URINARY TRACT CARCINOMA - TRANSURETHRAL RESECTION AND BIOPSY
STRUCTURED REPORTING PROTOCOL
(1st Edition 2018)

Incorporating the:
International Collaboration on Cancer Reporting (ICCR)
Dataset for the reporting of carcinoma of the urinary tract - biopsy and transurethral resection specimen
www.ICCR-Cancer.org
Core Document versions:

1. ICCR Dataset for the reporting of carcinoma of the urinary tract - biopsy and transurethral resection specimen
2. AJCC Cancer Staging Manual 8th edition
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   o Numbering of Standards and Guidelines must be retained in the checklist, but can be reduced in size, moved to the end of the checklist item or greyed out or other means to minimise the visual impact.

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The Royal College of Pathologists of Australasia ("College") has developed these protocols as an educational tool to assist pathologists in reporting of relevant information for specific cancers. Each protocol includes “standards” and “guidelines” which are indicators of ‘minimum requirements’ and ‘recommendations’, which reflect the opinion of the relevant expert authoring groups. The use of these standards and guidelines is subject to the clinician’s judgement in each individual case.

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Scope

This protocol contains standards and guidelines for the reporting of transurethral resection (TUR) specimens and biopsies of the urinary bladder, urethra, ureter and renal pelvis. The protocol applies to primary carcinomas (non-invasive and invasive), with or without associated epithelial lesions. Urothelial tumours diagnosed as papilloma or papillary urothelial neoplasm of low malignant potential are not carcinomas and this protocol does not apply to those diagnoses. The most distal portion of the penile urethra in the region of the glans penis is not included in this protocol, it is covered in the carcinoma of the penis protocol. Biopsy of the kidney is dealt with in a separate protocol.

Structured reporting aims to improve the completeness and usability of pathology reports for clinicians, and improve decision support for cancer treatment. The protocol provides the framework for the reporting of any urinary tract urothelial tumour, whether as a minimum data set or fully comprehensive report.
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>AJCC</td>
<td>American Joint Committee on Cancer</td>
</tr>
<tr>
<td>BCG</td>
<td>Bacillus Calmette-Guerin</td>
</tr>
<tr>
<td>CIS</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>CG</td>
<td>Commentary for a guideline</td>
</tr>
<tr>
<td>CS</td>
<td>Commentary for a standard</td>
</tr>
<tr>
<td>HG</td>
<td>High grade</td>
</tr>
<tr>
<td>ICCR</td>
<td>International Collaboration on Cancer Reporting</td>
</tr>
<tr>
<td>ISUP</td>
<td>International Society of Urological Pathology</td>
</tr>
<tr>
<td>LIS</td>
<td>Laboratory information system</td>
</tr>
<tr>
<td>LG</td>
<td>Low grade</td>
</tr>
<tr>
<td>LVI</td>
<td>Lymphovascular invasion</td>
</tr>
<tr>
<td>PBS</td>
<td>Pharmaceutical Benefits Scheme</td>
</tr>
<tr>
<td>RCPA</td>
<td>Royal College of Pathologists of Australasia</td>
</tr>
<tr>
<td>TCC</td>
<td>Transitional cell carcinoma</td>
</tr>
<tr>
<td>TNM</td>
<td>Tumour-node-metastasis</td>
</tr>
<tr>
<td>TUR</td>
<td>Transurethral resection</td>
</tr>
<tr>
<td>TURB</td>
<td>Transurethral resection of bladder</td>
</tr>
<tr>
<td>UICC</td>
<td>International Union Against Cancer</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
Definitions

The table below provides definitions for general or technical terms used in this protocol. Readers should take particular note of the definitions for ‘standard’, ‘guideline’ and ‘commentary’, because these form the basis of the protocol.

Ancillary study
An ancillary study is any pathology investigation that may form part of a cancer pathology report but is not part of routine histological assessment.

Clinical information
Patient information required to inform pathological assessment, usually provided with the specimen request form, also referred to as “pre-test information”.

Commentary
Commentary is text, diagrams or photographs that clarify the standards (see below) and guidelines (see below), provide examples and help with interpretation, where necessary (not every standard or guideline has commentary).

Commentary is used to:

- define the way an item should be reported, to foster reproducibility
- explain why an item is included (e.g. how does the item assist with clinical management or prognosis of the specific cancer).
- cite published evidence in support of the standard or guideline
- state any exceptions to a standard or guideline.

In this document, commentary is prefixed with ‘CS’ (for commentary on a standard) or ‘CG’ (for commentary on a guideline), numbered to be consistent with the relevant standard or guideline, and with sequential alphabetic lettering within each set of commentaries (e.g. CS1.01a, CG2.05b).

General commentary
General commentary is text that is not associated with a specific standard or guideline. It is used:

- to provide a brief introduction to a chapter, if necessary
- for items that are not standards or guidelines but are included in the protocol as items of potential importance, for which there is currently insufficient evidence to recommend their inclusion. (Note: in future reviews of protocols, such items may be reclassified as either standards or guidelines, in line with diagnostic and prognostic advances, following evidentiary review).
Guideline | Guidelines are recommendations; they are not mandatory, as indicated by the use of the word ‘should’. Guidelines cover items that are unanimously agreed should be included in the dataset but are not supported by NHMRC level III-2 evidence.\textsuperscript{1} These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.

Guidelines include 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 eg macroscopic tumour details, block identification key, may be included as either required or recommended elements by consensus of the expert committee. Such findings are essential from a clinical governance perspective, because they provide a clear, evidentiary decision-making trail.

Guidelines are not used for research items.

In this document, guidelines are prefixed with ‘G’ and numbered consecutively within each chapter (eg G1.10).

<table>
<thead>
<tr>
<th>Macroscopic findings</th>
<th>Measurements, or assessment of a biopsy specimen, made by the unaided eye.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microscopic findings</td>
<td>In this document, the term ‘microscopic findings’ refers to histomorphological assessment.</td>
</tr>
<tr>
<td>Predictive factor</td>
<td>A predictive factor is a measurement that is associated with response or lack of response to a particular therapy.</td>
</tr>
<tr>
<td>Prognostic factor</td>
<td>A prognostic factor is a measurement that is associated with clinical outcome in the absence of therapy or with the application of a standard therapy. It can be thought of as a measure of the natural history of the disease.</td>
</tr>
<tr>
<td>Standard</td>
<td>Standards are mandatory, as indicated by the use of the term ‘must’. Standards 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 NHMRC levels of evidence\textsuperscript{1} document). In rare circumstances, where level III-2 evidence is not available an element may be made a Standard where there is unanimous agreement in the expert committee. An appropriate staging system eg Pathological TNM staging would normally be included as a required element. These elements must be recorded and at the discretion of the pathologist included in the pathology report according to the needs of the recipient of the report.</td>
</tr>
</tbody>
</table>

The summation of all standards represents the minimum dataset.
for the cancer.

In this document, standards are prefixed with 'S' and numbered consecutively within each chapter (eg S1.02).

<table>
<thead>
<tr>
<th>Structured report</th>
<th>A report format which utilises standard headings, definitions and nomenclature with required information.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synoptic report</td>
<td>A structured report in condensed form (as a synopsis or precis).</td>
</tr>
<tr>
<td>Synthesis</td>
<td>Synthesis is the process in which two or more pre-existing elements are combined, resulting in the formation of something new.</td>
</tr>
</tbody>
</table>

The Oxford dictionary defines synthesis as “the combination of components or elements to form a connected whole”.

In the context of structured pathology reporting, synthesis represents the integration and interpretation of information from two or more modalities to derive new information.
Introduction

Urinary tract biopsies or transurethral resections are commonly performed as a first step in establishing the diagnosis and extent of tumours arising from the urothelium. They are also performed in the follow-up of these patients after treatment, in particular, to assess if there is residual tumour.

Importance of histopathological reporting

Information in the pathology report of the macroscopic and microscopic findings in transurethral resection (TUR) specimens and biopsies of the bladder, urethra, ureter and renal pelvis is of both clinical and prognostic utility. The information gained from these specimens is used to guide clinical management of patients, particularly in relation to the role of definitive and adjuvant therapy and surveillance.

While the report must contain all information necessary for tumour staging, the treating clinician will often look for additional information in the report to further refine the patient’s likely prognosis and optimal treatment.

Benefits of structured reporting

The pathology report lays the foundation for a patient’s cancer management and conveys information which:

- Provides the definitive diagnosis
- Includes critical information for Tumour-Node-Metastasis (TNM) staging
- Evaluates the adequacy of the surgical excision
- Provides morphological and biological prognostic markers which determine personalised cancer therapy

However, the rapid growth in ancillary testing such as immunohistochemistry, flow cytometry, cytogenetics, and molecular studies, have made the task of keeping abreast of advances on specific cancer investigations extremely difficult for pathologists. The use of structured reporting checklists by pathologists ensures that all key elements are included in the report specifically those which have clinical management, staging or prognostic implications. Consequently minimum or comprehensive datasets for the reporting of cancer have been developed around the world. Both the United Kingdom,2 and United States3 have produced standardised cancer reporting protocols or “datasets” for national use for many years.

The use of cancer reporting checklists improves completeness and quality of cancer reporting and thereby ensures an improved outcome for cancer patients. This has long term cost implications for public health by ensuring the most effective and timely treatment based on accurate and complete information.
The use of a structured reporting format also facilitates easy extraction of the necessary information by secondary users of the information ie cancer registries.

International Collaboration on Cancer Reporting

The International Collaboration on Cancer Reporting (ICCR), founded in 2011 by the Australasian (RCPA), US (CAP) and UK (RCPA) Colleges of Pathology and the Canadian Association of Pathology (CAP-ACP) in association with the Canadian Partnership Against Cancer (CPAC), was established to explore the possibilities of a collaborative approach to the development of common, internationally standardised and evidence-based cancer reporting protocols for surgical pathology specimens.

The ICCR, recognising that standardised cancer datasets have been shown to provide significant benefits for patients and efficiencies for organisations through the ease and completeness of data capture\textsuperscript{4-7} undertook to use the best international approaches and the knowledge and experience of expert pathologists, and produce cancer datasets which would ensure that cancer reports across the world will be of the same high quality – ensuring completeness, consistency, clarity, conciseness and above all, clinical utility.

Representatives from the four countries participating in the initial collaboration undertook a pilot project in 2011 to develop four cancer datasets - Lung, Melanoma, Prostate (Radical Prostatectomy), and Endometrium. Following on from the success of this pilot project, the ICCR was joined by the European Society of Pathology (ESP) in 2013 and in 2014 incorporated a not-for-profit organisation focussed on the development of internationally agreed evidence-based datasets developed by world leading experts. The ICCR Datasets are made freely available from its website www.ICCR-Cancer.org

Design of this protocol

This structured reporting protocol has been developed using the ICCR dataset on the reporting of carcinoma of the urinary tract - biopsy and transurethral resection specimen, as the foundation.

This protocol includes all of the ICCR cancer dataset elements as well as additional information, elements and commentary as agreed by the RCPA expert committee. It provides a comprehensive framework for the assessment and documentation of pathological features of carcinoma of the urinary tract.

ICCR dataset elements for carcinoma of the urethra are included verbatim. ICCR Required elements are mandatory and therefore represented as standards in this document. ICCR Recommended elements, that is, those which are not mandatory but are recommended, may be included as guidelines or upgraded to a standard based on the consensus opinion of the local expert committee.
The ICCR elements are identified in each chapter with the ICCR logo placed before the Standard or Guideline number or bullet and the ICCR element description and commentary is boarded by a grey box as shown below:

<table>
<thead>
<tr>
<th>G3.02</th>
<th>The intraglandular extent should be recorded as a percentage.</th>
</tr>
</thead>
</table>

Additional commentary by the RCPA expert committee may be added to an ICCR element but is not included in the grey bordered area eg

<table>
<thead>
<tr>
<th>G2.03</th>
<th>If present, the laterality of the lymph nodes submitted may be recorded as left, right or bilateral.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS2.03a</td>
<td>If present, record site and number. All lymph node tissue should be submitted for histological examination.</td>
</tr>
</tbody>
</table>

Further information on the ICCR is available at [www.iccr-cancer.org](http://www.iccr-cancer.org)

**Checklist**

Consistency and speed of reporting is improved by the use of discrete data elements recorded from the checklist. Items suited to tick boxes are distinguished from more complex elements requiring free text or narrative. A structured or discrete approach to responses is favoured, however the pathologist is encouraged to include free text or narrative where necessary to document any other relevant issues, to give reasons for coming to a particular opinion and to explain any points of uncertainty.

**Report format**

The structure provided by the following chapters, headings and subheadings describes the elements of information and their groupings, but does not necessarily represent the format of either a pathology report (Chapter 7) or checklist (Chapter 6). These, and the structured pathology request form (Appendix 1) are templates that represent information from this protocol, organised and formatted differently to suit different purposes.

**Key documentation**

- *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols, Royal College of Pathologists of Australasia, 2009*[^8]
Updates since last edition

Not applicable.
Authority and development

This section provides information about the process undertaken to develop this protocol.

This 1st edition of the protocol is an amalgam of two separate processes:

1. This protocol is based on the ICCR Dataset for the Reporting of Carcinoma of the urinary tract - biopsy and transurethral resection specimen 1st edition. All ICCR elements from this dataset, both required (mandatory) and recommended (optional), are included in this protocol, verbatim. (It should be noted that RCPA feedback from all Anatomical Pathology fellows and specifically the local expert committee was sought during the development process of the ICCR dataset.) Details of the ICCR development process and the international expert authoring committee responsible for the ICCR dataset are available on the ICCR website: iccr-cancer.org.

2. Additional elements, values and commentary have been included as deemed necessary by the local expert committee. In addition, the standard inclusions of RCPA protocols eg example reports, request information etc, have also been added.

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ACT Health
ACT Cancer Registry
Australian Pathology
Australian Cancer Network
Australian Commission on Safety and Quality in Health Care
Australian Digital Health Agency
Australian Institute of Health and Welfare
Cancer Australia
Cancer Council ACT
Cancer Council Queensland
Cancer Council Victoria
Cancer Council Western Australia
Cancer Institute NSW
Cancer Services Advisory Committee (CanSAC)
Cancer Voices NSW
Clinical Oncology Society of Australia (COSA)
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Health Informatics Society of Australia (HISA)
Independent Review Group of Pathologists
Medical Software Industry Association (MSIA)
National Pathology Accreditation Advisory Council (NPAAC)
New Zealand Cancer Registry
Northern Territory Cancer Registry
Public Pathology Australia
Queensland Cooperative Oncology Group (QCOG)
RCPA Anatomical Pathology Advisory Committee (APAC)
Representatives from laboratories specialising in anatomical pathology across Australia
Royal Australasian College of Physicians (RACP)
South Australia Cancer Registry
Standards Australia
Tasmanian Cancer Registry
Development process

This protocol has been developed following the ten-step process set out in *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols.*

Where no reference is provided, the authority is the consensus of the local expert group for local inclusions and the ICCR Dataset Authoring Committee for ICCR components denoted with the ICCR logo.
1 Pre-analytical

This chapter relates to information that should be recorded on receipt of the specimen in the laboratory.

The pathologist is reliant on the quality of information received from the clinicians or requestor. Some of this information may be received in generic pathology request forms; however, the additional information required by the pathologist specifically for the reporting of carcinoma of the urinary tract is outlined in Appendix 1. Appendix 1 also includes a standardised request information sheet that may be useful in obtaining all relevant information from the requestor.

Surgical handling procedures affect the quality of the specimen and recommendations for appropriate surgical handling are included in Appendix 1.

S1.01 All demographic information provided on the request form and with the specimen must be recorded.

CS1.01a The Royal College of Pathologists of Australasia (RCPA) The Pathology Request-Test-Report Cycle — Guidelines for Requesters and Pathology Providers must be adhered to. This document specifies the minimum information to be provided by the requesting clinician for any pathology test.

CS1.01b Whether or not the patient identifies as Aboriginal and/ or Torres Strait Islander. This is in support of a government initiative to monitor the health of indigenous Australians particularly in relation to cancer.

CS1.01c The patient’s health identifiers may include the patient’s Medical Record Number as well as a national health number such as a patient’s Individual Healthcare Identifier (IHI) (Australia) or the National Healthcare Identifier (New Zealand).

S1.02 All clinical information as documented on the request form must be recorded verbatim.

CS1.02a The request information may be recorded as a single text (narrative) field or it may be recorded in a structured format.

CS1.02b The copy doctors requested on the request form must be recorded.

S1.03 The pathology accession number of the specimen must be recorded.

S1.04 The principal clinician involved in the patient’s care and responsible for investigating the patient must be recorded.

CS1.04a The principle clinician should provide key information regarding the clinical presentation of the patient. Follow
up may be required with the principle clinician for a number of reasons:

- The clinical assessment and staging may be incomplete at the time of procedure.

- The pathology request is often authored by the clinician performing the surgical excision/biopsy rather than the clinician who is investigating and managing the patient.

- The identity of this clinician is often not indicated on the pathology request form

- In practice therefore, it is important in such cases that the reporting pathologist should be able to communicate with the managing clinician for clarification.

G1.01 Any clinical information received in other communications from the requestor or other clinician should be recorded together with the source of that information.
2 Specimen handling and macroscopic findings

This section relates to the procedures required after the information has been handed over from the requesting clinician, and the specimen has been received in the laboratory.

Tissue Banking
➢ Pathologists may be asked to provide tissue samples from fresh specimens for tissue banking or research purposes. The decision to provide tissue should only be made if the pathologist is sure that the diagnostic process will not be compromised. As a safeguard, research use of the tissue samples may be put on hold until the diagnostic process is complete.

Specimen handling
➢ Detailed fixation and specimen handling instructions are available from the RCPA online Cut-up Manual:

www.rcpa.edu.au/Library/Practising-Pathology/Macroscopic-Cut-Up
➢ The entire specimen must be blocked.

Macroscopic findings

S2.01 The labelling of the specimen(s) must be clearly recorded.

<table>
<thead>
<tr>
<th>S2.02</th>
<th>The operative procedure must be recorded.</th>
</tr>
</thead>
<tbody>
<tr>
<td>S2.03</td>
<td>The specimen site(s) sampled must be recorded.</td>
</tr>
<tr>
<td>CS2.03a</td>
<td>Since this dataset applies to the full length of the urinary tract the specific anatomic site is essential to the correct site identification and interpretation. The differential diagnostic considerations will have many site specific alternatives. Although the key staging landmarks have much overlap there are also several that will be site specific such as the renal stroma in renal pelvis tumours, prostatic stroma in the prostatic urethra and corporal bodies in the penile urethra. Location within individual sites can also be important to interpretation. In the urinary bladder specimens from the dome/anterior wall will include urachal lesions in the differential diagnosis. In the posterior wall/trunk/bladder neck secondary tumours from adjacent organs become important considerations in differential diagnosis. The distribution of muscularis mucosae fibres also vary by location in the urinary bladder and so knowledge of location can assist in evaluation of smooth muscle in the context of staging</td>
</tr>
</tbody>
</table>
In males the urethra is divided into four regions, the preprostatic, prostatic, membranous and penile. Knowing the origin of a “urethral” biopsy or transurethral resection is important as there are histologic differences between regions as well as different glandular elements that may be relevant to the interpretation of a given specimen.

If biopsies are from different locations then a separate dataset should be completed for each specimen site.

<table>
<thead>
<tr>
<th><strong>S2.04</strong></th>
<th><strong>In a biopsy the number of pieces must be recorded.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S2.05</strong></td>
<td><strong>For TURBT specimens an indication of the size of the specimen must be given – this may be by weight or measured in mm.</strong></td>
</tr>
<tr>
<td><strong>S2.06</strong></td>
<td><strong>A block identification key listing the nature and origin of all tissue blocks must be recorded.</strong></td>
</tr>
</tbody>
</table>

- **CS2.06a**
  - The origin/designation of all tissue blocks should be recorded and it is preferable to document this information in the final pathology report. This is particularly important should the need for internal or external review arise. The reviewer needs to be clear about the origin of each block in order 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 example for further immunohistochemical or molecular analysis, research studies or clinical trials.

- **G2.01**
  - A descriptive or narrative field should be provided to record any macroscopic information that is not recorded in the above standards and guidelines, and that would normally form part of the macroscopic description.

- **CG2.01a**
  - The traditional macroscopic narrative recorded at the time of specimen dissection is often reported separately from the cancer dataset. Although this remains an option, it is recommended that macroscopic information be recorded within the overall structure of this protocol.

- **CG2.01b**
  - Much of the information recorded in a traditional macroscopic narrative is covered in the standards and guidelines above and in many cases, no further description is required.
3 Microscopic findings

This section relates to purely histological (morphological) assessment. Information derived from multiple investigational modalities, or from two or more chapters, is described in Chapter 5.

<table>
<thead>
<tr>
<th>S3.01</th>
<th>Histological tumour type and sub-type/variant must be recorded.</th>
</tr>
</thead>
</table>
| CS3.01a | The 2016 World Health Organization (WHO) classification is utilised for assigning histological tumour type.\textsuperscript{13} As in the 2004 WHO Classification,\textsuperscript{14} a tumour is classified as a urothelial carcinoma if there is any identifiable urothelial component no matter how small and including urothelial carcinoma \textit{in situ} (CIS). The one exception to this rule is for cases with a (small cell neuroendocrine carcinoma or large cell neuroendocrine carcinoma) where classification is now in the neuroendocrine tumour category. For those cases that are mixed, the other elements should be reported with an estimated percentage. In the above scheme, this would be managed by placing the other component in the histological tumour type element. For example, a mixed tumour with 70% small cell neuroendocrine carcinoma and 30% urothelial carcinoma would be reported under the histological tumour type as Neuroendocrine tumour (small cell neuroendocrine carcinoma) and then under histological tumour type – Other, specify - urothelial carcinoma (30%).

For biopsies and TURs that contain pure adenocarcinoma or pure squamous cell carcinoma, they should be diagnosed as such. Without evaluation of the entire lesion it is not however possible to exclude the possibility of a urothelial carcinoma with squamous or glandular differentiation and consider a comment explaining that should always be included. The presence of keratinizing squamous metaplasia particularly when there is dysplasia would support the diagnosis of primary squamous cell carcinoma.\textsuperscript{15} Similarly the presence of intestinal metaplasia with dysplasia would support the diagnosis of primary adenocarcinoma. None the less a definitive diagnosis of either should be made with caution in biopsy or transurethral resection of bladder tumour (TURBT) material. There are no reliable immunohistochemical markers to distinguish these possibilities with certainty in the individual case. In urothelial carcinoma with glandular differentiation, the glandular component may retain its “urothelial” profile including expression of p63, GATA3 and high molecular weight cytokeratin but often these are lost with the tumour showing an enteric immunohistochemical profile. Markers of squamous differentiation such as desmoglein 3, CK14 and MAC387. |
have not been proven to reliably separate pure squamous cell carcinoma from urothelial carcinoma with squamous differentiation. Further for both adenocarcinoma and squamous cell carcinoma the diagnosis of primary origin in the urinary bladder requires clinical correlation to exclude the possibility of origin at another site.

The 2016 WHO classification now includes carcinomas arising in the urachus as a separate category. These are defined as carcinomas arising from urachal remnants. In general it is not possible to diagnose these in biopsy and TURBT material based on the morphologic findings alone. Criteria for the diagnosis of urachal carcinoma include location in the bladder dome or anterior wall, an epicentre in the bladder wall or perivesical tissue, the absence of diffuse cystitis glandularis/ intestinal metaplasia outside of the dome/anterior wall region and the absence of a known primary elsewhere. The majority (over 80%) of urachal carcinomas are adenocarcinoma followed by urothelial carcinoma, squamous cell carcinoma and small cell neuroendocrine carcinoma. If a diagnosis of urachal carcinoma is rendered the histologic type should be specified. Adenocarcinomas of the urachus are most often mucinous and can be either solid or cystic. Other variants of adenocarcinoma including enteric and signet ring-cell also occur. The WHO does include a category of “mucinous cystic tumour of low malignant potential” that could not be diagnosed with certainty in biopsy/TURBT material. There are no reliable immunohistochemical markers to distinguish adenocarcinomas of urachal origin from primary adenocarcinomas of the bladder proper or from secondary adenocarcinomas of gastrointestinal origin.

Also new in the 2016 WHO classification is the category of Müllerian tumours. For the purposes of this dataset this consists primarily of clear cell carcinoma and rare examples of endometrioid carcinoma. These tumours are morphologically the same as their counterparts in the female genital tract. They are rare tumours and most often when clear cell carcinoma presents as a primary bladder tumour it represents secondary involvement most often originating in a urethral diverticulum. Diagnosis therefore requires clinical correlation to support diagnosis as a primary bladder tumour. Clear cell carcinoma and endometrioid carcinoma may arise from endometriosis or rarely Müllerianosis. Clear cell carcinoma must also be distinguished from urothelial carcinoma with divergent differentiation along Müllerian lines in which case it would be classified under urothelial carcinoma. Expression of markers such as p63, GATA3 and high molecular weight cytokeratin are not present in clear cell carcinoma and in the absence of a recognisable
urothelial component would suggest this possibility. Müllerian type clear cell carcinoma has similar immunohistochemical profile to primary tumours of the female genital tract and cannot be used to distinguish a primary from a secondary origin.

The neuroendocrine tumour category includes small cell neuroendocrine carcinoma, large cell neuroendocrine carcinoma, well-differentiated neuroendocrine tumour and paraganglioma. Small cell neuroendocrine carcinoma is by far the most common of these. By definition this is a malignant neoplasm with neuroendocrine differentiation. About one-half of cases are pure and one-half are mixed with another component with urothelial carcinoma being most frequent. Cases with mixed differentiation are included in this category. There does remain some controversy regarding the percentage of the neuroendocrine component required to classify a tumour as a neuroendocrine carcinoma. From a practical standpoint cases with a small cell neuroendocrine carcinoma component irrespective of the amount are managed as small cell neuroendocrine carcinoma with the larger series in the literature including cases with only a focal component of small cell carcinoma. For example the National Comprehensive Cancer Network (NCCN) includes tumours with “any small-cell component” in the category of non-urothelial cell carcinoma. The diagnosis is defined by morphologic criteria but most cases do demonstrate evidence of neuroendocrine differentiation by immunohistochemistry. The most sensitive immunohistochemical markers are CD56 and synaptophysin. TTF-1 is expressed in about 50% of cases. In cases with pure small cell morphology the possibility of direct spread from an adjacent organ or metastasis must be excluded clinically.

Lastly there are carcinomas arising in the urinary bladder that have no specific differentiation and based on exclusion of metastasis from another site are considered to be primary in the urinary tract. In the 2004 WHO classification these were included as a variant of urothelial carcinoma but given that by definition they have no urothelial differentiation these should be reported using the “carcinoma, type cannot be determined” category.

**Histologic subtype/variant**

The 2016 WHO classification includes a number of recognised morphologic variants as outlined in the table below. Because urothelial carcinoma has a remarkable capacity for morphologic variation the number of histologic variants that have been described in the literature is extensive. In the development of the 2016 WHO classification not all of these are included. In general the variants that have been
specifically recognised fall into three broad categories. Variants that have a deceptively bland morphology, such as the nested variant, could be misdiagnosed as benign or considered low grade although their behaviour is the same as for high grade tumours. In the second category are tumours that have a morphology that mimics other tumours. Lastly are those tumours that have important prognostic or therapeutic implications.

The importance of variant histology in clinical management decisions has been receiving increasing clinical attention. Some variants have been highlighted because of the high frequency of under staging when present in biopsy or TURBT specimens. There are an increasing number of therapeutic algorithms that incorporate variant histology as a significant factor. For T1 urothelial carcinoma, the presence of variant histology is one feature that is used in determining whether to consider immediate cystectomy.

The level of evidence for specific variants having independent prognostic information varies from the variant having no clinical significance but being important diagnostically (e.g. nested, microcystic, etc), to no data, to data indicating the variant has prognostic significance (e.g. micropapillary, plasmacytoid, sarcomatoid). Rather than making reporting of specific subtypes that have some supporting data mandatory and others lacking data recommended it is considered best to make the entire category a required element.

Reporting the percentage of variant histology when present is recommended (this is recommended in the WHO 2016 monograph). The data supporting this is very limited and only available for selected variants (micropapillary, sarcomatoid, lymphoepithelioma-like), with divergent differentiation (glandular, squamous). There is also insufficient data available for setting specific amounts of each specific variant in order for it to be clinically significant. Given the lack of data, if variant histology is identified, it should be reported and the estimated percentage of the tumour it makes up reported. For cases with more than one variant present, the percentage of each is recommended to be documented.

**CS3.01b** The classification of tumours is from the WHO 2016 classification (refer to Appendix 4).

**S3.02** The presence of non-invasive carcinoma must be reported.

**CS3.02a** The majority of patients with urothelial carcinoma present initially with non-invasive disease. Most of
these have a non-invasive papillary tumour and much less frequently have urothelial CIS as the initial diagnosis. Non-invasive papillary tumours account for 70% to 75% of newly diagnosed cases with over one-half being in the lower grade categories (papillary urothelial neoplasm of low malignant potential, low grade papillary carcinoma). Urothelial CIS in its pure form counts for 1% to 3% of newly diagnosed urothelial tumours and is by definition high grade. Much more often it coexists with high grade papillary urothelial carcinoma and is found in association with invasive urothelial carcinoma in up to 65% of cases. Papillary tumours range from benign (papilloma, papillary urothelial neoplasm of low malignant potential) to low and high grade carcinomas. CIS and papillary carcinoma develop by different genetic pathways and have different biologic behaviour and so are considered as different entities within the non-invasive category.

Classification of non-invasive urothelial tumours into the papillary and in situ categories has both prognostic and management implications. Further the identification of CIS coexisting with papillary carcinoma also has significance for prognosis and treatment. In biopsy and TURBT specimens both diagnoses can be rendered when the papillary carcinoma and the CIS are present on different tissue fragments or in specimens submitted from different sites. When flat lesion is present adjacent to and in continuity with a papillary tumour the question becomes whether the flat part represents a “shoulder” of the papillary tumour or coexisting CIS. There are no generally accepted criteria for making this decision even though the diagnosis does have clinical significance. We would recommend making the diagnosis of associated CIS in this situation if (i) there is a gap of normal urothelium between the papillary tumour and the flat lesion or (ii) if the morphology of the flat lesion is different than that of the epithelium on the surface of papillary fronds.

For patients presenting with invasive urothelial carcinoma the recognition and documentation of an associated non-invasive papillary carcinoma and/or CIS remains important. For patients with T1 disease the presence of CIS indicates a significantly increased risk of subsequent recurrence and of progression to muscle invasive disease. For patients with CIS of the bladder unresponsive to BCG therapy this is an indication for early cystectomy. The presence of associated CIS in newly diagnosed high grade T1 disease may also be used to support early cystectomy. For patients presenting with invasive urothelial carcinoma there are data that such cases arising through the “papillary” pathway have stage for stage a better prognosis that those developing via the “flat” pathway.
There is also evidence that the extensiveness of the CIS is significant and so distinguishing between a single focus and diffuse (or multifocal) disease is important. For the purpose of this dataset, diffuse is defined as the presence of CIS in more than one site as indicated by biopsies submitted separately or involving more than one tissue fragment in a TURBT specimen.

Lastly non-urothelial CIS can also occur in the urinary tract. Most frequently this is squamous cell CIS typically in association with keratinizing squamous metaplasia. This can be identified in patients with invasive squamous cell carcinoma but also can be diagnosed in the absence of invasive disease. Adenocarcinoma in situ is not a well-defined lesion in the urinary tract. In cases of intestinal metaplasia varying degrees of atypia can be seen up to high grade dysplasia, a term we would prefer rather than adenocarcinoma in situ. Urothelial CIS can show areas of squamous and glandular differentiation and these should not be diagnosed as squamous or adenocarcinoma in situ respectively.

<table>
<thead>
<tr>
<th>CS3.02b</th>
<th>The extent of bladder CIS may have an impact on the risk of upper tract recurrence.55</th>
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<tr>
<th>G3.01</th>
<th>The presence of associated epithelial lesions should be reported.</th>
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<tr>
<td>CG3.01a</td>
<td>A variety of neoplastic lesions that fall short of carcinoma are recognised in the urinary tract. These include papillary lesions such as urothelial papilloma, papillary urothelial neoplasm of low malignant potential and inverted urothelial papilloma. Similarly flat lesions such as urothelial dysplasia, keratinizing squamous metaplasia with dysplasia and intestinal metaplasia with dysplasia can be seen. Identification of these may have diagnostic implications (e.g. the presence of keratinizing squamous metaplasia with dysplasia supporting the diagnosis of primary squamous cell carcinoma) but do not have known proven prognostic or clinical significance otherwise. While for completeness it may be useful to report such findings, it is not considered to be a required element in the context of a carcinoma diagnosis.</td>
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<tr>
<th>S3.03</th>
<th>The histological grade must be reported.</th>
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<tr>
<td>CS3.03a</td>
<td>Histologic grading of urothelial tumours is best considered in two categories, non-invasive papillary tumours and invasive carcinoma. For non-invasive papillary tumours the 2016 WHO remains the same as in the 2004 WHO and continues to recommend the grading system first put forward by the International Society of Urological Pathology (ISUP) in 1997.56 The</td>
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55. The extent of bladder CIS may have an impact on the risk of upper tract recurrence.

56. Histologic grading of urothelial tumours is best considered in two categories, non-invasive papillary tumours and invasive carcinoma. For non-invasive papillary tumours the 2016 WHO remains the same as in the 2004 WHO and continues to recommend the grading system first put forward by the International Society of Urological Pathology (ISUP) in 1997.
system is now recommended by almost all major pathology and urology organisations as the preferred grading system.\textsuperscript{41,57}

Papillary urothelial neoplasm of low malignant potential is not reported using this dataset. It is nonetheless a significant diagnosis and does indicate an increased risk for the development of other neoplasms in the urinary tract. In one large study that included 1,006 non-invasive papillary tumours (papillary urothelial neoplasm of low malignant potential, 212 [21%]; low grade papillary carcinoma, 603 [60%]; high grade papillary carcinoma, 191 [19%]), treated by TUR with or without intravesical therapy, recurrence occurred in 18%, 35% and 34% of each respectively and progression in 2%, 7% and 29% respectively.\textsuperscript{58} The majority of studies have had similar results with no or minimal risk of progression in grade or stage for papillary urothelial neoplasm of low malignant potential.\textsuperscript{58-61}

There are significant differences in the risk of progression to invasive carcinoma and death from bladder cancer between low and high grade papillary urothelial carcinoma.\textsuperscript{58,62,63} The grade of non-invasive papillary carcinoma is the major variable in the choice of therapy in these patients.\textsuperscript{43} Other features of importance in predicting outcome of patients with Ta papillary tumours are number of tumours/multifocality,\textsuperscript{63-66} tumour size,\textsuperscript{63,67-69} the presence of associated CIS,\textsuperscript{63} and a history of prior recurrence.\textsuperscript{63} It has also been suggested that for low grade papillary tumours the frequency of follow up cystoscopies can be reduced.\textsuperscript{70}

Grade heterogeneity is not uncommon in papillary urothelial carcinoma being reported in up to 32% of cases.\textsuperscript{71,72} It is currently recommended that tumour grade be assigned based on the highest grade present. Some authors have recommended considering a tumour low grade if the high grade component accounts for less than 5% of the tumour volume.\textsuperscript{71,73} The 2016 WHO recommends grading based on the highest grade component and acknowledges the uncertainty of how to approach cases with a small proportion of high grade tumour. It does indicate that "it may be prudent to state the proportion of high-grade disease."

The use of the 1973 WHO grading system for papillary tumours remains in use in many regions and some published guidelines specifically recommend the reporting of both the current WHO grade with the 1973 grade,\textsuperscript{43,74,75} while others provide for the 1973 to be provided by institutional choice.\textsuperscript{13,41,57}

The grading of invasive urothelial carcinoma is another
area of controversy. In North America the vast majority of invasive urothelial carcinomas have been diagnosed as high grade in contrast to European studies where a substantial percentage of invasive tumours have been graded as 2 or even 1. Currently there is general agreement that grade 1 tumours (WHO 1973), largely corresponding to papillary urothelial neoplasm of low malignant potential, lack the capacity to invade.\textsuperscript{76-78} In studies using the 1998 ISUP/WHO 2004 grading system the vast majority of invasive tumours are high grade.\textsuperscript{79,80} The 2016 WHO recommends continuing to grade invasive carcinoma using the WHO 2004 system recognising that the vast majority of tumours will be high grade.\textsuperscript{13} If invasive tumours are graded using an alternative grading system this should be indicated.

For further information refer to the ICCR dataset.\textsuperscript{81}

CS3.03b Squamous cell carcinoma is graded using criteria used for these tumours in other viscera.\textsuperscript{82} Invasive SCC may be well differentiated with well defined nests of squamous cells with prominent keratinisation, intercellular bridges and minimal nuclear pleomorphism, moderately differentiated with more cellular atypia, minimal keratinisation but with obvious squamous features or poorly differentiated with marked nuclear pleomorphism and only focal evidence of squamous differentiation.

CS3.03c There is no generally accepted grading system for adenocarcinoma of the bladder.\textsuperscript{9}

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<th>S3.04</th>
<th>The status of the muscularis propria must be reported.</th>
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<tr>
<td>CS3.04a</td>
<td>The presence or absence of muscularis propria is a vital piece of information in determining the adequacy of a biopsy or TUR specimen that contains an invasive carcinoma.\textsuperscript{41,43,74} For such patients, the absence of muscularis propria in a TURBT would be an indication for a repeat TUR to be performed if treatment is other than cystectomy. It is well documented that absence of muscularis propria in a TURBT specimen is associated with a significantly increased risk of residual disease and early recurrence.\textsuperscript{83} The current European Association of Urology (EAU) guidelines recommend repeat TUR (i) after an incomplete initial TUR, (ii) if there is no muscle in the specimen after initial resection with the exception of Ta, LG/G1 tumours and primary CIS, (iii) in all T1 tumours and (iv) in all HG/G3 tumours except primary CIS.\textsuperscript{43} It generally is also considered appropriate to comment on the presence or absence of muscularis propria in a biopsy or TUR specimen, irrespective of the presence or absence of invasive carcinoma.</td>
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### S3.05

**The microscopic extent of invasion must be given.**

| CS3.05a | Reporting the extent of invasion is a critical part of the assessment of carcinomas arising in the urinary tract. The elements included reflect the anatomic landmarks that are essential to the pathologic staging of each tumour and vary by site within the urinary tract.\(^{84}\) It is not appropriate to assign pathologic stage on biopsy or TUR specimens and pathologic stage is not an element within this dataset. It is however possible, based on the assessment of the extent of invasion to recognize the least pathological stage possible in a given case.

The diagnosis of invasion can be challenging. Throughout the urothelial tract histologic features that are indicative of stromal invasion include individual tumour cells, irregular nests or cords of cells, retraction artefact around nests, increased cytoplasmic eosinophilia and a myxoid or desmoplastic stromal response.\(^{85,86}\) Several studies have documented the difficulty with the diagnosis of invasion.\(^{87-89}\) Two large studies based on central review of patients being entered on clinical trials have demonstrated the over diagnosis of invasion in 35% to 53% of cases.\(^{90,91}\) Studies have also demonstrated lack of agreement among pathologists with special interest in urologic pathology.\(^{92}\) In some cases immunohistochemistry with a pan cytokeratin marker is helpful in identifying individual cells particularly when there is a heavy inflammatory infiltrate present. Following the principles of the AJCC-TNM staging system the diagnosis of invasion should be limited to cases with unequivocal invasion.\(^{84}\)

Identification of invasion of smooth muscle fibres in specimens from the renal pelvis, ureter and urethra all indicate T2 disease. In the urinary bladder the presence of the muscularis mucosae complicates the interpretation as involvement of these fibres still represents a T1 tumour.\(^{93}\) Muscularis mucosae fibres can be present throughout the bladder.\(^{12}\) The trigone/bladder neck region least often has recognisable muscularis mucosae fibres and from a practical perspective involvement of smooth muscle in this location essentially always indicates muscularis propria invasion. Muscularis mucosae fibres are typically thin and wispy forming small bundles that taper at the ends and usually are only a few cells thick. They lack the dense eosinophilic cytoplasm characteristic of muscularis propria. Often the fibres are seen in association with a layer of thick walled blood vessels. The muscularis mucosae can however occasionally be thickened and better defined, more closely mimicking muscularis propria. Smoothelin, a cytoskeletal protein is differentially expressed in the muscularis propria and not the muscularis mucosae.\(^{94}\)
Application in challenging cases can be helpful but for the most part the marker has not gained widespread application. Regarding the use of smoothelin for staging, the ISUP states "limited experience and conflicting data preclude smoothelin or vimentin to be recommended routinely for subclassifying muscle type at this time." In some cases it is not possible to be certain if the smooth muscle involvement represents muscularis mucosae or muscularis propria. In those cases this should be specifically commented upon. Repeat TUR on these cases is necessary to determine the true depth of involvement.

Assessment of the presence or absence of muscularis propria invasion can also be hampered by cautery artefact. This can result in stromal changes that mimic smooth muscle leading to over staging or make muscularis propria unrecognisable leading to under staging. Pathologists have used histochemistry (trichrome stain) or immunohistochemistry (desmin) to help determine if muscle is represented in cauterized tissue but no controlled studies of the reliability of these approaches is available.

Urothelial carcinoma can be primary in the prostatic urethra but in the majority of cases involvement is seen in association with a bladder tumour. Among all male patients with bladder cancer the prostate is involved in approximately 4% of cases. Prostatic involvement is found in 15% to 48% of patients undergoing cystoprostatectomy for urothelial carcinoma of the bladder. Involvement is usually by urothelial CIS but occasionally papillary tumours are seen. Extension into the prostatic ducts is frequently present in these cases and should not be mistaken for invasion. Inflammation can be present around the ducts in the absence of invasion. Usually invasion of the subepithelial connective tissue or the prostatic stroma elicits a desmoplastic response. Immunohistochemistry is frequently required to distinguish urothelial carcinoma from high grade prostatic carcinoma. Glandular and or squamous differentiation can be present as with urothelial carcinoma elsewhere.

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<tr>
<th>G3.02</th>
<th>The substaging of T1 disease should be reported.</th>
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<tr>
<td>CG3.02a</td>
<td>There have been many efforts to establish the optimum method of identifying T1 tumours with low and high risk for recurrence, progression and death from bladder cancer. One focus of many of these reports has been to &quot;substage&quot; T1 tumours. Recent guidelines have generally recommended that pathologists provide some indication of volume or depth of invasion without specifying a preferred method. In the ICUD recommendations for</td>
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quantitation, Amin et al stated “It is recommended that pathologists provide some form of estimate of the LP invasion in pT1 tumours (e.g. focal, multifocal, extensive, etc)” and “Involvement of the MM may be included in a comment to provide information on the depth/extent of invasion.” The 2016 WHO follows this recommendation as do the recently released College of American Pathologists reporting guidelines.\textsuperscript{13,57}

Clinical guidelines have also noted the importance of depth of invasion. In the ICUD section on treatment of high grade Ta, CIS and T1 urothelial carcinoma, the author’s first recommendation is “The assessment of T1 urothelial carcinoma should be based on tumour grade, early recurrence, multiplicity, tumour size, concomitant CIS, urothelial carcinoma involving the prostatic mucosa or ducts, and depth of invasion.”\textsuperscript{105}

Because of the potential for additional information in T1 tumours to directly impact clinical decision making the ICCR guidelines have included substaging of TI disease as a non-required element. The dataset also provides for alternative methods for reporting as there is insufficient data to recommend one alternative over the others.

For further information refer to the ICCR dataset.\textsuperscript{81}

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<th>S3.06</th>
<th>The presence or absence of lymphovascular invasion (LVI) must be recorded.</th>
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| CS3.06a | The data on lymphovascular invasion (LVI) in urothelial carcinoma in the urinary bladder has continued to grow with many large series now reported.\textsuperscript{106-110} These have included very large multi-institutional series (e.g. Kluth et al\textsuperscript{109} – 8102 patients), cases from phase 3 clinical trials (von Rundstedt et al\textsuperscript{110} – SWOG4B951/NCT00005047) and in the generation of prognostic scores (Eisenberg et al\textsuperscript{108} – SPARC Score) all of which have found LVI to be a highly significant predictor of outcome.  

Studies that have evaluated the significance of LVI on biopsy or TURBT material specifically are much more limited.\textsuperscript{111-121} These have almost all been based on H&E evaluation with limited utilisation of immunohistochemistry. The frequency of identification of LVI has ranged from <10% to as high as 67%. Among the better studies are the paper by Olsson et al (2013) which is population based [all newly diagnosed T1 tumours (N=211)] in the Southeastern region of Sweden with relatively uniform treatment.\textsuperscript{121} These authors identified LVI in 8% of cases and also included an indeterminate category (22% of cases).\textsuperscript{121} The presence of LVI was an independent predictor of recurrence free-, progression free- and cancer specific
survival.\textsuperscript{121} The prospective study by Orsola \textit{et al} (2005) in contrast found no significant association with progression-free or cancer specific survival.\textsuperscript{122} This study is limited by the short follow up. Overall the majority of these studies have found LVI to be important but, as indicated, data is limited.

Specific data on LVI determination in biopsy/TUR specimens of upper tract and urethra are not available. There are several reports that have found LVI to be significant (various endpoints) in resection specimens for upper tract urothelial carcinoma.\textsuperscript{123-126} These large, contemporary series have consistently identified LVI as a significant parameter in upper tract urinary cancer. For example, the study by Cha \textit{et al} (2012) was a multi-institutional retrospective analysis of 2244 patients treated by radical nephroureterectomy.\textsuperscript{123} The cases were divided into a development and an external validation cohort. LVI (based on the pathology reports) was an independent predictor of recurrence free survival and cancer specific survival in both cohorts and was included in the 2-year and 5-year recurrence-free and cancer-specific survival nomograms.\textsuperscript{123}

For urethral carcinoma there is no substantive literature available. In the 2013 Guidelines on Urethral Carcinoma by the EAU, LVI is not recognised as a prognostic indicator.\textsuperscript{127}

The role of immunohistochemistry in determining the presence or absence of LVI has been limited. The problem with recognising LVI on H&E sections has been demonstrated for urothelial carcinoma. Algaba\textsuperscript{128} and Lopez-Beltran\textsuperscript{74} among others have pointed out the importance of utilising strict criteria and these should be followed. Criteria recommended by Algaba (2006) included tightly cohesive tumour cells with a smooth border and the cells at the periphery having a shell-like appearance, the tumour thrombus floating free in the lumen of a space with an unequivocal endothelial cell lining, the presence of fibrin and/or red blood cells around the thrombus, and the space preferably associated with an arteriole with the surrounding stroma appearing normal.\textsuperscript{128}

The possibility of routinely performing immunohistochemistry on T1 cases is much discussed but with little data.\textsuperscript{113,111} The general use of immunohistochemistry in the routine setting cannot be recommended since performing immunohistochemical stains on even selected paraffin blocks with bladder cancer would be extremely time consuming and cost intensive.\textsuperscript{129}

Although the data on LVI in biopsy/TUR specimens is limited, the compelling evidence in large resection studies of urothelial carcinoma of the urinary bladder
and upper tract support inclusion as a required element in this dataset.

For further information refer to the ICCR dataset.\textsuperscript{81}

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<tr>
<th>CS3.06b</th>
<th>Criteria used in other locations also apply here.</th>
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<tr>
<th>G3.03</th>
<th>Any coexistent pathology should be recorded.</th>
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<tr>
<td>CG3.03a</td>
<td>Biopsy and endoscopic resection specimens from throughout the urinary tract that are diagnosed with carcinoma can also show a number of non-neoplastic conditions. Although some findings such as keratinizing squamous metaplasia and diffuse intestinal metaplasia may be relevant in a specific case the reporting of these findings does not have sufficient significance to be considered a required element.</td>
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| G3.04       | Any additional relevant microscopic comments should be recorded. |
4 Ancillary studies findings

Ancillary studies may be used to determine lineage, clonality or disease classification or subclassification; as prognostic biomarkers; or to indicate the likelihood of patient response to specific biologic therapies.

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<tr>
<td><strong>G4.01</strong></td>
<td>Whether or not ancillary tests are performed should be recorded and the results incorporated into the pathology report.</td>
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<tr>
<td><strong>CG4.01a</strong></td>
<td>Currently there are no ancillary studies that are recommended for routine use in urothelial carcinoma of the urinary tract. If immunohistochemical studies are performed for differential diagnosis or to assist in staging or the detection of LVI they could be listed in this section. If ancillary studies are performed at the request of the clinician or in following an institutional policy or for any other reason, these should be included in the report.</td>
</tr>
<tr>
<td><strong>CG4.01b</strong></td>
<td>While most bladder tumours can be identified on histological examination, some difficulties may be encountered in differentiating some subtypes of urothelial carcinoma from metastatic malignancy. A variety of studies has investigated the utility of immunohistochemistry in distinguishing between tumour types and may be helpful in some cases.</td>
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5 Synthesis and overview

Information that is synthesised from multiple modalities and therefore cannot reside solely in any one of the preceding chapters is described here. For example, tumour stage is synthesised from multiple classes of information – clinical, macroscopic and microscopic.

By definition, synthetic elements are inferential rather than observational, often representing high-level information that is likely to form part of the report ‘Summary’ or ‘Diagnosis’ section in the final formatted report.

Overarching case comment is synthesis in narrative format. Although it may not necessarily be required in any given report, the provision of the facility for overarching commentary in a cancer report is essential.

G5.01 The “Diagnostic summary” section of the final formatted report should include:

a. Tumour type with different subtypes specified
b. Tumour grade
c. Tumour extent (Level of invasion)
d. Lymphovascular invasion
e. Presence of non-invasive carcinoma

S5.01 The reporting system must provide a field for free text or narrative in which the reporting pathologist can give overarching case comment.

CS5.01a This field may be used, for example, to:

• document any noteworthy adverse gross and/or histological features
• explain any elements of clinicopathological ambiguity
• express any diagnostic subtlety or nuance that is beyond synoptic capture
• document further consultation or results still pending.

CS5.01b Use of this field is at the discretion of the reporting pathologist.

G5.02 The edition/version number of the RCPA protocol on which the report is based should be included on the final report.
For example, the pathology report may include the following wording at the end of the report: “the data fields within this formatted report are aligned with the criteria as set out in the RCPA document “ XXXXXXXXXXX” XXXX Edition dated XXXXXXXX”.
6 Structured checklist

The following checklist includes the standards and guidelines for this protocol which must be considered when reporting, in the simplest possible form. The summation of all “Standards” is equivalent to the “Minimum Data Set” for bladder cancers. For emphasis, standards (mandatory elements) are formatted in bold font.

S6.01 The structured checklist provided below may be modified as required but with the following restrictions:

a. All standards and their respective naming conventions, definitions and value lists must be adhered to.

b. Guidelines are not mandatory but are recommendations and where used, must follow the naming conventions, definitions and value lists given in the protocol.

G6.01 The order of information and design of the checklist may be varied according to the laboratory information system (LIS) capabilities and as described in Functional Requirements for Structured Pathology Reporting of Cancer Protocols.

CG6.01a Where the LIS allows dissociation between data entry and report format, the structured checklist is usually best formatted to follow pathologist workflow. In this situation, the elements of synthesis or conclusions are necessarily at the end. The report format is then optimised independently by the LIS.

CG6.01b Where the LIS does not allow dissociation between data entry and report format, (for example where only a single text field is provided for the report), pathologists may elect to create a checklist in the format of the final report. In this situation, communication with the clinician takes precedence and the checklist design is according to principles given in Chapter 7.

G6.02 Where the checklist is used as a report template (see G6.01), the principles in Chapter 7 and Appendix 2 apply.

CG6.02a All extraneous information, tick boxes and unused values should be deleted.

G6.03 Additional comment may be added to an individual response where necessary to describe any uncertainty or nuance in the selection of a prescribed response in the checklist. Additional comment is not required where the prescribed response is adequate.
Values in italics are conditional on previous responses.

Values in all caps are headings with sub values.

<table>
<thead>
<tr>
<th>S/G</th>
<th>Item description</th>
<th>Response type</th>
<th>Conditional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-analytical</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S1.01</td>
<td>Demographic information provided</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S1.02</td>
<td>Clinical information provided on request form</td>
<td>Text OR Structured entry as below:</td>
<td></td>
</tr>
</tbody>
</table>

**CLINICAL INFORMATION**

- Previous history of urinary tract disease or distant metastasis
  - Single selection value list:
    - Information not provided
    - No previous history
  - OR
  - Text, *provide details including site(s)*

- Previous therapy
  - Single selection value list:
    - Information not provided
    - No previous therapy
  - OR
<table>
<thead>
<tr>
<th>Text, provide type of therapy if present, if applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystoscopic appearance</td>
</tr>
<tr>
<td><strong>Single selection value list:</strong></td>
</tr>
<tr>
<td>• Information not provided</td>
</tr>
<tr>
<td>• Normal</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td><strong>Multi select value list (select all that apply):</strong></td>
</tr>
<tr>
<td>• Papillary</td>
</tr>
<tr>
<td>• Polypoid</td>
</tr>
<tr>
<td>• Red (erythematous) area</td>
</tr>
<tr>
<td>• Other, specify</td>
</tr>
<tr>
<td>Other clinical information</td>
</tr>
<tr>
<td>Text</td>
</tr>
<tr>
<td>Clinical extent of disease</td>
</tr>
<tr>
<td>Text</td>
</tr>
<tr>
<td><strong>Operative procedure</strong></td>
</tr>
<tr>
<td><strong>Single selection value list:</strong></td>
</tr>
<tr>
<td>• Not specified</td>
</tr>
<tr>
<td>• Transurethral resection</td>
</tr>
<tr>
<td>• Biopsy</td>
</tr>
<tr>
<td>• Other, specify</td>
</tr>
<tr>
<td><strong>Site(s) sampled</strong></td>
</tr>
<tr>
<td><strong>Single selection value list:</strong></td>
</tr>
<tr>
<td>• Not specified</td>
</tr>
<tr>
<td>• Renal pelvis</td>
</tr>
</tbody>
</table>
| Field | Description | Value

S1.03 | Pathology accession number | Alpha-numeric

S1.04 | Principal clinician caring for the patient | Text

G1.01 | Other clinical information received | Text

## Macroscopic findings

| Field | Description | Value |

S2.01 | Specimen labelled as | Text

S2.02 | Operative procedure | Single selection value list:
- Not specified
- Transurethral resection (TUR)
- Biopsy
- Other, specify

*If biopsy, record the number of pieces submitted S2.04.
If TUR, record size per S2.05

S2.03 | Specimen site | Single selection value list:
- Renal pelvis
- Ureter
- Bladder, specify site/s
| S2.04 | Number of pieces submitted (Applicable to biopsies only) | Numeric: ____ |
| S2.05 | TUR size | Numeric: ____g OR Numeric: ____mm |
| S2.06 | Block identification key | Text |
| G2.01 | Other macroscopic comment | Text |

**Microscopic findings**

<table>
<thead>
<tr>
<th>S3.01</th>
<th>Histological tumour type</th>
<th>Single selection value list:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>- Urothelial carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Squamous cell carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Adenocarcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Neuroendocrine tumour</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Small cell neuroendocrine carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If urothelial carcinoma, record the Histological sub-type/variant</td>
</tr>
</tbody>
</table>
- Large cell neuroendocrine carcinoma
- Tumours of Müllerian type
  - Clear cell carcinoma
  - Endometrioid carcinoma
- Other, specify

<table>
<thead>
<tr>
<th>Histological subtype(s)/variant(s) (urothelial carcinoma)</th>
<th>Single selection value list:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Not identified</td>
</tr>
<tr>
<td></td>
<td>• Present</td>
</tr>
</tbody>
</table>

If present, record subtype/variant and estimated % for each applicable variant

<table>
<thead>
<tr>
<th>Sub-type/variant</th>
<th>Multi select value list (select all that apply):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Squamous</td>
</tr>
<tr>
<td></td>
<td>• Glandular</td>
</tr>
<tr>
<td></td>
<td>• Nested</td>
</tr>
<tr>
<td></td>
<td>• Micropapillary</td>
</tr>
<tr>
<td></td>
<td>• Plasmacytoid</td>
</tr>
<tr>
<td></td>
<td>• Sarcomatoid</td>
</tr>
<tr>
<td></td>
<td>• Other, specify</td>
</tr>
</tbody>
</table>

| Percentage       | Numeric: ____%                                    |

<table>
<thead>
<tr>
<th>Non-invasive carcinoma</th>
<th>Single selection value list:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Not identified</td>
</tr>
<tr>
<td></td>
<td>• Indeterminate</td>
</tr>
</tbody>
</table>

OR
<table>
<thead>
<tr>
<th></th>
<th>Multi select value list (select all that apply):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>▪ Carcinoma <em>in situ</em>, flat</td>
</tr>
<tr>
<td></td>
<td>□ Multifocal</td>
</tr>
<tr>
<td></td>
<td>□ Focal</td>
</tr>
<tr>
<td></td>
<td>▪ Papillary carcinoma, non-invasive</td>
</tr>
<tr>
<td></td>
<td>□ Other, <em>specify</em></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>G3.01</th>
<th>Associated epithelial lesions</th>
<th>Single selection value list:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>□ Not identified</td>
<td></td>
</tr>
<tr>
<td></td>
<td>□ Present, <em>specify</em></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>S3.03</th>
<th>Histological grade</th>
<th>Single selection value list:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>□ Not applicable</td>
<td></td>
</tr>
<tr>
<td></td>
<td>□ Cannot be determined</td>
<td></td>
</tr>
</tbody>
</table>

**Urothelial carcinoma**
- □ Low-grade
- □ High-grade
- □ Other, *specify*

**Squamous cell carcinoma or adenocarcinoma**
- □ GX: Cannot be assessed
- □ G1: Well differentiated
- □ G2: Moderately differentiated
- □ G3: Poorly differentiated
- □ Other, *specify*
<table>
<thead>
<tr>
<th>S3.04</th>
<th>Status of muscularis propria</th>
<th>Single selection value list:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not present/submitted</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>S3.05</th>
<th>Extent of invasion</th>
<th>Single selection value list:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cannot be assessed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Papillary carcinoma, non-invasive</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Urothelial carcinoma <em>in situ</em>, flat</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tumour invades subepithelial connective tissue (lamina propria)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tumour invades muscularis propria (detrusor muscle)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tumour involving prostatic urethra</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tumour involving prostatic ducts and acini</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tumour invasive into prostatic stroma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tumour invasive into renal stroma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tumour invasive into periurethral muscle</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tumour invasive into corpus spongiosum</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tumour invasive into corpus cavernosum</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other, specify</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>G3.02</th>
<th>Substaging T1 disease</th>
<th>Single selection value list:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Invasion superficial to muscularis mucosae</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Invasion involving and/or deep to muscularis mucosae</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Lymphovascular invasion</strong></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th></th>
<th><strong>Coexistent pathology</strong></th>
<th><strong>Single selection value list:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>• None identified</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Present, <em>specify</em></td>
</tr>
</tbody>
</table>

|   |   | **Other microscopic comment** | **Text** |
|   |   |   |   |

**Ancillary test findings**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th><strong>Ancillary studies</strong></th>
<th><strong>Single selection</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Not performed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Performed, <em>specify</em></td>
</tr>
</tbody>
</table>

**Synthesis and overview**
<table>
<thead>
<tr>
<th><strong>G5.01</strong></th>
<th>Diagnostic summary</th>
<th><strong>Text</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Include:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a. Tumour type with different subtypes specified</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. Tumour grade</td>
<td></td>
</tr>
<tr>
<td></td>
<td>c. Tumour extent (Level of invasion)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>d. Lymphovasular invasion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>e. Presence of non-invasive carcinoma</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>S5.01</strong></th>
<th><strong>Overarching comment</strong></th>
<th><strong>Text</strong></th>
</tr>
</thead>
</table>

| **G5.02** | Edition/version number of the RCPA protocol on which the report is based | **Text** |
7 Formatting of pathology reports

Good formatting of the pathology report is essential for optimising communication with the clinician, and will be an important contributor to the success of cancer reporting protocols. The report should be formatted to provide information clearly and unambiguously to the treating doctors, and should be organised with their use of the report in mind. In this sense, the report differs from the structured checklist, which is organised with the pathologists’ workflow as a priority.

Uniformity in the format as well as in the data items of cancer reports between laboratories makes it easier for treating doctors to understand the reports; it is therefore seen as an important element of the systematic reporting of cancer. For guidance on formatting pathology reports, please refer to Appendix 2.
Appendix 1  Pathology request information and surgical handling procedures

This appendix describes the information that should be collected before the pathology test. Some of this information can be provided on generic pathology request forms; any additional information required specifically for the reporting of carcinoma of the renal pelvis and ureter may be provided by the clinician on a separate request information sheet. An example request information sheet is included below. Elements which are in bold text are those which pathologists consider to be required information. Those in non-bold text are recommended.

Also included in this appendix are the procedures that are recommended before handover of specimens to the laboratory.

Patient information

➢ Adequate demographic and request information should be provided with the specimen.
  
  ▪ Items relevant to cancer reporting protocols include:
    i  patient name
    ii  date of birth
    iii  sex
    iv  identification and contact details of requesting doctor
    v  date of request
  
  ▪ Whether or not the patient identifies as Aboriginal and/ or Torres Strait Islander. This is in support of a government initiative to monitor the health of indigenous Australians particularly in relation to cancer.

➢ The patient’s health identifiers should be provided.
  
  ▪ The patient’s health identifiers may include the patient’s Medical Record Number as well as a national health number such as a patient’s Individual Healthcare Identifier (IHI) (Australia) or the National Healthcare Identifier (New Zealand).

➢ The Australian Healthcare identifiers i.e. Healthcare Provider Identifier - Individual (HPI-I) and Healthcare Provider Identifier - Organisation (HPI-O) should be use, where possible, to identify the requesting doctor.
### Clinical Information

<table>
<thead>
<tr>
<th>Clinical information should be recorded.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Knowledge of any relevant history is critical in the accurate diagnosis of tumours throughout the urinary tract.(^{41,57,131,132}) This may be relevant to the specific diagnosis being entertained. This is a recommended rather than a required item as it is the responsibility of the clinician requesting the pathological examination of a specimen to provide information that will have an impact on the diagnostic process or affect its interpretation. Patients with a history of urothelial neoplasia are at risk for urothelial tumours throughout the urinary tract and this may inform the interpretation in subsequent specimens. Urothelial tumours in the urinary bladder and upper tract may have been treated with therapies such as Bacillus Calmette-Guerin (BCG), mitomycin C and others. These can be associated with morphologic changes that have the potential for misdiagnosis if the pathologist is unaware of the prior treatment.(^{133,134}) Radiation therapy (to the bladder or to adjacent organs) can be associated with pseudocarcinomatous hyperplasia that can be misdiagnosed as invasive carcinoma.(^{135,136}) Nephrogenic adenoma can be seen following biopsy or TUR and can mimic recurrent tumour clinically and pathologically.(^{137,138}) Knowledge of the cystoscopic appearance can also be helpful in some cases.(^{131,132}) For example, when evaluating a biopsy for the presence or absence of papillary neoplasia, knowledge of the cystoscopic finding of a papillary lesion can inform the interpretation. Finally knowledge of a history of carcinoma elsewhere such as prostatic adenocarcinoma, colorectal adenocarcinoma, cervical squamous cell carcinoma, and others can greatly assist in the interpretation of biopsy/TUR specimens in the right circumstances.</td>
</tr>
</tbody>
</table>

| Relevant past medical history, family history and known risk factors associated with bladder cancers should be provided. The past history of urothelial neoplasms elsewhere in the urinary tract should be recorded. |

<table>
<thead>
<tr>
<th>Previous history of bladder disease may include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Superficial bladder disease</td>
</tr>
<tr>
<td>• Muscle invasive disease.</td>
</tr>
</tbody>
</table>

| Distant metastasis refers to the spread of cancer of the same histologic type as the original (primary) tumour to distant organs or distant lymph nodes. |

| This information will provide an opportunity for previous reports to be reviewed during the reporting process, which may provide valuable information to the pathologist. This information also has implications for recording cancer incidence and evidence based research. |

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50
• Previous chemotherapy may cause extensive or complete tumour necrosis. This must be taken into account by the reporting pathologist.

• Chemotherapy or radiation therapy induced changes may simulate malignancy. For example, radiation therapy or chemotherapy can produce pseudo-carcinomatous urothelial proliferation mimicking invasive urothelial or squamous cell carcinoma\textsuperscript{139} or CIS-like changes.\textsuperscript{140}

➢ Information regarding the extent of disease as determined from clinical assessment, cystoscopy, prior histology and imaging should be provided.

➢ Relevant information regarding the extent of disease, particularly biopsy positivity gives extra information that is useful for adequately sampling for accurate staging. For example, the principal tumour may not be the most invasive. There may be non-papillary tumours that are deeply invasive.

➢ The operative procedure and nature of specimen(s) sampled should be stated.
The above Request Information Sheet is published to the RCPA website.
Appendix 2  Guidelines for formatting of a pathology report

Layout

Headings and spaces should be used to indicate subsections of the report, and heading hierarchies should be used where the LIS allows it. Heading hierarchies may be defined by a combination of case, font size, style and, if necessary, indentation.

- Grouping like data elements under headings and using ‘white space’ assists in rapid transfer of information.\(^\text{141}\)

Descriptive titles and headings should be consistent across the protocol, checklist and report.

When reporting on different tumour types, similar layout of headings and blocks of data should be used, and this layout should be maintained over time.

- Consistent positioning speeds data transfer and, over time, may reduce the need for field descriptions or headings, thus reducing unnecessary information or ‘clutter’.

Within any given subsection, information density should be optimised to assist in data assimilation and recall.

- Configuring reports in such a way that they ‘chunk’ data elements into a single unit will help to improve recall for the clinician.\(^\text{141}\)
- ‘Clutter’ should be reduced to a minimum.\(^\text{141}\) Thus, information that is not part of the protocol (e.g. billing information, SNOMED codes, etc) should not appear on the reports or should be minimized.
- Injudicious use of formatting elements (e.g. too much bold, underlining or use of footnotes) constitutes clutter and may distract the reader from the key information.

Where a structured report checklist is used as a template for the actual report, any values provided in the checklist but not applying to the case in question must be deleted from the formatted report.

Reports should be formatted with an understanding of the potential for the information to mutate or be degraded as the report is transferred from the LIS to other health information systems.

As a report is transferred between systems:

- text characteristics such as font type, size, bold, italics and colour are often lost
- tables are likely to be corrupted as vertical alignment of text is lost when fixed font widths of the LIS are rendered as proportional fonts on screen or in print
- spaces, tabs and blank lines may be stripped from the report, disrupting the formatting
- supplementary reports may merge into the initial report.
Appendix 3  Example of a pathology report

BLADDER TUR, BIOPSY STRUCTURED REPORT

CLINICAL INFORMATION RECEIVED

Prev. hx of urinary tract disease: No previous history
Previous therapy: No previous therapy
Cystoscopic appearance: Papillary tumour
Other clinical information: Haematuria
Clinical extent of disease: Tumour in posterior wall of bladder. Invasive?
Operative procedure: TUR Bladder tumour
Site(s) sampled: Posterior wall of bladder

MACROSCOPIC

Specimen labelled as: TUR Bladder tumour
Operative procedure: Transurethral resection (TUR)
Specimen site(s): Posterior wall of bladder
Number of pieces submitted: Numerous pieces
Block identification key: A-E (In toto)
Other macroscopic comment: Soft friable tissue

MICROSCOPIC

Tumour
Histological tumour type: Papillary Urothelial carcinoma with micropapillary urothelial carcinoma comprising 25% of invasive carcinoma
Non-invasive carcinoma: Urothelial carcinoma in situ
Histological grade: High-grade

Extent of invasion
Tumour invades Subepithelial connective tissue (lamina propria)
Lymphovascular invasion: Present
Status of muscularis propria: Present
SUBSTAGING T1 DISEASE
Invasion involving and/or deep to muscularis mucosae

Associated epithelial lesions: Not identified
Co-existing pathology: None identified

ANCILLARY TESTS Not performed

Diagnostic Summary

Transurethral resection:
High grade papillary urothelial carcinoma with micropapillary urothelial carcinoma (25%)
In invading into lamina propria and deep to muscularis mucosa;
No invasion into muscularis propria;
Lymphovascular invasion present;
Carcinoma in situ present

Reported by Dr Bernard Beckstein  Authorised 4/9/2017
Appendix 4  WHO Classification of Tumours

WHO 2016: Variants of Urothelial Carcinoma⁹

Urothelial carcinomas with divergent differentiation
  Squamous differentiation
  Glandular differentiation
  Trophoblastic differentiation
  Müllerian differentiation
Nested, including large nested
Microcystic
Micropapillary
Lymphoepithelioma-like
Plasmacytoid/diffuse
Sarcomatoid
Giant cell
Lipid-rich
Clear cell
Poorly differentiated tumours (including those with osteoclast-like giant cells)
References


8. RCPA (Royal College of Pathologists of Australasia (2009 ). *Guidelines for Authors of Structured Cancer Pathology Reporting Protocols*. RCPA, Surry Hills NSW.


Van Der Meijden A, Sylvester R, Collette L, Bono A and Ten Kate F (2000). The role and impact of pathology review on stage and grade assessment of stages Ta and T1 bladder tumors: a combined analysis of 5 European


