***Appendix C: STUDY PROCEDURE***

**Enrolment Consultation**

Verbal information and written PICF provided

Consent form signed

Completion Form A (Registration Form)

**Day of Surgery**

On the day of patient’s surgery after general anaesthesia is administered the patient will undergo routine positioning in the operating theatre.

As per standard practise an examination under anaesthesia will be performed.

**ICG injection protocol**

If suitable to proceed with laparoscopic / robotic surgery, the patient will have injection of ICG dye as follows:

* 25mg of ICG powder diluted in 20ml of Normal Saline (final concentration 1.25mg per ml)
* Speculum examination of cervix
* Spinal needle used to inject cervix at 3 and 9 o’clock position
	+ 0.5ml injected 1-3mm into cervix submucosa (superficial injection) and 0.5ml injected 1cm into cervix stroma (deep injection) at 3 o’clock position
	+ 0.5ml injected 1-3mm into cervix submucosa (superficial injection) and 0.5ml injected 1cm into cervix stroma (deep injection) at 9 o’clock position
	+ Total volume 2ml equivalent to ICG dose 5.0mg
* Injection time of ICG recorded

***SLN Mapping Protocol***

* da Vinci Si or Xi surgical robot or laparoscopic platform capable of NIRF imaging used in all patients
* After entry into peritoneal cavity and placement of all ports peritoneal survey conducted
* Mapping proceeds as per SLN mapping algorithm



* If obvious extrauterine disease then SLN mapping not carried out and retroperitoneal spaces explored to remove any suspicious or bulky lymph nodes only
* If no extra-uterine peritoneal or lymph node disease then proceed with mapping
* Round ligaments divided
* Retroperitoneal spaces explored and NIRF imaging used to follow ICG tracer in lymphatic channels to a sentinel lymph node
* Successful mapping defined by observing a channel leading from cervix into at least one candidate lymph node in at least one hemi-pelvis
* Identified sentinel lymph node retrieved and labelled for location
* Documentation of commencement of dissection per hemi-pelvis and time of detection of SLN per hemi-pelvis recorded on Form B
* All patients proceed to hysterectomy with intra-operative frozen section as per current practise
* If SLN mapping failed in a hemi-pelvis then side specific pelvic lymphadenectomy (on the side of failed mapping) will be performed in those patients who have high risk factors for lymph node metastasis based on frozen section as per Appendix A (>50% myoinvasion, Grade 3 tumour with any myoinvasion or bulky tumour >2cm)
	+ on the successfully mapped hemi-pelvis, these patients will not need to undergo further comprehensive lymphadenectomy
	+ those patients without high risk factors on frozen section (Grade 1 or 2 tumour with <50% myoinvasion) will not need to undergo side specific pelvic lymphadenectomy, even if SLN mapping fails in a hemi-pelvis, as these patients have >90% 5-year survival based on current practise which does not require lymph node staging
	+ those patients with ultra-high risk features for nodal disease (Grade 3 tumour with > 50% myoinvasion or UPSC and clear cell tumours with any degree of myoinvasion) will not need to undergo comprehensive pelvic lymphadenectomy if there is failed SLN mapping to a hemi-pelvis, as they will qualify for high risk protocol adjuvant chemotherapy and external beam radiation as per current practise
* All SLN mapping and details of additional lymph nodes removed to be documented on Form B by the operating surgeon

***Ultra-staging Protocol***

* SLN halved
* Each half-SLN was sectioned at 3-mm intervals
* Each section analysed at four parallel divisions of 100 μm
	+ one of these divisions was used for H&E staining
	+ H&E negative sections examined by IHC with an anticytokeratin antibody cocktail including AE1 and AE3
* Non –sentinel lymph nodes handled according to institutional standard of care practices and hence negative H&E slides from non-sentinel lymph nodes are not subjected to IHC staining
* Metastatic disease categorized and reported in standardized fashion according to the American Joint Committee on Cancer definitions with macrometastases defined as foci of metastasis greater than 2mm, micrometastasis defined as disease volume 0.2mm – 2mm and isolated tumour cells defined as foci of disease measuring <0.2mm in greatest dimension or individual pathological cells staining positive for pan-cytokeratins.
* Standardized synoptic reporting of all sentinel lymph node specimens

**Follow-up**

* Histopathology and SLN biopsy results documented on Form C along with final FIGO staging and adjuvant treatment recommendation based on Multidisciplinary team discussion
* Form D will be completed by the attending Gynaecological Oncologist at the 3-month post-operative visit and details length of post-operative hospitalization, immediate or delayed post-operative complications, post-surgical therapies (radiotherapy / chemotherapy) and the presence or absence of any recurrent disease.
* Subsequent sections of Form D will be completed at the 6, 12, 24 and 36 month post-operative visits and again details any delayed complications, any development of recurrent disease since last follow-up and treatment thereof.