

**Datasets for the Histopathological Reporting of Neoplasms of the Ovaries and Fallopian Tubes and Primary Carcinomas of the Peritoneum**

**Version History**

<b>Version</b>	<b>Date</b>	<b>Summary of Change/Process</b>
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This is a national document produced by the Royal College of Pathologists ([www.rcpath.org](http://www.rcpath.org)) and is the latest version.

## 1. Scope of the guideline

This document is to inform and assist with the reporting of cervical neoplasia.

## 2. Guideline background

At Network Site Specific Group (NSSG) meetings the group acknowledged the need for pathology guidance for gynaecology. The NSSG recommended the guidance produced by the Royal College of Pathologists (RCP) and both Gynae and Cellular Pathology NSSGs agreed to adopt this guidance.

## Monitoring of the guideline

Adherence to the Network guidelines may from time to time be formally monitored.

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## References

[http://www.rcpath.org/resources/pdf/g070\\_vulvadataset\\_jun08.pdf](http://www.rcpath.org/resources/pdf/g070_vulvadataset_jun08.pdf)

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The Royal College of Pathologists

Pathology: the science behind the cure

## Standards and datasets for reporting cancers

### Datasets for the histopathological reporting of neoplasms of the ovaries and fallopian tubes and primary carcinomas of the peritoneum

July 2008

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<b>Comments</b>	<p>In accordance with the College's pre-publications policy, this document was put on The Royal College of Pathologists' website for consultation from 3 June – 1 July 2008. 20 pieces of feedback were received and the authors considered them and amended the document accordingly.</p> <p>Please email <a href="mailto:publications@rcpath.org">publications@rcpath.org</a> if you wish to see the responses and comments.</p> <p>This edition replaces the 1<sup>st</sup> edition of the Minimum dataset for the histopathological reporting of ovarian tumours, and Fallopian tube and primary peritoneal carcinomas, published in March 2005.</p> <p><b>Professor Carrock Sewell</b> <b>Director of Communications</b></p>

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## 1 Introduction

This document provides the datasets for the histopathological reporting of ovarian neoplasms in resection specimens and replaces the original 2005 dataset.<sup>1</sup> The new dataset is largely based on the original, although there are some important changes. Datasets for primary fallopian tube carcinoma and primary peritoneal carcinoma are included, but the dataset for reporting of non-epithelial tumours has been removed as it was the view of the authors and the British Association of Gynaecological Pathologists (BAGP) Working Group that, given the diverse nature and the rarity of many of these neoplasms, each with differing prognostic factors, an all-encompassing dataset is of little value.

Strict criteria should be used for the diagnosis of a primary fallopian tube or peritoneal carcinomas. The World Health Organization (WHO) criteria<sup>2</sup> for a primary fallopian tube carcinoma are:

- i. the tumour must be located macroscopically within the tube or its fimbriated end
- ii. the uterus and ovary must either not contain carcinoma or, if they do, it must be clearly different from the fallopian tube lesion.

The presence of *in situ* carcinoma in the tube adjacent to the carcinoma may also be useful in helping to confirm a tubal primary. Most tubal carcinomas are of serous or endometrioid type. For primary fallopian tube carcinomas, it is useful to record the site of the tumour within the tube since it has been suggested that fimbrial tumours have a worse prognosis due to easy access to the peritoneal cavity.<sup>3</sup> The Association of Directors of Anatomic and Surgical Pathology have recently provided guidelines for the reporting of fallopian tube neoplasms.<sup>4</sup>

The following criteria for a primary peritoneal carcinoma, used by the WHO<sup>2</sup> and adopted from the Gynecologic Oncology Group (GOG), should be used:

- i. both ovaries should be normal in size or enlarged by a benign process
- ii. the involvement in extraovarian sites must be greater than the involvement of the surface of either ovary
- iii. ovarian tumour involvement must be either non-existent, confined to the ovarian surface epithelium without stromal invasion or involve the cortical stroma with tumour size less than 5 x 5 mm.

Most primary peritoneal carcinomas are of serous type.

An important change from the previous dataset is that it is now recommended that serous carcinomas of the ovary, fallopian tube or peritoneum are graded using a two-tier system. More specific guidance is provided regarding the grading of other morphological subtypes.

Meticulous and accurate recording of the pathological parameters in the datasets have important implications for the staging and prognosis of individual patients and play a large part in assessing the need for adjuvant chemotherapy.

Use of the datasets is advocated in the context of the multidisciplinary team meeting (MDTM) as an adjunct to clinical decision making relevant to the treatment of each individual patient. This will also facilitate regular audit and review of all aspects of the service, facilitate the collection of accurate data for cancer registries and provide feedback for those caring for patients with cancer.

It is important to have robust local mechanisms in place to ensure that the MDTM Clinical Leads and other key members and Cancer Registries are apprised of supplementary or revised histology reports that may affect patient treatment and data collection.

Evidence for this revised dataset was obtained from a review of the literature up to 2007.

The following organisations were consulted during the preparation of the dataset:

- the Working Group of the British Association of Gynaecological Pathologists (BAGP), comprising BAGP Council and co-opted members
- the British Gynaecologic Cancer Society (BGCS).

## **2 Clinical information required on the specimen request form**

The specimen request form should include full patient details and the results of any previous biopsy or cytology specimens, such as peritoneal or omental biopsies. If there is a history of a prior neoplasm, this should be stated. If pre-operative chemotherapy has been administered, this information should be provided, as it is often not possible to type or grade an ovarian neoplasm reliably after chemotherapy as the morphological features may differ markedly from the chemo-naïve tumour and/or residual tumour cells may be sparse or no residual tumour may be present.<sup>5</sup>

The results of tumour marker studies, e.g. CA125, CEA, CA19.9 and inhibin, should be provided. For ovarian neoplasms, it is important to know if there have been problems during the operation which might have resulted in loss of capsular integrity and if there has been any evidence of leakage of cyst contents during surgery.

The details of surgical specimens from multiple sites should be provided and specimen pots should be labelled to correspond to the specimen details on the request form.

## **3 Preparation of the specimen before dissection**

Staging laparotomy for ovarian, tubal and primary peritoneal carcinoma usually includes a hysterectomy and bilateral salpingo-oophorectomy, omentectomy and lymphadenectomy together with peritoneal biopsies, washings and appendicectomy and diaphragmatic scrapes in certain instances. However, especially in young women who wish to retain their fertility, unilateral salpingo-oophorectomy and omentectomy may be performed.

There are no particular steps that need to be taken before dissection of the ovarian mass or masses. Some pathologists ink the capsular surface (although most do not); this practice is left to the discretion of the pathologist as some find it useful in easy identification of capsular blocks and capsular integrity. Prior slicing of the neoplasm may be undertaken to allow adequate fixation. It is recommended that these steps are only undertaken following careful examination of the capsular surface of the ovary and documentation of the presence or absence of surface tumour and/ or capsular breach and of the presence of and integrity of the fallopian tube. Prior opening of the uterus may be indicated to enable fixation of the endometrium.

A photographic record of the specimen may be useful on an individual case basis.

## **4 Specimen handling and block selection**

The origin/designation of all tissue blocks should be recorded and it is the view of the BAGP working group that it is preferable that this information be documented on 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. In particular, an accurate record of the block origin is useful in highlighting the capsular blocks and the blocks taken from areas of capsular disruption. If this information

is not included on the final pathology report, it should be available on the laboratory computer system and relayed to the reviewing pathologist. The principles applied to primary ovarian neoplasms also apply to primary tubal and peritoneal neoplasms.

#### **4.1 Ovarian masses**

Ovarian carcinomas may be unilateral or bilateral. Each ovary should be weighed and measured in three dimensions. The presence of an associated fallopian tube should be documented and this measured.

It is important to identify if the ovarian capsule is intact or if there is any evidence of capsular disruption or involvement by tumour and a thorough study of the capsular surface is indicated. The presence or absence of gross tumour involvement of the capsular surface should be documented. It may be impossible to know whether capsular disruption occurred preoperatively or intra-operatively and this may be discussed at the MDTM. The presence or absence of gross tumour involvement should be noted. As stated earlier, it may be helpful to ink the capsular surface since this may facilitate recognition of those blocks that include the capsule; this may be important in correct staging of the tumour. Inking may also help to ensure that the block is fully faced when sections are examined.

Following examination of the capsular surface, the neoplasm is sliced at 1 cm intervals and the nature of the cut surface noted, i.e. predominantly a solid lesion, a partly solid and partly cystic lesion or an entirely cystic lesion. The colour and consistency of solid areas and the presence of haemorrhage or necrosis should be noted. If the lesion is cystic, the nature of the cyst contents should be noted. At this point, if the neoplasm is cystic, it is usual to describe the cyst lining, which may have papillary excrescences. For a predominantly cystic lesion with papillary excrescences on the internal or external surface, it is useful to estimate the percentage of the internal or external surface with papillary excrescences.

After appropriate measurements have been documented, the blocks from the neoplastic ovaries are taken. Any unusual or heterogeneous areas should be sampled and a significant number of blocks should include the capsule. There is little evidence base for the number of blocks to be sampled but some authors recommend that at least one block per cm of maximum dimension of the ovarian neoplasm should be taken. However, with a large homogenous neoplasm or a simple, thin-walled, cystic lesion without capsular thickening or papillary processes, more limited sampling may be appropriate with the option of further sampling should this be indicated. One piece of tissue per cassette is recommended. However, if the lesion is predominantly a thin walled cyst, more than one piece of tissue might be submitted in an individual cassette. Mucinous neoplasms may be extremely heterogeneous with close proximity of benign, borderline and malignant areas and more generous sampling may need to be undertaken, especially from grossly solid or suspicious areas, depending on the histological findings in the original sections.<sup>6</sup> For cystic lesions with papillary processes on the internal or external surface, the papillary areas should be extensively blocked.

If one of the ovaries is grossly normal, one or two blocks will suffice. In patients with BRCA1 or 2 mutations the entire "normal" ovary should be submitted for histological examination.

#### **4.2 Hysterectomy specimens**

The uterus should be measured in three dimensions and weighed if local protocol indicates. The serosal surface of the uterus should be examined carefully, particularly the posterior aspect around the cornua and the pouch of Douglas where tumour deposits or endometriosis might be identified. If there is any gross abnormality, these areas should be sampled.

Sections from the uterus and cervix should be taken according to local protocols for a benign hysterectomy specimen. This will usually include two cervical blocks, most commonly one each from the anterior and posterior lip, and two blocks to include the endometrium and the

full thickness of the myometrium. Any tumour deposits on the uterine serosa should be sampled. If a synchronous endometrial tumour is present<sup>7,8</sup> (not a rare scenario), this should be sampled as indicated in the uterine carcinoma dataset.

#### **4.3 Biopsies and resection of omentum**

An infracolic omentectomy is usually performed as part of the staging procedure for a suspected ovarian carcinoma. On occasions, only an omental biopsy will be performed. The omentum should be measured in three dimensions and weighed. The presence or absence of gross tumour involvement should be documented and the size of the largest tumour nodule measured. The latter is important in the substaging of stage III ovarian carcinoma. With obvious gross tumour involvement, one or two representative blocks to confirm the presence of tumour should suffice. With a grossly normal omentum in a patient with an ovarian carcinoma or borderline tumour (especially of serous type), more extensive sampling is indicated since microscopic foci of tumour or implants may be identified histologically. However, there is little evidence base regarding the number of blocks necessary and, in most institutions, four to six blocks are taken.<sup>9,10</sup>

#### **4.4 Biopsies of lymph nodes**

Lymph nodes should be submitted in separate pots that are labelled according to their site of origin. The number of lymph nodes retrieved from each site should be recorded. The presence of macroscopic involvement of lymph nodes by tumour should be recorded. All retrieved lymph nodes must be examined histologically. Those obviously involved by tumour need only be sampled, while others should be submitted in their entirety for histological examination. It is advocated that, where possible, one lymph node in its entirety should be blocked in each cassette. Nodes smaller than 5 mm can be bisected or processed whole while larger nodes may require examination in more than one block.

#### **4.5 Peritoneal biopsies**

These should be submitted in separate pots and labelled as to their site of origin. They should be submitted in their entirety for histological examination and sectioned at multiple levels.

#### **4.6 Resection of the appendix**

The appendix may be removed, most often in the context of a suspected mucinous ovarian neoplasm. The appendix should be measured. The nature of any gross tumour involvement should be recorded, i.e. mucosal or serosal. In most cases with synchronous mucinous tumours in the appendix and the ovary (this usually occurs in the setting of pseudomyxoma peritonei), the appendix is the primary neoplasm and the ovarian and peritoneal disease is secondary to direct spread from the appendiceal neoplasm. In such cases, this is not to be regarded as a primary gynaecological neoplasm but as a primary gastrointestinal neoplasm. However, rarely there are synchronous independent primary neoplasms. In the setting of pseudomyxoma peritonei and with no visible lesion in the appendix, the appendix should be submitted in its entirety for histological examination because a microscopic lesion may be identified which is not grossly visible.

### **5 Core histological data items**

The following features are regarded as core histological data items:

- tumour type
- tumour grade
- microinvasion
- lymph node status
- peritoneal biopsies
- omentum



- peritoneal washings or ascitic fluid
- fallopian tubes
- staging.

## 5.1 Tumour type

The tumour type should be designated according to the WHO classification.<sup>2</sup> The most common morphological subtypes of primary ovarian carcinoma are serous, endometrioid, clear cell and mucinous.<sup>11</sup> Most primary tubal carcinomas are of serous or endometrioid type and most primary peritoneal carcinomas are of serous type. Mixed tumours also occur. The WHO states that a diagnosis of mixed tumour should only be made if the minor component represents more than 10% of the tumour after examination of multiple blocks.<sup>2</sup> However, it is recommended that all different morphological subtypes in an ovarian carcinoma are documented, even if comprising less than 10% of the neoplasm since it is possible that, especially in an early stage neoplasm, even a minor component of a more aggressive subtype may be prognostically important, although there is little evidence base for this. It may be useful to document the approximate percentage of each component. All tumour types should be SNOMED coded separately. It is recognised that there is considerable interobserver variation in the typing of ovarian cancers, especially in the distinction between high grade serous and endometrioid carcinoma,<sup>12,13</sup> and in this regard WT1 immunohistochemical staining may be of value (see below).<sup>14-16</sup> Borderline tumours should also be typed, the most common being serous and mucinous, although other subtypes also occur. Mucinous borderline tumours should be subclassified as intestinal (more common) or endocervical (Mullerian) type.<sup>6,17</sup>

## 5.2 Tumour grade

There are several different grading systems for ovarian carcinomas, including the FIGO, WHO and Silverberg systems,<sup>2,18-20</sup> but it is recommended that different morphological subtypes are graded using different systems (see below). Similar grading should be used for primary tubal and peritoneal cancers.

### 5.2.1 Serous carcinoma

In this dataset, there has been a change in the grading of serous carcinoma to reflect significant recent developments regarding the pathogenesis of this tumour type.<sup>12,21-26</sup> Serous carcinoma of the ovary, fallopian tube or peritoneum should be graded using a binary grading system as high grade or low grade. This distinction is based primarily on the assessment of nuclear atypia in the worst area of the tumour.<sup>12,21-26</sup> A recent study has demonstrated that the two-tier grading system is highly reproducible.<sup>27</sup> In low grade serous carcinoma, the nuclei are uniform with only mild atypia and less than or equal to 12 mitoses per 10 high power fields (the mitotic count is usually approximately 2 per 10 high power fields). There is no necrosis or multinucleate cells. High grade serous carcinoma exhibits moderate to marked nuclear atypia and greater than 12 mitoses per 10 high power fields. Necrosis and multinucleate tumour cells are often present.

The two-tier grading system is in keeping with the widespread acceptance that there are two distinct types of ovarian serous carcinoma, termed 'low grade' and 'high grade'.<sup>12,21-26</sup> These arise via two distinct pathways. Low grade serous carcinomas, which are much less common than high grade, arise in many instances from a pre-existing benign or borderline tumour with a well developed adenoma-carcinoma sequence. In contrast, the much more common high grade serous carcinoma is thought to arise directly from the ovarian surface epithelium or the epithelium of cortical inclusion cysts from an as yet unknown precursor. It is important to stress that these are two distinct tumour types, rather than high grade and low grade variants of the same neoplasm. It is also stressed that the distinction is based mainly on nuclear features and that many architecturally well differentiated tumours fall into the high grade category. It is also recognised that, in occasional cases, the distinction between a low grade

and high grade carcinoma may be difficult and intradepartmental discussion or specialist review may be useful.

### **5.2.2 Endometrioid carcinoma**

It is recommended that endometrioid carcinomas are graded as I, II or III (well, moderately or poorly differentiated) using the FIGO grading system which is used for the grading of uterine endometrioid adenocarcinomas.<sup>28</sup>

### **5.2.3 Mucinous carcinoma**

There is no separate grading system for mucinous carcinomas of the ovary, but it is recommended that they are graded in a similar manner to endometrioid carcinomas, as is done in the uterus. It may also be useful to describe the pattern of invasion as either expansile/confluent or infiltrative/destructive<sup>12</sup> (see non-core data items).

### **5.2.4 Clear cell carcinoma and carcinosarcoma**

Ovarian clear cell carcinomas are regarded as automatically high grade or grade III, as are similar carcinomas in the uterine corpus. It is recognised that carcinosarcomas (malignant mixed Mullerian tumours) in the ovary, as in the uterus, are of epithelial derivation<sup>29,30</sup> and they are automatically regarded as grade III. With carcinosarcomas, it may be useful to detail the relative percentages of the epithelial and mesenchymal components and the individual subtypes of these, since this may be of prognostic significance<sup>31</sup>.

## **5.3 Microinvasion**

Microinvasion may occur within an otherwise typical borderline tumour, usually of serous or mucinous type. In most studies, microinvasion has been found to have no adverse effect on prognosis, although foci of microinvasion in serous borderline tumours often coexist with other features which may be indicative of a worse prognosis, such as a micropapillary growth pattern.<sup>32-34</sup> There is no universally agreed upper size limit for microinvasion but most use 5 mm and this is recommended by the BAGP Working Group. Microinvasion may be multifocal and, if the foci of microinvasion are clearly separate, these can be regarded as multiple distinct foci of microinvasion and the size of the separate foci need not be added together. It has been suggested that microinvasion in a mucinous borderline tumour should be classified as borderline tumour with microinvasion or as microinvasive carcinoma,<sup>6</sup> but this is a controversial area and likely to be poorly reproducible from a histological viewpoint. However, we feel this should be routinely attempted using published criteria<sup>6,12</sup>.

## **5.4 Lymph nodes**

The total number of lymph nodes examined from each anatomical site and the number involved by tumour should be recorded. It is noted that in serous borderline tumours, lymph node involvement may comprise borderline tumour rather than carcinoma and that this may not be associated with an adverse outcome.<sup>35,36</sup> This is a difficult area and may require specialist internal or external review.

## **5.5 Peritoneal biopsies**

The presence or absence of tumour involvement in biopsies from each anatomical site should be recorded. Peritoneal involvement in association with an ovarian borderline tumour, especially of serous type, may take the form of invasive or non-invasive implants which may coexist. This is a difficult area and may require specialist internal or external review. Tumour deposits on the uterine serosa in association with borderline tumours may also take the form of invasive or non-invasive implants.

## **5.6 Omentum**

The size of the largest omental metastatic deposit should be documented. This should be evaluated in conjunction with the gross appearance and is important for substaging of FIGO

stage III ovarian carcinomas. Omental involvement in association with a borderline tumour, especially of serous type, may take the form of invasive or non-invasive implants. This is a difficult area and may require specialist internal or external review. Since invasive and non-invasive implants may, on occasions, coexist and since invasive implants are associated with an adverse prognosis and are often an indicator for adjuvant chemotherapy, extensive omental sampling should be undertaken when non-invasive implants are identified in the original sections.

### 5.7 Peritoneal washings or ascitic fluid

Cytological assessment of peritoneal fluid forms part of the staging system for ovarian carcinoma and in stage I tumours the presence or absence of tumour cells in peritoneal washings may be critical in determining the need for adjuvant therapy. It is recommended, especially in stage I ovarian cancers, that the results of peritoneal fluid sampling (if undertaken) are integrated into the histopathology report. An area of difficulty is the presence of serous epithelial cells in peritoneal fluid in patients with serous borderline tumour; in such cases, there should be close correlation between the histology and cytology specimens since if the cytology is reported in isolation, this may erroneously be diagnosed as malignant. Pleural fluid may also be sent for examination.

### 5.8 Fallopian tubes

The presence or absence of tubal involvement should be documented as well as the site of tubal involvement, for example mucosal or serosal. Tubal involvement in ovarian carcinoma is not uncommon and the fimbria is the most common site. It has, in fact, been suggested that the tubal fimbria is the site of origin of many pelvic serous carcinomas.<sup>37,38</sup>

### 5.9 Staging

Tumours should be staged according to both the FIGO and TNM staging systems (see Appendix A). Although it is useful to record the provisional stage on the histopathology report, the final stage should be determined at the MDTM where the results of all clinical, radiological and pathological parameters can be correlated. Borderline tumours should be staged in the same way as invasive carcinomas. It should be noted that there is no staging system for primary peritoneal carcinomas.

## 6 Non-core data items

Non-core data items are those that may be included as part of a complete report but which are of uncertain prognostic relevance. These may be recorded as a separate comment or within a complementary text report.

- The weight of the ovaries
- The presence or absence of lymphovascular permeation.
- The results of any immunohistochemical studies.
- Presence of micropapillary architecture. It has been suggested that in serous borderline tumours, the presence of a micropapillary architecture is associated with an increased likelihood of extraovarian invasive implants and an adverse outcome.<sup>39,40</sup> This is a controversial area but the presence of a micropapillary growth pattern (strict criteria for this should be employed) in a serous borderline tumour might be documented. It is not recommended that the term 'micropapillary serous carcinoma' be used for borderline tumours with a micropapillary architecture but rather the term serous borderline tumour with a micropapillary architecture is used.
- For stage I fallopian tube carcinomas, it may be useful to document the depth of invasion into the wall of the tube i.e. mucosal, submucosal, muscle coat, serosa.
- For mucinous carcinomas, it may be useful to describe the pattern of invasion as expansile/confluent or infiltrative/destructive.

- Some of the features noted in the gross examination of the ovary (section 4.1) (for example, solid/cystic appearance; colour/consistency etc) are not included in the reporting proforma and can be included as a separate comment or within a complimentary text report.
- In carcinosarcomas, it may be useful to detail the relative percentages of the epithelial and mesenchymal components and the individual subtypes of these, since this may be of some prognostic significance
- The weight of the omentum.
- Whether microinvasion is unifocal or multifocal.

## **7 Tumour classification and diagnostic coding**

Primary tumours of the ovaries, Fallopian tubes and peritoneum should be classified according to the WHO histological classification of tumours of the ovary and coded using SNOMED codes (see Appendix A). Tumours should be staged by both the TNM and FIGO systems (see Appendix B).<sup>2</sup> Most gynaecological oncologists use the FIGO staging system for gynaecological cancers. However, TNM staging is included in this dataset to allow standardisation of staging across all cancer sites. Depending on local protocols, clinicians may elect to include TNM staging in gynaecological cancer datasets.

## **8 Small biopsy specimens**

Most ovarian carcinomas are removed without a preoperative histological diagnosis, the diagnosis being made on the basis of a combination of clinical, serological and radiological features in an MDTM setting. Cytological examination of ascitic fluid may have been undertaken to confirm malignancy and markers may be undertaken on this to help to establish the ovary as the primary site of origin.

Sometimes radiologically guided core biopsies, usually of the omental metastatic disease, are performed to confirm the diagnosis preoperatively or prior to chemotherapy or in patients who are too ill to undergo a laparotomy. The number of core biopsies should be stated and the length of each core documented. Tissue may need to be preserved so that a range of immunohistochemical markers can be performed.

Small biopsies may also be undertaken at laparotomy or laparoscopy to confirm or exclude the ovary as the primary site or when the disease is so extensive that optimal surgical debulking is not thought to be possible.

## **9 Reporting of frozen sections**

Intra-operative assessment of ovarian tumours varies with local guidelines. In most institutions in the United Kingdom frozen sections are rarely carried out in the evaluation of an ovarian neoplasm while in a few centres this is routinely performed. There may be problems with intra-operative assessment due to issues associated with sampling. Situations where frozen section examination might be performed include:

- Intra-operative assessment of a neoplasm confined to the ovary to assess whether this is benign, borderline or malignant; this may direct whether lymphadenectomy or other staging procedures are undertaken
- for confirmation of an epithelial neoplasm, for subtyping of an epithelial malignancy and, in cases of obvious malignancy, to distinguish between a primary ovarian and a metastatic neoplasm.

Other situations where frozen section examination might be requested are outside the remit of this document. It is recognised that accurate diagnosis is not always possible on the

limited sampling available at the time of intra-operative consultation, but discussion of the case with the surgeon may result in information that can be used to plan the extent of surgery.

## 10 Specific aspects of individual tumours not covered elsewhere

With a mucinous ovarian carcinoma, especially if bilateral or with extraovarian spread, a metastatic neoplasm should always be considered. It is beyond the remit of this document to discuss this subject in detail but a combination of clinical, gross pathological, microscopic and immunohistochemical features assist in distinguishing between a primary and secondary ovarian mucinous neoplasm.<sup>41-43</sup>

Immunohistochemistry has many applications in the field of ovarian neoplasia and the use of immunohistochemistry has significantly increased in recent years.<sup>44-46</sup> The results of any immunohistochemical stains should always be carefully interpreted in conjunction with the clinical, gross and microscopic features. It is beyond the remit of this document to discuss the uses of immunohistochemistry in detail. However, areas where immunohistochemistry may contribute significantly include the following.

- The distinction between a primary ovarian adenocarcinoma and a metastatic adenocarcinoma from various sites. Potentially useful markers include: cytokeratins 7 and 20, CA125, CEA, CA19.9, WT1, TTF1, oestrogen receptor and CDX2.
- Typing of an ovarian adenocarcinoma. Most ovarian serous carcinomas (as well as primary tubal and peritoneal serous carcinomas) exhibit nuclear positivity with WT1, while most of the other morphological subtypes are negative.
- The distinction between an epithelial and a sex cord-stromal tumour. Some primary ovarian adenocarcinomas, especially of endometrioid type, may closely mimic an ovarian sex cord-stromal tumour. Potentially useful markers include: inhibin and calretinin (positive in sex cord-stromal tumours) and epithelial membrane antigen and cytokeratin 7 (positive in epithelial neoplasms).

## 11 Acknowledgements

Members of the British Association of Gynaecological Pathologists (BAGP) Working Group and Professor Simon Herrington and Dr Laurence Brown, authors of the 2005 dataset for the reporting of ovarian cancers.

## 12 References

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## Appendix A WHO classification and SNOMED 'M' coding of surface epithelial-stroma neoplasms

### Serous tumours

Malignant	
Adenocarcinoma	84413
Surface papillary adenocarcinoma	84613
Adenocarcinofibroma (malignant adenofibroma)	90143
Borderline	84421
Papillary cystic tumour	84621
Surface papillary tumour	84631
Adenofibroma, cystadenofibroma	90141
Benign	
Cystadenoma	84410
Papillary cystadenoma	84600
Surface papilloma	84610
Adenofibroma and cystadenofibroma	90140

### Mucinous tumours

Malignant	
Adenocarcinoma	84803
Adenocarcinofibroma (malignant adenofibroma)	90153
Borderline	84721
Intestinal type	
Endocervical-like	
Benign	
Cystadenoma	84700
Adenofibroma and cystadenofibroma	90150
Mucinous cystic tumour with mural nodules	
Mucinous cystic tumour with pseudomyxoma peritonei	84803

### Endometrioid tumours including variants with squamous differentiation

Malignant	
Adenocarcinoma, not otherwise specified	83803
Adenocarcinofibroma (malignant adenofibroma)	83813
Malignant Mullerian mixed tumour (carcinosarcoma)	89503
Adenosarcoma	89333
Endometrioid stromal sarcoma (low grade)	89313
Undifferentiated ovarian sarcoma	88053
Borderline	
Cystic tumour	83801
Adenofibroma and cystadenofibroma	83811
Benign	
Cystadenoma	83800
Adenofibroma and cystadenofibroma	83810

## Clear cell tumours

Malignant	
Adenocarcinoma	83103
Adenocarcinofibroma (malignant adenofibroma)	83133
Borderline	
Cystic tumour	83101
Adenofibroma and cystadenofibroma	83130
Benign	
Cystadenoma	83100
Adenofibroma and cystadenofibroma	83100

## Transitional cell tumours

Malignant	
Transitional cell carcinoma (non-Brenner type)	81203
Malignant Brenner tumour	90003
Borderline	
Borderline Brenner tumour	90011
Proliferating variant	90011
Benign	
Brenner tumour	90000
Metaplastic variant	90000

## Squamous cell tumours

Squamous cell carcinoma	80703
Epidermoid cyst	33410

## Mixed epithelial tumours (specify components)

Malignant	83233
Borderline	83231
Benign	83230

## Undifferentiated and unclassified tumours

Undifferentiated carcinoma	80203
Adenocarcinoma, not otherwise specified	81403

## Appendix B TNM and FIGO classification of tumours of the ovary <sup>2</sup>

This classification applies to malignant surface epithelial-stromal tumours, including those of borderline malignancy.

TNM category	FIGO stage	Descriptor
TX		Primary tumour cannot be assessed
T0		No evidence of primary tumour
T1	I	Tumour limited to the ovaries
T1a	IA	Tumour limited to one ovary, capsule intact, no tumour on ovarian surface; no malignant cells in ascites or peritoneal washings
T1b	IB	Tumour limited to both ovaries, capsule intact, no tumour on ovarian surface; no malignant cells in ascites or peritoneal washings
T1c	IC	Tumour limited to one or both ovaries with any of the following: capsule ruptured, tumour on ovarian surface; malignant cells in ascites or peritoneal washings
T2	II	Tumour involves one or both ovaries with pelvic extension
T2a	IIA	Extension and/or implants on uterus and/or tube(s); no malignant cells in ascites or peritoneal washings
T2b	IIB	Extension to other pelvic tissues; no malignant cells in ascites or peritoneal washings
T2c	IIC	Pelvic extension (2a or 2b) with malignant cells in ascites or peritoneal washings
T3 and/or N1	III	Tumour involves one or both ovaries with microscopically confirmed peritoneal metastases outside the pelvis and/or regional lymph node metastasis
T3a	IIIA	Microscopic peritoneal metastasis beyond pelvis
T3b	IIIB	Macroscopic peritoneal metastasis beyond pelvis, 2 cm or less in greatest dimension.
T3c and/or N1	IIIC	Peritoneal metastasis beyond pelvis more than 2 cm in greatest dimension and/or regional lymph node metastasis
M1	IV	Distant metastasis * (excludes peritoneal metastasis)

N – Regional lymph nodes **		
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Regional lymph node metastasis

M – Distant metastasis *		
MX		Distant metastasis cannot be assessed
M0		No distant metastasis
M1		Distant metastasis

**Notes**

- \* Liver capsule metastasis is T3/stage III; liver parenchymal metastasis is M1/stage IV; pleural effusion must have positive cytology for M1/stage IV.
- \*\* Regional lymph nodes are: hypogastric (obturator), common iliac, external iliac, lateral sacral, para-aortic and inguinal nodes.

## Appendix C Reporting proforma for non-benign epithelial ovarian tumours

Surname ..... Forenames ..... Date of birth .....

Hospital..... Hospital no ..... NHS no .....

Date of receipt ..... Date of report ..... Report no .....

Pathologist ..... Surgeon .....

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### MACROSCOPIC FEATURES

Specimen type: .....

#### Ovaries

Right: Dimensions ..... x ..... x ..... mm

Tumour involvement: Yes  No

Capsule: Intact  Disrupted  Involved by tumour  Not assessable

Surface involvement Y/N

Left: Dimensions ..... x ..... x ..... mm

Tumour involvement: Yes  No

Capsule: Intact  Disrupted  Involved by tumour  Not assessable

Surface involvement Y/N

#### Fallopian tubes

Right Length.....mm Normal  Abnormal

Comment .....

Left Length.....mm Normal  Abnormal

Comment .....

#### Uterus

Normal  Abnormal  Comment .....

#### Omentum

Biopsy  Omentectomy  Dimensions .....x..... x.....mm

Not involved by tumour  Involved by tumour  Size of largest tumour nodule.....mm

Comment .....

**Peritoneal biopsies:** Not received  Received

**Lymph nodes:** Not received  Received

### MICROSCOPIC FEATURES OF OVARIES

#### Right ovary

Borderline tumour: Absent  Serous  Mucinous  Endometrioid

Other  .....

Microinvasion: Not present  Present

Invasive carcinoma: Not present  Present

Tumour subtype (tick all that apply)

**Differentiation**

- Serous  { High Grade   
Low Grade
- Mucinous
- Endometrioid
- Clear cell (automatically grade 3)  { Well/Grade 1   
Moderate/Grade 2   
Poor/Grade 3
- Transitional
- Carcinosarcoma (automatically grade 3)
- Undifferentiated (automatically grade 3)
- Mixed epithelial types
- Others .....

**Left ovary**

Borderline tumour: Absent  Serous  Mucinous  Endometrioid

Other  (specify) .....

Microinvasion: Not present  Present

Invasive carcinoma: Not present  Present

Tumour subtype (tick all that apply)

**Differentiation**

- Serous  { High Grade   
Low Grade
- Mucinous
- Endometrioid
- Clear cell (automatically grade 3)  { Well/Grade 1   
Moderate/Grade 2   
Poor/Grade 3
- Transitional
- Carcinosarcoma (automatically grade 3)
- Undifferentiated (automatically grade 3)
- Mixed epithelial types
- Others (specify) .....

**MICROSCOPIC FEATURES OF OTHER TISSUES**

**Fallopian tubes:** Right: Not involved  Involved   
Left: Not involved  Involved

**Endometrium:** Normal  Abnormal   
Comment .....

**Myometrium:** Normal  Abnormal   
Comment .....

**Uterine serosa:** Not involved  Non-invasive borderline implants   
Invasive carcinoma / invasive implants

**Omentum:** Not involved  Non-invasive borderline implants   
Invasive carcinoma / invasive implants

**Peritoneal biopsies**

Sites (insert)	Not involved	Non-invasive borderline implants	Invasive carcinoma / invasive implants
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Lymph nodes Sites (insert)	Not sampled	No. harvested	No. involved
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**Peritoneal cytology sample (if received):** Not involved  Involved  Equivocal

**Comments/additional information:**

**Provisional FIGO stage** ..... (may change following MDTM discussion).

**Provisional TNM stage** .....

**SNOMED codes** T..... M.....

**Signature**..... **Date**...../...../.....

## Appendix D Reporting proforma for fallopian tube carcinoma

Surname ..... Forenames ..... Date of birth .....  
Hospital..... Hospital no ..... NHS no .....  
Date of receipt ..... Date of report ..... Report no .....  
Pathologist ..... Surgeon .....

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### MACROSCOPIC FEATURES

Nature of specimen: .....

#### Fallopian tubes

Right: Length.....(mm) Normal  Abnormal   
Size of tumour .....(mm)  
Site of tumour Isthmus  Ampulla  Fimbrial   
Serosal involvement Yes  No   
  
Left: Length.....(mm) Normal  Abnormal   
Size of tumour .....(mm)  
Site of tumour Isthmus  Ampulla  Fimbrial   
Serosal involvement Yes  No

#### Ovaries

Right: Dimensions ..... x ..... x ..... mm Tumour involvement: Yes  No   
Left: Dimensions ..... x ..... x ..... mm Tumour involvement: Yes  No

**Uterus and cervix** Normal  Abnormal

Comment .....

#### Omentum

Biopsy  Omentectomy  Dimensions.....x.....x.....mm  
Not involved by tumour  Involved by tumour   
Size of largest tumour nodule.....mm  
Comment:.....

**Peritoneal biopsies:** Not received  Received

---

### MICROSCOPIC FEATURES OF FALLOPIAN TUBES

#### Right fallopian tube

Borderline tumour: Absent  Serous  Mucinous  Endometrioid  Other   
Microinvasion: Not present  Present   
Invasive carcinoma: Not present  Present



Tumour subtype (tick all that apply)

**Differentiation**

Serous	<input type="checkbox"/>	} High Grade <input type="checkbox"/> Low Grade <input type="checkbox"/>
Mucinous	<input type="checkbox"/>	
Endometrioid	<input type="checkbox"/>	} Well/Grade 1 <input type="checkbox"/> Moderate/Grade 2 <input type="checkbox"/> Poor/Grade 3 <input type="checkbox"/>
Clear cell (automatically grade 3)	<input type="checkbox"/>	
Transitional	<input type="checkbox"/>	
Carcinosarcoma (automatically grade 3)	<input type="checkbox"/>	
Undifferentiated (automatically grade 3)	<input type="checkbox"/>	
Mixed epithelial types	<input type="checkbox"/>	
Others .....	<input type="checkbox"/>	

**Left fallopian tube**

Borderline tumour: Absent  Serous  Mucinous  Endometrioid  Other

Microinvasion: Not present  Present

Invasive carcinoma: Not present  Present

Tumour subtype (tick all that apply)

**Differentiation**

Serous	<input type="checkbox"/>	} High Grade <input type="checkbox"/> Low Grade <input type="checkbox"/>
Mucinous	<input type="checkbox"/>	
Endometrioid	<input type="checkbox"/>	} Well/Grade 1 <input type="checkbox"/> Moderate/Grade 2 <input type="checkbox"/> Poor/Grade 3 <input type="checkbox"/>
Clear cell (automatically grade 3)	<input type="checkbox"/>	
Transitional	<input type="checkbox"/>	
Carcinosarcoma (automatically grade 3)	<input type="checkbox"/>	
Undifferentiated (automatically grade 3)	<input type="checkbox"/>	
Mixed epithelial types	<input type="checkbox"/>	
Others (specify) .....	<input type="checkbox"/>	

**MICROSCOPIC FEATURES OF OTHER TISSUES**

**Ovaries:** Right: Not involved  Involved  (see Notes)  
Left: Not involved  Involved  (see Notes)

**Endometrium:** Normal  Abnormal  Comment .....

**Myometrium:** Normal  Abnormal  Comment .....

**Uterine serosa:** Not involved  Borderline changes (non-invasive implants)   
Invasive carcinoma

**Omentum:** Not involved  Non-invasive borderline implants   
Invasive carcinoma / invasive implants

**Peritoneal biopsies**

Sites (insert)	Not involved	Non-invasive borderline implants	Invasive carcinoma / invasive implants
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**Lymph nodes**

Sites (insert)	Not sampled	No. harvested	No. involved
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**Peritoneal cytology sample (if received):** Not involved  Involved  Equivocal

**Comments/additional information:**

**Provisional FIGO stage** ..... (may change following MDTM discussion).

**Provisional TNM stage** .....

**SNOMED codes** T..... M.....

**Signature**..... **Date**...../...../.....

**Appendix E Reporting proforma for primary peritoneal carcinoma**

Surname ..... Forenames ..... Date of birth .....  
 Hospital..... Hospital no ..... NHS no .....  
 Date of receipt ..... Date of report ..... Report no .....  
 Pathologist ..... Surgeon .....

**MACROSCOPIC FEATURES**

Nature and site of specimen (s): .....

**Peritoneal biopsies** Not received  Received

**Omentum**

Biopsy  Omentectomy  Dimensions.....x.....x.....mm  
 Not involved by tumour  Involved by tumour   
 Size of largest tumour nodule.....mm  
 Comment:.....

**Ovaries**

Dimensions ..... x ..... x ..... mm Tumour involvement: Yes  No   
 Dimensions ..... x ..... x ..... mm Tumour involvement: Yes  No

**Fallopian tubes**

Right: Normal  Abnormal   
 Left: Normal  Abnormal  Comment .....

**Uterus and cervix:** Normal  Abnormal  Comment .....

**MICROSCOPIC FEATURES – PERITONEUM AND OMENTUM**

**Peritoneum**

Borderline tumour: Absent  Serous  Mucinous  Endometrioid  Other

Microinvasion: Not present  Present

Invasive carcinoma: Not present  Present

Tumour subtype (tick all that apply)

Serous	<input type="checkbox"/>	{ High Grade <input type="checkbox"/> Low Grade <input type="checkbox"/>
Mucinous	<input type="checkbox"/>	
Endometrioid	<input type="checkbox"/>	{ Well/Grade 1 <input type="checkbox"/> Moderate/Grade 2 <input type="checkbox"/> Poor/Grade 3 <input type="checkbox"/>
Clear cell (automatically grade 3)	<input type="checkbox"/>	
Transitional	<input type="checkbox"/>	
Carcinosarcoma (automatically grade 3)	<input type="checkbox"/>	
Undifferentiated (automatically grade 3)	<input type="checkbox"/>	
Mixed epithelial types	<input type="checkbox"/>	
Others .....	<input type="checkbox"/>	

**Omentum**

Borderline tumour: Absent  Serous  Mucinous  Endometrioid   
 Other  .....

Microinvasion: Not present  Present

Invasive carcinoma: Not present  Present

Tumour subtype (tick all that apply)

**Differentiation**

Serous	<input type="checkbox"/>	} High Grade <input type="checkbox"/> Low Grade <input type="checkbox"/>
Mucinous	<input type="checkbox"/>	
Endometrioid	<input type="checkbox"/>	} Well/Grade 1 <input type="checkbox"/> Moderate/Grade 2 <input type="checkbox"/> Poor/Grade 3 <input type="checkbox"/>
Clear cell (automatically grade 3)	<input type="checkbox"/>	
Transitional	<input type="checkbox"/>	
Carcinosarcoma (automatically grade 3)	<input type="checkbox"/>	
Undifferentiated (automatically grade 3)	<input type="checkbox"/>	
Mixed epithelial types	<input type="checkbox"/>	
Others .....	<input type="checkbox"/>	

**MICROSCOPIC FEATURES OF OTHER TISSUES**

**Ovaries:** Right: Not involved  Involved  (see Notes)  
 Left: Not involved  Involved  (see Notes)

**Fallopian tubes:** Right: Not involved  Involved   
 Left: Not involved  Involved

**Endometrium:** Normal  Abnormal  Comment .....

**Myometrium:** Normal  Abnormal  Comment .....

**Uterine serosa:** Not involved  Borderline changes  Invasive carcinoma

**Appendix (if received):** Not involved  Involved  Comment .....

<b>Lymph nodes</b>	Not sampled	No. harvested	No. involved
Sites (insert)			
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**Peritoneal cytology sample (if received):** Not involved  Involved  Equivocal

**Comments/additional information:**

**SNOMED codes:** T..... M.....

**Signature..... Date...../...../.....**