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| **Core/ Non-core** | **Element name** | **Values** | **Commentary** | **Implementation notes** |
| Non-core | CLINICAL INFORMATION | Multi select value list (choose all that apply): • Not provided • Radiological appearance  • History of previous cancer • Other (describe) | Clinical information is essential to proper processing and evaluation of pathological specimens as it can influence pre-test probability of a particular diagnosis. This allows the pathology laboratory to accurately triage processing, including extent of sampling. It also informs the pathologist as to decisions ultimately influencing the number of slides to be examined (serial sections, levels) and potential ancillary studies to be performed1, thus avoiding error. For malignant mesothelioma, the radiologic growth pattern and history of previous cancer are important guides to further analysis of a particular specimen. A radiologic nodular growth pattern may prompt correlation with surgical thoracoscopic observations with regard to nodule sampling, while a diffuse growth pattern may lead to a request for deeper or more extensive samples. History of prior cancer could suggest a different panel of immunohistochemical stains to definitively rule out metastasis from a known tumour. A cancer history can prompt a request to review prior outside material or to review an archival in house slide record.1 Other valuable clinical information includes presence of a pleural effusion and its characteristics (e.g. transudative, bloody, exudative); this can trigger review of and correlation with a concurrent cytological specimen. A history of asbestos exposure is not relevant for the diagnosis of samples in which malignant mesothelioma is a consideration, as this history does not influence sample processing or ultimate diagnosis.2  References  1 Wick MR (2007). Medicolegal liability in surgical pathology: a consideration of underlying causes and selected pertinent concepts. Semin Diagn Pathol 24(2):89-97.  2 Husain AN, Colby TV, Ordonez NG, Allen TC, Attanoos RL, Beasley MB, Butnor KJ, Chirieac LR, Churg AM, Dacic S, Galateau-Salle F, Gibbs A, Gown AM, Krausz T, Litzky LA, Marchevsky A, Nicholson AG, Roggli VL, Sharma AK, Travis WD, Walts AE and Wick MR (2017). Guidelines for Pathologic Diagnosis of Malignant Mesothelioma: 2017 Update of the Consensus Statement From the International Mesothelioma Interest Group. Arch Pathol Lab Med doi: 10.5858/arpa.2017-0124-RA. [Epub ahead of print] |  |
| Non-core | NEOADJUVANT THERAPY | Single selection value list: • Not administered  • Information not provided • Administered (describe) | A history of neoadjuvant therapy is important in the pathology analysis. Assessment of residual tumour, including nodal status, is critical to staging and prognostication in the neoadjuvant setting.1,2    References  1 Van Schil PE, Opitz I, Weder W, De Laet C, Domen A, Lauwers P, Hendriks JM and Van Meerbeeck JP (2014). Multimodal management of malignant pleural mesothelioma: where are we today? Eur Respir J 44(3):754-764. 2 de Perrot M, Feld R, Cho BC, Bezjak A, Anraku M, Burkes R, Roberts H, Tsao MS, Leighl N, Keshavjee S and Johnston MR (2009). Trimodality therapy with induction chemotherapy followed by extrapleural pneumonectomy and adjuvant high-dose hemithoracic radiation for malignant pleural mesothelioma. J Clin Oncol 27(9):1413-1418. |  |
| Core | OPERATIVE PROCEDURE | Single select value list: • Not provided • Core biopsy • Open biopsy • VATS biopsy • Decortication • Radical pleurectomy • Extrapleural pneumonectomy • Debulking • Other (specify) | Documentation of the operative procedure is useful, as correlation of the type of procedure with the material received can be important for patient safety. In resection specimens, the type of surgical procedure is important in determining the assessment of surgical margins. Due to advanced age, clinical status, or extent of disease, few mesothelioma patients are suitable for extrapleural pneumonectomy or radical pleurectomy and therefore, diagnosis is usually based upon biopsy alone. Although the volume of tissue sampled is more restricted than for surgical resection specimens, biopsy assessment may contribute significant observations for clinical management and prognosis, in addition to the crucial distinction between secondary tumours affecting the serosal membranes and mesothelioma, and between mesothelioma and benign reactive mesothelial proliferations.  The type of biopsy is important as it affects the extent to which a diagnosis may be made with any certainty. Accurate typing of mesothelioma1-4 has been shown to vary by procedure - 83% for open biopsy in comparison to 74% for Video-assisted thoracoscopic surgery (VATS) biopsy, and 44% for X-ray computed tomography (CT)-guided biopsy, when compared with the subtype assessed in a follow-up series of 83 extrapleural pneumonectomy (EPP) specimens.4  References  1 Bueno R, Reblando J, Glickman J, Jaklitsch MT, Lukanich JM and Sugarbaker DJ (2004). Pleural biopsy: a reliable method for determining the diagnosis but not subtype in mesothelioma. Ann Thorac Surg 78(5):1774-1776. 2 Greillier L, Cavailles A, Fraticelli A, Scherpereel A, Barlesi F, Tassi G, Thomas P and Astoul P (2007). Accuracy of pleural biopsy using thoracoscopy for the diagnosis of histologic subtype in patients with malignant pleural mesothelioma. Cancer 110(10):2248-2252. 3 Attanoos RL and Gibbs AR (2008). The comparative accuracy of different pleural biopsy techniques in the diagnosis of malignant mesothelioma. Histopathology 53(3):340-344. 4 Kao SC, Yan TD, Lee K, Burn J, Henderson DW, Klebe S, Kennedy C, Vardy J, Clarke S, van Zandwijk N and McCaughan BC (2011). Accuracy of diagnostic biopsy for the histological subtype of malignant pleural mesothelioma. J Thorac Oncol 6(3):602-605. |  |
| Core | SPECIMEN(S) SUBMITTED | Multi select value list (choose all that apply): • Not provided Pleura/Thoracic • Diaphragm • Lung  • Right  • Wedge  • Lobe  • Entire Lung  • Left  • Wedge  • Lobe  • Entire Lung • Mediastinal fat • Pericardium • Parietal pleura • Contralateral pleura • Visceral pleura • Endothoracic fascia • Chest wall • Rib • Spine • Port site  Peritoneum • Peritoneum • Omentum • Left ovary • Right ovary • Left fallopian tube • Right fallopian tube • Uterus • Other intra-abdominal organs (specify)  Other submitted specimens • Lymph nodes (specify site(s)) • Other submitted specimens (specify) |  |  |
| Non-core | TUMOUR SIZE |  | For pleural mesotheliomas that are received as radical surgical (EPP or P/D) specimens, attempting to measure the dimensions of individual tumour nodules is neither simple (because the distinction between tumour and fibrotic reaction may be difficult to assess) nor informative. Rather, measuring the maximum thickness of tumour appears to be a more useful indicator of tumour burden and can often be compared to radiologic measurements.1 For peritoneal mesotheliomas, the specimen is normally received in multiple parts and dimensions of the dominant mass should be measured. Where multiple nodules are present, the dimensions of the largest nodule should be recorded.  References  1 College of American Pathologists (2015). Cancer protocol templates. Available from: http://www.cap.org/web/home/resources/cancer-reporting-tools/cancer-protocol-templates?\_adf.ctrl-state=10jd5draq2\_17&\_afrLoop=78742816534289#!%40%40%3F\_afrLoop%3D78742816534289%26\_adf.ctrl-state%3D4596lsm96\_4. http://www.cap.org/apps/cap.portal?\_nfpb=true&cntvwrPtlt\_actionOverride=%2Fportlets%2FcontentViewer%2Fshow&\_windowLabel=cntvwrPtlt&cntvwrPtlt%7BactionForm.contentReference%7D=committees%2Fcancer%2Fcancer\_protocols%2Fprotocols\_index.html&\_state=maximized&\_pageLabel=cntvwr (Accessed 19th Feb 2016). | Heading |
| Non-core | TUMOUR SIZE - Pleural specimens |  |  | Record both Maximum thickness of any mass AND Dimensions of dominant mass |
| Non-core | Maximum thickness of any mass | Numeric:\_\_\_mm  OR Indeterminate |  |  |
| Non-core | Dimensions of dominant mass | Numeric: \_\_\_x\_\_x\_\_mm OR indeterminate |  |  |
| Non-core | TUMOUR SIZE - Peritoneal specimens |  |  | Record Maximum thickness of any mass OR Dimensions of dominant mass |
| Non-core | Dimensions of dominant mass | Numeric: \_\_\_x\_\_x\_\_mm OR indeterminate |  |  |
| Non-core | Dimensions of largest nodule | Numeric: \_\_\_x\_\_x\_\_mm OR indeterminate |  |  |
| Core | MACROSCOPIC TUMOUR SITE | Multi select value list (choose all that apply): • Indeterminate Pleura/Thoracic • Diaphragm • Lung  • Right  • Left • Mediastinal fat • Pericardium • Parietal pleura • Contralateral pleura • Visceral pleura • Endothoracic fascia • Chest wall • Rib • Spine • Port site  Peritoneum • Peritoneum • Omentum • Left ovary • Right ovary • Left fallopian tube • Right fallopian tube • Uterus • Other intra-abdominal organs (specify)  Other  • Lymph nodes • Other site (specify) |  |  |
| Non-core | MITOTIC COUNT | Numeric:\_\_\_\_per mm2 | In pleural malignant mesothelioma, mitotic count has not been definitively established as an independent parameter in the diagnostic setting or as a determinant of prognosis. However among epithelioid peritoneal malignant mesothelioma, increased mitotic count (greater than 4 in 10 HPF )1 was reported as a poor prognostic indicator, and, more recently, was validated in a multi-observer study of an independent group of patients2, establishing a lower cut-off of 5 mitoses in 50 HPF.  Ki-67 fraction may also have prognostic significance, but its use as an adjunct to mitotic count has not been investigated. References  1 Borczuk AC, Taub RN, Hesdorffer M, Hibshoosh H, Chabot JA, Keohan ML, Alsberry R, Alexis D and Powell CA (2005). P16 loss and mitotic activity predict poor survival in patients with peritoneal malignant mesothelioma. Clin Cancer Res 11(9):3303-3308. 2 Krasinskas AM, Borczuk AC, Hartman DJ, Chabot JA, Taub RN, Mogal A, Pingpank J, Bartlett D and Dacic S (2016). Prognostic significance of morphological growth patterns and mitotic index of epithelioid malignant peritoneal mesothelioma. *Histopathology* 68(5):729-737 | Applicable to peritoneal specimens only |
| Core | HISTOLOGICAL TUMOUR TYPE | Single selection value list: • Epithelioid (Epithelial) • Sarcomatoid (Sarcomatous) • Biphasic (Mixed epithelial and sarcomatous) • Malignant mesothelioma, NOS | The major histological tumour types of malignant mesothelioma as recognized by the World Health Organisation (WHO) classification (4th edition)1 are epithelioid, sarcomatoid and biphasic/mixed. By convention a biphasic mesothelioma is diagnosed if the lesser component reaches 10% of the tumour examined.  There are a number of histological patterns of malignant mesothelioma which are important to be aware of primarily because of diagnostic confusion. For epithelioid mesothelioma these include common patterns such as solid, tubulopapillary, and trabecular, also less common forms such as micropapillary, adenomatoid (microcystic), clear cell, transitional, deciduoid, small cell and pleomorphic mesothelioma. It should be noted that, at present, there is no uniformity among pathologists for the definition of many of these patterns nor any clear prognostic significance to most of them, and we do not recommend these names be included as part of a diagnosis; their importance lies in the recognition by the pathologist that these are patterns seen in mesotheliomas. For sarcomatoid mesothelioma these histological variants may comprise heterologous (osteosarcomatous, chondrosarcomatous and rhabdomyosarcomatous) elements, and desmoplastic mesothelioma. Desmoplastic mesothelioma is characterized by atypical spindle cells and dense hyalinised fibrous stroma, the latter comprising at least 50% of the tumour.2  The conventional immunohistochemical panel of markers may require modification with some of these patterns to prevent misdiagnosis. Some of these patterns may have prognostic significance; however, until these prognostic patterns are clearly defined and accepted, the current recommendation is to diagnose mesotheliomas as epithelioid, sarcomatoid/desmoplastic, or biphasic/mixed, particularly since radical surgical approaches depend on these general classifications.  In some cases, such as small biopsy specimens, a definitive tumour type cannot be assigned and in this situation a value of “mesothelioma not otherwise specified (NOS)” would be used.   WHO classification of tumours of the pleura  References  1 WHO (World Health Organization) (2015). WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart. Fourth edition Travis WD, Brambilla E, Burke AP, Marx A and Nicholson AG. IARC Press, Lyon, France.  2 Husain AN, Colby TV, Ordonez NG, Allen TC, Attanoos RL, Beasley MB, Butnor KJ, Chirieac LR, Churg AM, Dacic S, Galateau-Salle F, Gibbs A, Gown AM, Krausz T, Litzky LA, Marchevsky A, Nicholson AG, Roggli VL, Sharma AK, Travis WD, Walts AE and Wick MR (2017). Guidelines for Pathologic Diagnosis of Malignant Mesothelioma: 2017 Update of the Consensus Statement From the International Mesothelioma Interest Group. Arch Pathol Lab Med doi: 10.5858/arpa.2017-0124-RA. [Epub ahead of print] | Note that permission to publish the WHO classification of tumours may be needed in your implementation. It is advisable to check with the International Agency on Cancer research (IARC) |
| Non-core | RESPONSE TO NEOADJUVANT THERAPY | Single selection value list: • Cannot be assessed • Prior treatment not known • No prior treatment • No response • Positive response  • No or minimal tumour response   • Partial tumour response   • Complete or near-complete response | There is no recommended or agreed system for tumour regression grading of mesothelioma that has been treated with neoadjuvant therapy, however a general indication of residual viable tumour may be useful. |  |
| Core | MARGIN STATUS | Single selection value list: • Cannot be assessed • Not applicable • Not involved • Cannot be assessed • Involved, Specify margin(s), if possible | In extrapleural pneumonectomy specimens (EPP) the bronchial resection margin status is evaluated by intraoperative frozen section examination. In the surgical pathology specimen, the soft tissue margin status is difficult to assess because the entire pleura represents a margin. Usually in patients with extrapleural pneumonectomy (EPP), the surgeon is performing a blind dissection beneath the endothoracic fascia between the pleura and chest wall. | Applicable to extrapleural pneumonectomy specimens only |
| Non-core | COEXISTENT PATHOLOGY | Single selection value list: • None identified OR Specify | It is recommended that pathologists comment upon any coexistent non-neoplastic findings present in the submitted materials. These include, for extrapleural pneumonectomy specimens, such findings as emphysema, small airways disease, respiratory bronchiolitis, asbestosis, asbestos bodies, talc granulomas and pleural plaques.1 For diagnosing asbestosis, it is recommended that the criteria published by the asbestosis committee of the College of American Pathologists and Pulmonary Pathology Society be used.2 For peritoneal resection specimens, additional findings such as endometriosis, endosalpingiosis and mesothelial inclusion cysts should be noted. Reference  1 Mark EJ (1981). The second diagnosis: the role of the pathologist in identifying pneumoconioses in lungs excised for tumor. Hum Pathol 12(7):585-587. 2 Roggli VL, Gibbs AR, Attanoos R, Churg A, Popper H, Cagle P, Corrin B, Franks TJ, Galateau-Salle F, Galvin J, Hasleton PS, Henderson DW and Honma K (2010). Pathology of asbestosis - An update of the diagnostic criteria: Report of the asbestosis committee of the College of American Pathologists and Pulmonary Pathology Society. Arch Pathol Lab Med 134(3):462-480. |  |
| Core | EXTENT OF INVASION | Multi select value list (choose all that apply): • Cannot be assessed • No evidence of primary tumour • Parietal pleura without involvement of the ipsilateral visceral pleura • Parietal pleura with focal involvement of the ipsilateral visceral pleura • Endothoracic fascia (as determined by surgeon/radiologist) • Mediastinal fat • Localised focus of tumour invading the soft tissue of the chest wall • Diffuse or multiple foci invading soft tissue of chest wall • Through the pericardium or diaphragm • Into but not through the pericardium or diaphragm • Rib(s) • Peritoneum through the diaphragm • Great vessels/oesophagus/trachea or other mediastinal organ • Extension into contralateral pleura • Spine • Myocardium • Confluent visceral and parietal pleural tumour (including fissure) • Mediastinal organ(s) (specify) • Other (specify) | Extent of invasion is part of staging for radical pleural surgical specimens. In biopsies the presence of invasion is the most important parameter for separating benign from malignant mesothelial proliferations.  Invasion into the endothoracic fascia is a staging parameter and should be determined only by the surgeon or radiologist, since there are no characteristic pathological features appreciable by gross or microscopic examination.  The endothoracic fascia represents a connective tissue plane that lies between the parietal pleura and the innermost intercostal muscle. Its histology is not well defined. Sections from parietal pleura that appose the chest wall showing histologic involvement of skeletal muscle is the best surrogate indicator that the endothoracic fascia has been breached. |  |
| Core | LYMPH NODE STATUS | Single selection value list: • No nodes submitted or found • Cannot be assessed OR Record  • Involved  • Not involved for each Lymph node station/location or specimen identification | Thoracic or abdominal lymph nodes may be sampled to obtain a diagnosis or for the staging of an already diagnosed tumour. If thoracic, they should be identified by standard station; for abdominal lymph nodes, a suitable specimen identifier or descriptor should be used. A lymph node station should be regarded as positive for mesothelioma regardless of the number of malignant mesothelial cells present or the number of lymph nodes involved provided one node contains malignant mesothelial cells. However, the identification of mesothelial cells in lymph nodes does not necessarily indicate metastasis. Rarely may they represent incidental inclusions.1,2 The diagnosis of metastatic mesothelioma should only be made when there is good evidence of a serosa based tumour whether diffuse or, very rarely, localized.   References  1 Parkash V, Vidwans M and Carter D (1999). Benign mesothelial cells in mediastinal lymph nodes. Am J Surg Pathol 23(10):1264-1269.  2 Goyal M, Kodandapani S, Sharanabasappa SN and Palanki SD (2010). Mesothelial cell inclusions mimicking adenocarcinoma in cervical lymph nodes in association with chylous effusion. Indian J Med Paediatr Oncol 31(2):62-64. |  |
| Non-core | ANCILLARY STUDIES | Single selection value list: • Not performed • Performed | The three most common molecular alterations in malignant mesothelioma are loss of neurofibromin 2 (Merlin, NF2), cyclin-dependent kinase inhibitor 2A (CDKN2A, p16), and BRCA1 associated protein-1 (BAP1). While to date NF2 loss has not been exploited diagnostically, p16 Fluorescence in situ hybridization (FISH) and BAP1 appear to be useful markers for separating benign from malignant mesothelial proliferations.1 Thus far both these markers have been reported as only lost in malignant mesotheliomas when strict cut-offs are applied. One outcome of the strict cut-off is the major problem of low sensitivity. Overall, studies reporting loss of p16 by FISH in mesotheliomas show a sensitivity around 50%, albeit significantly higher in pleural (67% ) than peritoneal mesothelioma (25%).1  Loss of p16 by FISH in pleural mesothelioma is correlated with adverse survival.2,3 Retention of p16 by immunohistochemistry is a useful prognostic indicator in peritoneal epithelioid malignant mesothelioma, with a significantly prolonged survival in that group.4 The sensitivity for loss of nuclear expression of BAP1 is not well defined but probably on the order of 50 to 70% for epithelioid mesotheliomas, and very low for sarcomatoid mesotheliomas.1 But these markers are only useful when lost; positive staining does not rule out a mesothelioma.  BAP1 immunohistochemistry in addition is useful as a screening tool for BAP1 germline mutation syndromes, in which there are familial aggregations of mesotheliomas, melanomas including ocular melanomas, renal cell carcinomas, and probably a variety of other tumours.5 Interestingly, patients with BAP1 germline mutation mesotheliomas are reported to have dramatically better survival rates.6 However, BAP1 immunohistochemistry is no more than a screening tool in this context, since the vast majority of mesotheliomas that show BAP1 loss only have somatic mutations, and formal genetic analysis is required to confirm germline tumours. Positive immunohistochemistry for EMA , Glut1 , IMP3 and CD 146 have all been proposed as single markers for malignant mesothelioma when compared to benign proliferations.1 Since small but significant proportions of benign proliferations are positive for each of these markers, combinations of markers have been proposed, but the correlations are weak.7-10 Therefore in the absence of morphologic invasion (cytology, small biopsy, or cellular atypia alone) these markers should not be relied upon as the sole determinant of malignancy.  References  1 Churg A, Sheffield BS and Galateau-Salle F (2016). New Markers for Separating Benign From Malignant Mesothelial Proliferations: Are We There Yet? *Arch Pathol Lab Med* 140(4):318-321.  2 Dacic S, Kothmaier H, Land S, Shuai Y, Halbwedl I, Morbini P, Murer B, Comin C, Galateau-Salle F, Demirag F, Zeren H, Attanoos R, Gibbs A, Cagle P and Popper H (2008). Prognostic significance of p16/cdkn2a loss in pleural malignant mesotheliomas. Virchows Arch 453(6):627-635.  3 Lopez-Rios F, Chuai S, Flores R, Shimizu S, Ohno T, Wakahara K, Illei PB, Hussain S, Krug L, Zakowski MF, Rusch V, Olshen AB and Ladanyi M (2006). Global gene expression profiling of pleural mesotheliomas: overexpression of aurora kinases and P16/CDKN2A deletion as prognostic factors and critical evaluation of microarray-based prognostic prediction. Cancer Res 66(6):2970-2979.  4 Borczuk AC, Taub RN, Hesdorffer M, Hibshoosh H, Chabot JA, Keohan ML, Alsberry R, Alexis D and Powell CA (2005). P16 loss and mitotic activity predict poor survival in patients with peritoneal malignant mesothelioma. Clin Cancer Res 11(9):3303-3308.  5 Carbone M, Yang H, Pass HI, Krausz T, Testa JR and Gaudino G (2013). BAP1 and cancer. Nat Rev Cancer 13(3):153-159.  6 Baumann F, Flores E, Napolitano A, Kanodia S, Taioli E, Pass H, Yang H and Carbone M (2015). Mesothelioma patients with germline BAP1 mutations have 7-fold improved long-term survival. Carcinogenesis 36(1):76-81.  7 Minato H, Kurose N, Fukushima M, Nojima T, Usuda K, Sagawa M, Sakuma T, Ooi A, Matsumoto I, Oda M, Arano Y and Shimizu J (2014). Comparative immunohistochemical analysis of IMP3, GLUT1, EMA, CD146, and desmin for distinguishing malignant mesothelioma from reactive mesothelial cells. Am J Clin Pathol 141(1):85-93.  8 Lagana SM, Taub RN and Borczuk AC (2012). Utility of glucose transporter 1 in the distinction of benign and malignant thoracic and abdominal mesothelial lesions. Arch Pathol Lab Med 136(7):804-809.  9 Monaco SE, Shuai Y, Bansal M, Krasinskas AM and Dacic S (2011). The diagnostic utility of p16 FISH and GLUT-1 immunohistochemical analysis in mesothelial proliferations. Am J Clin Pathol 135(4):619-627.  10 Lee AF, Gown AM and Churg A (2013). IMP3 and GLUT-1 immunohistochemistry for distinguishing benign from malignant mesothelial proliferations. Am J Surg Pathol 37(3):421-426. | If performed, record results under applicable headings |
| Non-core | Immunohistochemistry (List stains) | Text |  |  |
| Non-core | Other (specify) | Text |  |  |
| Core | PATHOLOGICAL STAGING (TNM 8th edition) |  |  | PLEURAL SPECIMENS only  Note that permission to publish cancer staging tables may be needed in your implementation. It is advisable to check. |
| Core | Suffixes | Choose if applicable: • m - multiple primary tumours at a single site • r - recurrent tumours after a disease free period • y - classification is performed during or following multimodality treatment |  |  |
| Core | Primary tumour (T) | Per 8th edition |  |  |
| Core | Regional lymph nodes (N) | Per 8th edition |  |  |