

## **Appendix 1. In Vitro Fertilization Protocol**

Stimulation protocols for fresh embryo transfer cycles utilized gonadotropin-releasing hormone (GnRH) antagonists, GnRH agonists for downregulation, estradiol priming or low-dose GnRH agonist flare protocols.<sup>16-19</sup> For cryopreserved embryo transfer cycles, both natural and programmed protocols were utilized, with the aim to achieve an endometrial thickness of 7 mm by ultrasound. The day of embryo transfer and number of embryos transferred were determined according to internal protocols and patient history. In the majority of cryopreserved embryo transfer cycles, luteal support was provided with intramuscular progesterone in oil (locally compounded at Village Fertility, Waltham, Massachusetts, or Freedom Fertility, Byfield, Massachusetts), initiated at a dose of 25-100 mg per night, starting in the evening three to five days prior to transfer. In cases in which the serum level was below 20 ng/mL on the day of transfer, the dose of progesterone was increased by 25 mg. In those patients with adverse reactions to intramuscular progesterone, one applicator (90 mg) of vaginal progesterone gel (Crinone® 8%, Actavis Pharma, Inc.) was used twice daily. The majority of patients undergoing fresh embryo transfer used vaginal progesterone gel (one applicator daily), beginning two days after oocyte retrieval for luteal support. Regardless of fresh or frozen transfer, luteal phase support was continued through 10 weeks of gestation.