Massachusetts House of Representatives
Health Care Committee Members
State House
Boston, MA. 02133

re: Massachusetts House Bill # 2062

Testimony in support of the 'Fertility Clinic Regulation Bill'

Dear Health Care Committee Member:

It has been said that 'the power of an idea can be measured by the degree of resistance it attracts'. This adage seems especially apt for the issue at hand, given the Fertility Industry's fierce determination to remain regulation free and the delay in enacting this piece of legislation.

Incredibly, this country has national and international laws regulating the use of lab animals, but no laws regulating the use of women in reproductive technologies; and we have established policy on the protection of fetuses, frozen embryos, and dead sperm, yet there are no policies for the protection of women and children involved with reproductive technologies.

True, the American Fertility Society has produced minimum performance guidelines and made generic ethical statements. These were hailed as fundamental policy created by credible professionals and were promoted as such to the public. The publication of the American Fertility Society's reports contained no disclosure that these unenforceable guidelines were crafted by the very individuals advancing and profiting from these technologies. It does not take a doctorate to know you don't have the fox guarding the poultry.

The U.S. seems to watch idly as other countries respond to bioethical issues, and responsibly address and regulate reproductive technologies. To consider the technological, ethical, biological, societal, scientific, medical, legal, and future ramifications of these issues is indeed a formidable task. Regulation and laws have lagged far behind the technologies, and the Industry seems to increase its pace correspondingly.

Just in the 12 months since this bill's last hearing, human embryo's have been cloned, and the possibility to transplant aborted fetuses' ovaries into women has emerged. To bear one's own brother, or to be the offspring of an unborn non-person are now more than a theoretical possibility. The concept of "life" as we've known it is now challenged, and the U.S. needs to face this challenge and its sequelae

But there is no regulation of reproductive technologies in this country today because our government has chosen to avert rather than act upon these issues. Simultaneously the Fertility Industry has replicated itself and it's agenda; and in doing so the Industry has attained such a critical mass that it's prevalence alone conveys the impression that the technologies are accepted, approved, safe, and effective. This burgeoning, multi-billion dollar technological market is colorfully painted as science ... yet there is no

data to support safety.

While Massachusetts House # 2062 does not attempt to deal with the broader bioethical issues, it is nonetheless a "first in the nation" attempt to establish regulation of a fertility clinic; and this, in and of itself, is a major first step. But Boston does not appear to be fertile ground or friendly soil for this first step.

This city and surrounding areas contain a large concentration of fertility clinics (and sperm banks): since there is no license required to operate a fertility clinic, the exact number of clinics performing IVF will remain unknown. In addition, the world's largest manufacturer of fertility drugs, Serono, has begun a $50 million expansion just outside of Boston - a development the Governor of Massachusetts has hailed as "good for Massachusetts". And 'Resolve' an active arm of the Fertility Industry, centers its national office in Somerville; and regularly receives perks from local fertility clinics and Serono.

But while the Industry has scores of lobbyists deflecting regulation, the consumer is left without protection, without advocacy, and without a voice.

'Resolve' alleges itself to be a non-profit organization dedicated to support, advocate, and educate the infertile population. 'Resolve' submitted testimony in opposition to this 'Fertility Clinic Regulation Bill' in March 1993; in a June 1993 Newsletter, Resolve informed its members about the existence of this bill for the first time. Since 'Resolve' could not issue a statement on behalf of members whom it had not informed or polled, this 'opposition to regulation' was an administrative position. Yet, 'Resolve' is promoted by the American Fertility Society, fertility clinics, fertility doctors, Serono, and the media as THE authority that "speaks" for the infertile. There are those of us who chose to speak for ourselves.

Therefore, the 'Fertility Clinic Regulation Bill' speaks to issues of consumer protection that should be legislated, despite the vested interests that are in opposition. Mandatory licensure, minimum standards, quality assurance, quality control, informed consent, record keeping, and data tracking of the women and offspring are more than reasonable safeguards. These measures become even more paramount when one considers that the Fertility Industry is exploitive at best, and dangerous at worst.

In my 1993 testimony and addendum, I cited the Journal of Assisted Reproduction and Genetics (Vol. 9, No. 3, 1992) in 'Hormonal stimulation for IVF' : "Since oocytes used in IVF are harvested after hormonal stimulation, it is not unlogical to assume an effect of this stimulation on the oocyte quality ... whether different types of hormonal stimulation have different effects on the nuclear oocyte quality is not yet clear."

We've already had the debacle of DES, and the tragedy of thalidomide. In 1962, following birth defects from thalidomide, I have read that the Kefauver Amendments were passed requiring efficacy data before a drug can be marketed. Wouldn't these amendments address a necessity to thoroughly determine a drug's safety? Yet in 1967 and 1969, respectively, clomid and pergonal were approved by the FDA, and have been prescribed for over a quarter of a century - but both remain lacking in epidemiologically sound data, and without long term study design.

Stanford released a study last year which showed an increased risk of developing ovarian cancer after

using fertility drugs. Following this study's release, 'Fertility & Sterility' (the trade journal of the American Fertility Society) had an article in February 1993 titled "Fertility drugs and ovarian cancer: red alert or red herring?". Commenting on this study, the first paragraph states "To our knowledge, these are the first reports of a significant association between ovarian cancer and fertility drugs"

"Significant" defined by Webster is "important, representative of something, standing as a sign of something". A visit to a medical library reveals the following reports:

- American Journal of Obstetrics & Gynecology (March 1992) in 'Ovarian carcinoma of low malignant potential, infertility, and induction of ovulation - Is there a link?': "All the patients in our series received Pergonal therapy for induction of ovulation, and serous ovarian tumors of low malignant potential developed in all" ... "the clinical observation (of three case reports) is important and one that we believe requires evaluation and follow-up. It might be prudent to set up a national registry for patients <35 years old with ovarian carcinoma. If this confirms our observation and the common denominator is infertility with subsequent ovulation induction, further study regarding this issue appears warranted."

- Iatrogenics (1991: 1: 7-16), 'The risks associated with ovulation induction' : "Predominant medical opinion has it that CC and hMG (clomid and pergonal) are safe and effective, although serious side-effects sometimes occur. This presumption of safety must be regarded with measured skepticism. By current standards, CC and hMG were never properly evaluated prior to their introduction into clinical practice. Today, nearly 30 years later, methodologically sound research is still lacking. Widespread use of these drugs has led health policy-makers, researchers and the public to voice concerns about the risks of ovulation induction". "Ovulation induction may be a risk factor for certain types of hormonally-dependent cancers, particularly ovarian cancer

- British Medical Journal (September 1989) in 'Follicular stimulation and ovarian cancer' : "Drs. Fishel and Jackson correctly warned about the possible long term sequelae of ovarian stimulation, especially epithelial malignancies in the ovary, endometrium, and the breast".

- British Medical Journal (July 29, 1989); 'Follicular stimulation for high tech pregnancies: are we playing it safe?' discusses the "potential risk of cancer from excessive ovarian stimulation".

- Congress of the United States, Office of Technology Assessment. "Infertility: medical and social choices." Washington D.C., U.S. Government Printing Office, 1988', as cited by The Lancet (October 28, 1989): "Complications linked with induction of superovulation by fertility drugs include the ovarian hyperstimulation syndrome, cysts, coagulation abnormalities leading to thromboembolism, stroke, and myocardial infarction, molar pregnancy, and ovarian cancer"

There are additional sources which address the relationship between the use of fertility drugs and ovarian cancer, as well as there being information identifying a relationship of fertility drug use and birth defects:

- The National Perinatal Statistics Unit and the Fertility Society of Australia, "In Vitro Fertilization Pregnancies, Australia and New Zealand, 1979 - 85", National Perinatal Statistics Unit (Sydney, 1987): IVF babies have 'four times higher than normal mortality rate for the first 28 days after birth, five times the expected rate of spina bifida, and nearly seven times the expected rate of a serious heart defect'

- Iatrogenics (1991: 1: 7-16), 'The risks associated with ovulation induction': "In humans, CC and hMG significantly increase the incidence of chromosomal abnormalities in the embryo. In a study ... they conclude that fertility drugs increase the risk of releasing oocytes which carry a chromosomal anomaly."

- The Lancet (July 15, 1989), 'Ovulation induction and neural tube defects': "A relation between ovulation induction and some congenital anomalies cannot be excluded."

- New England Journal of Medicine (September 23, 1982), 'Hepatoblastoma in an infant born to a mother after hormonal treatment for sterility' : "We suggest a possible association between the hormonal treatment the mother received before pregnancy and the hepatoblastoma in her offspring".

- The Lancet (June 2, 1973), 'Anencephaly and ovulation stimulation' : "We think that the possibility of a causal relationship between ovulation-stimulating treatment and central nervous system abnormality should not be dismissed lightly."

Clearly, all of these must be seen as "significant": "important, representative of something, standing as a sign of something". And none of these should be dismissed lightly. And while there are reports which refute a cancer or congenital defect association, the predominant opinion from both camps is that "further investigation is needed".

In the Fertility & Sterility article (February 1993) in which it was stated "to our knowledge, these are the first reports of a significant association", the conclusion of the paper states: "At present, there is no need to change medical practice regarding use of fertility-enhancing drugs. There is enough cause for concern, however, to slightly alter the physician's approach to counseling patients. We suggest advising patients receiving fertility drugs as to the possible increased risk of ovarian cancer. ... Careful records must be maintained identifying each patient, including Social Security number, date and place of birth, maiden name, and an address and telephone number where the patient may be reached. Such information will help individual physicians contact their patients should more definitive evidence of a causal relationship between fertility drugs and ovarian cancer be found."

But historically, fertility doctors have shown a poor track record in maintaining records; DES being one example. This can be further illustrated by another past fertility drug "misadventure" practiced by the U.S. (as well as in other countries). Human pituitary gland hormone (hGH), derived from cadavers, was administered beginning in 1963 as a fertility drug to infertile women and as a growth hormone to children with pituitary insufficiency. But in 1985, after two deaths in the U.S., investigation yielded the discovery that a fatal neurological disorder, Creutzfeldt-Jakob Disease (CJD), was associated with human pituitary gland hormone.

Quoting 'Overdue Acknowledgement? The Legacy of CJD for Australian Women Treated With Human Pituitary Gland Hormone for Infertility' from Lynette Dumble, Senior Research Fellow, the University of Melbourne, Parkville, 3052, Australia, and Renate Klein, School of Social Inquiry, Geelong, 2317, Australia (1992), (Synopsis also found in The Lancet, October 3, 1992): "It was suggested in 1985 that the first of the hGH-associated CJD deaths might represent the beginning of an iatrogenic epidemic, but

by 1988, despite the emergence of further cases of CJD (in the U.S., U.K., and Australia), the basis for an international silence was established." "In the United States, where hGH use was abandoned in 1985, monitoring, surveillance and counseling of subjects at risk commenced immediately after the first CJD death in 1985 under the auspices of the FDA, CDC, NIH, and the Institutions who were responsible for hGH administration".

"More recent reviews of the U.S.A. and U.K. experiences have reported that CJD continues to occur in their respective hGH-treated populations and that they must remain under long-term review. The U.S.A. review points out that only 10% of their 6,284 recipients had been followed-up for the 15 year average incubation interval from midpoint of hGH treatment to the onset of CJD symptoms. As a result the great majority of potentially exposed patients have not yet attained the requisite incubation period for expression of CJD."

Therefore, as women in this country take approved fertility drugs that have never been properly tested, with evidence pointing to carcinogenic and teratogenic effects, and with no monitoring ... women (and children) exposed to a former, now-recognized-as-deadly fertility drug remain unsurveilled and presently are at risk for death. That this is disturbing is an understatement.

Given that the U.S. abandoned the use of the human pituitary gland hormone after two deaths, it would appear that two deaths from a fertility drug are the requisite red flag for intervention. I offer Gilda Radner and Barbara Mays as a tragic pair of deaths arising from current, approved, never properly tested, readily available, fertility drugs. Both took currently used fertility drugs and both died of ovarian cancer. (Was this why Barbara May's baby was "switched at birth"? Could someone have feared a relationship might be established with Barbara Mays use of fertility drugs and her offspring's congenital heart defect? Mother and child may well be victims from these drugs). While their names are high profile, how many other unknowns are there out there? Without data tracking, we'll never know.

The number of women and children in the world who were exposed to the human pituitary gland hormone associated with CJD are estimated at 13,000 to 30,000; exact figures are unknown. As of 1988, 1.9 million women were estimated to have taken currently approved fertility drugs - and again, exact numbers are unknown. Clearly data tracking is in order here.

To my knowledge there has been only one attempt to data track. According to Congressional testimony by Medical Research International (MRI) at the Subcommittee on Regulation and Business Opportunities (March 9, 1989), MRI testified on the "IVF/ET Registry": "The Registry is a collaborative effort of the American Fertility Society (AFS), the Society for Assisted Reproductive Technology (SART), and MRI. Since its inception, the Registry has been financially supported exclusively by Serono Laboratories, Inc.. In June 1988, MRI was awarded a contract by the National Institute of Child Health and Human Development to study the potential adverse health effects on women undergoing assisted reproductive technology treatment. The NICHD funding complements that of Serono and is specifically targeted at enrolling 13,000 women." "Resolve is collaborating with us on our NICHD project by offering cooperating subjects gift memberships as an incentive for volunteering in the study subject".

This study was completed last year, Resolve denies offering free membership as an incentive, and less than 4000 women were enrolled. It would appear that this Industry-sponsored study fell far short of its

goal, and was rife with conflict of interest.

At a Resolve sponsored forum in June 1993, a representative from MRI stated: "This study was the largest cohort of women, but it's still too small to address this hypothesis now. We have identified one case of ovarian cancer, possibly two, but since all the numbers aren't in, I can't make any definitive statements". Also stated at this forum by other panel members were the following: "Be prepared to see media reports of an increase in ovarian cancer amongst your population - but don't be alarmed. You people are one of the most observed in medicine; if we were monitoring healthy, fertile women as closely as we monitor you ... we[1]d be finding their ovarian cancers as well", "ovulation induction drugs may protect you against ovarian cancer because in the majority of cases they are successful, and pregnancy is a protection against ovarian cancer."

Although MRI states in its 1989 Congressional testimony that a critical role of the Registry is to 'disseminate the results'; once 'all the numbers were in', MRI would not release the results of this study upon my request.

Massachusetts currently has an epidemic of breast cancer, and has awarded millions of dollars in grants to study breast cancer. Though there has been a number of case reports of developing breast cancer following ovulation induction (bilaterally in several instances), not one grant in this high concentration of fertility clinics chose to examine this issue.

Ovarian cancer is the fourth leading killer cancer of women. Despite the lack of knowledge on the effects of superovulation on infertile women, now fertile women are being groomed for taking these drugs; to serve as either egg donors or gestational carriers, to undergo IVF for their infertile partners, for purposes of preimplantation diagnosis, or for menopausal pregnancies.

It is reported that there is a shortage of egg donors, yet there are an estimated 200,000-plus frozen embryos worldwide. Infertility and treatment options are prevalent and hyped in this country, yet the disasters of excess fertility are of paramount concern in the Third World and measures of sterilization and birth control reign. Fertility drugs are touted as safe, yet have never been tested. These deductions and concepts are baffling.

Equally baffling is the widespread use of lupron, a Category X drug, as an ovulatory adjunct in assisted reproductive procedures. Quoting the 1993 PDR under 'warnings', 'contraindications', and 'precautions': "Safe use of lupron in pregnancy has not been established clinically. Before starting treatment with lupron, pregnancy must be excluded" ... "Lupron is contraindicated in women who are or may become pregnant while receiving the drug. Lupron may cause fetal harm when administered to a pregnant woman. Major fetal abnormalities were observed in rabbits but not in rats. There was increased fetal mortality and decreased fetal weights in rats and rabbits. The effects on fetal mortality are expected consequences of the alterations in hormonal levels brought about by the drug. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, she should be apprised of the potential hazard to the fetus" ... "safe use of the drug in pregnancy has not been established clinically. Therefore, a nonhormonal method of contraception should be used during pregnancy."

As mentioned in my 1993 testimony "the routine use of GnRH-a (lupron) for all patients undergoing IVF

has practical but no significant medical advantages ... there have been very few prospective randomized studies comparing the use of GnRH-a with conventional stimulation regimens" - citing 'Fertility and Sterility' April 1992 in '[1]The routine use of GnRH-a for all patients undergoing IVF. Is there any medical advantage?" The 'practical advantage' referenced is the fact that the clinic can schedule the woman for an 8:00 A.M. retrieval, thereby avoiding the disruption a 2:30 A.M. wakeup would create. But what dangers does this chemical compound pose to the woman (either alone or synergistically with the fertility drug), how long does the chemical remain in her system, and what effect might it have on an embryo and/or offspring? Again, without data, these questions cannot be answered ... but they must be asked.

And I must also ask why is tamoxifen being used as an ovulatory adjunct in assisted reproductive procedures? During recent Senate hearings on tamoxifen, the consent form designed for the control women required revisions to make certain it was understood that they should not become pregnant while taking tamoxifen. In 'Fertility and Sterility', May 1993, the following article can be found: "A clomid and tamoxifen combination therapy: a novel therapy for ovulation induction" ... 'A clomid and tamoxifen combination therapy and a clomid alone therapy produced ovulation rates of 75% and 43.9% respectively. The combination therapy is effective in ovulation induction'

The 1993 PDR cites the following for tamoxifen: "Warnings. Pregnancy Category D. Tamoxifen may cause fetal harm when administered to a pregnant woman. Individuals should not become pregnant while taking tamoxifen and should use barrier or nonhormonal contraceptive measures. Effects on reproductive functions are expected from the antiestrogenic properties of the drug. In fertility studies in rats and in teratology studies in rabbits using doses at or below those used in humans, a lower incidence of embryo implantation and a higher incidence of fetal death or retarded in utero growth were observed, with slower learning behavior in some rat pups. There are no adequate and well-controlled studies in pregnant women. There have been reports of spontaneous abortions, birth defects, fetal deaths, and vaginal bleeding. If this drug is used during pregnancy or the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazards to the fetus". Again ... what dangers does this drug pose to the woman (either alone or synergistically with the fertility drug), how long does the drug remain in her system, and what effect might it have on an embryo and/or offspring? Again, without data, these questions cannot be answered ... but they must be asked.

Both lupron and tamoxifen are not approved by the FDA for the indication of ovulation induction. Both lupron and tamoxifen "are not to be used by women who are or who may become pregnant", and both lupron and tamoxifen's effect on human embryos and offspring are "unknown". Yet ... both lupron and tamoxifen are being administered as an ovulatory adjunct to women undergoing assisted reproductive technologies with the goal of conception!

Recently I forwarded a request to the Attorney General's office to investigate the claims of several fertility clinics regarding the safety of the drugs. Local fertility clinic brochures were enclosed, and relevant statements were: “no known serious side effects”, “none of these medications have been shown to be harmful", "effective and safe hormonal drugs", "the medications, if carefully monitored, are not harmful to you. There is no clinical evidence of increased incidence of birth defects, congenital abnormalities or spontaneous miscarriage".

Although I have not had a response from the Attorney General's Office, elsewhere I have learned that the brochures I forwarded were outdated, and do not reflect current brochures. If these brochures have indeed been changed, then there are only two questions. Has the theme of 'no known serious side effects' been removed and replaced with full disclosure? Or is there simply removal of the libelous statements? To put this in other words ... were changes made for the protection of the patient, or for the protection of the clinic?

Presently, the lack of laws, regulations, and standards creates an atmosphere in which there is no accountability or culpability on the part of the Industry. The sucking sound from the legal vacuum can be heard in Mexico (where, incidentally, the price of pergonal is one fifth the cost in the U.S.). A review of legal literature shows some case law is being established in the areas of paternity/maternity issues in surrogacy and egg donor scenarios, privacy and freedom rights violations, pre-implantation misdiagnosis, preconceptus torts, and property rights matters. Aside from the privacy and freedom rights cases, all these situations deal with 'successful cycles'

But if one is generous and applies a success rate of 20%, this means that these fertility clinics are churning out an 80% failure rate. Without standards, laws, and regulations, there will be no accountability or culpability for the manner and methods of the failures that result from substandard or negligent management. How many of these failures are due to improper or mismanaged stimulation regimes, miscalculation of retrieval, wrong culture medium, faulty equipment, lab errors, improper implantation techniques, etc., etc.? While there could never be a guarantee of 'success', the high paying customer should be guaranteed appropriate treatment.

Massachusetts House Bill # 2062 would and should establish standards for quality control and quality assurance in a fertility clinic. Since billing audits and quality management are most certainly exercised in the financial division of the fertility clinics - quality management needs to be applied to the clinical arena as well.

Massachusetts House Bill # 2062 would and should provide for mandated record keeping and data collection. And systematic analysis of that data should follow.

Massachusetts House Bill # 2062 would and should mandate informed consent. Women must be given the knowledge regarding the efficacy of treatment, and that drug-free IVF cycles are available and appropriate in many instances. And women must be given the knowledge that these fertility drugs have never been properly tested, and that evidence indicates a carcinogenic and teratogenic potential.

Massachusetts House Bill # 2062 would and should require a fertility clinic to obtain a license. A dog kennel, hair transplant clinic, and cosmetologist require a license to operate, to just name a few. Clearly a fertility clinic, manipulating human gametes and utilizing powerful drugs and invasive techniques, should be required to obtain licensure.

Massachusetts requires that grease traps in restaurants be monitored and measured routinely, and has mandated such within the restaurant's license to operate. If this state or this country does not value and ensure the health, safety, and protection of women and children in the marketplace of fertility clinics, then we're all going down the drain.

Respectfully submitted,
Lynne Millican, R.N.

April 6, 1994