I. Protocol for Work Up Prior to Requesting Authorization of Services for Induction of Ovulation or Assisted Reproductive Technology

**Evaluation of Fallopian Tubes** (or previous study from the referring MD)
Tubal occlusive disease must be specifically excluded for all patients by using one or more of the following tests:

- Hysterosalpingography (HSG) – primary
- Laparoscopy and “Chromopertubation” when indications other than infertility
- Fluoroscopic or Hysteroscopic selective tubal cannulation in cases of proximal tubal occlusion on HSG

**Evaluation of Uterine Cavity** (or previous study from the referring MD)
In cases of abnormal endometrial cavity on HSG, or pre-IVF:

- Hysterosonography (HSN) – primary
- Hysteroscopy if HSN is abnormal or not diagnostic

**Criteria for the Evaluation of Ovarian Reserve:**
The following patients must be screened to provide prognostic information:

- Women at age > 35
- Any women with unexplained infertility
- Any patient with a family history of early menopause
- Any patient with a single ovary, history of previous ovarian surgery or prior chemotherapy or pelvic irradiation
- Any patient with documented poor response to exogenous gonadotropin stimulation

Ovarian Reserve must be screened during infertility treatment cycles:

- Annually for patients < 40 years of age
- Recommended every 6 months for patients > 40 years of age. Required annually.

**Diagnostic Studies for the Evaluation of Ovarian Reserve**
The following diagnostic studies are to be used to evaluate ovarian reserve:

- Cycle day 3 FSH/E2
- AMH (Anti-Mullerian Hormone)

**Evaluation of Semen Specimens**

- Two semen analysis are recommended prior to categorization of the male as subfertile or infertile
- A comprehensive semen analysis must be completed prior to infertility treatment cycles (e.g. IUI/IVF). If normal, the submitted semen analysis should be within 2 year of cycle start. If abnormal, the semen analysis should be updated within 1 year of cycle start.
- A minimum of 5 M/ml motile sperm is recommended in a specimen for IUI-
  specimens with lower counts are associated with significantly lower success rates with IUI and may be indications for IVF w/ ICSI.
- Evaluation of semen parameters are based on WHO criteria and/or Strict Kruger Morphology. * WHO criteria for normal values:
  - Volume > 1.5 ml
  - Concentration/Count 15M/ml or greater
  - Motility 40% or more with forward progression in > 32%
  - Morphology of greater than or equal to 4%
  * Strict Kruger Morphology of > 14% is optimal, 4 to 14% is suboptimal but still offers fair to good prognosis
II. Protocol for the allowable number of IUI cycles

- **Natural Cycles**
  - 4 cycles for women < 35 and 3 or less cycles for older women (there is no requirement for natural cycle IUI prior to use of clomiphene citrate with IUI)

- **Clomid Cycles**
  - For unexplained infertility, a maximum of 3-4 cycles
  - For anovulation, a maximum of 6 ovulatory cycles.

- **Gonadotropin Cycles (Gonadotropin cycles are NOT required prior to advancing to IVF)**
  - For unexplained infertility, a maximum of 4 cycles.
  - For anovulation, a maximum of 6 ovulatory cycles.

NOTE: Higher success rates have been demonstrated with IUI compared with intracervical or intravaginal insemination. There is no evidence that having 2 IUI’s on successive days is more successful than a single well timed IUI. IUI is NOT indicated in patients with severe tubal disease or in cases with significant male factor infertility.

III. Protocol for step therapy requirements

- **Patients 40 and under with unexplained infertility**
  - Should undergo 3 to 4 cycles of clomiphene citrate with IUI before attempting more advanced treatments such as IVF or IUI with gonadotropins*.

- **Patients 41 and over with unexplained infertility**
  - May move directly to IVF or IUI with gonadotropins* and bypass the clomiphene IUI treatments given their very low efficacy.

- **Patients 43 and over**
  - Should be discouraged from attempting clomiphene IUI and should move directly IVF, or oocyte donation, when appropriate, given the absence of efficacy of clomiphene IUI in this age group.

The rate of conception with clomiphene citrate IUI diminishes with advancing maternal age. Women aged 41 to 42 years old have a pregnancy rate of approximately 3 to 5% per cycle with clomiphene IUI, and only a 7 to 8% cumulatively after 4 cycles with this modality. This is less than half the pregnancy rate per patient of women under age 40. Thus, patients over age 40 with unexplained infertility should be counseled appropriately and may move directly to IVF or IUI with gonadotropins, and bypass the clomiphene IUI treatments, given their low efficacy in this age group.

*Gonadotropin/IUI therapy is not a required or recommended step*
IV. Protocol for ICSI Guidelines
- Oligozoospermia (< 15 M/ml)
- Asthenozoospermia (<40%)
- Teratozoospermia (Kruger < 4% or WHO <30%)
- History of poor or failed fertilization after conventional IVF
- Positive anti-sperm antibodies
- Cryopreserved sperm from cancer patients in remission
- Spinal cord injury patients – electroejaculated sperm
- Surgically retrieved sperm (epididymal or testicular)

V. Protocols for ovarian stimulation for IVF
Protocols vary depending on numerous prognostic factors including the patient’s age, ovarian reserve, infertility diagnosis, and prior response to gonadotropins. Protocols include gonadotropin therapy and accessory medications that are used to program cycles and prevent premature LH surges (leuprolide acetate ganirelix, or cetrotide). Certain protocols (GnRH antagonist or microdose leuprolide acetate) have been demonstrated to have greater utility than others for the poor responder patient. There no proven benefit to gonadotropin doses greater than 450 IU per day. Daily gonadotropin doses above 450 IU are discouraged, and a maximum daily dose of 600 IU should be adhered to.

VI. Protocol for Numbers of Embryos Transferred (ASRM)
ASRM guidelines recommending limits on the number of embryos to transfer depending on the developmental stage of the embryos, the quality of the embryos, and the patient’s personal history, must be followed. Use of elective single embryo transfer for those patients who are good candidates (under 35, high quality embryos, first IVF cycle, and embryos available for cryopreservation) is strongly encouraged.

1. Indications for Embryo Cryopreservation (ASRM)
- To reduce the risks of multiple gestation and encourage the transfer of fewer embryos (including elective single embryo transfer).
- To preserve fertility potential in the face of certain necessary medical procedures (e.g., chemotherapy, radiotherapy for cancer)
- To increase the chance of having one or more pregnancies from a single cycle of ovarian stimulation
- To minimize the medical risk and cost to the patient by decreasing the number of induced ovulations and egg retrievals
- To temporarily delay pregnancy when OHSS occurs by freezing all embryos.