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## OVULATION INDUCTION CONSENT FORM

Your physicians have advised that you consider treatment with medications that stimulate ovulation. These medications are known as clomiphene citrate (Clomid, Serophene) or human menopausal gonadotropins (HMG) (Follistim, Gonal-F, Repronex). These two classes of hormones are potent medications commonly used in the treatment of infertility of many different causes, including 1) irregular ovulation or lack of ovulation, 2) sperm abnormalities, 3) poor postcoital tests, 4) advanced age of the woman, 5) longstanding infertility of unknown cause, 6) endometriosis and 7) persistent infertility despite other forms of treatment.

Clomid and Serophene are the trade names for clomiphene citrate. It works by signaling the brain to trigger the release of luteinizing hormone (LH) and follicle stimulating hormone (FSH), the two hormones that are responsible for the development and release of the egg from the ovary. It is a tablet and is commonly taken for five days each menstrual cycle. It is usually well tolerated, with minimal adverse reactions. The most common side effects are bloating, breast tenderness, hot flashes, and headaches. If you should experience visual disturbances, this needs to be reported to the physician. The visual changes are reversible. Oftentimes treatment with clomiphene citrate is combined with an injection of another hormone called hCG (Ovidrel) to trigger ovulation. HCG is a very safe medication, without side effects, except in the extremely rare circumstance of an allergic reaction. The goal of treatment with clomiphene citrate is to 1) stimulate ovulation to occur in a woman who doesn't spontaneously cycle, 2) produce predictable ovulation in women with irregular menstrual cycles, 3) to gently stimulate women with prolonged infertility to produce one or two extra eggs per month.

Follistim, Gonal-F and Repronex, are the trade names for HMG's, hormones that are normally made and secreted by the pituitary gland. Repronex contains a mixture of LH and FSH. Follistim and Gonal-F are FSH only. When these hormones are given, multiple follicles can be stimulated to grow. When the follicles are mature, hCG is given to induce the release of the egg from the ovary. This is commonly referred to as "controlled superovulation".

Ovulation induction requires careful monitoring with sonograms to measure follicle size, and blood tests for estrogen, progesterone, and at times, LH levels. Every woman responds differently to these medications, and the same woman may respond differently from one cycle to another. Thus, monitoring of each cycle is essential to determine the proper dose of the medication, the correct time to trigger ovulation with hCG and to minimize the risks of treatment.

*All* medications have the potential to cause adverse reactions. There are 3 potential risks associated with ovulation induction that you must be aware of prior to starting treatment. The first is the



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increased possibility of a multiple gestation (a pregnancy with more than 1 baby), which occurs in 5% of clomiphene citrate-induced pregnancies and approximately 20% of pregnancies conceived with HMG therapy. A twin pregnancy is often a welcome event, however it carries a greater risk of pregnancy complications than a singleton pregnancy. When triplets or greater are conceived, the likelihood of premature delivery and other pregnancy complications are quite high. To minimize the risk of a multiple pregnancy, ultrasound monitoring is performed. If an excessive number of mature follicles are found, you may be instructed not to take the hCG (the hormone that triggers ovulation) and cancel the cycle. Unfortunately, despite all measures to minimize the likelihood of a triplet or greater gestation, it occasionally occurs. In these cases, selective fetal reduction is an option. This procedure, however, is associated with a 5% risk of losing the entire pregnancy.

The second risk associated with HMG therapy (it is exceedingly uncommon with clomiphene citrate) is a poorly understood condition called Ovarian Hyperstimulation Syndrome (OHSS). Most women who receive HMG's develop a mild degree of hyperstimulation and this is not worrisome. Severe hyperstimulation occurs infrequently (less than 1% of cases); however, it is a serious medical condition. The signs and symptoms include fluid retention with pooling of large amounts of fluid in the abdominal and lung cavities. This can result in abdominal swelling, pain, weight gain, difficulty breathing, and a decreased amount of urine production. Abnormalities in kidney function can occur. The thickening of fluid in the blood vessels increases the risk of clotting. Deaths have been reported, but are exceedingly rare. The ovaries may become quite enlarged and cause pelvic discomfort. If the pain worsens it can indicate a ruptured ovarian cyst or a twisted ovary, which may require surgery. In some cases of severe OHSS, hospitalization is required. If a pregnancy does not occur, the symptoms are self-limiting and will resolve when your period starts. The condition is often more serious and lasts longer if you become pregnant, but it will eventually resolve. There is no treatment for OHSS so our goal is to avoid it; withholding additional medications and avoiding pregnancy, thus canceling the treatment cycle in those circumstances where we feel the risks are high, accomplishes this goal. There is a relatively good correlation between excessive pre-ovulatory response to the medications and the post-ovulatory risk of being hyperstimulated. However, it may also occur in a woman who did not have an excessive number of follicles or a very high estrogen level. Although OHSS is a serious medical condition it is important to remember that it occurs infrequently, and it resolves completely over time.

Cancellation of a stimulation cycle is disappointing, however, it must be viewed positively as a means to ensure your health and to increase the chances of an uncomplicated pregnancy and a healthy baby. The next treatment cycle will be changed in a manner that will produce a more controlled ovarian response and thus increase the likelihood of a successful and healthy pregnancy.

The third concern is that of ovarian cancer, which to this day remains a theoretic (i.e., not definitely proven) increased risk in women who have used fertility medications. Since it is known that long term use of birth control pills, which block ovulation, decreases the lifetime risk of developing



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ovarian cancer, many physicians have questioned whether the additional ovarian stimulation with fertility medications may increase the chances of developing ovarian cancer in the future. Over the past 20 years numerous studies have been done to try and answer this question. Unfortunately the results are contradictory. One reason to explain the controversy is that there are so many variables that increase or decrease an individual woman's likelihood of ovarian cancer. Many of the studies include few women and do not have the power to give a definitive answer. Finally, these medications have been used for only thirty years. Most women who have taken them are still quite young. Since ovarian cancer tends to occur in women who are greater than 50 years old, we need to follow them for a lifetime to have the true answers.

A large study investigating the potential risk of ovarian cancer in women with a history of infertility and the use of various medications was recently published (6/04). In this report, 12,193 eligible subjects were evaluated for infertility treatment between 1965-1988. The women were cared for at 5 different medical centers within the United States. The follow-up of these women was completed in 1999. During this time, 45 ovarian cancers were found. When compared to the general population, the infertility patients had a 2-fold greater likelihood of developing ovarian cancer, a statistic that has been known for decades. However, the overall incidence of ovarian cancer was not elevated when comparing infertile women who received treatment with ovulation induction medications versus the infertile women who did not receive treatment. Higher rates of ovarian cancer were found in women who were followed for a longer period of time (greater than 15 years), but the results were not statistically significant, therefore not conclusive.

Once you have decided to undergo treatment with medications that stimulate ovulation, you will be given an appointment for an "Injection Teaching Session". HMG's are given as subcutaneous injections because they do not remain active if taken orally. During the teaching session you and/or your partner (or whoever will be giving you the injections) will be instructed how to mix the appropriate dose of medications and to administer the injections. Although most people are nervous about injections, everyone feels comfortable at the end of a session. Another aspect of the teaching session is to understand how our office conducts an ovulation induction cycle. Clomid is typically taken between cycle day 3 through 7. In general, HMG injections are given daily, starting on the 2<sup>nd</sup> day of a menstrual cycle (the day after your period begins). On the 6-8<sup>th</sup> day of the menstrual cycle, you will be scheduled to have the first sonogram and blood tests. In the afternoon you will call the office (before it closes at 4 pm) to get the results and receive the instructions to continue and eventually complete the treatment cycle. The results of these tests will help us determine whether we need to change the medication dose, when you should return for additional testing, and when is the appropriate time to take hCG to trigger ovulation. After the hCG is given, you will not need additional injections or sonograms. If your treatment includes inseminations, they will be scheduled the 2 days following the hCG injection. Approximately a week after ovulation, you will be seen in the office and evaluated for any signs or symptoms of hyperstimulation, to obtain a blood test for a



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progesterone level (to confirm ovulation and an adequate luteal phase), and to discuss any possible changes in the next treatment cycle if a pregnancy does not occur.

Ovulation induction cycles are labor intensive and require a great deal of time and commitment. We are also committed to assist you through the process and be available for questions and support.

I have been given the opportunity to ask questions and they have been answered fully and satisfactorily.

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Patient Date

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RN/MD. Date

Ver.7/05