Squamous Cell Carcinoma of the Anus
Abdominoperineal Excision Specimen
Histopathology Reporting Guide

Family/Last name

Given name(s)

Date of birth DD – MM – YYYY

Patient identifiers

Date of request DD – MM – YYYY

Accession/Laboratory number

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

☐ indicates multi-select values ◯ indicates single select values

SCOPE OF THIS DATASET

CLINICAL INFORMATION (Note 1)

◯ Information not provided
◯ Information provided

Previous chemo/radiotherapy

◯ Information not provided
◯ No
◯ Yes, *specify*

Previous biopsy/local excision

◯ Information not provided
◯ No
◯ Yes

Clinical diagnosis and relevant history (e.g., HIV status, solid organ transplant), *specify*

Surgery for residual or recurrent disease, *specify*

Other clinical information, *specify*

ADDITIONAL TISSUES/ORGANS SUBMITTED (Note 2)

(select all that apply)

◯ Not submitted
☐ Bladder
☐ Prostate
☐ Vagina
☐ Uterus
☐ Other, *specify*

SPECIMEN DIMENSIONS (Note 3)

Length of specimen
(proximal resection margin to perianal skin margin)

mm

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

◯ Not specified
☐ Anal canal
☐ Perianal skin
☐ Anus, not otherwise specified
☐ Other, *specify*

TUMOUR DIMENSIONS (Note 5)

Greatest dimension

mm → ◯ Macroscopic ◯ Microscopic

◯ Cannot be assessed, *specify*

BLOCK IDENTIFICATION KEY (Note 6)

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

HISTOLOGICAL TUMOUR TYPE (Note 7)

◯ Squamous cell carcinoma
◯ Verrucous squamous cell carcinoma

HISTOLOGICAL TUMOUR GRADE (Note 8)

◯ Low grade
◯ High grade

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EXTENT OF INVASION (Note 9)

- ◯ Not applicable (no adjacent tissue/organ attached to this specimen)
- ◯ No invasion of adjacent tissue/organ(s) (e.g., vagina, prostate) attached to this specimen
- ◯ Invasion into adjacent tissue(s)/organ(s), *specify*

LYMPHOVASCULAR INVASION (Note 10)

- ◯ Not identified
- ◯ Present

PERINEURAL INVASION (Note 11)

- ◯ Not identified
- ◯ Present

MARGIN STATUS (Note 12)

Proximal/distal margin

- ◯ Cannot be assessed
- ◯ Involved
- ◯ Not involved

Distance to closest margin[a] ____ mm

Specify margin

Circumferential margin

- ◯ Cannot be assessed
- ◯ Involved
- ◯ Not involved

Distance to margin ____ mm

[a] *Can use macroscopic measurement instead.*

LYMPH NODE STATUS (Note 13)

- ◯ No nodes submitted or found

Number of lymph nodes examined

- ◯ Not involved
- ◯ Involved

Number of positive mesorectal lymph nodes

Number of positive internal iliac/ inguinal lymph nodes, if submitted

Number of positive external iliac lymph nodes, if submitted

- ◯ Number cannot be determined

POST-TREATMENT TUMOUR REGRESSION (Note 14)

- ◯ Not applicable
- ◯ No viable carcinoma cells (i.e., complete response)
- ◯ Single cells or rare small groups of carcinoma cells (i.e., near complete response)
- ◯ Residual cancer with evident tumour regression, but more than single cells or rare small groups of carcinoma cells (i.e., partial response)
- ◯ Extensive residual carcinoma with no evident tumour regression (i.e., poor or no response)

ADDITIONAL FINDINGS (select all that apply) (Note 15)

- ◯ None identified
- ☐ Low grade squamous intraepithelial lesion (LSIL) (includes condyloma acuminatum/viral wart)
- ☐ High grade squamous intraepithelial lesion (HSIL)
- ☐ Anal fistula
- ☐ Crohn's disease
- ☐ Other, *specify*

ANCILLARY STUDIES (Note 16)

- ◯ Not performed
- ◯ Performed
  - ◯ p16 immunohistochemistry
  - ◯ Other, *record test(s), methodology and result(s)*

Representative blocks for ancillary studies

NON-NEOPLASTIC TISSUE BLOCK

Block number

- ◯ Not available

CARCINOMA BLOCK

Block number

- ◯ Not available

Neoplastic cell proportion (number of carcinoma cells/ total number of nucleated cells) (to the nearest 10%) ____ %

HISTOLOGICALLY CONFIRMED DISTANT METASTASES (Note 17)

- ◯ Not applicable
- ◯ Not identified
- ◯ Present, *specify site(s)*

PATHOLOGICAL STAGING (UICC TNM 9th edition)[b] (Note 18)

TNM Descriptors (only if applicable) (select all that apply)

- ☐ m - multiple primary tumours
- ☐ y - post-therapy
- ☐ r - recurrent

Primary tumour (pT)

- ◯ TX[c] Primary tumour cannot be assessed
- ◯ T0 No evidence of primary tumour
- ◯ Tis Carcinoma in situ, HSIL, anal intraepithelial neoplasia II–III (AIN II–III) anal squamous intraepithelial neoplasia H (ASIN-H)[d]
- ◯ T1 Tumour 2 cm or less in greatest dimension
- ◯ T2 Tumour more than 2 cm but not more than 5 cm in greatest dimension
- ◯ T3 Tumour more than 5 cm in greatest dimension
- ◯ T4 Tumour of any size invades adjacent organ(s), e.g., vagina, urethra, bladder[e]

Regional lymph nodes (pN)

- ◯ NX[c] Regional lymph nodes cannot be assessed
- ◯ N0 No regional lymph node metastasis
- ◯ N1 Metastasis in regional lymph node(s)
  - ◯ N1a Metastases in inguinal, mesorectal, and/or internal iliac nodes
  - ◯ N1b Metastases in external iliac nodes
  - ◯ N1c Metastases in external iliac and in inguinal, mesorectal and/or internal iliac nodes

[b] *Reproduced with permission. Source: UICC TNM Classification of Malignant Tumours, 9th Edition, eds by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, Elizabeth Van Eycken. 2025, Publisher Wiley (incorporating any errata published up until 21st January 2026).*

[c] *TX and NX should be used only if absolutely necessary.*

[d] *The AJCC v9 staging system for anal cancer has removed Tis. The ICCR dataset authors also do not encourage use of the pTis category.*

[e] *Direct invasion of the rectal wall, perianal skin, subcutaneous tissue, or the sphincter muscle(s) alone is not classified as T4.*

Definitions

CORE elements

CORE elements are those which are essential for the clinical management, staging or prognosis of the cancer. These elements will either have evidentiary support at Level III-2 or above (based on prognostic factors in the National Health and Medical Research Council (NHMRC) levels of evidence[1]). In rare circumstances, where level III-2 evidence is not available an element may be made a CORE element where there is unanimous agreement by 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 III-2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.

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

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Scope

This dataset is currently intended only for squamous cell carcinoma (SCC) of the anus. It has been developed for the pathological reporting of local excision specimens only; there is a separate ICCR dataset for abdominoperineal excision (APE) specimens. Diagnostic biopsy specimens are exempt from ICCR reporting requirements.

The term ‘anal SCC’ is used hereafter as an umbrella one to include both anal canal and perianal SCC. Adenocarcinomas and neuroendocrine neoplasms are excluded (see below for reasoning). Malignant tumours that are not epithelial, e.g., melanoma, lymphoma and sarcoma, are also excluded.

In accordance with current World Health Organization (WHO) recommendations,[2] the term squamous intraepithelial lesion (SIL) is used throughout this dataset instead of for example, anal intraepithelial neoplasia (AIN) or squamous dysplasia. The dataset does not apply to APE specimens which only demonstrate SIL and do not contain carcinoma.

NOTE: PRIOR TO PUBLICATION THE DATASET CONTENT WILL BE UPDATED TO REFLECT WHO 6TH EDITION.

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

For reasons explained below, oncological therapy, defined as radiotherapy and/or chemotherapy, administered before excision of an anal SCC does not represent true neo-adjuvant management and is therefore referred to hereafter as 'prior chemo/radiotherapy'. Knowing whether a patient has received prior chemo/radiotherapy will influence pathological staging and microscopic assessment of the primary tumour excised.

Local excision of smaller anal canal and/or perianal SCC is rarely preceded by oncological therapy. Therefore, patients who undergo APE typically fall into one of two groups: those who have persistent disease despite first line oncological therapy, and are therefore operated on sooner, and those who have previously obtained a complete clinical response but then develop recurrent disease, and are therefore operated on later.[3,4] Knowledge of which of these groups a patient belongs to will determine whether T staging should have the prefix ypT (for the 'persistent' disease group) or rpT (for the 'recurrent' disease group).

Knowledge of previous sampling of the tumour may help explain an absence of malignancy and/or any artefactual changes in an excision specimen.

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Note 2 – Additional tissues/organs submitted (Core)

The term APE includes both conventional and extended versions. The latter may include excision of further soft tissue and/or organs in addition to the sphincter complex and coccyx. Whether an APE is extended is only relevant to pathological reporting of anal SCC if invasion of tissues/organs that are excised beyond conventional APE defines a pT4 stage, e.g., bladder or uterus.[5,6] Therefore, it is more important to be told and to record the presence of such tissues/organs in the surgical specimen than the type of APE performed.

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Note 3 – Specimen dimensions (Non-core)

The length of an APE specimen has no clinical relevance and is not used for surgical audit purposes either; this dimension is therefore regarded to be a non-core item.

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Note 4 – Tumour site (Core)

TNM9 classifies all "anal margin tumours and perianal tumours arising within 5 centimetres (cm) of the anal margin" as carcinomas of the anus.[5,6] The term 'anal margin' has been used in different ways, for example, to mean the area below the dentate line or the zone of perianal skin up to 5 cm (50 mm) beyond the anal verge.[4,7] This dataset therefore avoids use of the term 'anal margin' and uses the terms 'perianal skin', 'anal verge', and 'anal canal'. The term 'anus' encompasses these regions.

Distinguishing between an anal canal cancer and a perianal cancer can be clinically important in view of recommendations that pT1 perianal SCCs can be initially managed by local excision as opposed to chemoradiotherapy, which is first line therapy for anal canal SCCs.[3,4]

It is acknowledged that the precise origin of larger tumours cannot be assessed especially when they cross the anal verge. While the option of 'cannot be assessed' is applicable here, the patient would most likely be managed as for an anal canal carcinoma because the larger size of the tumour would usually exceed a pT1 tumour, and involvement of the anal canal increases the risk of spread to internal pelvic nodes which are better managed with oncological therapy.

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Note 5 – Tumour dimensions (Core)

The TNM9 definitions of pT1, 2 and 3 for anal cancer are based on tumour size.[5,6] On the assumption that the histological block(s) demonstrate(s) the maximum dimension of the tumour, a microscopic measurement provides a more accurate tumour dimension and is therefore preferable. However, if the whole tumour is not blocked as one slide or across composite slides, then a macroscopic measurement of maximum size is acceptable instead. It should be stated whether the tumour size was measured macroscopically or microscopically. Including both macroscopic and microscopic measurements of maximum tumour size in one dataset may confuse its users and is strongly discouraged.

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Note 6 – Block identification key (Non-core)

The origin/designation of all tissue blocks should be recorded. This information should ideally be documented in the final pathology report and is particularly important when further internal or external review arises. The reviewer needs to have an unequivocal description of the origin of each block to provide an informed specialist opinion. 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.

Recording the origin/designation of tissue blocks also facilitates retrieval of blocks for future immunohistochemical or genomic analysis, research studies, or clinical trials.

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Note 7 – Histological tumour type (Core)

All SCCs of the anus should be classified based on the 5th edition WHO Classification of Digestive System Tumours, 2019.[2] Adenocarcinoma is far less common than SCC in the anal canal and perianal skin.[2] The TNM staging for anal carcinoma is primarily designed for SCC, e.g., it using similar, size-based criteria as per skin and oral SCC staging.[5,6] It remains uncertain if there is equal clinical merit in applying this anal staging system to adenocarcinoma, which might be better staged according to extent of invasion through the anatomical layers of the anal canal/rectal wall,[8] akin to rectal adenocarcinoma. Indeed, a proportion of adenocarcinomas presenting in the anal canal may actually be low primary rectal adenocarcinomas. Adenosquamous carcinoma and neuroendocrine carcinoma also arise within the anus, although both

subtypes are much rarer than anal SCC and there remains a lack of evidence to indicate what staging system is best applied to either carcinoma. Therefore, this dataset and its TNM based staging will pertain only to SCC and its WHO recognised variant, verrucous carcinoma.[2] Future iterations of this dataset may include adenocarcinoma and/or the other rare anal carcinoma subtypes, as further research emerges on how best to stage them in the anus.

Diagnostic criteria for verrucous carcinoma are outlined in detail elsewhere,[2] but by definition this subtype of SCC should be low grade and should not show evidence of human papillomavirus. In line with current WHO recommendations,[2] there is no requirement to document other morphological subtypes of SCC, e.g., basaloid or mucoepidermoid carcinoma, although recognition of their existence is important to permit distinction from possible morphological mimics such as small cell neuroendocrine carcinoma.

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Note 8 – Histological tumour grade (Non-core)

Previously reported associations between tumour grade, i.e., the degree of differentiation, and prognosis of anal SCC may have been compounded by association with stage,[4] and there remains a lack of evidence that tumour grade represents an independent prognostic indicator.[9] Further, there are no internationally accepted criteria for defining different grades for anal SCC and in keeping with this, interobserver reproducibility of such grading has not been validated. The current National Comprehensive Cancer Network (NCCN) guidelines for anal cancer uses carcinoma differentiation to help determine whether a perianal SCC should be managed by local excision alone.[3] However, the current European Society for Medical Oncology (ESMO) guidelines do not recommend that tumour differentiation be used to make this management decision because its authors were unaware of any supporting evidence for this.[4]

For all these reasons, the consensus of the DAC was that histological tumour grade should not currently be a non-core element for anal SCC. However, if grade is reported, the following two-tier system is suggested because this will intrinsically yield less interobserver variability than a system with more categories: low grade is equivalent to well (grade 1) or moderately (grade 2) differentiated, whereas high grade is equivalent to poorly (grade 3) differentiated.

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Note 9 – Extent of invasion (Core)

Invasion of an adjacent organ defines a pT4 stage tumour.[5,6]

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Note 10 – Lymphovascular invasion (Non-core)

The presence of lymphovascular invasion has not been confirmed as an independent prognostic predictor for anal SCC nor does it currently influence patient management after excision. It is therefore considered a non-core element and as such, there is no clinical requirement to distinguish lymphatic from blood vessel invasion.

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Note 11 – Perineural invasion (Non-core)

The presence of perineural invasion has not been confirmed as an independent prognostic predictor for anal SCC and its presence does not currently influence patient management after excision of this cancer type.

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Note 12 – Margin status (Core)

The definition of an involved margin is the presence of carcinoma within 1 mm of the margin. There is less evidence for the use of this definition for anal SCC compared to surgically excised rectal adenocarcinoma[10] and oesophageal cancer.[11] However, of UKCCCR Anal Cancer Trial patients who underwent salvage APE, 25% developed locoregional recurrence (LRR) when tumour distance from the circumferential resection margin was >1 mm, whereas 60% developed LRR at a distance of ≤1 mm.[12] Further, the current ESMO guidelines recommend oncological therapy for any patient whose anal SCC lies ≤1 mm from a margin in a local excision specimen.[4] Therefore, until evidence emerges to change the definition, an involved margin remains defined as presence of SCC within 1 mm of the surgical margin.

Involvement of a peripheral margin by SIL is clinically relevant only for local excision specimens because if present, this may impact the frequency of clinical surveillance of the area thereafter.

The proximal (large bowel) margin will rarely be involved by anal SCC in APE specimens. Clearance from the distal (perianal skin) margin can be based on a microscopic measurement if both carcinoma and the margin are in the same standard size or mega block. If not, a macroscopic measurement will suffice. Macroscopic is less precise than microscopic assessment but there is less clinical need for absolute precision if the clearance is already >15-20 mm, i.e., the smaller dimension of a standard size block.

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Note 13 – Lymph node status (Core)

The nodal group involved defines sub-staging of N1 for TNM9.[5,6]

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Note 14 – Post-treatment tumour regression (Non-core)

In view of the two clinical indications for APE for anal SCC (as discussed in **NOTE 1 – CLINICAL INFORMATION**), a good response to prior chemo/radiotherapy would not be expected for patients with persistent disease, and it can be argued that recurrent carcinomas have regrown only after earlier tumour regression. Therefore, grading of tumour regression is less clinically relevant in the former scenario and not applicable to the latter.

Perhaps for this reason, there is no known tumour regression system that has been validated specifically for anal SCC. Therefore, if tumour regression is to be graded, word descriptions are favoured and a four category system akin to that of Ryan is arbitrarily proposed.[13]

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Note 15 – Additional findings (Non-core)

These are recognised potential associations of anal SCC.

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Note 16 – Ancillary studies (Non-core)

p16 immunohistochemistry may be used to help diagnose and/or grade SIL.[2,14] However, its role for anal SCC remains to be fully validated. For oropharyngeal SCC, p16 expression is used as a surrogate marker for HPV infection and as a predictor of better response to chemoradiotherapy, therefore guiding patient management.[15,16] While there is growing clinical interest in similarly using p16 immunohistochemistry for diagnostic biopsies of anal SCC, like cervical SCC, the majority are HPV-associated cancers; first line management for anal SCC currently remains local excision if the tumour is small and perianal, and chemoradiotherapy if not.[3,4] Finally, there is only limited evidence (only six studies could be used for a recent meta-analysis[17]) that p16 expression predicts for a better prognosis for anal SCC. p16 immunohistochemistry therefore has even less relevance for anal SCC which has been excised and especially when the patient has already undergone oncological therapy.

PDL1 may emerge as a future therapeutic biomarker for anal SCC.[4]

Prospective recording of neoplastic and non-neoplastic tissue blocks can facilitate future research and can expedite tissue processing for genomic testing in the future. If such testing involves RNA or DNA extraction, prospective recording of neoplastic cell proportion will further expedite tissue processing.

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Note 17 – Histologically confirmed distant metastases (Core)

For anal SCC, the sites of distant metastases include lymph nodes beyond the groups defining N1 disease and any organ outside the anal canal, especially the liver.[5,6] The element is only needs to be recorded if a histological specimen proving distant spread (e.g., a core or fine-needle aspiration biopsy of a liver metastasis) was submitted together with the excision specimen.

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Note 18 – Pathological staging (Core)

TNM staging should be assessed according to the agreed criteria of the UICC and AJCC 9th editions.[5,6] The only exception is that pT in situ is not recognised for anal cancer in this dataset. This omission acknowledges that it is difficult to histologically distinguish between high grade squamous dysplasia and so-called squamous 'carcinoma-in-situ'.

Note that in the setting of completion surgery following a diagnosis of carcinoma in a local excision specimen, an overall tumour stage should be provided based on the pathological findings within both specimens, usually taking into consideration extent of local invasion in the local excision specimen and any residual local or nodal metastatic tumour in the subsequent surgical resection specimen.

Reporting of pathological staging categories (pT,pN,pM) is based on the evidence available to the pathologist at the time of reporting the resection specimen. A pT category is not assigned on biopsy. As indicated in the UICC/AJCC TNM 9th edition,[5,6] the final stage grouping of a patient's tumour is based on a combination of pathological staging and other clinical and imaging information.

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References

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