

Morphology code	Allowed topography codes	Not allowed topography codes
8261, 8262	C15-C26, C52-C57	
8263	C15-C26, C34, C52-C57, C64	
8265	C18-C20, C26, C34	
8270-8273, 8280, 8281, 8300	C64, C751	
8290	C07, C08, C64, C73, C74.0, C75.1, C80	
8311, 8312, 8316-8320	C56, C64	
8313, 8444	C56	
8314, 8315	C50	
8322	C75.0	
8330-8332, 8335-8337, 8339-8350	C73	
8370	C74.0	
8380-8383	C48.1, C48.2, C52-C57, C80	
8384	C53	
8390, 8400, 8402-8410, 8413	C30.0, C44, C51, C60, C63.2	
8401	C30.0, C44, C50, C51, C60, C63.2	
8420	C44.2	
8440	C07, C08, C18, C25, C48.1, C48.2, C50, C54, C56, C57, C80	
8441, 8460	C48.1, C48.2, C53, C54, C56, C57, C80	
8442, 8450, 8451, 8461-8463, 8471-8474	C48.1, C48.2, C54, C56, C57	
8452, 8453	C24, C25, C56	
8470	C18.1, C25, C56, C57, C80	
8500	C07, C08, C23 -C25, C50, C61, C80	

Table 8. *Continued*

Morphology code	Allowed topography codes	Not allowed topography codes
8501-8509, 8512-8514, 8519-8524, 8530, 8540, 8541, 8543	C50	
8510	C16, C18, C50, C80 The combination topography C73 and morphology 8510 should be reviewed and changed (morphology 8345)	
8525	C00.3-C00.5, C01-C08, C30.0, C31	
8542	C30.0, C44, C51, C60, C63.2	
8550, 8551	C00.3-C00.5, C01-C08, C16, C18-C20, C25, C30-C34, C50, C61, C80	
8580-8586	C37	
8588, 8589	C73	
8590-8650	C56, C62	
8670	C56	
8690, 8691	C755	
8692	C75.4	
8700	C74.1	
8710, 8711, 8714		C42.0, C42.1, C77 If the primary site cannot be identified, topography should be C809.
8720		C38, C40-C42, C47-C49, C77 If the primary site cannot be identified, topography should be C809.
8721-8723, 8730	C21, C30.0, C44, C51, C60, C63.2, C69, C80	
8728	C70	
8740, 8761	C44	
8741, 8743, 8745	C30.0, C44, C51, C60, C63.2, C69.0	
8742	C44, C51, C60, C63.2	
8744	C44.6, C44.7, C44.9	

Table 8. *Continued*

Morphology code	Allowed topography codes	Not allowed topography codes
8746	C00-C06, C09-C11, C15, C20, C21, C30, C31, C68.0 The combination topography C44 and morphology 8746 should be reviewed and changed.	
8770-8772	C30.0, C44, C51, C60, C63.2, C69, C80	
8773, 8774	C69	
8780	C44	
8800-8811, 8814-8831, 8840-8921, 8963, 8990, 8991, 9040-9043, 9120-9150, 9170, 9540, 9550, 9561, 9580, 9581		C42.0, C42.1, C77 If the primary site cannot be identified, topography should be C809.
8812	C40, C41	
8832, 8833	C44, C51, C60, C63.2	
8930, 8931	C48.1, C48.2, C52-C57	
8933, 8934	C52-C57	
8936	C15-C20, C25, C26, C48.1, C48.2, C80	
8940	C00.3-C00.5, C04-C08, C30.0, C44 If the topography is C62 morphology should be reviewed and a possible code could be 9085.	
8941	C00.3-C00.5, C04-C08, C30.0	
8950, 8951	C48.1, C48.2, C52-C57, C80	
8959, 8960, 8964	C64	
8970	C22.0	
8971	C25	
8972, 8973	C34	
8983	C50	
8744	C44.6, C44.7, C44.9	

Table 8. *Continued*

Morphology code	Allowed topography codes	Not allowed topography codes
8746	C00-C06, C09-C11, C15, C20, C21, C30, C31, C68.0 The combination topography C44 and morphology 8746 should be reviewed and changed.	
8770-8772	C30.0, C44, C51, C60, C63.2, C69, C80	
8773, 8774	C69	
8780	C44	
8800-8811, 8814-8831, 8840-8921, 8963, 8990, 8991, 9040-9043, 9120-9150, 9170, 9540, 9550, 9561, 9580, 9581		C42.0, C42.1, C77 If the primary site cannot be identified, topography should be C809.
8812	C40, C41	
8832, 8833	C44, C51, C60, C63.2	
8930, 8931	C48.1, C48.2, C52-C57	
8933, 8934	C52-C57	
8936	C15-C20, C25, C26, C48.1, C48.2, C80	
8940	C00.3-C00.5, C04-C08, C30.0, C44 If the topography is C62 morphology should be reviewed and a possible code could be 9085.	
8941	C00.3-C00.5, C04-C08, C30.0	
8950, 8951	C48.1, C48.2, C52-C57, C80	
8959, 8960, 8964	C64	
8970	C22.0	
8971	C25	
8972, 8973	C34	
8983	C50	

Table 8. *Continued*

Morphology code	Allowed topography codes	Not allowed topography codes
9000	C56	
9013-9015	C48.1, C48.2, C56-C57, C80	
9020	C50	
9044	C49, C80	
9045	C30.0, C31, C80	
9050-9053	C38.0, C38.4, C48.1, C48.2, C63.7, C80	
9060	C38.1-C38.3, C48.0, C56, C71, C751, C75.3 If the topography is C62 morphology should be reviewed and a possible code could be 9064.	
9061-9063	C38.1-C38.3, C48.0, C62	
9064, 9065	C38.1-C38.3, C48.0, C49.5, C56, C62, C71, C75.1, C75.3, C80	
9070-9073, 9080-9086, 9101, 9102	C38.1-C38.3, C48.0, C49.5, C52-C57, C62, C71, C72, C75.1, C75.3, C80	
9090,9091	C56	
9100	C38.1-C38.3, C48.0, C56-C58, C62, C80	
9104, 9105	C58	
9124	C22.0	
9161	C71-C72	
9180	C40, C41, C48.0, C49, C50, C80	
9181-9187, 9250	C40, C41	
9192-9195, 9221	C40, C41	
9220, 9230, 9231, 9240-9243	C30.0, C31, C32.3, C33, C40, C41, C48.0, C49, C80	
9251, 9252	C49	
9260, 9364		C70-C72, C42, C77
9261	C40.0, C40.2, C41.9	
9270-9342	C03, C31.0, C41.0, C41.1, C41.9	
9350	C75.1, C75.2	

Table 8. *Continued*

Morphology code	Allowed topography codes	Not allowed topography codes
9351, 9352	C75.2	
9360-9362	C75.3	
9370-9372	C11, C41, C49	
9380-9385, 9391-9393, 9396, 9400-9431, 9440-9460, 9478	C71, C72, C75.1, C75.3	
9390	C71.5, C71.9	
9394	C72	
9395	C75.3	
9432	C75.1	
9470-9472, 9474-9477, 9480, 9493	C71.6, C71.9	
9490, 9500, 9503	C38.1-C38.3, C47, C48.0, C71-C72, C74.1, C75.5, C80	
9492, 9505-9509	C71, C72, C75.3	
9501, 9502	C69.4, C71	
9510-9513	C69.2	
9521-9523	C30.0, C31, C72.2	
9530-9539	C70	
9560	C38, C47, C48.0, C71-C72, C80	
9582	C75.1	
9590-9596, 9670-9675, 9680-9688, 9690-9699, 9702, 9705, 9714, 9715, 9724,9728, 9729, 9735, 9737, 9738, 9750-9760, 9762		C42.0, C80
9597, 9700, 9709, 9718, 9725, 9726	C30.0, C44, C51, C60, C63.2 If the primary topography is not available, it should be coded as C44.9.	
9650-9667	C02.4, C09-C11, C14, C22.0, C42.1, C42.2, C77	
9678	C38.0, C38.4, C48.1, C48.2	
9679	C37.9, C38.1, C38.3, C77.1	

Table 8. *Continued*

Morphology code	Allowed topography codes	Not allowed topography codes
9689	C42.2	
9701	C42.1, C44, C77	
9708	C44, C49	
9712	C49	
9716	C22.0, C42	
9717	C16-C20, C26.0	
9719	C01-C06, C09-C14, C30-C32, C44, C69.6, C77	
9727 (BPDCN)[1]	C42.1, C44	
9731	C40, C41	
9734		C40, C41, C42.0, C42.1, C80
9732, 9733, 9742, 9800-9810, 9820-9822, 9831-9836, 9838-9920, 9931-9968, 9975-9989, 9991-9993	C42.1	
9741	C22.0, C42, C44, C77	
9761	C42.0	
9764	C17	
9827	C42.1, C77	
9930		C42.0, C42.1, C80

(1) In ICD-O-3, 9727 was used for precursor cell lymphoblastic lymphoma, NOS; in the 2011 updates to ICD-O-3, 9727 is used for blastic plasmacytoid dendritic cell neoplasm (BPDCN). The topography codes allowed refer to BPDCN only.

- Consistency between morphology/ behaviour

Although according to the Rule F of the ICD-O-3 it is exceptionally possible to have morphology and behaviour combination not listed in the ICD-O-3, it is recommended to review all records with morphology and behaviour combination not included in any version of the ICD-O-3. Nevertheless, some of these combinations are not rare among the European CRs.

Therefore, **Table *9*** reports the accepted morphology and behaviour codes that are not included in the ICD-O-3.

Table 9. Accepted morphology and behaviour codes that are not included in the ICD-O-3.

8000/2	8011/2	8051/2	8053/2	8053/3	8071/2	8072/2	8075/2
8078/2	8083/2	8084/2	8100/3	8103/3	8121/2	8123/2	8124/2
8131/2	8143/2	8144/2	8160/2	8211/2	8213/2	8220/2	8221/2
8248/3	8250/2	8251/2	8252/2	8253/2	8255/2	8260/2	8262/2
8271/3	8310/2	8380/2	8382/2	8384/2	8400/2	8401/2	8402/2
8403/2	8409/2	8410/2	8440/1	8441/2	8443/3	8444/3	8480/2
8481/2	8482/2	8490/2	8502/2	8507/3	8508/2	8510/2	8540/2
8542/2	8543/2	8550/2	8560/2	8570/2	8573/2	8590/3	8721/2
8722/2	8723/2	8740/2	8743/2	8744/2	8745/2	8746/2	8770/2
8771/2	8772/2	8825/3	8832/1	8940/2	8941/2	8983/3	9013/3
9061/2	9084/2						

3.1.4 Consistency between follow-up variables and basis of diagnosis

- Consistency between vital status, incidental finding of cancer at autopsy (autopsy), basis of diagnosis and duration of survival (survival)

In addition to the checks between date of the last known vital status and date of incidence/date of birth described in section 3.1, **Table 10, Table 11, Table 12, Table 13, Table 14, Table 15** include several edits related to the combination of the following variables: vital status, autopsy, basis of diagnosis and survival.

Table 10. Consistency between vital status, autopsy and basis of diagnosis.

Vital status = 1 (alive)	Autopsy (incidental finding of cancer at autopsy) should be ≠ 1
	Basis of diagnosis ≠ 0 (DCO-Death Certificate Only)

Table 11. Consistency between basis of diagnosis, vital status, survival, dates of incidence/last known vital status.

Basis of diagnosis = 0 (DCO)		Vital status = 2 (dead)
		Survival (in days) = 0
		Date of incidence = Date of the last known vital status

Table 12. Consistency between autopsy, vital status, survival and dates of incidence/last known vital status.

Autopsy = 1 (yes)	Vital status = 2 (dead)
	Survival (in days) = 0
	Date of incidence = Date of the last known vital status

Table 13. Combinations of dates allowing computation of missing/unknown survival time.

Survival (in days) = missing/unknown	Date of the last known vital status (MoF, YoF) should be ≠ missing/unknown
	Month of Incidence should be ≠ missing/unknown

Table 14. Consistency between survival and dates of incidence/last known vital status.

Survival (in days) ≠ missing/unknown	Survival (days) should be inside the interval: [(DoF-DoI)max_days, (DoF-DoI)min_days], where: DoI (MoI,YoI) = Date of incidence DoF(MoF,YoF) = Date of the last known vital status (DoF-DoI)max_days = exact number of days calculated from 1st day of DoI (MoI,YoI) to the last day of DoF (MoF,YoF) (DoF-DoI)min_days = exact number of days calculated from last day of DoI (MoI,YoI) and 1st day of DoF (MoF,YoF)]

Table 15. Consistency between survival time, autopsy and basis of diagnosis for cases that could have been potentially detected by autopsy or by death certificate only.

Survival (in days) = 0	Basis of diagnosis could be 0 (DCO-Death Certificate Only) OR Autopsy (incidental finding of cancer at autopsy) could be 1

3.1.5 Consistency between stage/ treatment variables and other tumour variables

The stage at diagnosis is particularly useful information for the interpretation of international survival comparisons, for the evaluation of screening programs, patient care and clinical and epidemiological research purposes.

CRs have been using TNM system for staging solid tumours and lymphomas (13, 23-26). In addition, some CRs are collecting and coding childhood cancer stage according to the Toronto guidelines (27, 28).

Table 16 contains the cancer entities and staging systems other than TNM classification used by the European CRs for coding the extent of disease for specific cancer entities.

Table 16. Staging systems other than TNM classification by cancer entities.

Staging System	Cancer entities
Ann Arbor	Lymphomas (Hodgkin Lymphoma and Non-Hodgkin lymphoma)
Lugano	Lymphomas (Hodgkin Lymphoma and Non-Hodgkin lymphoma)
Dukes'(*)	Colorectal tumours
FIGO	vulva, vagina, cervix uteri, corpus uteri, ovary and primary peritoneal carcinoma, fallopian tube, and gestational trophoblastic tumours

(*) Obsolete classification, mentioned because of historical series

- Other additional checks related to stage and treatment variables

Behaviour and TNM/stage at diagnosis

- If behaviour >2 then pT≠pTis.

  If behaviour is higher than 2 then pT category should not be coded as in situ tumour (pTis)

- If behaviour=2 then pT = is and Stage = 0.

  If behaviour is 2 (in situ tumour), stage should be coded as 0.

TNM/stage at diagnosis and BoD

- If pT ≠ TX and pT ≠ 9 and pT ≠ blank then BoD = 7 or 6 or 5.

  If pT category has a value different than missing and unknown, the base of diagnosis should be coded as 5, 6 or 7 (histology) .

- If pN ≠ NX and pN ≠ 9 and pN ≠ blank then BoD = 7 or 6 or 5.

  If pN category has a value different from missing and unknown, the base of diagnosis should be coded as 5, 6 or 7 (histology).

- If pM = 1 then BoD = 7 or 6 or 5.

  cT ≠Tis and pT ≠Tis.

  If pM category has the value 1 (tumour with metastasis at diagnosis) the base of diagnosis should be coded as 5, 6 or 7 (histology). In addition, the cT and pT categories cannot be coded as Tis (in situ tumour)

TNM/stage at diagnosis

- If Stage = 9 or blank, or Stage is not valid (out of range, invalid format), then (cT or pT) ≠ (TX or 9 or blank) and (cN or pN) ≠ (NX or 9 or blank) or (cM or pM) = 1.

If Stage is unknown/missing/invalid, it can be computed only if T,N values are available (M is considered 0 if missing/unknown), or if cM or pM is 1 (Stage 4).

Stage at diagnosis/staging system (ToS)

- If Stage is valid (in range, valid format), and Stage ≠ 9 and Stage ≠ blank, then ToS should be valid and ToS ≠ 9 and ToS ≠ blank.

If Stage is valid and not unknown or missing, then ToS should bevalid and not unknown or missing

Treatment variables, BoD and TNM stage

- If surgery ≠ 0 or surgery ≠ 9 or surgery ≠ blank, then BoD = 7.

  If surgery variable has a value different from zero, unknown or missing, the base of diagnosis should be coded as 7 (histology).

- If surgery = 0 and the BoD ≠ 7 and Autopsy ≠ 1 , then pT = 9 or pT = blank.

  If surgery variable was coded as 0 (no surgery) and the autopsy variable was coded as 1 (no autopsy), and the BoD is not coded as 7, the pT category should be coded as unknown/missing value. The pT category can be coded only when using the piece of the surgery or autopsy.

4. Quality checklist for Multiple Primary Malignant Tumours

The Multiple Primary Malignant Tumours (MPMTs) quality checklist for **computing incidence** was developed by the JRC according to the current International Rules for Multiple Primary Cancers published in 2004(16).

The steps for checking solid MPMTs are the following:
Step 1. The two topographies are compared according to the current International Rules for Multiple Primary Cancers published in 2004.
In addition to the groups of topography codes considered as a single site in table 1 of the 2004 international rules, **for checking** other groups are considered as a single topography (see ***16***).
C80 (unknown primary site) and C768 (overlapping lesion of ill-defined sites) are considered as a single site with any topography.

Table 17. Groups of topography codes considered as a single site for solid tumours.

Topography code	Definition
C00	Lip
C03	Gum
C04	Floor of mouth
C05	Palate
C06	Other and unspecified parts of mouth
C76.0	Head, face or neck, NOS
C01	Base of tongue
C02	Other and unspecified parts of tongue
C76.0	Head, face or neck, NOS
C07	Parotid gland
C76.0	Head, face or neck, NOS
C08	Other and unspecified major salivary glands
C76.0	Head, face or neck, NOS
C09	Tonsil
C10	Oropharynx
C12	Pyriform sinus
C13	Hypopharynx
C14	Other and ill-defined sites in lip, oral cavity and pharynx
C76.0	Head, face or neck, NOS
C11	Nasopharynx
C76.0	Head, face or neck, NOS
C15	Oesophagus
C26.8	Overlapping lesion of digestive system
C26.9	Gastrointestinal tract, NOS
C76.1	Thorax, NOS
C16	Stomach
C26.8	Overlapping lesion of digestive system
C26.9	Gastrointestinal tract, NOS
C76.2	Abdomen, NOS
C17	Small intestine
C26	Other and ill-defined digestive organs
C76.2	Abdomen, NOS

Table 17. *Continued*

Topography code	Definition
C18	Colon
C26	Other and ill-defined digestive organs
C76.2	Abdomen, NOS
C19	Rectosigmoid junction
C20	Rectum
C26	Other and ill-defined digestive organs
C76.2	Abdomen, NOS
C21	Anus and anal canal
C26	Other and ill-defined digestive organs
C76	Other and ill-defined sites
C22	Liver and intrahepatic bile ducts
C26.8	Overlapping lesion of digestive system
C76.2	Abdomen, NOS
C23	Gallbladder
C24	Other and unspecified parts of biliary tract
C268	Overlapping lesion of digestive system
C26.9	Gastrointestinal tract, NOS
C76.2	Abdomen, NOS
C25	Pancreas
C26.8	Overlapping lesion of digestive system
C76.2	Abdomen, NOS
C30	Nasal cavity and middle ear
C39	Other and ill-defined sites within respiratory system and intrathoracic organs
C76.0	Head, face or neck, NOS
C31	Accessory sinuses
C39	Other and ill-defined sites within respiratory system and intrathoracic organs
C76.0	Head, face or neck, NOS
C32	Larynx
C39	Other and ill-defined sites within respiratory system and intrathoracic organs
C76.0	Head, face or neck, NOS
C33	Trachea
C34	Bronchus and lung
C39	Other and ill-defined sites within respiratory system and intrathoracic organs
C76.0	Head, face or neck, NOS
C76.1	Thorax, NOS
C37	Thymus
C76.1	Thorax, NOS
C38	Heart, mediastinum, and pleura
C39.8	Overlapping lesion of respiratory system and intrathoracic organs
C76.1	Thorax, NOS
C39	Other and ill-defined sites within respiratory system and intrathoracic organs
C76.0	Head, face or neck, NOS
C76.1	Thorax, NOS
C40	Bones, joints and articular cartilage of limbs
C41	Bones, joints and articular cartilage of other and unspecified sites
C76	Other and ill-defined sites

Table 17. *Continued*

Topography code	Definition
C44 C76	Skin Other and ill-defined sites
C47 C76	Peripheral nerves and autonomic nervous system Other and ill-defined sites
C48 C76	Retroperitoneum and peritoneum Other and ill-defined sites
C49 C76	Connective, subcutaneous and other soft tissues Other and ill-defined sites
C50 C76.1	Breast Thorax, NOS
C51 C57.8 C57.9 C76.3	Vulva Overlapping lesion of female genital organs Female genital tract, NOS Pelvis, NOS
C52 C57.8 C57.9 C76.3	Vagina Overlapping lesion of female genital organs Female genital tract, NOS Pelvis, NOS
C53 C55 C57.8 C57.9 C76.3	Cervix uteri Uterus, NOS Overlapping lesion of female genital organs Female genital tract, NOS Pelvis, NOS
C54 C55 C57.8 C57.9 C76.3	Corpus uteri Uterus, NOS Overlapping lesion of female genital organs Female genital tract, NOS Pelvis, NOS
C56 C57.8 C57.9 C76.3	Ovary Overlapping lesion of female genital organs Female genital tract, NOS Pelvis, NOS
C57 C76.3	Other and unspecified female genital organs Pelvis, NOS
C58 C76.3	Placenta Pelvis, NOS
C60 C63.8 C63.9 C76.3	Penis Overlapping lesion of male genital organs Male genital organs, NOS Pelvis, NOS
C61 C63.8 C63.9 C76.3	Prostate gland Overlapping lesion of male genital organs Male genital organs, NOS Pelvis, NOS

Table 17. *Continued*

Topography code	Definition
C62	Testis
C63.8	Overlapping lesion of male genital organs
C63.9	Male genital organs, NOS
C76.3	Pelvis, NOS
C63	Other and unspecified male genital organs
C76.3	Pelvis, NOS
C64	Kidney
C68.8	Overlapping lesion of urinary organs
C68.9	Urinary system, NOS
C76	Other and ill-defined sites
C65	Renal pelvis
C66	Ureter
C67	Bladder
C68	Other and unspecified urinary organs
C76	Other and ill-defined sites
C69	Eye and adnexa
C76.0	Head, face or neck, NOS
C70	Meninges
C76.0	Head, face or neck, NOS
C71	Brain
C76.0	Head, face or neck, NOS
C72	Spinal cord, cranial nerves, and other parts of central nervous system
C76.0	Head, face or neck, NOS
C73	Thyroid
C76.0	Head, face or neck, NOS
C74	Adrenal gland
C76	Other and ill-defined sites
C75	Other endocrine glands and related structures
C76	Other and ill-defined sites

Note: topography codes C80 and C768 are considered as a single site in combination with any other topography.

a) If the two topographies are in the same group, the two morphologies should be compared (**step 2**).

b) If the two topographies are in different groups, each tumour should be considered as primary tumour.

Step 2. The two morphologies should be compared according to the "*groups of malignant neoplasms considered to be histologically 'different' for the purpose of defining multiple tumours, ICD-O-3.2*" prepared by the International Agency for Research on Cancer (IARC) and the International Association of Cancer Registries (IACR) (14).

Some unspecified morphologies were included **for checking** in the groups defined by the IACR/IACR (**Table**). Morphology codes 8000-8005 (Unspecified types of cancer) are considered as a single group in combination with any other morphology.

***Note*: For haematological malignancies, Kaposi sarcoma and mesothelioma only morphologies are compared**

Table 18. Groups of morphology codes considered as a single entity.

Morphology code	Definition
8051-8086, 8120-8131 8010-8015, 8020-8022, 8050 8000-8005	**Squamous and transitional cell carcinoma** Unspecified carcinomas (NOS) Unspecified types of cancer
8090-8110 8010-8015, 8020-8022, 8050 8000-8005	**Basal cell carcinomas** Unspecified carcinomas (NOS) Unspecified types of cancer
8140-8149, 8160-8163, 8190-8221, 8250-8552, 8570-8576, 8940-8941, 9110 8010-8015, 8020-8022, 8050 8000-8005	**Adenocarcinomas** Unspecified carcinomas (NOS) Unspecified types of cancer
8023, 8030-8046, 8150-8158, 8170-8180, 8230-8249, 8560-8562, 8580-8589 8010-8015, 8020-8022, 8050 8000-8005	**Other specific carcinomas** Unspecified carcinomas (NOS) Unspecified types of cancer
8680-8714, 8800-8921, 8930-8936, 8990-8992, 9040-9045, 9120-9125, 9130-9138, 9141-9252, 9370-9373, 9540-9582 8000-8005	**Sarcomas and soft tissue tumours** Unspecified types of cancer
9050-9055 8000-8005	**Mesothelioma** Unspecified types of cancer
9840, 9860-9931, 9945-9946, 9950, 9960-9964, 9966, 9975, 9980-9989, 9991-9993 9590-9591, 9596, 9727, 9760, 9800-9801, 9805-9809, 9820, 9832, 9835, 9965, 9967-9968, 9970- 9971 8000-8005	**Myeloid** Unspecified types of haematopoietic and lymphoid tissues Unspecified types of cancer
9597, 9670-9699, 9712, 9728, 9731-9738, 9761-9767, 9769, 9811-9819, 9823, 9826, 9833, 9836, 9940 9590-9591, 9596, 9727, 9760, 9800-9801, 9805-9809, 9820, 9832, 9835, 9965, 9967-9968, 9970-9971 8000-8005	**B–cell neoplasms** Unspecified types of haematopoietic and lymphoid tissues Unspecified types of cancer
9700-9709, 9714-9719, 9724-9726, 9729, 9768, 9827, 9831, 9834, 9837, 9948 9590-9591, 9596, 9727, 9760, 9800-9801, 9805-9809, 9820, 9832, 9835, 9965, 9967-9968, 9970- 9971 8000-8005	**T–cell and NK–cell neoplasms** Unspecified types of haematopoietic and lymphoid tissues Unspecified types of cancer
9650-9667 9590-9591, 9596, 9727, 9760, 9800-9801, 9805-9809, 9820, 9832, 9835, 9965, 9967-9968, 9970- 9971 8000-8005	**Hodgkin lymphoma** Unspecified types of haematopoietic and lymphoid tissues Unspecified types of cancer

Table 18. *Continued*

Morphology code	Definition
9740-9742 9590-9591, 9596, 9727, 9760, 9800-9801, 9805-9809, 9820, 9832, 9835, 9965, 9967-9968, 9970- 9971 8000-8005	**Mast–cell tumours** Unspecified types of haematopoietic and lymphoid tissues Unspecified types of cancer
9749, 9750-9759 9590-9591, 9596, 9727, 9760, 9800-9801, 9805-9809, 9820, 9832, 9835, 9965, 9967-9968, 9970- 9971 8000-8005	**Histiocytes and Accessory Lymphoid cells** Unspecified types of haematopoietic and lymphoid tissues Unspecified types of cancer
9140 8000-8005	**Kaposi sarcoma** Unspecified types of cancer
8590-8671, 8720-8790, 8950-8983, 9000-9030, 9060-9105, 9260-9365, 9380-9539 8000-8005	**Other specified types of cancer** Unspecified types of cancer

The 2004 International Rules for Multiple Primary Cancer also includes some **recommendations for recording tumours** related to**:** 1) tumours of different laterality with the same morphology diagnosed in paired organs; 2) cancers which occur in any 4th character subcategory of colon (C18) and skin(C44) (16).

In addition to the recommendations for recording tumours described in the 2004 International rules for Multiple Primary Cancer, the **ENCR recommendation** for **recording** tumours is to register separately tumours in the same patient when the 3 digits of ICD-O-3 topography are different even if they have the same morphology.

The ENCR Recommendations for coding tumours of the CNS include the tumour sites (topography codes) and the tumour types (morphology codes) to be considered as different (20). The ENCR encourage European CRs to register the CNS tumours according to these recommendations. For example, a patient with a tumour in the cerebrum (C71.0) and a tumour in ventricle (C71.5), both tumours should be registered even if both have the same morphology code. A patient with an oligoastrocytoma (9382/3) and an embryonal tumour with multilayered rosettes with C19MC alteration (9478/3), both tumours should be registered even if the two tumours have are in the same topography code.

An exception to the mentioned recommendation is where one tumour has a non-specific topography which covers a range of sites (e.g. C26, C80) and the other has a topography within this range of sites; these should be considered to be in the same organ.

This approach is giving more flexibility to the data use by clinicians, epidemiologist, policymakers and researchers.

Following this recommendation, for example, a renal pelvis tumours (C65) with 8120 morphology code diagnosed in a patient with bladder tumour (C67) with 8130 morphology code, both tumours should be registered, even if morphologies are in the same group. Nevertheless, a bladder tumour (C67) in the a patient with urinary system NOS (C68.9) or unknown primary site (C80.9), only bladder tumour should be registered if the morphologies are included in the same group according to the **Table** .

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List of abbreviations and definitions

ENCR	European Network of Cancer Registries
IACR	International Association of Cancer Registries
IARC	International Agency for Research on Cancer
CRs	Cancer registries
MPMT	Multiple Primary Malignant Tumours

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