Embryo research in the US
Lori Andrews¹ and Nanette Elster
Chicago-Kent College of Law, 565 W Adams, Chicago, IL 60661, USA
¹To whom correspondence should be addressed

In February of 1997, researchers at the Roslin Institute in Scotland, UK, announced that they had cloned a sheep by transferring nuclear material from an adult mammary tissue cell to an enucleated egg cell of an unrelated sheep. The resulting embryo was transferred to a third sheep for gestation and in July, 1996, Dolly, the sheep, was born (Wilmut et al., 1997). The announcement of successful mammalian cloning through nuclear transfer generated much discussion throughout the world about the possibility of applying this technique to humans. In the US, the legality, morality, and scientific reality of cloning have brought back to the forefront issues that have been continually debated since the 1978 birth of Louise Brown. ‘We are moving from unconscious cultural determination of human biological progression to a degree of conscious self-determination,’ notes Grobstein (1981). As we make that transition, the law grapples with whether there should be limitations on the study, transfer and use of embryos.

Developments over the past two decades, such as in-vitro fertilization (IVF), preimplantation genetic diagnosis, and cloning have caused a great deal of attention to be focused on research involving concepti. IVF itself was initially a research procedure and, although over the past 20 years it has become accepted as a standard medical practice, certain attempts to enhance the IVF success rates are still considered to be research. These adjuncts to IVF for infertile couples range from the relatively uncontroversial procedures of testing different media in which to fertilize the embryos to the more controversial techniques of embryo cryopreservation (freezing) for subsequent implantation and embryo twinning (splitting the embryo) and cloning by way of nuclear transfer.

In 1994, a panel of 19 members appointed by the National Institutes of Health (NIH), a US governmental body, issued recommendations concerning the types of research with human embryos that should and should not be federally funded (Gianelli, 1994). Found to be unacceptable were techniques such as cloning and the creation of chimeras. The study of preimplantation diagnosis and the fertilization process, though, were found to be acceptable. Soon after the panel issued its recommendations, President Clinton issued a directive which banned the use of federal funds for research that created embryos solely for research purposes (Marwick, 1995). The ban did not apply to the use of spare embryos that may be remaining after an IVF attempt. Subsequently, Congress passed bans (PL 104-91 and PL 104-208) on the use of federal funds by various government departments for any research that exposes embryos to risk of destruction or non-therapeutic research. In March 1997, President Clinton banned the use of federal funds for human cloning.

The federal embryo research ban was allegedly violated recently by an NIH researcher, who utilized government issued equipment and personnel to perform preimplantation genetic diagnosis (Varmus, 1997). Although preimplantation genetic diagnosis cannot be performed with federal funds, private IVF clinics can perform the technique, as well as other research, within the bounds of individual states’ law.

Categories of embryo research
Embryo research can have a variety of goals. In some instances, it is done to benefit the couple who provided the gametes; in others, to benefit the potential child, while in still other cases, it is undertaken to benefit a particular unrelated individual or even to increase general scientific understanding.

Some research has focused on helping infertile couples conceive children, or in assessing the genetic status of their embryos (Simpson and Carson, 1992). These procedures provide couples with information on which to base decisions about whether or not to implant particular embryos. For example, David and Renee Abshire of Louisiana lost a child to Tay–Sachs disease in 1989. They chose not to have another child until they had a guarantee that another child would not suffer from the same disease (Tennant, 1997). The Abshires are opposed to abortion, therefore amniocentesis or chorionic villi sampling were techniques they were unwilling to undergo. Preimplantation genetic diagnosis allowed them to choose an embryo free of Tay–Sachs disease, and they now have a healthy 3 year old daughter (Painter, 1997). Genetic testing on embryos also leads to the theoretical possibility of undertaking gene therapy or other therapeutic measures to benefit either the embryo itself or the resulting child.

Beyond procedures that might benefit the embryo or its progenitors, there are embryo research possibilities that would potentially benefit third parties. These include the embryo as a source of cell lines or tissue. In addition, research can be undertaken not to benefit any particular individual, but to benefit society at large. Such research is basic scientific research, which might include the study of embryonic development or the study of the effects of particular interventions (such as exposure to certain drugs). The creation of embryos in Petri dishes raises the possibility of using spare embryos for research purposes and the further possibility of creating embryos exclusively for research purposes (Grobstein, 1981).

There is a wide range of opinions about the moral permissibility of various types of research on embryos. Yet embryo
research, unlike fetal research, has not been the subject of extensive legislative consideration in individual states. In part, this may have been due to the fact that fetal research was thought to entail mainly basic scientific research, while embryo research first came to the public’s attention as part of a clinical procedure to aid infertile couples, a goal that many in society felt was laudable.

Since embryo research per se has rarely been the subject of state legislative scrutiny, the analysis of whether a particular state restricts embryo research requires scrutiny of a wide range of state statutes which were adopted for other purposes, but contain language which is broad enough to regulate certain aspects of embryo research. These statutes include laws addressing fetal research, IVF, tissue or organ transplantation, and payment for embryos.

Overview of state laws impacting embryo research
In the US, 10 (Florida, Louisiana, Maine, Massachusetts, Michigan, Minnesota, North Dakota, New Hampshire, Pennsylvania, Rhode Island) out of the 50 states have laws regulating research and/or experimentation on embryos, pre-embryos, fetuses, concepti or unborn children which arguably may apply to a variety of types of research including preimplantation genetic diagnosis and cloning. One state (New Hampshire) allows embryo research until 14 days’ development, but does not allow implantation of a researched-upon embryo. The other nine states ban certain types of research on concepti but each statute approaches the prohibited activities in a slightly different way, and thus a close analysis is necessary to determine whether a technique performed on an embryo is within a particular statute’s reach. Among the questions to be addressed are whether the technique fits the definition of ‘research’ or ‘experimentation’; ‘therapeutic’ or ‘non-therapeutic’; whether the entity being researched upon fits the definition of ‘live’ and, depending on the state, ‘pre-embryo,’ ‘embryo,’ ‘fetus,’ ‘conceptus,’ or ‘unborn child.’

Not all the existing statutes, however, will necessarily survive constitutional scrutiny. Some of the states’ laws governing fetal research and the disposal of fetal remains have already been declared unconstitutional. In addition, statutes that do not allow the use of experimental genetic and reproductive technologies would be open to constitutional challenge. Such a challenge was successful in a federal district court case, Lifchez v. Hartigan (1990), which held that a ban on embryo research was unconstitutional because it impermissibly infringed upon a woman’s fundamental right to privacy. Although the Illinois statute banning embryo research permitted IVF, it did not allow embryo donation, embryo freezing, or experimental prenatal diagnostic procedures. The court stated: ‘It takes no great leap of logic to see that within the cluster of constitutionally protected choices that includes the right to have access to contraceptives, there must be included within that cluster the right to submit to a medical procedure that may bring about, rather than prevent, pregnancy. Chorionic villi sampling is similarly protected. The cluster of constitutional choices that includes the right to abort a fetus within the first trimester must also include the right to submit to a procedure designed to give information about that fetus which can then lead to a decision to abort’.

The reach of the state statutes
Effects of state laws on particular types of research

Preimplantation genetic screening
Various prenatal diagnostic techniques have been developed to help couples or individuals decide whether or not to continue a particular pregnancy. Research on genetic testing of ex utero embryos is currently underway (Simpson and Carson, 1989). Four states specifically allow genetic screening, exempting the procedure from their bans on embryo research (Massachusetts, Michigan, North Dakota, Rhode Island). In five other states, preimplantation genetic screen would be prohibited unless it could be shown to be beneficial or risk-free to the embryo (Florida, Louisiana, Maine, Minnesota, and Pennsylvania). In New Hampshire, if preimplantation screening is considered a research procedure, tested embryos cannot be implanted.

In addition to the general embryo research bans that extend to preimplantation screening, the laws of at least two other states could conceivably affect this procedure. These laws do not apply to other types of embryo research, but may, through a quirk in their language, apply to preimplantation screening. They are statutes in Florida and Oklahoma that prohibit research prior to an abortion or on a conceptus intended to be aborted.

Embryo cryopreservation or donation
Health care providers performing embryo cryopreservation (Zeilmaker et al., 1984) or embryo donation (Lutjen et al., 1984) as part of IVF will, in Pennsylvania, have to comply with the statute on reporting. The report must include the names of all persons conducting or assisting in the fertilization or experimentation; location; name and address of any person, facility, or agency involved in the process except for donors or recipients of eggs or spermatozoa; the number of eggs fertilized, number of fertilized eggs destroyed or discarded and the number of women implanted with fertilized eggs. In Louisiana they will have to comply with a law regarding the personnel qualifications and in certain other states, they will have to comply with insurance laws specifying the qualifications of reimbursable IVF providers.

In addition to having to comply with these requirements, if these procedures are considered to be experimental, there is a concern that they will fall foul of the embryo research laws in certain states. Six states (Florida, Massachusetts, Michigan, North Dakota, Pennsylvania and Rhode Island) have laws which could be used to prohibit embryo cryopreservation and five states (Maine, Massachusetts, Michigan, North Dakota and Rhode Island) have laws which could be interpreted to prohibit embryo donation.

Embryo twinning is even more experimental. Embryos can be divided in half before implantation in order to enhance the probability of at least one live birth. The procedure is risky for the embryo, however, and could violate the bans on embryo research in the 10 states.
Cloning

Some couples might elect cloning for reproductive purposes. If both members of a couple are infertile, they may wish to clone one or the other of themselves. If one member of the couple has a genetic disorder that the couple does not wish to pass on to a child, they could clone the unaffected member of the couple. In addition, if both husband and wife are carriers of a debilitating recessive genetic disease and are unwilling to run the 25% risk of bearing a child with the disorder, they may seek to clone one or the other of them. This may be the only way in which the couple will be willing to have a child that will carry on their genetic line.

The state embryo research bans are less likely to ban cloning than the other techniques involving embryos. Eight of the states prohibit some form of research on some product of conception, referred to in the statutes as a conceptus (Minnesota), embryo (Michigan), fetus (Florida, Maine, Massachusetts, North Dakota, Rhode Island), or unborn child (Pennsylvania). However, an argument could be made that the experimentation is being done on an egg, not the product of conception, and thus these statutes should not apply. By the time the egg is re-nucleated, the experiment or research (which is prohibited) has already been completed. Since the statutes would not apply until after the cloning procedure is completed, it could be argued that the most protection these statutes supply would be protection from experimentation after the re-nucleation, it would not prevent the cloning itself.

Two statutes have provisions that are particularly likely to be applied to cloning. In New Hampshire, a pre-embryo may not be allowed to develop beyond 14 days post-fertilization, so cloning research may be permissible within the first 14 days of development. However, ‘no pre-embryo that has been donated for use in research shall be transferred to a uterine cavity.’ Thus, if a re-nucleated oocyte is considered to be a pre-embryo, it would be impermissible in New Hampshire to implant the resulting conceptus to create a child.

In Louisiana, the statute applies to an ‘in vitro fertilized human ovum ... composed of one or more living human cells and human genetic material so unified and organized that it will develop in utero into an unborn child.’ An entity meeting the definition cannot be cultured and farmed solely for research purposes, which would prohibit cloning research to study gene function, cellular development, and so forth. Another provision specifically states that such an entity may be used ‘solely for the support and contribution of the complete development of human in utero implantation.’ This creates the anomalous result that researchers could clone a whole individual in Louisiana, but could not do research ex utero on cloned cells.

Gene therapy and other treatment for embryos

The prospect of adding genetic material to an embryo in vitro has been suggested as a way to correct genetic defects. Because the goal of the procedure is to provide a health benefit to the embryo or the resulting child, it is likely to be permissible even in states with extremely restrictive general bans on embryo research. Eight of the state laws (Florida, Louisiana, Massachusetts, Michigan, Minnesota, North Dakota, Pennsylvania and Rhode Island) governing embryo research would seem to allow gene therapy on embryos. New Hampshire’s statute prohibiting transfer of a researched-upon embryo to a uterine cavity would likely be read to prohibit gene therapy.

Cell line development

All of the states that have laws banning embryo research would appear to prohibit the development of cell lines out of embryos, if the procedure is considered a research procedure, since it would not be seen as therapeutic or beneficial to the embryo. In addition, payment for the cell lines might violate the laws in states banning payment for embryos for research uses or for any uses.

An argument might be made that certain types of cell line development should not be considered to be research, but rather an accepted practice (taking them out of the reach of the research bans). At that point, the question of whether companies could commercialize the cell lines would depend on whether there is a state law banning payment for cell lines or for fetal parts for any uses (not just research uses).

While some state laws might prevent payment for embryonic cell lines, it is possible that because a cell line is new tissue produced from the genetic material of, but not originally a part of, the embryo, laws proscribing the sale of the embryonic tissue may not apply. In fact, a Minnesota law prohibits the sale of living conceptuses or non-renewable organs but does allow ‘the buying and selling of a cell culture line or lines taken from a non-living human conceptus ...’. In contrast, Nevada’s broadly worded statute making it a crime for anyone to use or ‘make available ... the remains of an aborted embryo or fetus for any commercial purpose’ could conceivably outlaw the production of cell lines from fetal tissue.

Basic scientific research

The statutes which totally prohibit non-therapeutic research on embryos could seriously impede development of diagnostic and treatment technologies that would ultimately benefit other embryos. Some use broad enough language that they could be interpreted to ban research even if there is no risk to the embryo, e.g. observational studies of embryonic development. Yet an understanding of the normal situation and the range of variation must precede the definition of the abnormal. For example, the development of the tests to be used in conjunction with amniocentesis were made possible by undertaking research that was not beneficial to the researched-upon fetus (such as the assessment of the level of certain enzymes in its amniotic fluid), but which was able to provide typology for normal and abnormal values.

It would be a mistake to assume that non-therapeutic research is invariably more risky than potentially therapeutic research. For example, there will be more risk involved in gene therapy (which is intended to be therapeutic) than in studies which involve only observations and the collection of data on embryonic development. The ethical evaluation of research on embryos should involve a consideration both of the purposes of the activities and the risk involved as an effect of these activities; and these two factors, the purpose and the effect, should be kept conceptually distinct. The extent and magnitude of risk to a research subject is not correlated with the purpose of the activity or in some way determined by whether or not the activity is intended to provide a health benefit.
The study of concepti has potential relevance in many areas of medicine, including cancer research (because cell division of concepti resembles cell division in cancer tumours) and contraceptive research (because understanding the mechanism of embryo development and implantation can lead to the development of ways to inhibit these processes). The creation of embryos in Petri dishes occasioned by the development of IVF raises the possibility of using spare embryos for research purposes and the further possibility of creating embryos exclusively for research purposes (Grobstein, 1981).

Research on the conceptus without an identifiable intended beneficiary seems to offer a more remote benefit than does research to benefit the conceptus, or the gamete providers. Nevertheless, medical knowledge has been gained through general research on concepti. Much information can be obtained through research on animals, but human research is ultimately necessary because of the unique functioning of humans. Rubella vaccination research in monkeys demonstrated that the vaccination did not cross the placenta, yet subsequent human research revealed that it did and thus was unsafe for use in pregnant women (Vaheri et al., 1972).

Nine states (Florida, Louisiana, Maine, Massachusetts, Michigan, Minnesota, North Dakota, Pennsylvania and Rhode Island) forbid general scientific research on embryos. Certain state laws would also forbid payment to women in exchange for donating their conceptus for general scientific research. Ironically, although the benefits may be seen as more remote than with tissue transplantation to an identifiable recipient, there are fewer laws that would prohibit payment in conjunction with pure research. Fifteen states (District of Colombia, Florida, Georgia, Illinois, Louisiana, Maine, Massachusetts, Michigan, Minnesota, North Dakota, Pennsylvania, Rhode Island, Texas, Utah and Virginia) ban payment for embryos used in scientific research, while between 16 and 19 states (California, Connecticut, Delaware, District of Colombia, Florida, Georgia, Illinois, Louisiana, Michigan, Minnesota, Nevada, Pennsylvania, Rhode Island, Texas, Utah and Virginia, plus New York, Virginia and Wisconsin) ban payment in connection with donation of tissue or organs for transplantation.

Conclusions
In the US, regulation of embryo research is primarily determined by each individual state through legislation and/or case law. The lack of a uniform, national standard makes it impossible to conclude that embryo research is permissible or is not permissible in the US as a whole. One must consider each state’s laws on IVF, fetal research, organ and tissue donation, and abortion, as well as the procedure sought to be performed to ascertain the legal permissibility of such technique in a given jurisdiction. Despite the significance of some types of embryo research such as that involving preimplantation genetic diagnosis, it has been difficult to achieve a consensus on permissibility due in large part to a lack of consensus regarding the moral status of embryos.

References
Lifchez v. Hartigan, (1990) 735 F.Supp. 1361 (N.D. Ill.), aff’d 914 F.2d 260 (7th Cir.).