

**STRUCTURED REPORTING  
PROTOCOL FOR**

**Intrahepatic  
Cholangiocarcinoma, Perihilar  
Cholangiocarcinoma and  
Hepatocellular Carcinoma**

**(1<sup>st</sup> Edition 2019)**

Incorporating the:

**International Collaboration on Cancer Reporting (ICCR)**

Intrahepatic Cholangiocarcinoma, Perihilar Cholangiocarcinoma  
and Hepatocellular Carcinoma Dataset

[www.ICCR-Cancer.org](http://www.ICCR-Cancer.org)

**Core Document versions:**

- ICCR dataset: Intrahepatic Cholangiocarcinoma, Perihilar Cholangiocarcinoma and Hepatocellular Carcinoma 1st edition v1.1
- AJCC Cancer Staging Manual 8th edition
- World Health Organization (2010) Classification of Tumours. Pathology and Genetics of Tumours of the Digestive System (4th edition).

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# Scope

This protocol contains standards and guidelines for the structured reporting of resection and explant specimens of the liver. It applies to specimens with intrahepatic and perihilar cholangiocarcinoma, and hepatocellular carcinoma.

Metastatic lesions to the liver are not included in the scope of this protocol, but essential elements to include in a report for metastatic disease of the liver are: margin status, the presence/absence of disease in the background liver, and assessment of response to therapy (if appropriate).<sup>1</sup>

This protocol also does not apply to neuroendocrine carcinomas, hepatoblastoma, carcinomas of the extrahepatic bile ducts and gall bladder, benign lesions such as adenomas, and non-epithelial malignancies.

Structured reporting aims to improve the completeness and usability of pathology reports for clinicians and improve decision support for cancer treatment. This protocol can be used to define and report the minimum dataset, but the structure is scalable and can equally accommodate a maximum data set or fully comprehensive report.

# Abbreviations

AJCC	American Joint Committee on Cancer
CC	Cholangiocarcinomas
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
IHC	Immunohistochemistry
IHI	Individual health identifier
LIS	Laboratory Information System
MRN	Medical Record Number
NHI	National Health Identifier (NZ)
NHMRC	National Health and Medical Research Council
PBS	Pharmaceutical Benefits Scheme
RCPA	Royal College of Pathologists of Australasia
TNM	tumour-node-metastasis
UHI	Unique Health Identifier
UICC	International Union Against Cancer
VI	Vascular invasion
WHO	World Health Organization

# 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	<p>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).</p> <p>Commentary is used to:</p> <ul style="list-style-type: none"><li>• define the way an item should be reported, to foster reproducibility</li><li>• explain why an item is included (eg how does the item assist with clinical management or prognosis of the specific cancer).</li><li>• cite published evidence in support of the standard or guideline</li><li>• state any exceptions to a standard or guideline.</li></ul> <p>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 (eg CS1.01a, CG2.05b).</p>
General commentary	<p>General commentary is text that is not associated with a specific standard or guideline. It is used:</p> <ul style="list-style-type: none"><li>• to provide a brief introduction to a chapter, if necessary</li><li>• 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).</li></ul>

Guideline	<p>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.<sup>2</sup> These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.</p> <p>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.</p> <p>Guidelines are not used for research items.</p> <p>In this document, guidelines are prefixed with 'G' and numbered consecutively within each chapter (eg G1.10).</p>
Macroscopic findings	Measurements, or assessment of a biopsy specimen, made by the unaided eye.
Microscopic findings	In this document, the term 'microscopic findings' refers to histomorphological assessment.
Predictive factor	A predictive factor is a measurement that is associated with response or lack of response to a particular therapy.
Prognostic factor	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.
Standard	<p>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<sup>2</sup> 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.</p> <p>The summation of all standards represents the minimum dataset for the cancer.</p> <p>In this document, standards are prefixed with 'S' and numbered consecutively within each chapter (eg S1.02).</p>

Structured report	A report format which utilises standard headings, definitions and nomenclature with required information.
Synoptic report	A structured report in condensed form (as a synopsis or precis).
Synthesis	<p>Synthesis is the process in which two or more pre-existing elements are combined, resulting in the formation of something new.</p> <p>The Oxford dictionary defines synthesis as “the combination of components or elements to form a connected whole”.</p> <p>In the context of structured pathology reporting, synthesis represents the integration and interpretation of information from two or more modalities to derive new information.</p>

# Introduction

## Primary liver cancer

1,778 new cases of primary liver and intrahepatic bile duct cancers were reported in Australia in 2013 with the incidence of cancer much higher among Indigenous Australians and 2.8 times higher in males than females. It is one of the top ten causes of cancer death in Australia with 1,732 deaths reported in 2014 and 1979 deaths estimated for 2017.<sup>3</sup> New Zealand reported 289 new cases in 2013 and similar trends to Australia with higher figures for Māori compared with non-Māori and males to females.<sup>4</sup>

The number of new cases of liver cancer is increasing in Australia,<sup>3</sup> with estimated increases in the age-standardised incidence rates for liver cancer rising 1.8 to 7.5 per 100,000 population between 1982 and 2017. Risk factors include alcohol consumption, hepatitis B and C infection and non-alcoholic fatty liver disease (NAFLD). 5 year survival rates remain poor, though they are improving.

The epidemiology of hepatocellular carcinoma (HCC) is changing. Since the launch of all-oral direct acting antiviral therapies in Australia in March 2016, it is estimated that almost 30% of the hepatitis C virus (HCV) infected population has been treated, including more than 70% of those with cirrhosis. With current therapies, sustained virologic response (SVR) rates of more than 95% are observed, and highly effective salvage therapy is now available for non-responders. Sustained virologic response is associated with a marked reduction (adjusted HR 0.28, 95% CI 0.22–0.36) in the risk of HCC<sup>5</sup> however patients with cirrhosis at the time of SVR retain a risk of HCC and are recommended for long-term ultrasound surveillance. At the same time, NAFLD-associated HCC is increasing in incidence, including in patients without cirrhosis, and is estimated to account for at least 14% of HCC cases.<sup>6</sup>

Surveillance with 6 monthly ultrasound and alpha-fetoprotein (AFP) is recommended for any patient with cirrhosis, and many non-cirrhotic patients with chronic hepatitis B. HCC diagnosed within a surveillance programme is associated with an increased chance of curative resection or liver transplantation, and improved survival.<sup>7</sup>

With an increasing number of clinical trials and ongoing drug development, particularly in cases of HCC, the search for tissue and serological biomarkers to determine response to other therapies is rapidly advancing. This may result in specific stains being recommended in the near future.

In Australia, there are plans to establish transplant programs for cholangiocarcinoma, according to the Mayo protocol in which neoadjuvant therapies are given in the lead up to transplant.<sup>8,9</sup>

## Benefits of structured reporting

The pathology report lays the foundation for a patient's cancer journey 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<sup>10,11</sup> around the world. Both the United Kingdom,<sup>12</sup> and United States<sup>13</sup> 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.

## **Importance of histopathological reporting**

The information contained within a pathology report includes prognostic information for the patient and treating clinical team. The content will assist in subsequent management, whether this may be surveillance, further surgery, radiotherapy or chemotherapy, or a combination of these modalities.

Liver cancer is one of the few cancers treatable by organ transplantation. Information from the pathology report of the explant specimen will have a key role in determining prognosis and patient management.

## **International Collaboration on Cancer Reporting**

The International Collaboration on Cancer Reporting (ICCR), founded in 2011 by the Australasian (RCPA), US (CAP) and UK (RCPath) Colleges of Pathology and the Canadian Association of Pathology - Association Canadienne des Pathologistes (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<sup>14-17</sup> 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](http://www.ICCR-Cancer.org)

## Design of this protocol

This structured reporting protocol has been developed using the ICCR dataset on Intrahepatic Cholangiocarcinoma, Perihilar Cholangiocarcinoma and Hepatocellular Carcinoma 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 Intrahepatic Cholangiocarcinoma, Perihilar Cholangiocarcinoma and Hepatocellular Carcinoma.

ICCR dataset elements for liver resections specimens 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:

 G3.02	The intraglandular extent should be recorded as a percentage.
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Additional commentary by the RCPA expert committee may be added to an ICCR element but is not included in the grey bordered area nor indicated with an ICCR logo eg

 G2.03	If present, the laterality of the lymph nodes submitted may be recorded as left, right or bilateral.
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CS2.03a If present, record site and number. All lymph node tissue should be submitted for histological examination.

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**

- ICCR dataset: Intrahepatic Cholangiocarcinoma, Perihilar Cholangiocarcinoma and Hepatocellular Carcinoma Dataset 1st edition v1.1<sup>18</sup>
- Guidelines for Authors of Structured Cancer Pathology Reporting Protocols, Royal College of Pathologists of Australasia, 2009<sup>19</sup>
- World Health Organization (2010) Classification of Tumours. Pathology and Genetics of Tumours of the Digestive System (4th edition)<sup>20</sup>

## **Changes 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 – Intrahepatic Cholangiocarcinoma, Perihilar Cholangiocarcinoma and Hepatocellular Carcinoma 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](http://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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## Acknowledgements

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## **Stakeholders**

ACT Cancer Registry

ACT Health

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)

Department of Health, Australia

Health Informatics Society of Australia (HISA)

Independent Review Group of Pathologists

Medical Oncology Group of Australia

Medical Software Industry Association (MSIA)

Ministry of Health, New Zealand

National Pathology Accreditation Advisory Council (NPAAC)

New Zealand Cancer Registry

Northern Territory Cancer Registry

Pathology Australia

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)

Royal Australasian College of Surgeons (RACS)

Royal Australian and New Zealand College of Radiologists (RANZCR)

Royal Australian College of General Practitioners (RACGP)  
Royal College of Pathologists of Australasia (RCPA)  
South Australia Cancer Registry  
Standards Australia  
Tasmanian Cancer Registry  
Victorian Cancer Registry  
Western Australia Clinical Oncology Group (WACOG)  
Western Australian 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*.<sup>19</sup>

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 liver cancer, 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.<sup>21</sup> This document specifies the minimum information to be provided by the requesting clinician for any pathology test.

CS1.01b Document whether or not the patient identifies as Aboriginal and/ or Torres Strait Islander in Australia, or Maori in New Zealand. This is in support of government initiatives to monitor the health of those who identify as indigenous, 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 In most cases all clinical information should be transcribed: however in a small number of cases the pathologist may exercise discretion regarding the inclusion of provided clinical information, for instance, possibly erroneous information or information that may impact on patient privacy. In such case reference should be made as to the location of the complete clinical information eg "Further clinical information is available from the scanned request form."

G1.01 The copy doctors requested on the request form should 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 can 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 biopsy.
- The pathology request is often authored by the clinician performing the 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.

CS1.04b The Australian Healthcare identifiers ie Healthcare Provider Identifier - Individual (HPI-I) and Healthcare Provider Identifier - Organisation (HPI-O) should be included, where possible, to identify the principal clinician involved in the patient's care.

G1.02 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 chapter 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.
- If tissue is sampled for banking or research then this should be done in consultation with a pathologist and recorded in the report.

### Specimen handling

- Detailed fixation and specimen handling instructions are available from the RCPA online Cut-up Manual:  
<https://www.rcpa.edu.au/Manuals/Macroscopic-Cut-Up-Manual>
- **The specimen must be handled in a systematic and thorough fashion to ensure completeness and accuracy of pathological data.**

### Macroscopic findings

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

G2.01 The operative procedure should be recorded.

	<b>S2.02 The specimen(s) submitted must be recorded.</b>
	CS2.02a Preoperative radiological/imaging reports should ideally be available for review during pathological reporting of the surgical specimen.
	CS2.02b In assessing macroscopic specimens which contain malignant epithelial tumours of the liver it is important to establish the nature of the surgical resection. <sup>22</sup> Liver tumours are resected either by segmental resection <sup>23</sup> following the planes of whole liver segments defined by intra-operative ultrasound, or non-anatomical (wedge) resection for small, accessible, subcapsular lesions. The

		<p>dataset should also be applied to total hepatectomy specimens from patients undergoing liver transplantation when tumour is present.</p> <p>The segmental anatomy of the liver is shown in Figure 1. The boundaries of the eight segments represent the watershed between portions of liver perfused by main branches of the hepatic artery and portal vein, and form the basis of the various surgical options for major liver resection.</p> <p>Segmentectomy procedures result in sizeable resection specimens. The surgeon should state which segments are included as this may not be clear from the topography of the specimen. The boundary of segments is defined by the course of intrahepatic vessels and cannot be inferred from surface landmarks. Wherever possible, the preoperative imaging report should be available to the pathologist at the time of specimen dissection.</p> <p>Surgical intervention for cholangiocarcinomas arising at the hilum (ie proximal to the junction of the cystic and common hepatic duct) will generally include a length of extrahepatic duct in continuity with segments or lobes of liver. There is considerable anatomical variability at the liver hilum, and the pathologist should consult the surgeon if the identity of the main hilar vessels and ducts is not clear from the information provided on the request form. Note that this reporting guide does not apply to more distal bile duct carcinomas resected without hepatectomy. Specimens may include lymph nodes, either dissected separately by the surgeon or found at the liver hilum in the resected specimen. A regional lymphadenectomy specimen will ordinarily include six or more lymph nodes for primary intrahepatic and gallbladder cancers, and 15 lymph nodes for perihilar cholangiocarcinomas (CC).<sup>24</sup> Regional lymph nodes are those in the hepaticoduodenal ligament: hilar, cystic duct, pericholedochal, hepatic artery, portal vein for perihilar CC. More distant nodes are occasionally resected and involvement of such nodes is classified as distant metastasis (M1). There is no pN2 category for intrahepatic cholangiocarcinomas, however pN2 has been added in TNM8 for perihilar cholangiocarcinoma, for cases with four or more lymph node metastases.<sup>24,25</sup></p>
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G2.02 Whether or not the liver capsule is normal should be recorded.

 G2.03	Specimen dimensions should be recorded in three dimensions (in millimetres).	
	CG2.03a	Indicate the greatest measurement for each parameter in an irregularly shaped specimen.
	CG2.03b	For perihilar cholangiocarcinoma specimens, the length of extrahepatic bile duct should also be recorded.

 G2.04	The weight of the specimen should be recorded.	
 G2.05	For hepatocellular carcinoma specimens, the presence or absence of satellitosis in the specimen should be recorded.	
	CG2.05a	Satellitosis is defined as “ <i>a nodule separated from the main tumour by a distance greater than that of the satellite diameter</i> ”.
	CG2.05b	<p><u>Hepatocellular carcinoma</u> In hepatocellular carcinoma (HCC) several studies have found that the presence of satellite tumours is related to recurrence but there is no consensus on the definition of satellitosis.<sup>26-33</sup> Roayaie et al<sup>31</sup> used a definition of tumours less than or equal to 2 cm and located of less than or equal to 2 cm from the main tumour. The Liver Cancer Study Group of Japan included in their definition that the satellite nodules should be histologically similar or less differentiated than the main tumour.<sup>27</sup> Reviewing the additional literature the ICCR has suggested the above definition in CG2.05a. It is acknowledged however that accurate distinction between satellitosis and intrahepatic metastasis can be difficult.</p> <p><u>Cholangiocarcinoma</u> No data are available on intrahepatic or perihilar cholangiocarcinoma.</p>
	CG2.05c	While satellitosis is recognised in cholangiocarcinoma, it should only be reported for hepatocellular carcinoma.
 G2.06	Whether there is macroscopic tumour rupture should be recorded.	
	CG2.06a	<p><u>Hepatocellular carcinoma</u> Rupture needs to be distinguished from peri-operative fragmentation of the capsule, which occasionally occurs with a large, bulging, soft/friable tumour. A review in 2006<sup>34</sup> summarises a number of small series of patients who either underwent immediate resection at the time of rupture, or staged resection. The largest of which was in a series of 60 patients.<sup>34</sup> Pathological stage and grade were not statistically different compared to non-ruptured series. Time to recurrence was shorter, but not survival.</p> <p><u>Cholangiocarcinoma</u> No data are available on intrahepatic or perihilar cholangiocarcinoma.</p>
 <b>S2.03</b>	<b>The tumour sites and number of tumours per site must be recorded, where possible.</b>	
	CS2.03a	<p><u>Hepatocellular carcinoma</u> Tumour site, size and number are important prognostic factors in hepatocellular carcinoma. Based on survival data, the 8th edition of the TNM system<sup>24</sup> has subdivided the T category by tumour size and number. For TNM staging, multiple tumours include satellitosis, multifocal tumours and intrahepatic metastases.</p>

		<p>Treatment guidelines for HCC based on the Barcelona Clinic Liver Cancer staging system (also proposed in Europe and the United States) recommend liver resection only for patients with a single HCC (without portal hypertension).<sup>35,36</sup></p> <p>The number of tumours is one of the most significant predictors of recurrence and overall survival<sup>37-41</sup> and it is correlated with the presence of microvascular invasion.<sup>42</sup> A tumour with an apparent surrounding satellite nodule(s) should be regarded as a single tumour when the co-nodule(s) is attached to the main tumour.<sup>43</sup> In this setting, the apparent satellite may represent an irregular leading edge of the tumour.</p> <p><u>Intrahepatic cholangiocarcinoma</u></p> <p>The number of tumours and tumour size (refer to <b>MAXIMUM TUMOUR DIMENSION</b>) have also been recognized as important prognostic factors in intrahepatic cholangiocarcinoma.<sup>44-48</sup> Multifocality has been incorporated into the TNM staging system (8<sup>th</sup> edition).<sup>24</sup> Patients with more than four lesions showed significantly lower disease free and overall survival.<sup>49</sup> For TNM staging, multiple tumours include satellites and intrahepatic metastases. The presence of satellite lesions has been demonstrated to negatively impact on overall survival on both univariate and multivariate analyses.<sup>50</sup></p> <p>There is currently no clear definition of satellites in the setting of intrahepatic cholangiocarcinoma.</p> <p>Location of all tumours (HCC and intrahepatic cholangiocarcinoma) should be reported since this is important for correlation with imaging. Representative sections should be obtained from each nodule.</p> <p><u>Perihilar cholangiocarcinoma</u></p> <p>Perihilar cholangiocarcinoma is defined as a cholangiocarcinoma arising above the junction of the common hepatic duct and the cystic duct, and up to the second order divisions of the left and right hepatic duct – corresponding to the ducts that have peribiliary glands. The site of the perihilar CC should be described according to the ducts involved macroscopically (right, left, common hepatic duct).</p>
 <b>S2.04</b>		<p><b>The maximum tumour dimensions for each tumour must be recorded, where possible. Note for a large number of tumours a range of dimensions can be recorded.</b></p>
	CS2.04a	<p>Tumour size is an important determinant of stage and should be recorded in all cases of both HCC and CC. The maximum diameter, measured to the nearest millimeter, can be assessed both on the unfixed or fixed specimen (measuring the unfixed specimen avoids underestimation resulting from formalin fixation-induced shrinkage). For cases with multiple tumours, it has been recommended that size of at least the 5 largest tumour nodules should</p>

		<p>be provided,<sup>51</sup> while a range can be expressed for additional tumour nodules.</p> <p><u>Hepatocellular carcinoma</u></p> <p>Large size (&gt;5 cm) and multiple tumour nodules are unfavorable prognostic factors for patients with HCC after hepatic resection.<sup>52,53</sup> TNM8 also uses a dimension of 2cm to divide stage pT1 into pT1a solitary HCC &lt;2 cm irrespective of microvascular invasion and pT1b for patients with solitary HCC &gt;2 cm without microvascular invasion.</p> <p><u>Intrahepatic cholangiocarcinoma</u></p> <p>One study used a large multi-institutional data set to demonstrate that there are certain threshold sizes that are relevant for prognosis in intrahepatic cholangiocarcinoma, and these thresholds have been incorporated into a prognosis nomogram with other significant factors.<sup>45</sup> In another study, unifocal intrahepatic cholangiocarcinoma &lt;2 cm diameter was shown to have a superior prognosis after liver transplantation compared with larger or multifocal tumours.<sup>54</sup></p> <p><u>Perihilar cholangiocarcinoma</u></p> <p>The maximum tumour dimension is more difficult to measure for perihilar cholangiocarcinoma, since the extent of the tumour requires histological confirmation for accurate assessment. Both the linear extent of the tumour along the bile duct, and the maximum diameter of any mass lesion should be included, for correlation with pre-operative imaging.</p>
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- G2.07 The distance of tumour to the closest point of the liver capsule should be recorded for intrahepatic lesions.
- G2.08 The distance of tumour to the closest resection margin and what that margin is (if orientated) should be recorded.
- G2.09 For intrahepatic tumour specimens, the macroscopic involvement of vessels should be recorded.
- G2.10 For perihilar cholangiocarcinoma specimens, the extent of invasion into the biliary tree should be described.
- G2.11 For perihilar cholangiocarcinoma specimens, the depth of invasion beyond the biliary tree should be described.
- G2.12 Whether or not the background liver parenchyma is normal (eg cirrhotic or non cirrhotic) should be recorded and if abnormal it should be described.

 <b>S2.05</b>	<b>A block identification key<sup>12</sup> listing the nature and origin of all tissue blocks must be recorded.</b>	
	CS2.05a	The origin/designation of all tissue blocks should be recorded and it is preferable to document this information

		<p>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. Photography of macroscopic specimens is considered best practice. Annotation of captured images can be very helpful and aids with review of the case at a later date. It can also provide useful information in the context of multidisciplinary meetings.</p> <p>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.</p> <p>Because of the importance of resection margin status, it is recommended that all surgical surfaces (hepatic transection plane and hilar tissues for perihilar cholangiocarcinoma) are painted prior to specimen dissection. Occasionally different colours can be used to identify specific surgical margins. This information should also be recorded in the block key.</p> <p>The precise blocks will vary according to specimen and tumour type.<sup>55-58</sup> The number of blocks is influenced by tumour type. For HCC, it is recommended that a minimum of three tumour blocks be examined and all macroscopically distinctive areas should be sampled. The following guidelines are provided for intrahepatic tumours:</p> <ul style="list-style-type: none"> <li>• Tumour with nearest hepatic resection margin (when this is close enough to the tumour to be included in the block).</li> <li>• Other blocks of tumour with adjacent liver tissue (for microscopic vascular invasion). It may be helpful to sample a full face of tumour if it has been treated to assess response.</li> <li>• Liver capsule if there is a possibility of capsular invasion, ie where there is subjacent tumour and overlying adherent tissue or macroscopic capsular invasion. Where the capsule appears intact over subcapsular tumour, with a smooth shiny surface, histology is not required to confirm capsular integrity.</li> <li>• Gallbladder bed and wall where there is adjacent intrahepatic tumour.</li> <li>• Any site macroscopically suggestive of vascular or bile duct invasion.</li> </ul>
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		<ul style="list-style-type: none"> <li>• Background liver (taken as far away as possible from the tumour).</li> </ul> <p>A block of representative background liver should be taken, whether or not it looks abnormal macroscopically.</p> <p>For perihilar cholangiocarcinoma, careful dissection and block taking from the biliary tree is necessary to delineate the extent and margin status. The distal margin of the biliary tree and the proximal margin of the left or right duct(s) should be identified prior to dissection. This is aided if the surgeon identifies and marks the structures, eg with a coloured tie/s. The resection margins of these ducts may be submitted separately by the surgeon, with or without a request for frozen section.</p>
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G2.13 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.

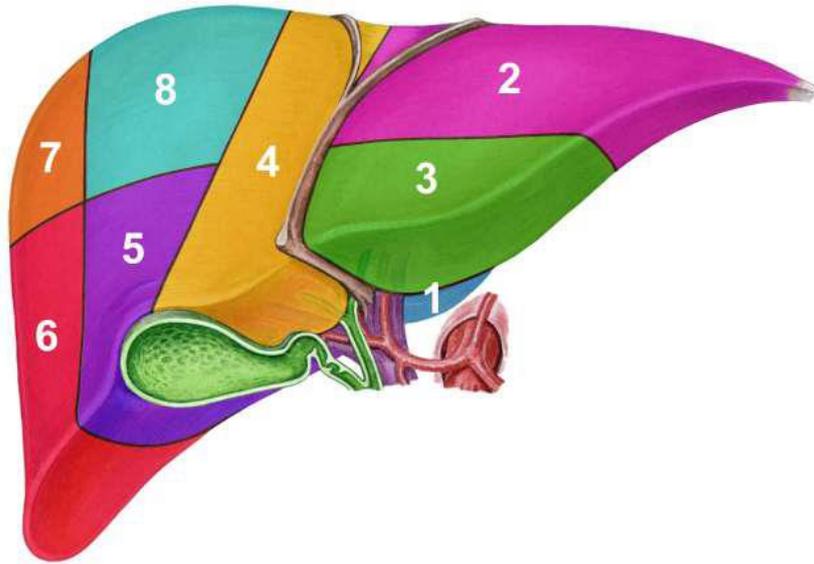
CG2.13a The traditional macroscopic narrative recorded at the time of specimen dissection is often reported separately from the cancer dataset. Although this remains an option, it is recommended that macroscopic information be recorded within the overall structure of this protocol.

CG2.13b 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.

CG2.13c A traditional macroscopic description may be required when the Laboratory Information System (LIS) does not allow a structured approach.

CG2.13d Where the LIS offers an electronic interface for structured data entry the need for narrative can be significantly reduced to describe only information not otherwise captured.

**Figure 1: Segmentectomy specimens<sup>59</sup>**



- Right hepatectomy, Segments 5-8
- Right trisegmentectomy, Segments 4-8
- Left lateral segmentectomy, Segments 2-3
- Left hepatectomy, Segments 2-4
- Left trisegmentectomy, Segments 1-5 and 8
- Total hepatectomy, Segments 1-8

### 3 Microscopic findings

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

 <b>S3.01</b>	<b>The histological tumour type must be recorded (refer to Appendix 4).</b>	
	CS3.01a	<p><u>Hepatocellular carcinoma</u></p> <p>With the exception of the fibrolamellar variant of HCC, (which is regarded in the current World Health Organisation (WHO) classification as a distinct tumour from HCC), the architectural and cytological variants of HCC (such as trabecular, compact, pseudoacinar, scirrhous, sarcomatoid, clear cell, steatohepatic etc) are all considered as HCC.</p> <p>Early HCC is a low grade and early stage HCC measuring 2 cm diameter with a vaguely nodular appearance that merges imperceptibly into the adjacent parenchyma.<sup>60</sup> It has a different blood supply and imaging profile compared with conventional (progressed) HCC, and can co-exist with progressed HCC giving a nodule-in-nodule appearance. It is not separately classified from HCC in the current WHO schema.</p> <p>Fibrolamellar HCC has a better prognosis when compared to conventional HCC as a whole, but the outcome is similar when compared to conventional HCC arising in non-cirrhotic liver.<sup>61,62</sup></p> <p><u>Cholangiocarcinoma</u></p> <p>Cholangiocarcinoma is further classified by site into intrahepatic, perihilar and distal types.<sup>63</sup> Intrahepatic cholangiocarcinoma is defined as being located upstream of the second degree bile ducts. Perihilar cholangiocarcinoma is localised to the area between second degree bile ducts and the insertion of the cystic duct into the common bile duct.</p> <p>Combined hepatocellular-cholangiocarcinoma is defined as containing unequivocal, intimately mixed elements of both hepatocellular carcinoma and cholangiocarcinoma.<sup>20</sup> Collision tumours are not considered combined neoplasms. The classical type shows areas of typical HCC and cholangiocarcinoma, which can be confirmed with histochemical (mucin) and immunohistochemical stains.<sup>64</sup> Some tumours exhibit putative stem cell or progenitor cell features, now</p>

		<p>recognised as a specific subtype in the 2010 WHO classification.<sup>20</sup> A variety of immunohistochemical markers can be used to support the diagnosis, but these tumours remain incompletely understood. Although the demographics and clinical features of combined HCC-ICCs including age, gender, association with HBV, HCV and cirrhosis resemble those of HCC in both TNM 8<sup>th</sup> edition and 7<sup>th</sup> edition of WHO classification such combined tumours are staged as for IH-CC and for reporting purposes we recommend that the data set is used as for typical IH-CCs.</p> <p>Intraductal papillary neoplasm (IPN) with an invasive component and mucinous cystic neoplasm with an associated invasive carcinoma should specify the type of invasive carcinoma.</p> <p>IPN with pancreatobiliary differentiation of the lining epithelium usually give rise to tubular adenocarcinoma, whilst those with intestinal-type lining may be associated with a mucinous (colloid) type of invasive carcinoma, which has a better prognosis.<sup>65</sup></p> <p>Intrahepatic CC typically has a microacinar glandular pattern with central sclerosis, and distinction from metastatic adenocarcinoma particularly from stomach or pancreas is based on the single or dominant intrahepatic mass and absence of a known extra-hepatic primary tumour. Most intrahepatic CCs are pure adenocarcinomas. Rare variants listed in the WHO classification include adenosquamous, squamous, mucinous, signet ring, clear cell, mucoepidermoid, lymphoepithelioma-like (Epstein-Barr Virus (EBV) associated) and sarcomatous intrahepatic CCs.</p> <p>There are other liver tumours such as hepatoblastoma, neuroendocrine tumours, rhabdoid tumour, carcinosarcoma etc, which have an epithelial component, however, it is not envisaged that this dataset would be used for such resections.</p>
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CS3.01b

The abbreviation cHCC-CCA is also used to denote "combined (or mixed) hepatocellular-cholangiocarcinoma." <sup>66</sup>. However, this terminology is different to that used in the WHO Classification of Tumours.

CS3.01c

Metastatic tumours

Metastatic lesions in the liver are not covered in the scope of this protocol.

The essential elements to record for liver metastases are margin status, the presence/absence of disease in the background liver, and assessment of response to therapy (if appropriate).

IC & CR	G3.01	The type of tumour growth pattern should be recorded.	
IC & CR	CG3.01a		<p><u>Hepatocellular carcinoma</u></p> <p>There are two principal forms of nomenclature about HCC growth pattern. In the WHO blue book 4th edition<sup>20</sup>; nodular, massive, and diffuse macroscopic types are described for progressed HCC. Early hepatocellular carcinoma is a separate entity, which is a low-grade, early-stage tumour. Grossly, early HCC usually is a poorly defined nodular lesion measuring <math>\leq 2</math> cm in diameter (hence the terms "vaguely nodular small HCC" and "small HCC with indistinct margins" that have been used for this tumour).</p> <p><u>Intrahepatic cholangiocarcinoma</u></p> <p>Four tumour growth patterns of intrahepatic cholangiocarcinoma are described: the mass-forming type, the periductal infiltrating type, the intraductal growth type and the mixed type.<sup>20</sup> Mass-forming intrahepatic cholangiocarcinoma (65% of cases) forms a well-demarcated nodule growing in a radial pattern and invading the adjacent liver parenchyma. The periductal-infiltrating type of cholangiocarcinoma (6% of cases) spreads in a diffuse longitudinal growth pattern along the bile duct, and the intra-ductal growth type (4% of cases) shows a polypoid or papillary tumour within the dilated bile duct lumen. The remaining 25% of cases of intrahepatic cholangiocarcinoma grow in a mixed mass-forming/periductal-infiltrating pattern.<sup>67</sup> Limited analyses suggest that the diffuse periductal-infiltrating type may be associated with a poor prognosis but the prognostic significance of growth pattern is controversial.<sup>47,68</sup></p> <p><u>Perihilar cholangiocarcinoma</u></p> <p>The periductal infiltrating growth pattern is the characteristic pattern for periductal cholangiocarcinoma, with or without an associated mass lesion. When present, mass lesions within the perihilar tissues are frequently sparsely cellular with abundant desmoplastic stroma. Unlike most intrahepatic tumours, in which the tumour margins are clearly evident macroscopically, the extent of perihilar cholangiocarcinoma cannot be distinguished by naked eye. There may be associated bile duct scarring or peritumoral fibrosis, while isolated tumour cells may be present in fatty tissue beyond the apparent tumour margin. Extensive sampling of hilar cholangiocarcinoma is necessary to identify the extent, dimension and margin status of these tumours. When there is direct invasion of the adjacent liver (pT2b) there is usually a more cellular, expansile growth pattern.</p>

	CS3.01b	<p><b>Figure 2: Schematic diagram of the macroscopic types of hepatocellular carcinoma</b></p> <table border="1" data-bbox="679 338 1355 987"> <tr> <td data-bbox="679 338 1026 450">Small nodular type with indistinct margin</td> <td data-bbox="1026 338 1355 450"></td> </tr> <tr> <td data-bbox="679 450 1026 584">Simple nodular type with distinct margin</td> <td data-bbox="1026 450 1355 584"></td> </tr> <tr> <td data-bbox="679 584 1026 719">Simple nodular type with extranodular growth</td> <td data-bbox="1026 584 1355 719"></td> </tr> <tr> <td data-bbox="679 719 1026 853">Confluent multinodular type</td> <td data-bbox="1026 719 1355 853"></td> </tr> <tr> <td data-bbox="679 853 1026 987">Margin irregular (infiltrative type)</td> <td data-bbox="1026 853 1355 987"></td> </tr> </table> <p>Refer to the ICCR dataset for further information.<sup>18</sup></p>	Small nodular type with indistinct margin		Simple nodular type with distinct margin		Simple nodular type with extranodular growth		Confluent multinodular type		Margin irregular (infiltrative type)	
Small nodular type with indistinct margin												
Simple nodular type with distinct margin												
Simple nodular type with extranodular growth												
Confluent multinodular type												
Margin irregular (infiltrative type)												
 <b>S3.02</b>	<b>The Histological grade must be recorded.</b>											

CS3.02a

Grade is a key component of determining entry into clinical trials and is therefore essential to record.

ICCR recommends the use of a three-point scale:

- Well differentiated/G1
- Moderately differentiated/G2
- Poorly differentiated/G3

Although a tumour may have varying grades within it, only the worse grade should be recorded, even if only a minor component of highest grade is present.

	CS3.02b	<p>For practical purposes, well-differentiated HCCs are those where the tumour cells closely resemble hepatocytes such that the differential diagnosis is with dysplastic nodule (in cirrhosis) or adenoma (in non-cirrhotic livers). Poorly differentiated HCC are those where the hepatocellular nature of the tumour is not evident from the morphology.</p> <p>Refer to the ICCR dataset for further information.<sup>18</sup></p>
 <b>S3.03</b>	<b>The extent of invasion must be recorded.</b>	
	CS3.03a	<u>Hepatocellular carcinoma</u>

		<p>HCC can directly invade adjacent organs. Perforation of visceral peritoneum or extension to adjacent organ (other than gallbladder) is classified as pT4 with the TNM staging system.<sup>24</sup></p> <p><u>Cholangiocarcinoma</u></p> <p>Intrahepatic cholangiocarcinoma extending to extra-hepatic structures is classified as stage pT4 by the TNM system. According to international guidelines,<sup>69</sup> stage pT4 ICC are considered unresectable tumours.</p>
	<b>S3.04 The presence or absence of vascular invasion must be recorded.</b>	
	CS3.04a	<p><u>Hepatocellular carcinoma</u></p> <p>Vascular invasion (VI) is an independent prognostic factor in HCC after resection<sup>58,70-76</sup> as well as after transplantation.<sup>77-82</sup> VI affects survival also in early HCC.<sup>83</sup> For the TNM staging system, vascular invasion is a component of the pT stage.<sup>24</sup></p> <p>VI is classified as macroscopic or microscopic (MiVI). Macroscopic VI is defined as invasion of tumour into a major vessel that can be identified during macroscopic examination or radiological imaging and is part of established staging systems, such as Barcelona Clinic Liver Cancer classification (BCLC).</p> <p>For the pathological classification in the 8<sup>th</sup> edition of TNM,<sup>24</sup> involvement of major branch of portal vein or hepatic vein is classified as pT4. This refers to the main right or left branch of the vein, as distinct from macroscopic vascular invasion which relates to macroscopically visible involvement of any vessel – the width of the vessel is not helpful as intravascular tumour may distend the calibre of the vein.</p> <p>MiVI is usually defined as tumour within a vascular or lymphatic space lined by endothelium, visible only on microscopy, identified in the liver tissue surrounding the tumour and venous vessels in the tumour capsule and/or non-capsular fibrous septa. However, there is a lack of consensus for the definition of MiVI.<sup>84</sup> Inter-observer and intra-observer variability in the evaluation of MiVI in HCC has been reported.<sup>31</sup></p> <p><u>Cholangiocarcinoma</u></p> <p>Vascular invasion is an important prognostic factor for ICC.<sup>85-89</sup> Macroscopic vascular invasion is a strong predictor of survival: 5-year survival has been reported to be 0% for patients with macroscopic vascular invasion.<sup>85,86</sup></p>

		For TNM staging system, vascular invasion is a component of the pT stage  Refer to the ICCR dataset for further information. <sup>18</sup>
	CS3.04b	The use of special stains and/or immunohistochemistry may be useful in many cases.
 G3.02	The presence or absence of perineural invasion should be recorded.	
	CG3.02a	The significance of perineural invasion is greater for intrahepatic cholangiocarcinoma than for hepatocellular carcinoma.  Perineural invasion is particularly common in perihilar CC and is a significant prognostic indicator for recurrence. <sup>90</sup> Recognition of perineural invasion, considered 'indeterminate' on H&E stains can be aided by S100 immunohistochemistry.  Refer to the ICCR dataset for further information. <sup>18</sup>
 G3.03	The response to loco-regional therapies for Hepatocellular Carcinoma should be recorded.	
	CG3.03a	If an incomplete response is noted then the percentage of necrosis observed should be recorded.
	CG3.03b	<u>Hepatocellular carcinoma</u>  Patients with HCC in cirrhosis increasingly undergo locoregional therapy using a wide variety of modalities such as radiofrequency ablation and transarterial chemo-embolization. In some instances, tumours that are beyond acceptable criteria for transplantation are successfully down-staged. <sup>91-93</sup> The response to therapy is assessed by imaging and/or decrease in AFP level.  Down-staging or total necrosis of the tumour following therapy has been associated with improved outcome after liver resection and transplantation. <sup>94-97</sup> There are limited data to determine the significance of pathologic quantification of tumour necrosis after locoregional therapy. Although figures such as 50% <sup>98</sup> and 90% <sup>99</sup> necrosis have been used in some studies, there is insufficient evidence to make definite recommendations about cut off values for necrosis that correlate with outcome. Although not required, an estimate of extent of necrosis can provide valuable feedback to the clinical team to correlate it with the down-staging observed on imaging. <sup>94,96</sup>  There are no definite guidelines on how to assess the extent of necrosis and the pathological analysis in most studies has not been performed in a systematic manner. Microscopic examination of the entire tumour should be done when feasible. For selective sampling, sampling an entire cross section has been recommended if the

		tumour is $\leq 2$ cm with an additional section for each 1 cm for larger tumours. <sup>100</sup> Additional sampling of areas that appear grossly viable is often necessary. The overall extent of necrosis should be estimated based on a combination of gross and microscopic findings. The extent of necrosis should be reported in up to 5 of the largest tumour nodules. <sup>100</sup>
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CG3.03c

Local regional therapies used include transarterial chemo-embolisation (TACE, either with lipiodol or drug-eluting beads), thermal ablation, cryoablation, transarterial radioembolisation (TARE) or stereotactic body radiation therapy (SBRT).

 G3.04	The response to neoadjuvant therapy for Cholangiocarcinoma should be recorded.	
	CG3.04a	If an incomplete response is noted then the percentage of necrosis observed should be recorded.
	CG3.04b	Neoadjuvant chemoradiotherapy has been used in patients with cholangiocarcinoma. The presence of complete tumour necrosis is associated with a favourable prognosis in patients subsequently undergoing liver transplantation for perihilar cholangiocarcinoma. <sup>101,102</sup> However, at the present time there are no definite guidelines on how to assess the extent of necrosis or other features that may be indicative of tumour regression in cholangiocarcinoma.
	<b>S3.05</b>	<b>Margin status<sup>103</sup> must be recorded.</b>
	CS3.05a	<p><u>Hepatocellular carcinoma</u></p> <p>Margins should be assessed macroscopically, and blocks taken to confirm microscopically, noting that in addition to the parenchymal margin there are hilar/porta hepatis, hepatic vein, and radial margins. For this reason, painting the surface of the specimen prior to dissection is important, so that the margins can be identified from the block key and assessed microscopically.</p> <p><u>Margin status is considered to be a required item for all three tumour types in the dataset, with the clearance in mm to be stated if under 10 mm.</u> The actual distance in mm up to 10 mm is a component of the Singapore nomogram predicting freedom from relapse.<sup>104</sup></p> <p>Margins <math>&lt;</math> or <math>&gt; 1</math> mm are reported in several series as significant on multivariate analysis, including for large HCC <math>&gt; 10</math> cm,<sup>105</sup> and predictive of margin recurrence.<sup>106</sup></p> <p>Therefore, tumours with a margin <math>&lt; 1</math> mm are generally regarded as R1 resection, although there is not</p>

		currently a specific evidence base for this approach in HCC or CC.
	CS3.05b	<p><u>Intrahepatic cholangiocarcinoma</u></p> <p>For cholangiocarcinoma there are a few publications citing margin status as a prognostic factor on multivariate analysis<sup>107-109</sup> A systematic review of intrahepatic CC did not include margin status among significant prognostic factors.<sup>89</sup> There are no systematic reviews or meta-analysis specifically addressing perihilar cholangiocarcinoma.</p> <p><u>Perihilar cholangiocarcinoma</u></p> <p>The question of microscopic margin involvement is considered in detail in the Royal College of Pathologists (RCPATH) dataset<sup>110</sup> for pancreatic, ampulla of Vater and common bile duct cancers (2010). The distinction between transection margin, dissection (circumferential) margin and peritoneal surface is well described. The recommendation is that involvement of dissection or transection margins of &lt;1 mm should be regarded as R1 positive margin, whereas peritoneal surface involvement requires carcinoma cells to be seen on the surface.</p> <p>There is evidence cited of the prognostic relevance of this approach in pancreatic and distal bile duct cancer. Given the absence of published evidence for perihilar cholangiocarcinoma, and the similarities between biliary and pancreatic duct cancer, the same approach to the definition of R1 resection - ie cancer cells &lt;1 mm from the transection or dissection margin - is appropriate. Using this approach, there is an association of positive margin with prognosis.<sup>111</sup></p>
	<b>S3.06</b>	<b>Lymph node status must be recorded.</b>
	CS3.06a	<p><u>Hepatocellular carcinoma</u></p> <p>It should be noted that lymph nodes may not always be present in specimens resected for hepatocellular carcinoma. There is no strong evidence of prognostic significance of local nodal metastases in hepatocellular carcinoma. Lymph node involvement is common in fibrolamellar variant of HCC.</p> <p><u>Cholangiocarcinoma</u></p> <p>The pattern of metastatic spread of intrahepatic cholangiocarcinoma to lymph nodes is in part determined by the location of the tumour. For those involving the right lobe of liver, the regional nodes include the hilar, periduodenal and peripancreatic chains. For left sided tumours the regional lymph nodes include hilar and</p>

		<p>gastrohepatic nodes. Spread to coeliac and/or periaortic and caval nodes is regarded as distant metastases.</p> <p>Lymph node metastases in intrahepatic and perihilar cholangiocarcinoma have been identified as an important predictor of prognosis.<sup>47,89</sup> As noted, a pN2 category has been introduced in TNM8 for perihilar CC with four or more lymph node metastases.</p>
 <b>S3.07</b>	<b>The presence or absence of relevant coexistent pathology must be recorded.</b>	

- G3.05 If fibrosis is present, consider recording the degree with an appropriate staging system.
- CG3.05a If a scoring system is used to assess the background liver disease, then it should be appropriate to the disease process, understood by the local clinicians, and relevant to local practice eg BRUNT, KLEINER for steatohepatitis, ISHAK or METAVIR for viral hepatitis, etc.
- G3.06 Comments should be included, if appropriate.
- CG3.06a Free text entry to allow any additional, unusual or unexpected findings to be reported.

## 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.

Some studies, such as Her-2 testing, are required under the Pharmaceutical Benefits Scheme, to enable certain specific therapies to be prescribed.

	G4.01	Any ancillary tests performed (where appropriate) should be recorded.
	CG4.01a	The recording of additional studies performed on tissue from resections with cholangiocarcinoma or hepatocellular carcinoma is regarded as good practice. This includes molecular analysis and immunohistochemistry. There is some evidence that immunoreactivity markers of "stemness" (eg K19, Epcam, etc) in hepatocellular carcinoma in >5% of cells may endow a poorer prognosis <sup>112</sup> but this is not yet widely applied in practice. <sup>113-115</sup>
	CG4.01b	Intrahepatic cholangiocarcinoma may show large duct or small duct patterns which may have prognostic significance, <sup>116</sup>
	CG4.01c	With increasing numbers of clinical trials and drug development, particularly in cases of HCC, the search for tissue and serological biomarkers to determine response to other therapies is rapidly advancing. This may result in specific stains being recommended in the near future.

## 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 '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.

 <b>S5.01</b>	<b>The tumour stage must be recorded according to the AJCC TNM system (8<sup>th</sup> edition).<sup>25</sup></b>
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**S5.02 The year of publication and edition of the cancer staging system used in S5.01 must be included in the report.**

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

- a. specimen submitted (S2.02)
- b. tumour type (S3.01)
- c. tumour stage (S5.01 & S5.02)
- d. whether or not the specimen margins are involved (S3.05)

**S5.03 The reporting system must provide a field for free text or narrative in which the reporting pathologist can give overarching case comment.**

CS5.03a This field may be used, for example, to:

- explain the decision-making pathway, or any elements of clinicopathological ambiguity, or factors affecting diagnostic certainty, thereby allowing communication of diagnostic subtlety or nuance that is beyond synoptic capture
- give recommendations for further action or investigation

- document further consultation or results still pending

CS5.03b 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.

CS5.02a 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 "XXXXXXXXXX" 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 prostate cancer. For emphasis, standards (mandatory elements) are formatted in bold font.

- S6.01 The structured checklist provided 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*.<sup>117</sup>
- 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.

Item descriptions in italics are conditional on previous responses.

Values in all caps are headings with sub values.

S/G	Item description	Response type	Conditional
<b>Pre-analytical</b>			
<b>S1.01</b>	<b>Demographic information provided</b>		
<b>S1.02</b>	<b>Clinical information provided on request form</b>	<b>Text</b> OR <b>Structured entry as below:</b>	
	<b>New primary lesion or recurrence</b>	<b>Single selection value list:</b> <ul style="list-style-type: none"> <li>• New primary</li> <li>• Recurrence – regional, <i>describe</i></li> <li>• Recurrence – distant, <i>describe</i></li> </ul>	
	<b>Radiological/imaging information</b>	<b>Text</b>	
	<b>Operative procedure</b>	<b>Text</b>	
G1.01	Copy To doctors recorded	<b>Text</b>	
<b>S1.03</b>	<b>Pathology accession number</b>	<b>Alpha-numeric</b>	
<b>S1.04</b>	<b>Principal clinician</b>	<b>Text</b>	
G1.02	Comments	<b>Text</b>	
<b>Macroscopic findings</b>			

<b>S2.01</b>	<b>Specimen labelled as</b>	<b>Text</b>	
G2.01	Operative procedure	<b>Text</b>	
 <b>S2.02</b>	<b>Specimen(s) submitted</b>	<p><b>Single selection value list:</b></p> <ul style="list-style-type: none"> <li>• Not specified</li> <li>• Indeterminate</li> </ul> <p>OR</p> <p><b>Multi selection value list (select all that apply):</b></p> <ul style="list-style-type: none"> <li>• Liver <ul style="list-style-type: none"> <li>○ Total hepatectomy</li> <li>○ Segmental resection, <i>list segments or type of segmentectomy</i></li> <li>○ Wedge resection, <i>Describe site/segment</i></li> </ul> </li> <li>• Extrahepatic bile duct</li> <li>• Gallbladder</li> <li>• Diaphragm</li> <li>• Lymph nodes, <i>specify site/s</i></li> <li>• Other, <i>specify</i></li> </ul>	

G2.02	Liver capsule	<p><b>Single selection value list:</b></p> <ul style="list-style-type: none"> <li>• Normal</li> <li>• Abnormal <ul style="list-style-type: none"> <li>○ Breached by tumour</li> <li>○ Nodular</li> <li>○ Evidence of previous biopsy or surgery <i>e.g scar or suture</i></li> </ul> </li> </ul>	
 G2.03	Specimen dimensions	<p><b>Numeric: __x__x__mm</b></p> <p><u>Notes:</u></p> <p>Indicate the greatest measurement for each parameter in an irregularly shaped specimen</p>	
	Length of extrahepatic bile duct (Applicable to perihilar cholangiocarcinoma only)	<p><b>Numeric: ____mm</b></p>	
 G2.04	Specimen weight	<p><b>Numeric: ____g</b></p>	
 G2.05	Satellitosis (Applicable to hepatocellular carcinoma only)	<p><b>Single selection value list:</b></p> <ul style="list-style-type: none"> <li>• Cannot be assessed</li> <li>• Not identified</li> <li>• Present</li> </ul>	

 G2.06	Macroscopic tumour rupture (Applicable to hepatocellular carcinoma and perihilar cholangiocarcinoma only)	<b>Single selection value list:</b> <ul style="list-style-type: none"> <li>• Fragmented specimen</li> <li>• Ruptured</li> <li>• Intact</li> </ul>	
 S2.03	<b>Tumour site and number</b>	No macroscopic residual tumour OR <b>Text:</b> <i>specify site</i> AND <b>Numeric:</b> Number of tumours per site (if possible) <u>Notes:</u> Repeat site and number of tumours per site for each tumour site identified.	

 S2.04	<b>Maximum tumour dimension</b>	<p>Cannot be assessed</p> <p>OR</p> <p><b>Text:</b> Tumour identification</p> <p>AND</p> <p><b>Numeric:</b> ___mm maximum dimension</p> <p><u>Notes:</u></p> <p>Repeat tumour identification and maximum dimension for each tumour identified.</p> <p>OR</p> <p>For a large number of tumours include a range: ___mm to ___mm</p>	
G2.07	<p>Minimum distance of tumour to liver capsule</p> <p>(Applicable to intrahepatic tumour specimens)</p>	<p><b>Numeric: ___mm</b></p>	
G2.08	<p>Distance of tumour to closest resection margin</p>	<p><b>Numeric: ___mm</b></p> <p><b>AND</b></p> <p><b>Text (margin, if possible)</b></p>	
G2.09	<p>Macroscopic involvement of vessels</p> <p>(Applicable to intrahepatic tumour specimens)</p>	<p><b>Single selection value list:</b></p> <ul style="list-style-type: none"> <li>• Not identified</li> <li>• Present, <i>specify vessel(s) involved</i></li> </ul>	

G2.10	Extent of invasion into biliary tree (Applicable to hilar cholangiocarcinoma specimens)	<b>Text</b>	
G2.11	Depth of invasion beyond biliary tree (Applicable to hilar cholangiocarcinoma specimens)	<b>Text</b>	
G2.12	Background parenchyma	<b>Single selection value list:</b> <ul style="list-style-type: none"> <li>• Normal</li> <li>• Abnormal, <i>describe eg cirrhotic/fibrotic/fatty change/nutmeg</i></li> </ul>	
 <b>S2.05</b>	<b>Block identification key</b>	<b>Text</b>	
G2.13	Additional macroscopic comments	<b>Text</b>	
<b>Microscopic findings</b>			
 <b>S3.01</b>	<b>Histological tumour type</b>	<b>Single selection value list:</b> <u>Primary tumour</u> <ul style="list-style-type: none"> <li>• Hepatocellular carcinoma</li> <li>• Hepatocellular carcinoma, fibrolamellar variant</li> </ul>	

		<ul style="list-style-type: none"> <li>• Cholangiocarcinoma</li> <li>• Combined hepatocellular – cholangiocarcinoma</li> <li>• Intraductal papillary neoplasm with an associated invasive carcinoma</li> <li>• Mucinous cystic neoplasm with an associated invasive carcinoma</li> <li>• Undifferentiated carcinoma</li> <li>• Carcinoma, type cannot be determined</li> </ul>	
 G3.01	Tumour growth pattern	<p><b>Single selection value list:</b></p> <p><u>Hepatocellular carcinoma</u></p> <ul style="list-style-type: none"> <li>• Cannot be determined</li> <li>• Small nodular type with indistinct margin</li> <li>• Margin distinct <ul style="list-style-type: none"> <li>○ Simple nodular type</li> <li>○ Simple nodular type with extranodular growth</li> <li>○ Confluent multinodular type</li> </ul> </li> <li>• Margin irregular (infiltrative type)</li> </ul> <p><u>Intrahepatic, and perihilar cholangiocarcinoma</u></p> <ul style="list-style-type: none"> <li>• Cannot be determined</li> <li>• Mass-forming</li> <li>• Intraductal-growth</li> </ul>	

		<ul style="list-style-type: none"> <li>• Periductal infiltrating</li> <li>• Mixed mass-forming and periductal infiltrating</li> </ul>	
ICCR S3.02	<b>Histological grade</b>	<b>Single selection value list:</b> <ul style="list-style-type: none"> <li>• Not applicable</li> <li>• Cannot be assessed</li> <li>• Well differentiated/G1</li> <li>• Moderately differentiated/G2</li> <li>• Poorly differentiated/G3</li> </ul>	
ICCR S3.03	<b>Extent of invasion</b>	<b>Single selection value list:</b> <ul style="list-style-type: none"> <li>• No evidence of primary tumour</li> <li>• Cannot be assessed</li> <li>• Macroscopic invasion <ul style="list-style-type: none"> <li>○ Tumour confined to liver</li> <li>○ Tumour confined to the extrahepatic bile ducts histologically (carcinoma in situ/high-grade dysplasia) (<i>Applicable to perihilar cholangiocarcinoma only</i>)</li> <li>○ Tumour involves visceral peritoneum</li> <li>○ Tumour directly invades gallbladder</li> </ul> </li> </ul>	

		<ul style="list-style-type: none"> <li>○ Tumour directly invades other adjacent organs</li> <li>• Microscopic invasion <ul style="list-style-type: none"> <li>○ Tumour confined to liver</li> <li>○ Tumour confined to the bile duct mucosa histologically (carcinoma in situ/high-grade dysplasia) <i>(Applicable to cholangiocarcinoma only)</i></li> <li>○ Tumour involves visceral peritoneum</li> <li>○ Tumour directly invades gallbladder</li> <li>○ Tumour directly invades other adjacent organs</li> </ul> </li> </ul>	
ICCR S3.04	<b>Vascular invasion</b>	<p><b>Single selection value list:</b></p> <ul style="list-style-type: none"> <li>• Not identified</li> <li>• Indeterminate</li> <li>• Present macroscopically (large portal or hepatic veins)</li> <li>• Present microscopically (small portal or hepatic veins)</li> </ul>	
ICCR G3.02	Perineural invasion (Applicable to intrahepatic and perihilar cholangiocarcinoma)	<p><b>Single selection value list:</b></p> <ul style="list-style-type: none"> <li>• Not identified</li> <li>• Indeterminate</li> </ul>	

		<ul style="list-style-type: none"> <li>• Present</li> </ul>	
G3.03	Loco-regional therapy ( <i>for Hepatocellular Carcinoma</i> )	<b>Single selection value list:</b> <ul style="list-style-type: none"> <li>• Complete necrosis (no viable tumour)</li> <li>• Incomplete necrosis (viable tumour present)</li> <li>• No necrosis</li> <li>• No prior treatment</li> <li>• Response cannot be assessed, <i>explain reasons</i></li> </ul>	<b>If incomplete, record the percentage necrosis</b>
	<i>Percentage necrosis</i>	<b>Numeric: ____ %</b>	
 G3.04	Response to neoadjuvant therapy ( <i>for Cholangiocarcinoma</i> )	<b>Single selection value list:</b> <ul style="list-style-type: none"> <li>• Complete necrosis (no viable tumour)</li> <li>• Incomplete necrosis (viable tumour present)</li> <li>• No necrosis</li> <li>• No prior treatment</li> <li>• Response cannot be assessed, <i>explain reasons</i></li> </ul>	<b>If incomplete, record the percentage necrosis</b>
	<i>Percentage necrosis</i>	<b>Numeric: ____ %</b>	
 S3.05	<b>Margin status</b>	<b>Single selection value list:</b> <ul style="list-style-type: none"> <li>• Cannot be assessed</li> <li>• Not involved by invasive carcinoma</li> <li>• Involved by invasive carcinoma</li> </ul>	<b>If not involved by invasive carcinoma record the distance of tumour to closest margin</b>

		<ul style="list-style-type: none"> <li>Involved by high-grade dysplasia/carcinoma in situ (<i>Applicable to cholangiocarcinoma only</i>)</li> </ul>	<b>If involved by invasive carcinoma or involved by high-grade dysplasia/carcinoma in situ (<i>Applicable to cholangiocarcinoma only</i>), specify the margins, if possible</b>
	<b>Distance of tumour to closest margin</b>	<b>Numeric: ___mm</b> OR Clearance is $\geq 10$ mm	
	<b>Margin(s) involved</b>	<b>Text</b>	
 S3.06	<b>Lymph node status</b>	<b>Single selection value list:</b> <ul style="list-style-type: none"> <li>No nodes submitted or found</li> <li>Not involved</li> <li>Involved</li> </ul>	<b>If involved record the number of LN examined and number of positive LN</b>
	<b>Number of lymph nodes examined</b>	Number cannot be determined OR <b>Numeric: ____</b>	
	<b>Number of positive lymph nodes</b>	<b>Numeric: ____</b>	<b>Not required if number cannot be determined is entered above.</b>
 S3.07	<b>COEXISTENT PATHOLOGY</b>	<b>None identified</b> OR complete the following elements	
	<b>Other histopathological features</b>	<b>Multi selection value list (select all that apply):</b>	

		<ul style="list-style-type: none"> <li>• Steatosis</li> <li>• Steatohepatitis</li> <li>• Iron overload</li> <li>• Biliary disease, <i>specify, if known</i></li> <li>• Chronic hepatitis, <i>specify type, if known</i></li> <li>• Other, <i>specify</i></li> </ul>	
	<b>Fibrosis</b>	<b>Single selection value list:</b> <ul style="list-style-type: none"> <li>• Not identified</li> <li>• Indeterminate</li> <li>• Present</li> </ul>	<b>If present, consider recording G3.05</b>
	<b>Dysplastic/pre-malignant lesions</b>	<b>None identified</b> OR complete the following:	
	<b>Biliary intra-epithelial neoplasia (BilIN)</b>	<b>Single selection value list:</b> <ul style="list-style-type: none"> <li>• Absent</li> <li>• Present <ul style="list-style-type: none"> <li>○ BilIN-1</li> <li>○ BilIN-2</li> <li>○ BilIN-3</li> </ul> </li> </ul>	
	<b>Low-grade hepatocellular dysplastic nodule</b>	<b>Single selection value list:</b> <ul style="list-style-type: none"> <li>• Absent</li> <li>• Present</li> </ul>	

	<b>High-grade hepatocellular dysplastic nodule</b>	<b>Single selection value list:</b> <ul style="list-style-type: none"> <li>• Absent</li> <li>• Present</li> </ul>	
	<b>Other</b>	<b>Text</b>	
G3.05	<b>Fibrosis - staging system</b>		
	<b>ISHAK stage</b>	<b>Numeric: ____/6</b>	<b>Report only if needed.</b>
	<b>KLEINER stage</b>	<b>Numeric: ____/4</b>	<b>Report only if needed.</b>
	<b>METAVIR stage</b>	<b>Numeric: ____/4</b>	<b>Report only if needed.</b>
	<b>BATTS-LUDWIG stage</b>	<b>Numeric: ____/4</b>	<b>Report only if needed.</b>
	<b>BRUNT stage</b>	<b>Numeric: ____/</b>	<b>Report only if needed.</b>
	<b>Other stage</b>	<b>Text (specify system and result)</b>	<b>Report only if needed.</b>
G3.06	Additional microscopic comment	<b>Text</b>	
<b>Ancillary findings</b>			
	G4.01 Ancillary studies	<b>Single selection value list:</b> <ul style="list-style-type: none"> <li>• Not performed</li> <li>• Performed, <i>describe</i></li> </ul>	
<b>Synthesis and overview</b>			
	<b>S5.01 PATHOLOGICAL STAGING (AJCC 8TH EDITION)</b>		
	<b>TNM descriptors</b>	<b>Multi select value list :</b>	

		<ul style="list-style-type: none"> <li>• m - multiple primary tumours</li> <li>• y - post therapy</li> <li>• r - recurrent</li> </ul>	
	<b>Primary tumour (T)</b>	<p><b>Single select value list :</b></p> <p><b>Liver</b></p> <p>TX Primary tumour cannot be assessed  T0 No evidence of primary tumour  T1 Solitary tumour <math>\leq 2</math> cm, or <math>&gt;2</math> cm without vascular invasion  T1a Solitary tumour <math>\leq 2</math> cm  T1b Solitary tumour <math>&gt;2</math> cm without vascular invasion  T2 Solitary tumour <math>&gt;2</math> cm with vascular invasion, or multiple tumours, none <math>&gt;5</math> cm  T3 Multiple tumours, at least one of which is <math>&gt;5</math> cm  T4 Single tumour or multiple tumours of any size involving a major branch of the portal vein or hepatic vein, or tumour(s) with direct invasion of adjacent organs other than the gallbladder or with perforation of visceral peritoneum</p> <p><b>Intrahepatic bile ducts</b></p> <p>TX Primary tumour cannot be assessed  T0 No evidence of primary tumour  Tis Carcinoma <i>in situ</i> (intraductal tumour)  T1 Solitary tumour without vascular invasion, <math>\leq 5</math> cm or <math>&gt;5</math>cm</p>	

		<p>T1a Solitary tumour <math>\leq</math> 5 cm without vascular invasion</p> <p>T1b Solitary tumour <math>&gt;</math>5 cm without vascular invasion</p> <p>T2 Solitary tumour with intrahepatic vascular invasion or multiple tumours, with or without vascular invasion</p> <p>T3 Tumour perforating the visceral peritoneum</p> <p>T4 Tumour involving local extrahepatic structures by direct invasion</p> <p><b>Perihilar bile ducts</b></p> <p>TX Primary tumour cannot be assessed</p> <p>T0 No evidence of primary tumour</p> <p>Tis Carcinoma <i>in situ</i>/high-grade dysplasia</p> <p>T1 Tumour confined to the bile duct, with extension up to the muscle layer or fibrous tissue</p> <p>T2 Tumour invades beyond the wall of the bile duct to surrounding adipose tissue, or tumour invades adjacent hepatic parenchyma</p> <p>T2a Tumour invades beyond the wall of the bile duct to surrounding adipose tissue</p> <p>T2b Tumour invades adjacent hepatic parenchyma</p> <p>T3 Tumour invades unilateral branches of the portal vein or hepatic artery</p> <p>T4 Tumour invades the main portal vein or its branches bilaterally, or the common hepatic artery; or unilateral second-order biliary</p>	
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		radicals with contralateral portal vein or hepatic artery involvement	
	Regional lymph nodes (N)	<p><b>Single selection value list :</b></p> <p>No nodes submitted or found</p> <p><b>OR</b></p> <p><b>Liver including intrahepatic bile ducts</b></p> <p>NX Regional lymph nodes cannot be assessed  N0 No regional lymph node metastasis  N1 Regional lymph node metastasis</p> <p><b>Perihilar bile ducts</b></p> <p>NX Regional lymph nodes cannot be assessed  N0 No regional lymph node metastasis  N1 One to three positive lymph nodes typically involving the hilar, cystic duct, common bile duct, hepatic artery, posterior pancreaticoduodenal, and portal vein lymph nodes.  N2 Four or more positive lymph nodes from the sites described for N1.</p>	
	<b>Distant metastasis (M)</b>	<p><b>Single selection value list :</b></p> <p>Not applicable</p> <p><b>OR</b></p>	

		M1 Distant metastasis	
<b>S5.02</b>	<b>Year and edition of staging system</b>	<b>Numeric:</b> year <b>AND</b> <b>Text:</b> Edition eg 1 <sup>st</sup> , 2 <sup>nd</sup> etc	
G5.01	Diagnostic summary Include: a. specimen submitted (S2.02) b. tumour type (S3.01) c. tumour stage (S5.01 & S5.02) d. whether or not the specimen margins are involved (S3.05)	<b>Text</b>	
<b>S5.03</b>	<b>Overarching comment</b>	<b>Text</b>	
G5.02	Edition/version number of the RCPA protocol on which the report is based	<b>Text</b>	

## 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. An example of a pathology report is shown in Appendix 3.

# Appendix 1 Pathology request form for liver cancer

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 Intrahepatic Cholangiocarcinoma, Perihilar Cholangiocarcinoma and Hepatocellular Carcinoma 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:
    - patient name
    - date of birth
    - sex
    - identification and contact details of requesting doctor
    - date of request
  - Document whether or not the patient identifies as Aboriginal and/or Torres Strait Islander in Australia, or Maori in New Zealand. This is in support of government initiatives to monitor the health of those who identify as indigenous, 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 ie 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

- The operative procedure should be recorded.
- **Preoperative radiological/imaging reports should ideally be available for review during pathological reporting of the surgical specimen, and key elements should be included with the clinical details (eg site and size).**
- **Record if this is a new primary cancer or a recurrence of a previous cancer, if known.**
  - The term recurrence defines the return, reappearance or metastasis of cancer (of the same histology) after a disease free period.

Recurrence should be classified as distant metastases or regional (local) recurrence.

Regional (local) recurrence refers to the recurrence of cancer cells at the same site as the original (primary) tumour or the regional lymph nodes.

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.
- Comments should be included, if appropriate.
  - Space for free text should be included to encourage reporting of ambiguity, or for the addition of other comments.

## Example Request Information Sheet

<b>Intrahepatic and Perihilar Cholangiocarcinoma and Hepatocellular Carcinoma</b> <b>Histopathology Request Information</b> 	
Family name <input type="text"/>	<b>Indigenous Status</b> <input type="radio"/> Aboriginal but not Torres Strait Islander origin <input type="radio"/> Torres Strait Islander but not Aboriginal origin <input type="radio"/> Both Aboriginal and Torres Strait Islander origin <input type="radio"/> Neither Aboriginal nor Torres Strait Islander origin <input type="radio"/> Not stated/inadequately described
Given name(s) <input type="text"/>	
Date of birth <input type="text" value="DD - MM - YYYY"/>	Date of request <input type="text" value="DD - MM - YYYY"/>
Patient identifiers e.g. MRN, IHI or NHI (please indicate which) <input type="text"/>	Requesting doctor - name and contact details <input type="text"/>
Copy to doctor name and contact details <input type="text"/>	
<b>RADIOLOGICAL/IMAGING INFORMATION</b> <input type="text"/> <input type="text"/> <input type="text"/>	<b>NEW PRIMARY LESION OR RECURRENCE</b> <input type="radio"/> New primary <input type="radio"/> Recurrence - regional, <i>describe</i> <input type="text"/> <input type="radio"/> Recurrence - distant, <i>describe</i> <input type="text"/>
<b>OPERATIVE PROCEDURE</b> <input type="text"/> <input type="text"/> <input type="text"/>	<b>PRINCIPAL CLINICIAN</b> <input type="text"/>
	<b>OTHER COMMENTS</b> <input type="text"/> <input type="text"/> <input type="text"/>
<small>V 1.0 Request Information from Intrahepatic and Perihilar Cholangiocarcinoma and Hepatocellular Carcinoma Structured Reporting Protocol 1st Edition</small>	

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.<sup>118</sup>

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. The following strategies should be used:

Configure reports in such a way that data elements are 'chunked' into a single unit to help improve recall for the clinician.<sup>118</sup>

Reduce 'clutter' to a minimum.<sup>118</sup> Thus, information that is not part of the protocol (eg billing information or SNOMED codes) should not appear on the reports or should be minimised.

Reduce the use of formatting elements (eg bold, underlining or use of footnotes) because these increase 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

<b>Citizen, Gerald W.</b> C/O Paradise Close Wreck Bay Resort Nar Nar Goon East, 3181		Lab Ref: <b>18/P28460</b> Referred: 30/8/2018	
Male DOB 1/7/1987 MRN M1196785	Copy to: Dr N.G.Chappie Rainforest Cancer Centre, 46 Smith Road, Woop Woop, 3478	Referred by: Dr V. Brown Suite 3, AJC Medical Centre, Bunyip Crescent Nar Nar Goon West, 3182	

**LIVER CANCER STRUCTURED REPORT** Page 1 of 2

### Diagnostic Summary

**Liver, segmental resection, segments V/VIII**

**Hepatocellular carcinoma, Stage pT1NX (AJCC 8<sup>th</sup> edition, 2016);  
Surgical margins negative**

Comment: Non neoplastic liver has cirrhotic nodules ranging between 3 and 5 mm; Severe fibrosis present (Ishak score 6) and Steatosis 5%.

### Supporting Information

#### CLINICAL INFORMATION RECEIVED

<b>Clinical history:</b>	Segment V/VIII liver resection. Cirrhosis secondary to past hepatitis C successfully treated. Liver lesions segment V/VIII consistent with HCC on imaging
<b>New primary lesion or recurrence:</b>	New primary

#### MACROSCOPIC

<b>Specimen labelled as:</b>	"Liver"
<b>Operative procedure:</b>	Minor hepatectomy (less than 3 segments)"
<b>Specimen submitted:</b>	Liver, segmental resection, segments V/VIII
<b>Liver capsule:</b>	Abnormal, nodular
<b>Specimen dimensions:</b>	160 x 95 x 65 mm
<b>Specimen weight:</b>	403g
<b>Tumour site and number:</b>	1 tumour in segment 8 in a subcapsular location
<b>Maximum tumour dimension:</b>	18mm
<b>Dist. of tumour to closest resection margin:</b>	25mm, parenchymal margin
<b>Macroscopic involvement of vessels:</b>	Not identified
<b>Background parenchyma:</b>	Abnormal, remaining liver has a nodular cut surface with nodules ranging between 3 and 5 mm
<b>Block identification key:</b>	A-C: tumour; D,E: parenchymal margin; F,G: tissue adjacent to tumour.
<b>Additional macroscopic comments:</b>	The parenchymal resection margin is inked blue

**MICROSCOPIC**

**Tumour**

<b>Histologic tumour type:</b>	Hepatocellular carcinoma
<b>Histological grade:</b>	Moderately differentiated/G2
<b>Tumour growth pattern:</b>	Margin distinct, simple nodular type

**Extent**

<b>Extent of invasion:</b>	Tumour confined to liver
<b>Vascular invasion:</b>	Not identified
<b>Perineural invasion:</b>	Not identified

**Margin status:** Not involved by invasive carcinoma

**Lymph node status:** No nodes submitted

**Coexistent pathology:**

**Other histopathological features:** Steatosis, 5%

**Fibrosis:** Present

**ISHAK stage:** 6/6

**ANCILLARY TESTS**

None performed.

*Reported by Dr Bernadette Beckstein*

*Authorised 4/9/2018*

## Appendix 4 WHO Classification of Tumours of the Liver and Intrahepatic Bile Ducts<sup>a</sup>

Descriptor	ICD-O codes
<b>Epithelial tumours: hepatocellular</b>	
<i>Malignant</i>	
Hepatocellular carcinoma	8170/3
Hepatocellular carcinoma, fibrolamellar variant	8171/3
Undifferentiated carcinoma	8020/3
<b>Epithelial tumours: biliary</b>	
<i>Malignant</i>	
Intrahepatic cholangiocarcinoma	8160/3
Intraductal papillary neoplasm with an associated invasive carcinoma	8503/3*
Mucinous cystic neoplasm with an associated invasive carcinoma	8470/3
<i>Malignancies of mixed or uncertain origin</i>	
Combined hepatocellular-cholangiocarcinoma	8180/3

<sup>a</sup> The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) and the Systematized Nomenclature of Medicine (SNOMED). Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours.

\* These new codes were approved by the IARC/WHO Committee for ICD-O at its meeting in March 2010.

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