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Stem Cell Patents: Challenges and Solutions

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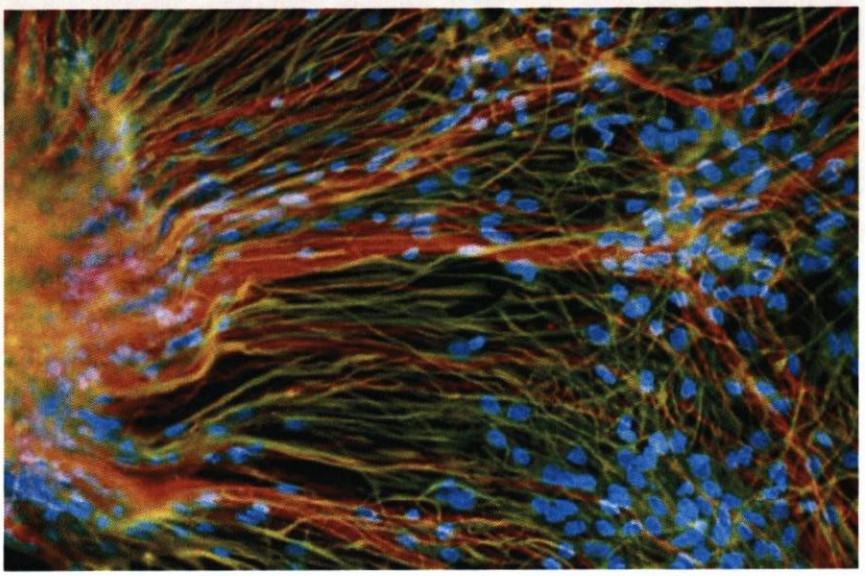
STEM CELL PATENTS: CHALLENGES AND SOLUTIONS



BY

SHIHAAM DONNELLY

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To my family – for all your support, love and constant reading of my work – I am eternally grateful. And to my superman: your relentless motivation and constant support is what made this possible. I am forever indebted to you

CONTENTS

ABSTRACT:

Stem cell research is 3 words which evokes an array of responses and emotions throughout societies. For Roman Catholics it evokes moral disgust and for scientists it symbolizes the promise and hope for the treatment and cure for crippling diseases. There exists an inherent tension between ethics and science in this context and both has to be taken into account in order for an effective and successful management solution for stem cells to operate. This paper will begin by exploring the science behind stem cell research and then explore both sides of the debate. It will argue that the medical benefits stem cell therapies offer is desirable and therefore stem cell research should be pursued. It will also take a look at the current patent stem cell landscape, specifically the USA WARF patents and illustrate how these patents along with those exclusively licensed to Geron has created a patent thicket. This has rendered the current intellectual property system inadequate and therefore this paper proposes an overhaul of this system through an endorsement of a clearinghouse model for the redistribution of patent rights. This clearinghouse mechanism will be supported by an international and regional network that will together perform an oversight function and act as an information provider.

CHAPTER ONE: UNDERSTANDING THE SCIENCE AND CONTROVERSY BEHIND STEM CELL RESEARCH

All cells come from cells

Rudolph Virchow, 1858

1.1 INTRODUCTION

On 09 March 2009, US President Barack Obama made an executive order lifting the ban on the use of federal funds for the creation of new stem cell lines.[1] Previously, scientists in the US involved in stem cell research had to rely on private funding and were only allowed to study the 21 stem cell lines that were available at the time.[2] This presidential action of allowing for government funding for stem cell research is expected to have the effect of speeding up research, to allow for increased development of treatments for diseases such as Parkinson's disease and will result in increased pharmaceutical activity. All of this will lead to an increase in patent activity and a further increase in the complexity of current stem cell related patents.

In light of these developments and the expected increase in patent activity, there is a need to re-examine the legal landscape of stem cell patents and to investigate alternative approaches of regulating stem cell research and its products. This paper is divided into four chapters and the first chapter will introduce the topic and give an overview of the stem cell biology and issues involved in stem cell patents. The issue of stem cell patents is unique in that it requires us to reconcile moral and ethical concerns with legal and commercial interests. This tension between ethics and science will be explored through a discussion of the controversy and debate surrounding stem cell research. In addition, this chapter will include a proposal for a joint meeting of all parties involved in the debate around stem cell research. This chapter will also look at the various types of stem cells and its definitions, specifically focusing on

[1] 'Removing barriers to responsible scientific research involving human stem cells', United States Executive Order 13505 of 09 March 2009.
[2] This was as a result of Executive Order 13435 of 20 June 2007 that banned the use of federal funds for the creation of new stem cell lines.

embryonic stem cells by looking at its biology, the technologies used to harvest these cells as well as its importance, its potential and value to the medical community in particular. It will conclude with a brief look at global attitudes towards stem cell research and the legal systems associated with those.

The second chapter begins with an overview of the USA patents through a case study of Wisconsin Alumni Research Foundation's patents, and continues with a look at the consequences of their stem cell patent portfolio. An examination of these patents were chosen because at present they hold the most fundamental of patents and it affects much of stem cell research and the direction it has taken. Two consequences of their patent portfolio, namely patent thickets and patent monopolies will be examined as well as its effects on stem cell research. Alternatives to the current patent landscape in the form of patent pools and cross licensing will also be investigated.

In the third chapter, this paper will propose a clearinghouse mechanism for the management of stem cell patents. This chapter will argue that the best solution for the regulation of stem cell patents is the redistribution of stem cell patent rights and related intellectual property rights through a clearinghouse system. This clearinghouse system will be supported by a global and regional network which will be setup via an international treaty. This network will provide an oversight and support function, along with the national governments who will assist with financial funding and further support mechanisms. A range of creative commons type licenses will be made available to all member of the clearinghouse and certain licenses will be made compulsory depending on the nature of the patent.

Essentially this paper will propose a complete overhaul of the governance of stem cell research and its products, beginning with working towards a shift in how society thinks about stem cell research. It is acknowledged that this will not be an easy task, however, the joint meeting proposed in chapter one is a step in the right direction. The estimated period for setup and functioning of the clearinghouse system along with the

global and regional network is five to ten years. This paper will now begin with an exploration into stem cell biology.

1.2 STEM CELL BIOLOGY

a) What are stem cells?

Despite the plethora of literature on stem cell biology, there is no universal definition of the term "stem cell"[3], instead scientists have taken to defining stem cells according to their functionality.[4] It is the proposition of this paper that the definition of a stem cell is constituent of two components – its key properties and its origin. In basic terms, a stem cell as the name suggests, is a cell from which other cells stem. More specifically, a stem cell is an unspecialised cell that has the ability to not only divide continuously into daughter cells but also replicate itself. [5] This self-replication ability is a key property of a stem cell and sets it apart from other cells in the body such as heart, skin and nerve cells that do not have self-renewal properties.[6] Another key property is the unspecialised nature of stem cells, which is unique because it means that these cells have the ability to differentiate into specialised cells. These two key properties of a stem cell form level 1 of the definition. Level 2 involves the origins of the stem cells, either from a blastocyst, from the gonadal ridge or from specific adult tissues.

The origin of a stem cell influences its properties and functionality in different ways as demonstrated in the table below. Embryonic stem cells are commonly derived from embryos that have been produced outside the body via in vitro fertilisation (IVF).[7] The 5 day old embryo known as the blastocyst is cultured to cause the separation of the inner cell mass from the surrounding trophectoderm. This

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[3] Marshak, Gardner and Gottlieb *Stem Cell Biology* (2001) at 2; Kelly *Stem Cells* (2007) at 3.
[4] Smith A 'Embryo derived stem cells: Of mice and men' in (2001) Vol. 17 *Annual Review of Cell and Developmental Biology* 435 at 451.
[5] A stem cell will divide continuously throughout the life of an organism or if in culture, will divide indefinitely.
[6] Kelly *Stem Cells* (2007) at 4; Sell *Stem Cells Handbook* (2004) at 1; *Understanding stem cells: An overview of the science and issues from the National Academies*, National Academies (2006); *Stem Cells: Scientific progress and future research directions,* Department of Health and Human Services (June 2001) at 1 accessed at http://stemcells.nih.gov/info/scireport/2001report.
[7] These embryos are sourced from fertility clinics with the informed consent of the donors.

inner cell mass is further subjected to a multi-step process in order to produce embryonic stem cell cultures.[8] These stem cell cultures can be directed to differentiate (also referred to as pluripotency) into any cell of the body and they have the ability to proliferate indefinitely. This pluripotency ability has sparked interest in stem cell research and has driven the continued efforts of scientists and doctors to use stem cells for various therapeutic purposes. The second source of embryonic stem cells are primordial germ cells located in the gonadal region of a 5 to 9 week foetus.[9] Similar with embryonic stem cells, the germ cells are cultured to isolate stem cells and the resultant cell cultures can proliferate and differentiate into most types of cells of the body. The difference between embryonic stem cells and embryonic germ stem cells lies in their ability to differentiate and proliferate with the former having greater potential to do so than the latter.[10] The third source of stem cells is the various tissues within the human body such as the skeletal muscles, hippocampus and liver. These stem cells are different from embryonic stem and germ stem cells in that it is limited to differentiate into specialised cells that are specific to the tissue in which it resides.[11]

Recent studies have suggested the possibility that adult stem cells have the ability to differentiate into specialised cells that are not specific to the tissue in which it resides, a phenomenon referred to as plasticity or trans-differentiation.[12] However, these claims of adult stem cell plasticity have been criticised mainly for being in contradiction to the orthodox certainty that the fate of somatic stem cells are committed during early development of the foetus.[13] This debate on the plasticity of

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[8] Thomson et al 'Embryonic stem cell lines derived from human blastocysts' in (1998) 282 *Science* 1145.

[9] These foetuses are obtained as a result of therapeutic termination of pregnancies: Shamblott et al 'Derivation and differentiation of human embryonic germ cells' in Lanza (ed) *Essentials of Stem Cell Biology* (2006) at 306; Bongso and Lee *Stem Cells: From Bench to Bedside* (2005) at 5. These cells are also referred to as embryonic germ stem cells.

[10] *Stem Cells: Scientific progress and future research directions,* Department of Health and Human Services (June 2001) at 14 accessed at http://stemcells.nih.gov/info/scireport/2001report; Sell *Stem Cells Handbook* (2004) at 4-6.

[11] *Stem Cells: Scientific progress and future research directions* (2001) at 2.

[12] *Stem Cells: Scientific progress and future research directions,* Department of Health and Human Services (June 2001) at 26 accessed at http://stemcells.nih.gov/info/scireport/2001report; Wobus *Stem Cells* (2008) at 390-391; Theise 'Stem Cell Plasticity: Validation versus valedictory' in Meyer et al (eds) *Fundamentals of Tissue Engineering and Regenerative Medicine* (2009) at 204.

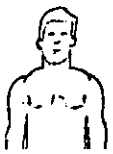
[13] See Cohen *Renewing the stuff of life: Stem Cells, Ethics and Public Policy* (2007) at 16 for a discussion on the debate regarding adult stem cell plasticity as well as Verfaillie 'Adult Stem Cells: Tissue Specific or Not? in Lanza (ed) *Essentials of stem cell biology* (2006) at 24-26 for criticisms on claims of adult stem cell plasticity; Wobus *Stem Cells* (2008) at 390.

adult stem cells is an important issue in the controversy surrounding stem cell research because it concerns the pluripotency of stem cells, which is the ability to differentiate into specialised cells from all three embryonic germ layers. This ability has made embryonic stem cell research a focus in the pursuit of therapeutics for diseases such as Parkinson's and for gaining a greater understanding of early human development particularly the prevention and treatment of birth defects. Unlike embryonic stem cells, adult human stem cells are not pluripotent and are limited in its ability to differentiate into specialised cells. Therefore, plasticity in adult stem cells was heralded as a 'breakthrough' because it was an alternative to the use of embryos as a source for pluripotent stem cells and therefore the solution to the controversy surrounding stem cell research.[14]

At present, the disagreement on the plasticity of adult stem cells continues and the claimed breakthrough has shown little progress or promise mostly due to the inability of reproducing the results of studies that claimed to prove plasticity in adult stem cells.[15] From the above discussion, it can be concluded that the minimum requirements for 'stemness' is both self-renewal and differentiation into a specialised cell. The stem cells are then further characterized by the degree of pluripotency, which is ultimately determined by its source. In terms of the definition, less focus should be placed on the source of these stem cells because embryonic, embryonic germ and adult stem cells all possess the same properties, as was mentioned above, its key difference lays only in the degree to which the differentiation property is present. Therefore, a basic definition of stem cell would be an unspecialised cell that has the ability to self replicate and differentiate.

[14] Vogel 'Breakthrough of the year: Capturing the promise of youth' in (1999) Vol. 286(5448) *Science* 2238-2243; Nielsen 'What happened to the stem cells?' in (2008) 34 *Journal of Medical Ethics* 852 at 854-855.
[15] See Cohen (note 13).

Table 1: Stem cells sources and properties

	Embryonic Stem Cells  **Blastocyst**	**Embryonic Germs Cells**  **Early Foetus**	**Adult Stem Cells**  **Adult Body**
Origin	*IVF Embryos*	*Gonadal ridge of early foetus sourced from aborted foetuses*	*Human Adult Tissues*
Property 1: Self Renewal	✓	✓	✓
Property 2: Unspecialised	✓	✓	✓
Proliferation in Culture	*Proliferates for long period in culture – several hundred population doublings*	*Doesn't have good growth in culture – 80 maximum population doublings*	*Rare to find*
Functionality: Differentiation	*Can differentiate into any specialised cell*	*Limited in its ability to differentiate into specialised cells*	*Differentiates into a specialised cell of the organ from which the stem cell is sourced*

b) Potential uses for stem cell research

Stem cells as has been illustrated in the discussion above have the unique ability to differentiate into a specialised cell for use by the organs in the body. These specialised cells can be used within the body for restorative or regenerative purposes. The potential restorative abilities of stem cells have been illustrated with regard to autoimmune diseases such as rheumatoid arthritis, multiples sclerosis and type 1 diabetes.[16] Autoimmune diseases generally presents as injury to a specific organ as a result of the immune system attacking that specific organ. These diseases are treated by using various anti-inflammatory and immunosuppressive medication but these are limited in its effectiveness and does not result in remission of the diseases. Stem cell therapy has the potential to not only be more effective but may also result in the remission of these diseases through the restoration of damaged tissues such as the pancreas in type 1 diabetes sufferers.[17]

One area in which stem cell therapy may be the most effective is the treatment of lupus, an autoimmune disease, which unlike other autoimmune diseases, attacks more than one organ in the body. At present, lupus is treated by first acquiring and accumulating from the patient, hematopoietic stem cells originating from the bone marrow of the patient.[18] In this treatment, the patient's immune cells are eliminated and are replaced by the accumulated stem cells via blood transfusion. The dangers of this therapy lie in the recovery period because the stem cells once inside the body has to find its way to the bone marrow and once there has to undergo differentiation into the specialised immune cells needed by the body to fend off diseases.[19] This leaves a dangerous open period for the patient where there will be no defense against infections. Furthermore, there is no guarantee that large enough amounts of immune

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[16] *Stem Cells: Scientific progress and future research directions (supra)* at 62; Giacomini, Baylis and Robert 'Banking on it: Public Policy and the Ethics of Stem Cell Research and Development' in (2007) 65(7) *Science* 1490; Augello, Tasso, Negrini et al 'Cell Therapy using Allogeneic Bone Marrow Mesenchymal Stem Cells Prevents Tissue Damage in Collagen-Induced Arthritis' in (2007) 56(4) *Arthritis and Rheumatism* 1175; Liu, Qu, Stewart et al 'Embryonic Stem Cells Differentiate into Oligodendrocytes and Myelinate in Culture and after Spinal Cord Transplantation' in (2000) 97(11) *Proceedings of the National Academy of Science of the USA* 6126.

[17] Assady, Maor, Amit et al 'Insulin Production by Human Embryonic Stem Cells' in (2001) 50(8) *Diabetes* 1691.

[18] *Stem Cells: Scientific progress and future research directions (supra)* at 62.

[19] Davis, King and Schultz *Fundamentals of Neurologic Disease* 2005 at 126.

cells will be generated by the stem cells and any surviving immune cells will kill off the stem cells, which means the process might have to be repeated numerous times to prevent progression or remission of the disease. [20] Embryonic stem cell therapy can play a vital role in solving the dilemmas and dangers of using this kind of therapy by offering stem cells that have more potential for self renewal. In addition, it has also been shown that embryonic stem cells are more receptive to genetic manipulation – a characteristic important in treatment of lupus since these stem cells can be engineered to remain undetected by the surviving immune cells of the patient.[21] An increase in the chances of self renewal and stem cells availability for differentiation has made embryonic stem cell therapy a sought alternative by doctors and scientists in the treatment of lupus and other autoimmune diseases. Another area where the use of embryonic stem cells for therapeutic purposes has also been sought is brain diseases such as Parkinson's and ALS.

Both Parkinson's disease and Amyotrophic lateral sclerosis (ALS) are degenerative diseases affecting neurons in the brain and spinal cord. Parkinson's disease is characterised by the gradual loss of mainly dopaminergic neurons and once this loss amounts to 70% of the total amount of neurons, the onset of symptoms of Parkinson's disease presents in patients.[22] At present, treatment of Parkinson's centers around relieving the symptoms such as bradykinesia, cogwheel rigidity and orthostatic hypotension as there is no therapy that can stop the progression of the disease.[23] Levodopa is the most commonly used drug as it can cross the blood brain barrier to be converted into the dopamine neurons needed by the brain, however, this drug has many side effects such as hallucinations and dyskinesias. [24] The advanced stages of the disease may also be treated by various surgical procedures such as thalamotomy or deep brain stimulation or transplantation surgery but each carries their own risk with minimal results.[25] ALS is a disease that causes the loss of the upper and lower motor neurons, with each loss causing varying symptoms such as

[20] *Ibid.*
[21] *Stem Cells: Scientific progress and future research directions (supra)* at 63.
[22] See note 19 at 128.
[23] *Ibid.*
[24] *Ibid.*
[25] *Ibid.*

limb spasticity or atrophy of the tongue and masseter muscles.[26] As with Parkinson's disease, there is no cure and the only effective drug solution for the treatment of the disease is the administering of riluzole that increases the lifespan of ALS patients by a few months. Other measures are also implemented to ensure that the patient lives out the remainder of his or her life comfortably.[27]

Stem cell research is believed to offer hope for the treatment of diseases because embryonic stem cells has potential to restore the lost neurons, something once thought impossible, thereby reversing the effects of these devastating diseases.[28] Not only does stem cell research allow for stem cell therapy but it also allows scientists to uncover various methods for stimulating the body's own stem cells to produce the necessary neural stem cells such as dopamine neurons in sufferers of Parkinson's disease.[29] It has also been suggested that stem cell therapy can be used for treating stroke patients, however, given the complexity of this disorder in terms of the various kinds of cell loss and the associated atrophy of the brain, the effectiveness of stem cell therapy may be limited.[30]

Bioethical roadblocks stunt much of the promise of stem cell research – not only do stem cell studies involve complex time consuming processes, of which some are not fully understood, but bioethical concerns has halted its progress in many ways. Therefore, much of stem cell research in recent years has been concerned with making stem cell therapy bioethically less problematic by looking to alternatives such as induced pluripotent stem cells and therapeutic cloning. The latter alternative has always been met with criticism and has been rejected because it involved procedures identical to those used in reproductive cloning.[31] Currently, stem cell therapy is at a slow moving point since there are still many unanswered questions relating to basic

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[26] See note 19 at 71-72.
[27] See note 19 at 73.
[28] This potential has been demonstrated in various animal studies: Kim, Auerbach et al, 'Dopamine neurons derived from embryonic stem cells function in an animal model of Parkinson's disease' in (2002) 418 *Nature* 50 and Takagi Y, Takahashi J et al. 'Dopaminergic neurons generated from monkey embryonic stem cells function in a Parkinson primate model' in (2005) 115 Journal of Clinical Investigation 102.
[29] Lindvall and Kokaia 'Stem cells for the treatment of neurological diseases' in (2006) 414 *Nature* 1094.
[30] Lindvall, Kokaia and Martinez-Serrano 'Stem cell therapy for neurodegenerative disorders – how to make it work' in (July 2004) *Nature Medicine* Review S46 at S47.
[31] See note 14 Nielsen 2008 at 855.

stem cell biology such as the plasticity of adult stem cells . In order to answer this and other questions, studies have to be undertaken, for which an adequate supply of embryonic stem cells are needed. However, given the opposition to the source of these stem cells, progress is hindered. This opposition not only prevents developments in embryonic stem cell research but also hinders resolving the dispute concerning plasticity of adult stem cells since the true measure of these induced pluripotent stem cells has to lie in a comparison with human embryonic stem cell research.[32]

1.3 THE EMBRYONIC STEM CELL DEBATE

There are two sides to the debate revolving around embryonic stem cell research: science and morality. On the science side, the main argument is based on the view that stem cell research has medical benefits and should therefore be pursued for the advancement of science and human health. Whereas on the morality side, the main arguments are that the human embryo should be protected because there is a moral obligation to do so and further, that this kind of research should be banned to protect our humanity. However, on closer inspection, the divide between the two sides are not as clear cut and there is no consensus on the ethical boundaries of the debate as there exists internal debates on each side particularly within the morality side.

a) Protecting the embryo

According to this view, when conception takes place, the resulting fertilized egg acquires the same moral status as a human therefore destruction of a blastocyst during the derivation of stem cells is considered tantamount to murder. Strong advocates of this view are the Roman Catholics who base their position on the *Donum Vitae*, a document released by the Vatican in 1987, which outlines their position on the dignity of human embryos and the morality of technological advancements in human reproduction.[33] According to this document, at the moment of conception two things occur sequentially: firstly, an individual possessing a unique genome is formed

[32] Holden and Vogel 'A Seismic Shift in Stem Cell Research' in (2008) 319 *Science* 560 at 561.
[33] Congregation for the Doctrine of the Faith, 'Instruction on Respect for Human Life in its Origin and on the Dignity of Procreation: Replies to Certain Questions of the Day (*Donum Vitae*) I:1' in (1987) *Bioethics* 596.

and secondly once this unique individual is created, it is implanted with a soul by the divine power. This ensoulment, which is a result of the individual's genomic uniqueness, establishes its moral status and provides immediate protection for the blastocyst.[34] This orthodox view of the time of establishment of the moral status of the embryo is however not shared by all Roman Catholic ethicists.

In January 1985, the Warnock Commission released its report on human fertilisation and embryology and recommended that research on embryos can only take place until the fourteenth day.[35] This recommendation is mainly based on *in vivo* embryo development in that on the fifteenth day, the primitive streak is formed. The formation of the primitive streak is vital in the development of the embryo since it establishes the bodily structure of the foetus in that the various parts such as the head and tail can be identified and it is also the beginning of gastrulation.[36] The end of the development of the primitive streak is marked by the formation of Henson's node, which leads to neurulation, a process in which the neural tube, the primordial structure of the brain and spinal cord, is formed.[37] Hence, the formation of the primitive streak is seen as the early beginning of the nervous system and any research on embryos can only be done up to the fourteenth day after fertilisation. Further to this, the primitive streak also marks the definitive individualization of the embryo, as twin formation can only occur within the first two weeks after fertilisation.[38] This recommendation was carried through by the United Kingdom government and became part of the Human and Fertilisation and Embryo Act.[39]

This 14 day rule as it is known, has been accepted by Roman Catholic ethicists such as Thomas Shannon who argues that conception is actually a two week process and is not marked by the fertilisation of the ovum, as argued by Roman Catholic theologians.[40] Shannon argues that biologically, conception takes place over a 2 week

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[34] *Ibid.*
[35] Priest 'The Report of the Warnock Committee on Human Fertilisation and Embryology' in (1985) 48 *Modern Law Review* 73 at 77.
[36] Gastrulation is the process in which the ectoderm, mesoderm and endoderm layers are formed: Moore, Persaud and Shiote *Colour Atlas of Clinical Embryology* (2000) at 13.
[37] Noback *The Human Nervous System: Structure and Function (2005)* at 104-105.
[38] Moore, Persaud and Shiote *Colour Atlas of Clinical Embryology* (2000) at 10-12.
[39] *Human Fertilisation and Embryology Act* (UK) 1990.
[40] Shannon 'Reflections on the Moral Status of the Pre-Embryo' in (1990) 51 *Theological Studies* 603 at 610-611; 'Human Embryonic Stem Cell Therapy' in (2001) 62 *Theological Studies* 811 at 816-817.

period, which encompasses various processes that result in an implanted embryo possessing a unique genome. At fertilisation, biologically, this uniqueness does not exist and therefore the argument that the uniqueness of the embryo leads to ensoulment and ultimately the activation of the moral imperative to protect the embryo, fails.[41] As evident from this discussion, there is no consensus within the argument of embryo protection albeit being the most vocal voice in the debate. Both Shannon's argument and that of the Roman Catholic Church posits that the embryo should be protected due to its moral status, but differs in the timing of the activation of moral protection. This question of the timing of moral status activation is key in the debate since the answer determines whether stem cell research is allowed. Whereas Shannon argues that the 14 day rule is demonstrated by biology, the Roman Catholic Church argues that moral status of the embryo is confirmed by biology.

b) Protecting humanity

The second argument on the morality side is based on the premise that humanity should be protected from ourselves, in other words, we should be prevented from making certain technological advancements since these can lead to later immoral technologies that we will regret and over which we will have no control. Advocates of the human nature protection argument believes stem cell research is a form of playing God which is inherently wrong since we are meant to appreciate our human nature, regardless of our limitations. [42] Leon Kass, a fierce advocate of this argument believes that stem cell research particularly the destruction of embryos and all other research involving the manipulation of human genes, ignites a feeling of repugnance within us and this feeling should direct us to rejecting and preventing technological advancements such as stem cell therapy.[43] This human nature protection argument can be seen as a precautionary approach that seeks to avoid a future filled with immoral technologies by preventing any advancement, which could contribute in any way to that feared future or which could potentially diminish our moral sensitivity.

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[41] *Ibid.*

[42] This argument is often referred to as the slippery slope argument – once you allow one action, there will be a snowballing of other actions, which eventually leads to not having any control over those actions at all. Peters 'The Stem Cell Debate in America and Around the Globe' in (1997) Collegium for Advanced Studies: Contemporary American Religion and its Global Impact – Paper.

[43] Kass, "Preventing a Brave New World: Why We Should Ban Human Cloning Now," (2000) 224 *The New Republic* 30-39.

From the above discussion, the anti stem cell research side is composed of two distinct arguments each arguing from a moral viewpoint. In the public arena however, the nature protection argument is not as strongly voiced as the embryo protection argument, which is largely advocated by religious groups and therefore it is often erroneously believed that the debate centers around religion versus science. This is not the case since various religious groups such as Jews, Muslims and Christian sects such as the Protestants support the pro anti stem cell argument. These groups base their support on the reasoning that stem cell research can assist in alleviating the pain and suffering caused by illnesses and injuries and argues that as humans we have the duty to alleviate others pain and suffering, the failure of which means we should be held accountable for the suffering.[44] In addition, both the Jewish and Muslim faiths believe that ensoulment only occurs after 40 days therefore the embryo has no moral status as a human being.[45] Further, it is argued that the medical benefits that can be realized by stem cell research outweigh the bioethical principle of nonmaleficience. These religious groups along with numerous scientists and researchers constitute the science side of the debate and their main philosophy centers around how we can contribute to a positive future by visualizing that future and working backward to the present and asking how medical science can realize that future.[46]

c) The argument for medical benefits

The stem cell debate has become much like the chaos on the trading floor of a stock exchange with everyone talking at the same time, resulting in no clear communication, no explanation of the viewpoint of either side. In addition, much of the debate has taken place in the public arena and in government between politicians and policy makers. This has resulted in no clear consensus on ethical issues and no clear understanding by the public of the basic science involved in stem cell research. It is my opinion that there should be a joint meeting with both sides present to explain their viewpoint and arguments. The focus of this meeting should not be on the scientific developments in regenerative medicine but rather, on the science side it

[44] Rabbi Elliott Dorff *Stem Cell Research* http://www.rabbinicalassembly.org/teshuvot/docs/19912000/dorff_stemcell.pdf
[45] *Ibid.* In Islam, ensoulment occurs at 120 days.
[46] See note 42: Peters 1997 at 14.

should be concerned with explaining the basic science of stem cell research. On the morality side, there should be an explanation of their viewpoint and arguments about the moral status of the embryo and their fears of humanity being led down a destructive path. The joint meeting has to be a world event, inviting scholars, religious leaders and scientists from around the world to participate because stem cell research is a topic that affects everyone either through their support or through opposition against stem cell research.[47] The aim of the joint meeting would be to try to reach an agreement in the future, with regards to the basic ethical principles, professional guidelines for scientists and a framework for a regulatory mechanism that allows for the free flow of benefits arising from this kind of research.

Within the agreement and guidelines arising out of this meeting, the four basic bioethical principles of autonomy, beneficence, non-maleficence and justice have to be upheld. As was mentioned above, the agreement and guidelines has to promote equal distribution of benefits and in doing so will satisfy the bioethical principle of justice. Autonomy in terms of the couple or woman choosing to donate spare IVF embryos should do so voluntarily and after being fully informed of the scientific fate of the donated embryos. Ultimately, there will have to be a balancing of the two opposing bioethical principles of beneficence (doing good by helping yourself and others) and non-maleficence (causing no harm unto others or yourself) and assessing which has more weight than the other does. The discussion on the potential uses of stem cell research is an illustration of the medical benefits of stem cell research (beneficence), however it can be argued that it does not outweigh the harm caused to the embryo (non-maleficence) but rather takes preference over it. Both harm to the embryo and medical benefits are equal in its strengths however, given the benefits derived from stem cell research, it takes preference over the harm caused to the embryo.

In my opinion, one of the key principles arising out the agreement has to be sanction of the 14 day rule as proposed by the Warnock Commission and later legislated by the UK government. It is the best solution scientifically and morally because it allows the embryo to have moral status while still allowing for medical

[47] Even the most dogmatic views can be changed as evidenced by the approval of Proposition 71 in California USA where pragmatism won over the conservative public view.

benefits. Therefore, from the moment of fertilization until the fourteenth day of development, embryos should be made available for research use. The fourteenth day is chosen because of the appearance of the primitive streak that marks the beginning of the primordial origins of the nervous system. It could be argued that the tenth day – the day of implantation in the uterus is a vital event in the development of the foetus, thereby establishing it as the moment at which the embryo has the most potential to be a human being and therefore should be protected. However, I think this argued should be rejected, particularly in light of potential technological advancements. It is not impossible to imagine that in the future scientists could develop an artificial life support system that replaces the womb, which will obliterate the significance of implantation in the womb as a vital step in fetal development. The appearance and development of the primitive streak however, is a key biological event, which not only establishes the nervous system but also marks the beginning of gastrulation and the organization of the various body parts in relation to each other. Therefore, the appearance of the primitive streak is a significant event and any research on embryos should be ceased before its formation.

Further to this, it is my suggestion that only IVF embryos are utilized for stem cell research and that therapeutic cloning should not be considered at this stage.[48] In Britain over the past 14 years, an estimated 1.2 million IVF embryos were destroyed either soon after creation or frozen to be destroyed after ten years.[49] This medical waste as it is labelled could have been derived into stem cell lines, which would have contributed significantly to stem cell research. Limiting the embryo source to IVF and only allowing research on embryos up until the fourteenth day allows for the recognition of the embryo as something to which special status should be accorded and for its respectful treatment. Respecting life and the right not to be killed are two different concepts as illustrated in legal frameworks where the death penalty is a form of punishment. Here, the prisoner on death row has basic rights and the government and its department are obligated to treat that prisoner with respect and dignity, which is entirely separate from the fact that his been sentenced to the death penalty.

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[48] Resolution 59/280 which included the United Nations Declaration on Human Cloning was adopted in 2005, where the majority voted in favour of the resolution, declaring reproductive cloning to be ethically repugnant.

[49] Woolf 'IVF Clinics destroy 1m 'waste' embryos
http://www.timesonline.co.uk/tol/life_and_style/health/article3108160.ece

d) Global attitudes and legal frameworks

The legal and regulatory frameworks through which stem cell research is governed can be divided into those that have a liberal, flexible or restrictive policy. As map A shows, the moral position of many countries do not always correspond with the legal position as indicated in map B, with the most noted examples being Japan and Israel. According to the BBVA survey, the majority in these countries believes that the embryo should be accorded moral status equivalent to a human being and more importantly, that stem cell research is immoral. [50] This is in contrast to their national laws, which permit stem cell research and a wide range of the associated technologies.[51] Comparing the data on both maps, one would expect to see red (immoral) and orange (restrictive) match ups as well as purple (moral) and green (liberal or flexible) match ups. Interestingly, the survey revealed that when people were informed of the specific benefits of stem cell research – their attitude changed from negative to positive. This shows that there is a lack of understanding about the basics of stem cell research and what it involves. It has also been shown that religious beliefs tie in closely with the attitude of society towards stem cell research but this is not necessarily always the case. In Germany and Austria, the rejection of stem cell research features strongly both within society and legal frameworks due to the atrocities perpetrated against these societies during the Holocaust, where cruel experiments were performed on Jewish people.[52] However, this prohibition only applies to German citizens – stem cell lines can still be imported from outside Germany's borders.[53]

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[50] Second BBVA Foundation International Study on Biotechnology: Attitudes to Stem Cell Research and Hybrid Embryos. Bilbao: Fundacio´n BBVA, May 2008. Only 15 countries were chosen as they were the focus of the BBVA survey on attitudes toward stem cell research hybrid embryos: Denmark, Sweden, Spain, UK, Italy, France, Ireland, Czech Republic, Netherlands, Germany, Poland, Austria, USA, Japan and Israel.

[51] Israel: Report of the Bioethics Advisory Committee of the Israel Academy of Sciences and Humanities: The Use of Embryonic Stem Cells for Therapeutic Research Report (August 2001) accessed at http://bioethics.academy.ac.il/english/report1/Report1-e.html; Japan: Law Concerning Regulation Relating to Human Cloning Techniques and Other Similar Techniques 2001 and the Guidelines for Derivation and Utilization of Human Embryonic Stem Cells 2001.

[52] Ronellenfitsch 'The Impact of the Holocaust on the Bioethical Controversy in Germany and the European Community' accessed at http://www.jura.uni-tuebingen.de/professoren_und_dozenten/ronellenfitsch/kooperationen/tel-aviv.pdf.

[53] See note 53 at 13.

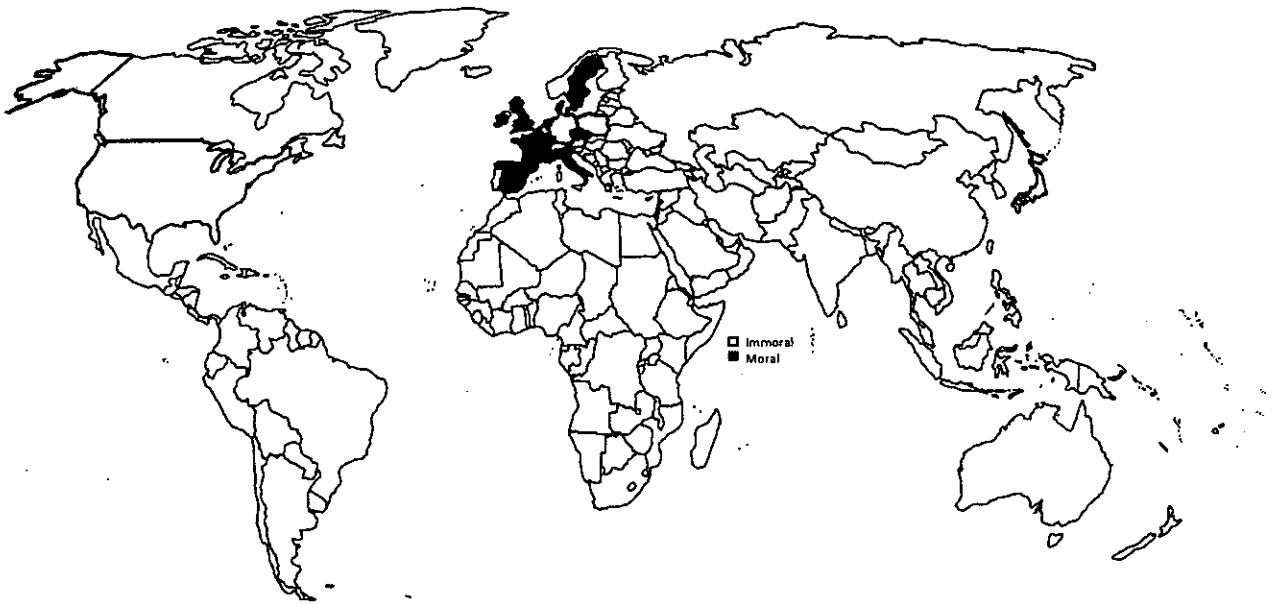

Figure 1: Map (A) showing citizen's attitude towards stem cell research – whether moral or immoral.

Figure 2: Map (B) indicating the legal approach of the selected countries towards stem cell research: liberal, flexible or restrictive.

Attitudes towards stem cell research depend on not only religious beliefs but also on the sociological, historical and cultural construct of society. As one can see from the map, there is a fair amount of disparity between these attitudes and the implemented legal framework in that country. This disparity has to be corrected via a meeting of the bioethics and the law because both are closely tied together. For the potential of stem cell research to be realized there has to be a system in place that adequately addresses ethical concerns, a system that works with both sides of the stem cell debate with the aim of benefiting mankind by both advancing technologically while simultaneously considering the consequences of our scientific progress. There is no denying that stem cell research is an ethical and legal minefield but there has to be impetus from both the scientific and moral side to navigate through this minefield for the benefit of humanity. One such initiative is the joint meeting proposed in this paper. Once this public dialogue is in progress and continues to take place, we will be a step closer to the implementation of a regulatory framework for stem cell research.

CHAPTER TWO: STEM CELLS AND THE LAW

2.1 STEM CELLS AND PATENTS

a) Case Study: The WARF Patents

Before the biotechnology explosion patent applications was a relatively straightforward process. An inventor could apply for a utility, design or plant patent and if successful could prevent others from using, selling or making that patented invention for 20 years. Now with various advances in science and technology, patent applications have become complex and the outcomes often controversial.

In 1995, Dr James Thomson made a breakthrough advancement in science by successfully creating stem cell lines from primate embryonic stem cells. [54] Soon thereafter, the Wisconsin Alumni Research Foundation (WARF), the owner of the lab at which he was employed, applied for a patent over his invention at the United States Patent and Trademark Office (USPTO). The application was later abandoned in 1997 but not before a continuation in part was filed in 1996 after the examining office rejected the original application.[55] Normally a continuation in part is meant to supplement an earlier claim by the addition of a new claim, to accommodate any new improvements to the invention since the original application was filed.[56] However, the WARF continuation was identical to the original application and was handled by a different examiner, resulting in two identical WARF patent applications handled by different examiners at the same USPTO office.[57] While the first examiner continually rejected the original application, the second examiner approved the continuation in part. Despite the efforts of John Doll, the director of the examining office, to stop the issuance of the patent, the examiner granted WARF patent 5,483,780: Primate Embryonic Stem Cells.[58] A few years later, patents 6,200,806[59] and 7,029,913[60] was approved, extending WARF's patent rights to human embryonic stem cells, so that by

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[54] Korobkin and Munzer *Stem Cell Century: Law and Policy for a Breakthrough Technology* (2007) 92.
[55] Loring and Campbell 'Intellectual Property and Human Embryonic Stem Cell Research' in (2006) 311 *Science* 1716 at 1716.
[56] Stim *Patent, Copyright and Trademark: A Desk Reference to Intellectual Property Law* (2009) 44.
[57] See note 55.
[58] Patent 5,483,780 issued on 20 January 1995 (hereinafter referred to as patent 780).
[59] Patent 6,200, 806 issued on 26 June 1998 (hereinafter referred to as patent 806).
[60] Patent 7,029,913 issued on 18 October 2001 (hereinafter referred to as patent 913).

the end of 2001 WARF had exclusive rights to the selling, making, using and importing of all primate embryonic stem cells both human and nonhuman.[61] Further to this, patent 913 extended WARF's patent rights to include a process patent for the proliferation of human embryonic stem cells in *in vitro* culture without the leukaemia inhibitory growth factor.[62]

The most far reaching of the WARF patents was claim one of patent 780, which allows for rights over the composition of matter for embryonic stem cells. This claim not only covers the embryonic stem cells itself but by implication also meant that WARF 'controlled' the derivation methods because the stem cells itself as a composition of matter belonged to WARF regardless of how it was derived. The granting of this patent had undoubtedly given WARF enormous control in stem cell research since they now owned both the stem cells and its derivation methods. In 1998, WARF established a non-profit subsidiary company called WiCell to engage in stem cell research as well as distribute stem cell lines therefore any individual or company wishing to work with stem cells have to obtain a license from this subsidiary. All commercial companies have to apply for a license which initially will cost $125 000 and a further $40 000 a year to renew the license while NIH funded organizations are only charged $500. Academic researchers have to pay $5000 but usage is limited, as the stem cells cannot be shared with any other academic.[63]

WARF shared certain intellectual property privileges related to stem cells with the United States National Institute of Health (NIH) and the Geron Corporation because of the funding provided to their labs by these entities. Specifically, due to the use of federal grants by Dr Thomson, the NIH has certain privileges with regards to patent 780.[64] To affirm these privileges they concluded a memorandum of understanding with WARF and could thereby ensure that the Federal Drug Agency (FDA) and Centre for Disease Control (CDC) researchers could make use of human

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[61] See http://www.warf.org/uploads/media/FactSheet_hESC_Patent_Descriptions.pdf for a summary of each patent.

[62] This growth factor is a protein expressed in the developing embryo to promote growth and cell differentiation.

[63] See note 55 at 1717; Bahadur and Morrison 'Patenting Human Pluripotent Cells: Balancing Commercial, Academic and Ethical Interests' (2010) 25(1) *Human Reproduction* 14 at 17; Wadman 'Licensing Fees Slow Down Advance of Stem Cells' in (2005) 435 *Nature* 272.

[64] Herder 'Proliferating Patent Problems with Human Embryonic Stem Cell Research' in (2006) *3 Bioethical Inquiry* 69 at 74.

embryonic stem cells in terms of a license.[65] Similarly, the Geron Corporation, who funded the human embryonic stem cell derivation methods received an exclusive license to derive cardiomyocytes, neural cells and pancreatic islet cells for stem cell based therapies, as well as non-exclusive rights to derive hematopoietic cells, osteoblasts and chondrocytes.[66]

WARF looked to extend its powers beyond US borders and filed an application at the European Patent Office (EPO) in 1996.[67] The EPO examining division rejected the application on the grounds that the invention violated Rule 28(c) and Article 53(a) of the European Patent Convention (EPC),[68] which states that no biotechnological invention will be granted if it concerns the use of a human embryo for industrial or commercial purposes or if its contrary to 'ordre public' or morality.[69] WARF appealed to the EPO's Enlarged Board of Appeal (EBoA), directing 4 questions to the panel, one of which was whether the prohibition in Rule 28(c) applied retrospectively to applications filed before the incorporation of Article 6(2)(c) of the Biotechnology Directive into the (EPC).[70] The EBA responded by stating that in the absence of transitional provisions in the EPC or any other evidence that inventions involving embryos were patentable prior to the incorporation of the Biotechnology Directive into the EPC, Rule 28 (c) operated retrospectively. [71] One other question that was posed was whether the availability of alternative technologies that do not result in the destruction of the embryo would make a difference in the decision to reject the patent application. The board responded by stating that any technological developments available after the filing date of the application could not be considered as it did not form part of the original application.[72] Their response leaves open the question of whether through using alternative technologies where no destruction of the embryo is caused, patents involving human embryonic stem cells will be

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[65] See note 55 at 1717.
[66] Geron Technology and Science – Stem Cell Lines accessed at http://www.geron.com/technology/stemcell/stemcelllines.aspx on 23 November 2009.
[67] EPO Patent Application No . 96903521.
[68] European Patent Office (EPO), *Convention on the Grant of European Patents (European Patent Convention),* 13th edition (Munich: EPO, 2007).
[69] Case G02/06, Examining Division Oral Proceedings 17 June 2004.
[70] Plaggenborg and Zimmer 'The EPO's Decision G 2/06 on the Patentability of Human Embryonic Stem Cells: Sounding the Bell for the Next Round?' in (2009) 28 *Biotechnology Law Report* 332 at 333-334.
[71] Decision of the Enlarged Board of Appeal of 25 November 2008, G0002_06, page 19.
[72] See note 71 at page 28.

allowed.[73] The United Kingdom Intellectual Property Office in response to the EBoA decision, released a practice note changing their previous policy to reflect a rejection of inventions using human embryonic pluripotent stem cells, which involves the destruction of the human embryo if there exists an alternative technology to derive stem cells. In addition, no patent application will be successful if it involves processes of obtaining stem cells from human embryos.[74] The EboA decision marked the end of WARF's pursuit of patent rights via the EPO but not the end of the challenges to the patent rights.

The Foundation for Taxpayer and Consumer Rights (FTCR) and the Public Patent Foundation (PUBPAT) challenged all three United States WARF patents pertaining to stem cell research by requesting a re-examination and revocation of the patents.[75] They argued that the patents hindered scientific progress and hampered the economic growth of the United States since taxpayer money have to be spent on license fees rather than the research itself. Their application for re-examination was successful and in 2007, the USPTO revoked WARF's patent rights on the basis that the claimed inventions were obvious, based on evidence of prior work by Robertson, Piedrahita and Williams.[76] Williams had taught a method of isolating embryonic stem cells from primates and other animals and his derived stem cells were able to retain their pluripotency and ability to differentiate.[77] While Robertson, taught a process of isolating mammalian embryonic stem cells that were pluripotent, that could be maintained over a long period and gave a detailed method for derivation of the stem cells through for example, the preparation of feeder layers, collection of blastocysts, expanding of and culturing stem cells.[78] Piedrahita taught a similar method to

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[73] Fitt 'New Guidance on the Patentability of Embryonic Stem Cell Patents in Europe' in (2009) 27(4) *Nature Biotechnology* 338 at 339.
[74] UKIPO Practice Note: Inventions involving Human Embryonic Stem Cells (3 February 2009).
[75] FTCR and PUBPAT request for *Inter Partes* Examination, see all documents concerning the challenge to the WARF patents at http://www.pubpat.org/warfstemcell.htm
[76] Robertson, et al "Isolation, Properties and Karyotype Analysis of Pluripotential (EK) Cell Lines From Normal and Parthenogenetic Embryos," (1983) 10 *Teratocarcinoma Stem Cells*, Cold Spring Harbor Laboratory 647663; Robertson and Elizabeth J "Embryo Derived Stem Cell Lines," *Teratocarcinomas and Embryonic Stem Cells; A Practical Approach*, (1987) Chapter 4; Piedrahita, et al., "On The Isolation Embryonic Stem Cells: Comparative Behavior Of Murine, Porcine And Ovine Embryos," (1990) 34(5) *Theriogenology* 879901.
[77] See page 4-8 for a detailed account of Williams patent (5,166,065) claims and a comparison with the claim of patent 780 in Request for *Inter Partes* Examination at http://www.pubpat.org/assets/files/warfstemcell/780Request.pdf.
[78] Robertson first published his findings in his 1983 paper and later expanded on it in the 1987 paper: see note 63.

Robertson's but used murine, porcine and ovine embryonic stem cells.[79] Based on these works and the support testimony by embryologist Dr Jeanne Loring, FCTR and PUBPAT had successfully argued that the inventions were obvious to those skilled in the art. WARF immediately appealed the decision and in 2008, the USPTO withdrew their rejections of the patent claims and the legal status of the patents affirmed.[80] According to the reasoning of the examiners, the inventions were not obvious because the prior art did not contain information on how to specifically derive human embryonic stem cells nor did it contain any information which suggested that they knew of a derivation method without having to experiment.[81] Patent 780 and 806 is now closed to any appeals however, patent 913 could still possibly be challenged by the FCTR and PUBPAT.

2.2 PATENT THICKETS AND PATENT MONOPOLIES

The complex intellectual property web woven by the WARF patents and its associated licenses have resulted in what is known as a patent thicket. Patent thickets are situations where it has become impossible for a company or individual to conduct research without infringing another's patent rights or being faced with overlapping intellectual property rights.[82] This situation is also further complicated when the invention is an upstream patent. Upstream inventions are patents that concern the basic research and early development of a product or range of products.[83] Therefore, in the case of stem cells, an example of an upstream invention would be basic research tools such as the derivation methods (patent 913) and basic biological compositions such as primate embryonic stem cells (patent 780 and 806).[84] It has been suggested that the increase in USA upstream patent applications is largely due to

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[79] See note 76 (Piedrahita 1990).

[80] USPTO Office: Application 95/000,154 (Art Unit 3991) - Inter Partes Re-examination: Action Closing Prosecution at pages 8, 10 and 16; Notice of Intent to Issue Ex Parte Re-examination Certificate, Application 90/008,139 at pages 4 and 6; and Notice of Intent to Issue Ex Parte Re-examination Certificate, Application 90/008,102 at pages 5-12

[81] Application 95/000,154 (Art Unit 3991) - Inter Partes Re-examination: pages 8, 10 and 16; Application 90/008,139 at pages 4 and 6; Application 90/008,102 at pages 5-12.

[82] Shapiro 'Navigating the Patent Thicket: Cross Licenses, Patent Pools and Standard Setting' in (2000) Vol 1 *Innovation Policy and the Economy* 119

[83] Holman 'Clearing a Path through the Patent Thicket' in (2006) 125 *Cell* 629. Downstream inventions are the opposite end of the spectrum and is essentially end products such as those produced by pharmaceutical companies for example.

[84] For a discussion on upstream patents see note 83 and Davis 'Patented Embryonic Stem Cells: The Quintessential "Essential Facility"?' in (2006) 94 *Georgetown Law Journal* 205.

the Bayh-Dole Act, which allowed universities and other non-profit organizations to apply for patents arising out of federally funded research.[85] Most university research is focused on the basic research and development and therefore most upstream inventions are likely to originate from these labs, as was the case with the WARF patents.[86] Some of the consequences of a patent thicket involving upstream inventions are the stifling of innovation due to restricted or prohibited conduct of research and the hampering of the flow of knowledge. Since there is no competition in terms of other available products, the patent holder can therefore exploit consumers by charging high prices and even fixing prices.[87]

Albeit, the potential of stem cell research is enormous, scientists are still far from developing a human embryonic stem cell based therapy in the form of a safe and marketable product that can be made available to the public.[88] The patent thicket has slowed down the progress of creating such a product because the basic research methodology is entangled in a highly restricted web of patents and licenses. Even though, academic organizations are granted a financial reprieve by only having to pay $500[89] for a license to legally use human embryonic stem cells in their research, as was mentioned before, universities are mostly concerned with the basic stem cell biology and the methodology behind deriving stem cell lines. It is the commercial companies such as pharmaceutical and other biotechnology companies that have and will in future inevitably be caught in this web and for startup companies there will undoubtedly be financial constraints. Another element in the WARF stem cell patent thicket is the exclusive license granted to the Geron Corporation, which includes exclusive rights to derive three kinds of cells from stem cell lines.[90] This essentially means that a company who wishes to derive and utilize more than one kind of stem cell will have to apply for a license to both Geron and WARF.

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[85] Rai and Eisenberg 'Bayh-Dole Reform and the Progress of Biomedicine' in (2002) 66 *Law and Contemporary Problems* 289 at 292-293.
[86] See note 83.
[87] See note 64 at 75-76.
[88] Goozner 'Innovation in Biomedicine: Can Stem Cell Research Lead the Way to Affordability?' in (2006) 3(5) *PLoS Medicine* 0611 at 0612.
[89] They are still restricted in terms of the purposes for which the stem cell lines can be used as well as sharing the derived stem cells with other researchers.
[90] WARF originally granted Geron exclusive rights to derive 6 kinds of stem cells – this number was reduced to 3 after public outcry and scrutiny.

The WARF patent situation is unique in that it presents itself as not only a patent thicket but also a patent monopoly because not only do the patents itself overlap with each other but all the key patents and licenses are held by WARF and Geron. It would therefore seem that these entities hold monopoly rights over human embryonic stem cell research since any researcher or scientist who wishes to use human embryonic stem cells for research or therapeutic purposes has to overcome these blocking patents, its associated licenses, the license fees and other royalty payments. An example of the practical effect of this patent thicket and monopoly was reported in an article in 2005 where Dr Jeanne Loring an embryologist who had founded Arcos BioScience, was unable to afford WARF's licensing fees. She was forced to merge with two other companies and convert the company from a commercial entity to an academic research one to be able to afford the costs associated with using stem cells.[91] To date WARF has signed 37 license agreements for various stem cell based technologies with each license agreement having its own set of restrictions and conditions.[92] Various authors have suggested ways of clearing the patent thicket two of which are cross licensing[93] as patent pooling[94] as methods of redistributing the existing patent rights in order to correct the stifling of innovation and promote the free flow of knowledge. These suggestions are not without criticisms and both the advantages and disadvantages of each will be explored.

2.3 CROSS LICENSING AND PATENT POOLS

A cross licensing agreement is a license agreement between two firms to allow for reciprocal use of patents and it normally carries no cost unless the patent portfolio of one firm is greater. In this case, the other company would have to pay the difference in value of the patents or the companies insist on other financial arrangements.[95] Shapiro and others have recommended cross licensing as a solution to patent thickets by using the Intel and IBM Corporations cross-licensing strategy as a

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[91] See note 65: Wadman 2005.
[92] See 'VistaGen and WARF Sign License Agreement for Human Embryonic Stem Cell Technology' accessed at http://www.warf.org/news/news.jsp?news_id=239.
[93] See note 82.
[94] Ebersole, Edmond and Schwartzman 'Stem Cells – Patent Pools to the Rescue' (2005) accessed at http://64.237.99.107/media/pnc/8/media.668.pdf.
[95] Motta *Competition Policy: Theory and Practice* (2004) at 206.

case study.[96] According to these authors, the advantages of these kinds of agreements are the enabling of better product delivery because companies combine production efforts, which in turn leads to reduced prices.[97] In addition, the combined participation of different companies allows for more efficient and specialised use of researchers, which together with the aforementioned advantage promotes and consequently leads to innovation within that field.[98] With respect, I submit that the same kind of intellectual property considerations and strategies that apply in the computer technology field is different from those in the biotechnology field. As was discussed previously, the intellectual property rights held by WARF and licensees such as Geron form part of a patent thicket, which has in essence blocked off much of stem cell research. A cross license would normally be beneficial in the case of patent thickets since it would allow for companies that possess broad upstream patents to open its resources for use by other companies thereby alleviating the dilemma of overlapping intellectual property rights.[99]

Applying these principles and elements to the human embryonic stem cell context yields different results. The principle of 'intellectual property for intellectual property' does not make sense because WARF owns the early development and basic research tools of both human and non-human embryonic stem cells, therefore there will not be any intellectual property for another company to exchange with WARF in terms of research tools and early development inventions. It would be more financially beneficial for WARF to enter into a license agreement with another company because they simply will not need to counter any infringements of intellectual property rights. It would only make practical sense for WARF and Geron to enter into a cross license agreement because of their ownership of upstream inventions but since both companies owns these fundamental patent rights it may be beneficial for them to grant reciprocal use of their patents. Such a cross license agreement would however only serve in the interests of these companies and would continue to contribute to the patent thicket and stifle innovation. It would mean the extension and strengthening of the embryonic stem cells monopoly because both

[96] Eswaran 'Cross-licensing of Competing Patents as a Facilitating Device' in (1994) 27(3) *The Canadian Journal of Economics* 689.
[97] See note 95.
[98] *Ibid.*
[99] American Bar Association *Intellectual Property and Antitrust Handbook* (2007) at 240.

Geron and WARF would be in control over fundamental patent rights, which will make it more difficult for companies to access and use these stem cells. There are also concerns about collusion between two companies to increase prices and the formation of a price cartel through a cross license agreement.[100]

Another option would be the patent pool system, where a group of companies agrees to allow access to their patents in a package form for which royalties are paid and members of the pool choose to license their patents to one another.[101] These patent pools are normally an economic response strategy to patent thickets or voluminous patent litigation since it facilitates wider access to patented inventions particularly where broad patents are involved. In the context of stem cell research, it would have been a suitable option if there were multiple stem cell patent holders because the patent pool system would allow for access to the technologies without having to negotiate with each patent holder.[102] However, in this context, it would be redundant because WARF owns the fundamental patents and associated derivation technologies needed for most stem cell research.[103]

One of the major problems with a patent pool for stem cells is that it would protect the validity of the WARF patents thereby strengthening its position. As it will be suggested later in this paper, the key solution to solving the stem cell research dilemma is unhindered access to basic stem cell science over which WARF currently has enormous control. Another concern is that because companies are exchanging information and technologies, one consequence of patent pooling could be anti-competitiveness, thereby stifling the progress and variation in downstream patents, which in this case would be the stem cell based therapies. In other words, since Geron and WARF patents would dominate the patent pool package due to the nature of their stem cell patent portfolio, companies participating in the patent pool might be forced to limit their research and development strategies to specific stem cell derivations based on WARF and Geron's objectives. [104]

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[100] See note 82 at 130.
[101] Verbeure, Zimmeren et al 'Patent Pools and Diagnostic Testing' in (2006) 24(3) *Trends in Biotechnology* 115.
[102] See note 101 at 119.
[103] *Ibid.*
[104] Clark, Piccolo et al 'Patent Pools: A Solution to the Problem of Access in Biotechnology Patents?' (2000) accessed at http://www.uspto.gov/web/offices/pac/dapp/opla/patentpool.pdf.

As one can see from the above discussion, the intellectual property approach is not always the best solution however, given the current complexity and far reaching consequences of the stem cell patents and the associated licenses, a replacement solution is not practical. Instead, what should be considered is a redistribution of stem cell intellectual property rights to allow for better access to technologies and the free flow of research information, which can lead to amongst other things, rapid progress regarding the creation of stem cell based therapies. Both cross licensing and patent pools has its advantages but at present, given the current stem cell patent landscape, is not the best suited solution for the problems created by the intellectual property approach. There needs to be an overhaul in not only the redistribution of patent rights but also in the way society thinks about stem cell research. The latter was argued in the previous chapter and the former will be proposed in the next chapter.

CHAPTER THREE: A CLEARINGHOUSE FOR STEM CELLS

3.1 THE CLEARINGHOUSE MODEL

As was discussed in the previous chapter, the intellectual property patent system is not the best mechanism for managing and regulating stem cell research and its products. At present the monopoly created by WARF and its associated licensees have stifled innovation and has slowed the progress from laboratory to a marketable product safe for human use. The alternatives of cross licenses and patent pools, albeit having its advantages, is not suited for the human embryonic stem cell context because it is difficult and moreover expensive for companies to negotiate both with WARF and possibly with Geron as well depending on the stem cell line they want to work with. In addition, patent pools although an attractive solution is not practiced widely enough for it to be beneficial. It is the proposal of this paper that the best suited solution for managing the intellectual property rights arising out of human embryonic stem cells is a clearinghouse mechanism combined with a distribution function. Before this proposal is explored, this paper shall look at the characteristics and functioning of a clearinghouse through a case study of PIPRA.

The concept of a clearinghouse first originated in the banking sector where it was used as a mechanism through which different banks would negotiate the payment of cheques and other bills of exchange. In the intellectual property sector, it has developed its own meaning. It is essentially a mechanism through which patent users are matched with patent holders so that information can be exchanged, licenses or similar agreements can be negotiated or it could be a means of collecting royalties. There are five types of clearinghouses, namely, information clearinghouse, technology exchange clearinghouse, open access clearinghouse, standardized license clearinghouse and royalty collection clearinghouse.

An information clearinghouse facilitates for access to information regarding the legal status of patents as well as technical and scientific knowledge – an example

of which is Espacenet, which provides information on various patents and patent applications from the EPO.[105] A technology exchange clearinghouse lists all available patented inventions that are available for licensing options as well as whether other negotiating options are available. A good example of this is Birchbob – a global initiative that aims to connect technology seekers and technology providers.[106] In both these examples of clearinghouses, access to the inventions is not facilitated by the clearinghouse but by the individual patent holder. The open access clearinghouse provides standardized free access to and use of inventions on a royalty free basis. The SNP Consortium is a non-profit organisation whose aim is to identify single nucleotide polymorphisms, identify and compare human genetic sequences and enable the free access to the human genome sequence.[107] A new type of clearinghouse is the standardized licenses model that provides free information on patented inventions as well as access and use to patented inventions based on standardised licenses. The final type is the royalty collection clearinghouse and it possesses the functions of the information, technology and standardized licenses clearinghouses. This clearinghouse also functions as a fee collector for patent holders for the use of their inventions and functions as a mediator for independent dispute resolutions.[108]

3.2 THE PIPRA CASE STUDY

The Public Sector Intellectual Property Resource for Agriculture (PIPRA) was established in 2003 mainly as a 'one stop shop' for agricultural patents and licenses information and a review of patenting and licensing practices, as a means to facilitate use of the basic research tools.[109] Its main aim is to provide unhindered access to technologies in the agricultural sector for the development and equitable distribution of subsistence crops in developing countries and for the maintenance of neglected speciality crops across the world. Some of their main functions are to draft and

[105] Espacenet – European Patent Office accessed at http://ep.espacenet.com/.
[106] Birchbob Technology Search Engine accessed at http://www.birchbob.com/.
[107] SNP Consortium – The International HapMap Project accessed at http://snp.cshl.org/index.html.en.
[108] Zimmeren, Verbeure et al. 'A clearinghouse for diagnostic testing: the solution to ensure access to and use of patented genetic inventions? In (2006) 84 *Bulletin of the World Health Organisation* 352 at 354.
[109] Atkinson et al 'Public Sector Collaboration for Agricultural IP Management' in (2003) 301 *Science* 174.

negotiate various kinds of agreements to ensure collaborative management of rights, teaching educational intellectual property management workshops as well as creating intellectual property handbooks, investigating ways of improving technology transfer and delivery and engaging in intellectual property policy analysis.[110] PIPRA consists of various member institutions who on joining must sign a memorandum of understanding that states that members will, in good faith, support, provide, promote and develop various core activities. It is further emphasised that the collaboration is not compulsory and does not commit any member to manage their patents in this way; instead, the collaboration is about identifying opportunities to work towards increased access to innovations for use across all fields.[111]

PIPRA operates in terms of what is known as 'freedom to operate' (FTO) which is essentially a combination of legal practice, scientific knowledge, business management and strategic planning.[112] The output of this operative tool is an opinion on whether a particular product within a particular context can be created, sold, used, distributed or imported without infringing any intellectual property rights or other related property rights.[113] The aim of this approach is to allow companies or other organisations to make informed decisions about potential downstream products before it reaches an advanced stage of development and more importantly, gives them the freedom to continue or proceed with research with a fairly low risk of infringing another's intellectual property rights.[114] Based on this information, the company or organisation makes the decision as to a legal, scientific (research and development) and business strategy which will best suit their needs.

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[110] Core activities accessed at http://www.pipra.org/about/.
[111] PIPRA Memorandum of Understanding accessed at http://www.pipra.org/documents/PIPRA%20MOU.pdf.
[112] Kowalski 'Freedom to Operate: The Preparations' in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices* (eds. Krattiger, Mahoney, Nelsen et al) 2007 at 1329.
[113] Krattiger 'Freedom to Operate, Public Sector Research and Product-Development Partnerships: Strategies and Risk-Management Options' in *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices* (eds. Krattiger, Mahoney, Nelsen et al) 2007 at 1317.
[114] See note 111 at 1318.

One of the key features of the PIPRA model is the establishment of a patent database, which has been made available to the public. This patent database presently lists over 6500 patents as well as information on the agricultural patent portfolio of 27 member institutions, which include universities and non-profit organisations. Full details of each patent are listed, starting from its application status – whether granted or still in process, to its licensing conditions if there any. [115] Another key feature in the PIPRA model is the practice of developing biotechnological resources. By identifying technologies that carry legal restrictions, they attempt to develop an alternative technology that will be made freely available to the public and a fee charged to companies who wish to use it in commercial ventures.[116] Through this initiative, PIPRA not only distributes technology but also contributes to the developing technologies in the field of agriculture.

3.3 THE STEM CELL CLEARINGHOUSE

It is the proposal of this paper that stem cell based inventions should be managed through a clearinghouse system that is part of a network of international, regional and national government support and co-operation, which in turn will be supported by various institutions, commercial companies and non-profit organisations. Essentially, there should be four levels of management and oversight – at the top level would be a global organisation that will perform an oversight function of the regional organisations, which comprises level two and will perform both an oversight and support function. Level three is the national governments that will be supported by level four organisations, which are the members of the clearinghouse such as universities and commercial companies. The clearinghouse for stem cells would be an amalgamation of all the types of clearinghouses mentioned elsewhere in this paper. It will not only be an informational hub but also a means through which basic research methodology and research tools is shared. It will list all stem cell related patented inventions per region including its legal status and whether its available for licensing, it will also provide compulsory and elective open access licenses and lastly, be a fee collector and mediator for dispute resolution.

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[115] Graff, Bergman et al. 'Intellectual property clearinghouses as an institutional response to the privatization of innovation in agriculture' in (2006) 3(3) *African Technology Development Forum* 11.
[116] *Ibid.*

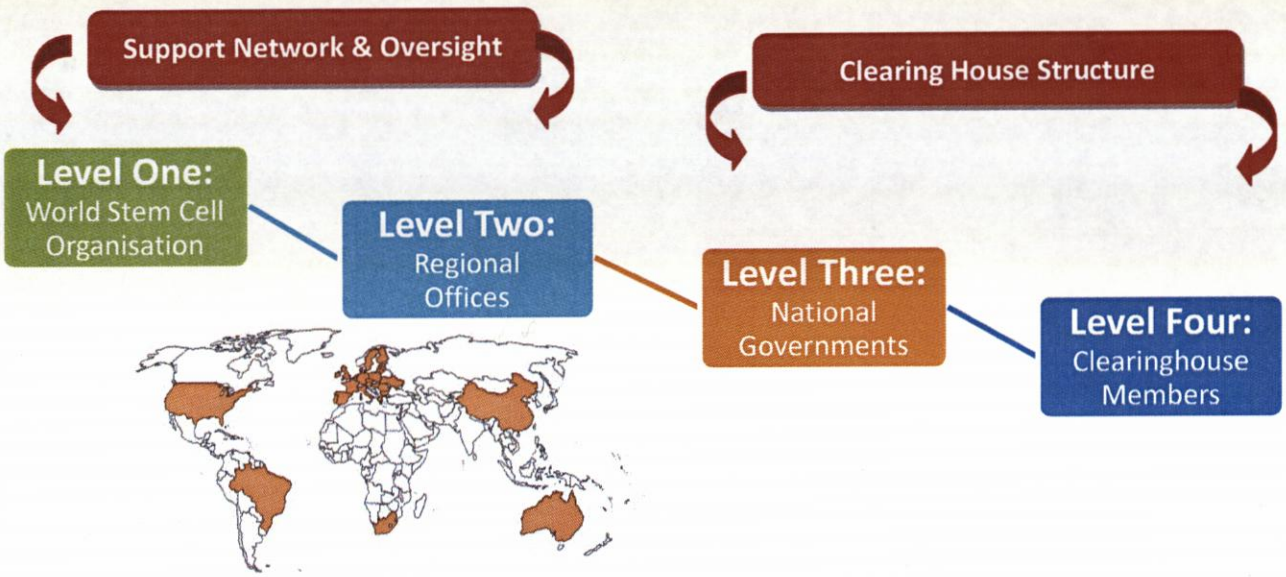

Figure 3: Conceptual Picture of the Stem Cell Clearinghouse Organisational Hierarchy

a) Laying the Foundation

As was mentioned in chapter one there has to be a consensus between the legal system or national policy and the attitude of a society towards stem cell research. In addition, much of the debate surrounding stem cell research is filled with internal debates and there is no clear communication from either side of the stem cell arena as to their arguments and reasoning. It was suggested that a global joint meeting should take place between the scholars, religious leaders, ethicists, scientists, lawyers and politicians. The aim of this meeting would be not only to reach a mutual understanding and agreement as to guidelines and conditions under which stem cell research is carried out but also to organise and participate in a series of talks that will lead to the signing of an international treaty. This international treaty will have as its objectives the following: the pursuit of stem cell research for the benefit of humankind, to be mindful of the special status accorded to the human embryo and for its respectful treatment. In addition, the members have to commit to the advance of stem cell science, to share and contribute to research and development, to encourage and promote unhindered access to basic stem cell research, to commit to promoting equitable and fair access to stem cell based therapy and to co-operate with other members of the treaty in their pursuit of these commitments. One of the more important purposes of the treaty would be the establishment of the World Stem Cell

Organisation (WSCO), whose membership will constitute both the parties to the treaty as well as all members of the clearinghouses established under their auspices. This organisation will amongst other things, perform an oversight function, release annual reports on the status and progress of stem cell research in all member countries as well as initiate and supervise surveys of people's attitudes towards stem cell research. It will provide oversight for the scientific guidelines and adherence thereto as well as ensure that parties fulfil their duties and obligations in terms of the treaty.

The treaty has to be incorporated into the national laws of the parties who have to ensure the creation and setup of a national clearinghouse. In addition, governments have to develop national policies around stem cell research and to engage in public dialogue with local citizens, with countries in their region and on an international scale. The WSCO will be supported by regional offices in each continent once a sufficient amount of national clearinghouses is setup within a particular region. These regional offices will essentially function as an information clearinghouse for governments in their region, consolidating the research and development efforts within the region as well as providing a stronger infrastructure and support for poorer countries to be able to participate in the WSCO efforts. In addition, the regional offices will each have its own stem cell related intellectual property database that will be connected to each country that ratified the treaty and both the regional and local databases will be connected to the international database so that there is a free flow of information taking place at an international, regional and national scale.

For poorer countries who lack basic unrestricted access to telephony and internet services, the regional office will ensure that these countries receive a quarterly printed publication informing them of new and modified entries to the database. Further to this, these poorer countries can provide to the regional office, information on the status and progress of their stem cell research efforts through printed or written documents – the duty of the regional office would be to make this information available to all other parties. The advantages of the international and regional levels are found in the support network it offers to governments, the dispute resolution mechanism, access to open source licenses, the flow of scientific and legal

information and the provision of equitable access to stem cell based therapies. If countries were to follow this model without ratifying the treaty, they will not be able to benefit from this network.

b) The national clearinghouses

As was mentioned previously, each government has to setup a national clearinghouse that has to be supported by national policies regarding stem cell research, intellectual property strategies and resource allocation. The government's key role in this proposal is the creation and maintenance of a patent database listing all stem cell related patents and patent applications. Closely connected to this patent database is the provision of reliable and speedy internet access, however, if this facility cannot be made available simultaneously with the patent database, the regional office practice of printing documents could be an option.[117] Alternatively, a country lacking this basic access could negotiate with a richer country within their region to provide them or assist with the financial and infrastructural support for creating and maintaining such a database. Running parallel to this database will be a comprehensive repository of research information on stem cell research, which will be classified into various categories. Each category will have access rules with the most basic being open and the more specialised knowledge having specific terms and conditions. The government will have the option of either running the clearinghouse as a specialised government agency or can elect an appropriate company to do so. Governments will be best suited both financially and logistically to carry out the required tasks. In addition, in countries such as South Africa, where the patent system follows a non-examining approach and where only selected people can gain access to the patent database, the government would be in the best position to extract the relevant information.[118] To support the clearinghouse financially, it may be negotiated at a later stage, for companies to plough back into the clearinghouse a small percentage of their profits in order to assist government to recover from initial start up costs.

[117] This could be done on recycled paper for environmental reasons.
[118] Burrells *South African Patent and Design Law* 3rd edition 1999 at paragraphs 2.70 and 2.81.

It is important to note that the international and regional roles are meant to be supportive and administrative and that this network will not follow a clearinghouse approach unlike the national governments whose role will be either to run the clearinghouse or elect a company to take on the role. For these national clearinghouses to run efficiently and make an impact there has to be infrastructure, a global network of support therefore I have proposed the international and regional levels. An example of this kind of system can be found in the Patent Cooperation Treaty 1970 where inventors can file one application to gain patent protection for their invention in 142 countries.[119] Once the request is filed, the International Search Authority (ISA) will perform a comprehensive search for prior art and will compile a report for the applicant.[120] In addition, the treaty also makes provision for, upon request by an applicant, for an international preliminary examination. This examination is a legal opinion on the validity of the patent based on novelty and other patentability requirements.[121] For the WSCO, the procedure will be similar: applicants will be able to access a patent database either at the international patent database which will list a general overview of all patents or at the regional level where a more detailed patent database can be found or lastly, by request to a particular clearinghouse, can access the information repository mentioned elsewhere in this paper as well as the comprehensive patent database of the clearinghouse.

c) The Clearinghouse Modus Operandi

The clearinghouse operations and management will be divided into a 3 tiered hierarchy beginning with the clearinghouse board, the management committee and lastly, the members. Membership to the WSCO clearinghouses will be open to all scientists, researchers, commercial companies or non-profit organisations involved in stem cell related work and research. There will be an initial standard membership fee of all new members and these funds will be allocated to contributing to the start up costs of the clearinghouse. In addition, on registration all members have to sign a memorandum of understanding, which states objectives of the WSCO clearing house, the parties to the memorandum of understanding as well as each members' duties and other agreements. A good example of the type of memorandum envisaged for this

[119] Patent Cooperation Treaty done at Washington on June 19, 1970, amended on September 28, 1979, modified on February 3, 1984, and October 3, 2001(as in force from April 1, 2002).
[120] See note 117 at article 15-18.
[121] See note 117 at Chapter II.

initiative is that of PIPRA.[122] Not only does it set out the objectives of the organisation but also requires through signing, members' acknowledgement of duties and their commitment to the good faith pursuit of these objectives. It specifically states that members should promote research and development and develop guidelines that encourage research innovation.[123] In addition, provision is also made for termination of the collaboration between PIPRA and a member. This memorandum of understanding not only sets out the cooperation between the clearinghouse and members but also between members as well.

Each member institution has to appoint a clearinghouse co-ordinator whose role will essentially be as representative of that institution. It will be the duty of the institution to educate and train the co-ordinator on the various national policies and intellectual property strategies employed in the clearinghouse as well as the management of their stem cell patent portfolio if available. This person will also have the responsibility of initiating discussions between the clearinghouse and their institution for any service rendered by the clearinghouse. In addition, the co-ordinator will become part of the management committee of the clearinghouse, which will be separate from the board, who will be responsible for creating, developing and adapting policies and guidelines.

The redistribution of patent rights will take place through a system of licensing options, which can be modified to the needs of either the patent owner or user. All clearinghouse patents on stem cell compositions of matter and any other fundamental stem cell patents (patents 806 and 780) will be subject to compulsory open licensing. Open licensing is essentially a process where companies such as Geron and WARF who have patent monopolies grant other companies full or conditional permission to use, reuse or redistribute their inventions. This kind of licensing is commonly used by software companies such as Microsoft ©, internet websites such as Wikimedia

[122] PIPRA Memorandum of Understanding accessed at www.pipra.org/documents/PIPRA%20MOU.pdf.
[123] *Ibid.*

Commons and organisations such as the Shuttleworth Foundation.[124] The most well known of this type of license is the creative commons license and in my opinion, a similar license would be the best suited for the stem cell context rather than patent pooling. In the case of patent pooling, the evolving stem cell field is not rigid so as to develop a set of conditions under which the pool will operate therefore a standard license would not serve the needs or be in the interests of parties concerned. With a creative commons type licensing solution, the patent owners will be able to place certain limitations on whether the work can be re-used, distributed or commercialised for example with the constant element being the open access to stem cell usage. Moreover, patent holders can request that all licensees will have to credit the inventors for their role in the end product or in the research conducted. [125] Therefore, patent holders will have a portion of their patent portfolio that contains a set of open licensed inventions. There will also be the normal licensing options for any other patent part of the members' patent portfolio. Members will have the option of either concluding an IP for IP agreement or an IP for fees agreement. If at any time information was technology was shared between the negotiating parties, the value of that exchange is to be subtracted from the license fee. In addition, these licensing options will be subject to specific terms and conditions such as the prohibition of exclusive licensing and any terms imposed by patent holders in relation to the open licenses have to be in accordance with the spirit and purport of the organisation and the memorandum of understanding. Any disputes relating to the licenses have to be reported to the dispute resolution arm of the organisation, which will be discussed elsewhere in this paper.

Two other offices have to be established as well within the clearinghouse system, namely, the information and technology exchange offices. The information office will have as its primary function the listing of all the stem cell related patents in each member's portfolio, any pending patent applications of any member as well as which patents are available for the various licensing options. This office will mainly serve as an information mechanism for members of the same clearinghouse but can be

[124] See the Shuttleworth Foundation – Open Licensing accessed at http://www.shuttleworthfoundation.org/about-us/our-philosophy/how-we-work/open-licensing.
[125] See the six creative commons license choices accessed at http://creativecommons.org/licenses/.

approached by other members of the WSCO. In addition, the information office will also be connected to the international and regional databases and any applicant that wishes to access specific patent information can request it directly from the relevant clearinghouse. To counter the costs involved with maintaining and updating these entries on the database, the co-ordinator mentioned earlier in this paper will have access to his or her company's portfolio on the database and will be responsible for updating the company portfolio or alternatively can elect to that delegate that task to another person. The technology exchange office will bear the responsibility of providing a comprehensive list of inventions available for various kinds of licensing both within and outside the WSCO. Members can not only search for patent holders of technology providers but can also request the assistance or announce the availability for an opening to collaborate with another company to create a downstream product. This would be beneficial since both members will be able to reduce and share the workload, which may speed up the development of the product. In addition, this office will raise awareness as to the inventions that are available for licensing and the negotiations needed to effect a license agreement. The negotiations between members will not fall under the functions of this office and their only role in that process will be as monitor of the negotiations.

Two additional and essential services are also to be offered by the clearinghouse, namely, fee collection and dispute resolution. In terms of the fee collection, the clearinghouse will provide a mechanism through which they will collect the license fees from both member and non-member licensees on behalf of patent holders who is then reimbursed by the management committee of the clearinghouse based on an allocation formula agreed to in the memorandum of understanding.[126] Examples of this practice are the Japanese Society Rights of Authors, Composers and Publishers (JASRAC) and the Authors Licensing and Collecting Society (ALSC) who are essentially societies that collect copyrights through collaboration with various artists and authors to share and license their works as well as set prices at a reasonable rate.[127] The dispute resolution mechanism will only be activated if a dispute arises between members of the clearinghouse while all 3rd party disputes have to be handled by members using their own funds. This

[126] See note 106 at 354.
[127] *Ibid.*

mechanism should be in the form of the alternative dispute resolution process arbitration, where the two parties will meet to try to settle their dispute. Lastly, provision should be made for a science division, which will be responsible for developing alternative technologies and contributing to the pursuit and progress of stem cell research.

CHAPTER FOUR: THE OVERHAUL OF THE LEGAL LANDSCAPE OF STEM CELL PATENTS

5.1 INTRODUCTION

This paper has proposed that a replacement solution for the current patent rights surrounding stem cell patents is not desirable and instead a system that facilitates for the redistribution of the associated intellectual property rights should be pursued. At present much of the stem cell is centred on finding ways around the ethical obstacles to the research therefore, as was suggested in the first chapter, there has to be a joint meeting between all sides in the debate surrounding stem cell research. Its purpose would be to engage in discussions that allows for a mutual and open dialogue between parties. This dialogue can aid in a better understanding and appreciation of the viewpoints of either side so that a compromise can be reached as to the methodology through which stem cell research will be performed.

Organizations that are intensely involved with stem cell research such as the NIH, WARF and other European organisations will ideally be at the forefront of this overhaul and it would be to their advantage if they were perceived as more global and responsible corporate citizens. Given the current stagnancy in the progress of stem cell research due to the patent thicket, it would be in their best interests to pursue the clearinghouse proposal because it would promote and encourage innovation. The idea of a clearinghouse system for stem cell patents is not new, as various scholars have suggested a similar solution for the management of stem cell patents.[128] This paper has suggested a system that extends beyond a clearinghouse system to include various support networks each having its own function and purpose. Clearinghouses that are formed by private companies or university organisations are not as well connected in a global manner as what would be necessary for the stem cell context therefore the clearinghouse at the national level would be the best solution. At a national level, the clearinghouse will have greater administrative capabilities and greater access to relevant and required information. However, it should be made clear that the principal

[128] Bergman and Graff 'The global stem cell patent landscape: implications for efficient technology transfer and commercial development' in (2007) 5(4) *Nature* 419; Collaborative IP Management for Stem Cell Research and Development Centre for Intellectual Property Studies-PIPRA 2007; see also the World Stem Cell Foundation site at http://www.worldscf.org/about.asp.

function of the national government is not to provide public funding for stem cell research, instead the funding is meant to provide for the administrative capacity of the clearinghouse. The research occurring at the science division mentioned in the previous chapter will have limited funding from government, with the bulk of the funding coming from the members and the fees paid for various non-essential services provided for by the clearinghouse.

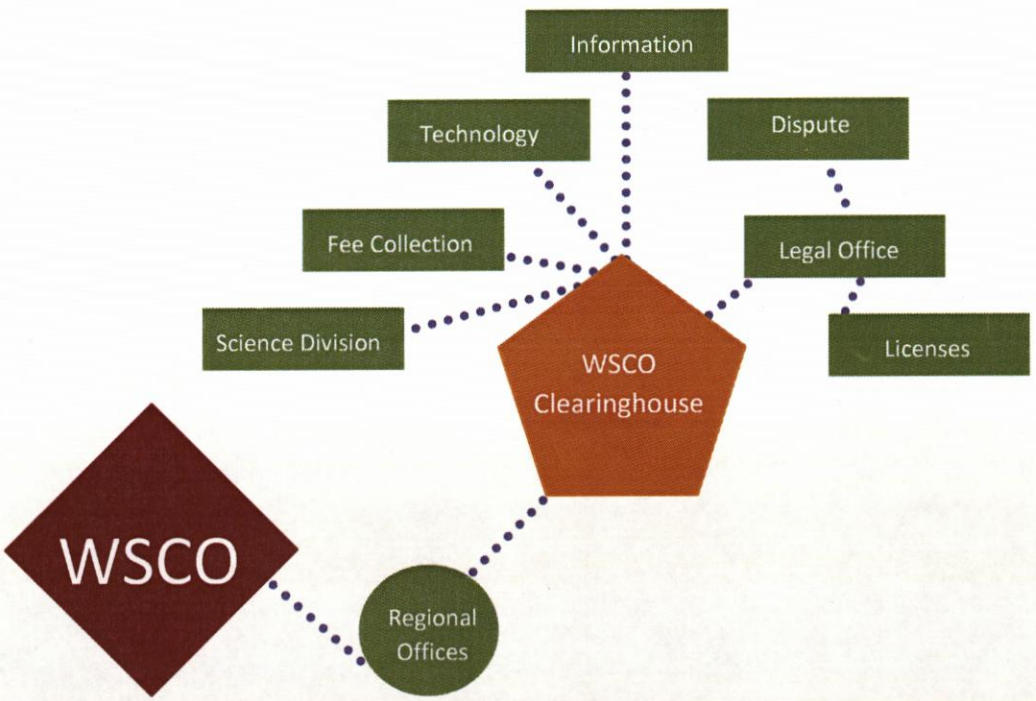

Figure 4: Conceptual picture providing an overview of the various offices within each clearinghouse and its connected to the WSCO and regional offices.

4.2 THE CLEARINGHOUSE PROPOSAL APPLIED IN THE STEM CELL CONTEXT

As one can see from the discussions in this paper, the clearinghouse and its support networks constitutes an all encompassing approach much like the PIPRA model. The key to the success of this proposal is the co-operation and collaboration between the WSCO and its members as well as between members. Initial startup costs for this organization and the clearinghouses will be costly in certain areas, however, with government support the appropriate funds can be allocated to this initiative. Therefore, it is best for the clearinghouse model to be rooted in the national

government structure, rather than on the international or regional scale. The support network of the WSCO will be mainly an informational and oversight mechanism, which makes it easy to set up as well as maintain since the databases will largely be updated by input from the clearinghouses. The main function of the information mechanisms is to provide transparency so that the public is well informed of the progress of stem cell research and through this may be able to show more confidence in and support this field of science.

To elucidate, as was mentioned before, each co-ordinator will have access to the patent portfolio of its company on the database. This national database is connected to the regional and international databases and it requires specific text entry inputs. The international database will be programmed to only show particular text entries per portfolio to give a searcher a general overview of the patents available and pending. In the same manner, the regional database will be programmed to show a more detailed account of these patents. The true costs for the regional and international network would therefore lie in the maintenance of the databases. Therefore, if member A searches the international database for pancreatic stem cell derivations, the database will show that members B have it included as part of their patent portfolio. The information will be fairly general and hence member A can request a more detailed account of the patent from the regional database. This process of information searching and exchange fosters an environment of market discovery, which leads to market exchanges and hence better collaboration of efforts to produce a downstream product.

At this point, the co-ordinator of the member B will be alerted to the request and will enter into discussions with member A. They have the responsibility to inform the relevant legal office of the negotiation processes. The open licenses are not automatically assigned to all members, but instead, if a member wants to negotiate such a license, their co-ordinator will have to initiate the process with members such as WARF and Geron. In this instance the aforementioned terms, conditions and restrictions will apply. The reasoning behind the open licensing is that the open sharing of knowledge and research can do much for speeding up the process of development of stem cell based therapies and together with the information

mechanisms can contribute to discovering ways of adopting procedures that are in line with the ethical and professional guidelines adopted at the joint meeting. In 2006, a South Korean University professor Hwang Woo-Suk was dismissed for research misconduct as he used eggs from his own researchers and paid other women to donate theirs. In addition, he also fabricated data used in a 2004 and 2005 publication on stem cell research that had earned him wide spread recognition and respect.[129] These violations of bioethics laws and research misconduct can be prevented if there are systems in place, such as the proposed information mechanisms to promote transparency and openness and the legal office oversight that records negotiation processes.

Based on the negotiation processes member A could enter either into an open license agreement or a commercial agreement with member B and for the legal procedures, the legal office will become involved. It is their duty to inform member A of the various options of open licensing as well as investigating and analyzing the needs of member A to match up those needs with the patent portfolio of member B where possible. The legal office has to be informed of the aims of the member A in terms of their work, whether it is for research or for commercial purposes so that the legal office can produce a report containing their analysis of the available patents and the licensing options. The analysis will be a collaborative effort between the legal office and the science division with the aim of not only operating within the rules of the clearinghouse but also to prevent the infringement of any 3rd party intellectual property rights. The flexibility of the open licensing agreement is more appealing than rigid standardized licenses because it allows large commercial companies to retain that sense of control over their patent portfolio even though the open license on stem cell related compositions of matter would be compulsory. Member A can therefore have access to the relevant stem cell patents and utilize this in their work. Depending on the terms agreed to in the license agreement, member A will either have to attribute the work to member A, or they are limited to replicating the work of member B or re-use their work only.[130] The set of open licensing options are:[131]

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[129] 'South Korea seeks 4 year prison term for stem cell fraud' accessed at http://www.reuters.com/article/idUSTRE57N1H320090824.

[130] This would most probably be the case where member A was a research institution and was pursuing stem cell research for academic purposes.

1. **Attribution:** This license allows others to use the patented invention without any restrictions with the only condition being that you have to credit and acknowledge the patent holder. This option will be appealing to those companies who wish to increase or strengthen their corporate identity.

2. **Attribution and Share Alike:** This license contains the attribution option and requires the licensee to allow \the resultant work to be used under the same conditions. This will ensure that a licensee must make their work available to be licensed in the same way so that the flow of information is continuous and ongoing.

3. **Attribution No Modification:** This license also contains the attribution option as well, however a member can only replicate the work but not modify it in any way. This could be particularly helpful where a member has an alternative technology, which can be made available to 3rd parties at a cheaper rate.

4. **Attribution Non-Commercial:** This license includes the attribution option and is only available to research and non-profit organizations. Any new work cannot be commercialized but can be licensed to others.

5. **Attribution Non-Commercial Share Alike:** This license is the same as the attribution non-commercial option and any resulting new work can only be made available for non-commercial licensing.

The establishment of the WSCO and its clearinghouses is not going to be an overnight venture, it is essentially an end product of what will start with the joint meeting and lead to many discussions on the issue. However, the joint meeting will alert the stem cell community to this proposed regulatory plan so as to give them to consider and possibly rethink current patent strategies and management so that when the system is up and running, the transition into the clearinghouse will be easier and less problematic. It could also give research institutions and universities impetus to move towards a greater stem cell research and development commitment since

[131] These options are based on the creative commons license options which can be accessed at http://creativecommons.org/about/licenses.

previously they were unwilling to consider stem cell research due to the exorbitant fees and legal entanglements.

4.3 CONCLUDING REMARKS

As was illustrated throughout this paper, there is a lot of uncertainty surrounding stem cell research at various levels. At the beginning of our discussions, it was discovered that there is no real consensus as to the definition of a stem cell or the properties of adult stem cells. This paper therefore proposed that to be classified as a stem cell, the minimum requirements are that it should be an unspecialised cell that has the ability to self replicate and differentiate. The degree to which these properties are found in stem cells are directly dependant on the source of the stem cells – either from the blastocyst which yields the most pluripotent of stem cells, or the early foetus or various organs in the body such as the liver and pancreas. Stem cell research has been pursued because it has the potential to alleviate crippling degenerative diseases such as lupus, Parkinson's disease and ALS and may provide the key to understanding and preventing various birth defects.

Stem cell research initiatives have however been faced with stark opposition by groups such as the Roman Catholics who believe that from the moment of conception an early embryo should be accorded moral status and protection. Further to this anti stem cell research stance is the argument that humanity has to protected from going down the slippery slope where we will end up in the scenario of being unable to control the consequences of our actions. Therefore, to prevent this kind of future, certain actions such as the allowing of the destruction of the embryo through the derivation of stem cells should be prohibited. Standing in opposition to these groups is the view that stem cell research is beneficial to humanity since it would aid in alleviating the plight of those suffering from crippling diseases. Essentially, there has to be a balancing exercise to weigh which viewpoint takes preference over the other. It has been the argument of this paper that the medical benefits argument should be preferred over the embryo protection and humanity protection arguments, in light of the many potential benefits this kind of research offers and its promise in the advancement of human health. Despite support of the pro stem cell research view, this paper has argued that a special status has to be conferred onto the early embryo and there should be a level of respect assigned to it.

Stem cell research is controversial because of the tension between morality and science – the dilemma it has been said, lies in whether we consider the potential life of early embryos or foetuses to be more valuable than adult life. As mentioned elsewhere in this paper, the potential life in the form of early embryos and foetuses should be accorded a special status and it should be respected. To this end, the 14 day rule was supported as a strict rule which will allow research to be performed on early embryos until the 14th day of development. The 14th day is significant because it signals the start of the formation of the primitive streak which is the primordial origin of the nervous system. Through this 14 day rule and accompanied by various guidelines which would have originated out of the joint meetings and later offered through the clearinghouse system, research on early embryos have to be performed with regard to the special status of the embryo and there has to be punishment for any scientist or researcher who fails to perform research within the guidelines. In addition, to ensure the prevention of the instrumentalisation of the embryo, therapeutic cloning should be prohibited because it would reduce the status of the early embryo to nothing more than a mere instrument in the treatment of a patient. In addition, this special status and respect for the embryo is carried through in the open compulsory licensing of patents 780 and 806 –embryonic stem cells will no longer be a commercial product of WARF and Geron but will be made available to all to use within the specified parameters.

In the brief overview of global attitudes and legal frameworks it was illustrated that there is a disparity between the societal view of stem cell research and the legal system of that society with regards to stem cell research. It was argued that for the potential of stem cell research to be realized there has to be considerations of the ethical dilemmas posed by this kind of research because of the issue of stem cells is inherently deeply embedded within morality. There has to be collaboration between all sides of the debate so that the legal and ethical minefield that constitutes stem cell research can be navigated for the benefit of humanity. As was mentioned elsewhere in this paper a survey of people's attitudes towards stem cell research revealed that once they were informed of the specific medical benefits of stem cell research, their attitudes changed from opposition to support of stem cell therapies. Therefore there is this need to inform and educate the public about what stem cell research involves. In

addition, this constructive public dialogue has to occur between the societies and the government, which can be achieved by the joint meeting and resultant offshoot discussion forums.

This public dialogue is a necessary precursor to the proposed system for the management of stem cell intellectual property rights because the envisaged system is one that takes into consideration the ethical viewpoints and will attempt to incorporate the essence of the viewpoints in the research guidelines to be issued. The management of these stem cell patents is necessary because of the current state of the legal landscape of these patents. This landscape is characterized by a monopoly by WARF and the Geron Corporation who owns fundamental stem cell patents that cover the composition of matter of both non-primate and primate embryonic stem cells. Through a licensing system these companies offer limited access to stem cell lines for the use by both commercial and non-commercial entities. This system is characterized by expensive license fees and for non-commercial entities such as universities and non-profit organisations the system imposes strict and prohibitive working conditions. The patent monopoly held by WARF and the Geron Corporation has resulted in a dense overlapping web of stem cell intellectual property rights that has made it impossible for companies wishing to pursue stem cell research to prevent patent infringement. Known as a patent thicket, it has resulted in the stifling of innovation and the hampering of the flow of knowledge.

Solutions for navigating the patent thicket has been suggested in the form of cross licensing and patent pooling. However, a discussion of these approaches revealed albeit its advantages, these solutions will not be suitable for the stem cell context given WARF and Geron's current stem cell patent portfolio. Instead, this paper has proposed an overhaul of the patent management of stem cells by proposing a system that provides for unhindered access to basic stem cell research – essentially the WARF patents covered by 780 and 806. This system will have as its foundation a support structure consisting of the World Stem Cell Organisation, an international effort which will be the result of a stem cell research treaty that has as its purpose the advancement of human health and science amongst other things. This organisation

will further be supported by regional offices, which will strengthen the support and oversight capabilities. Essentially the regional and international network will be part of the information highway to ensure the continued flow of knowledge.

All parties to the stem cell treaty has to establish a national clearinghouse whose function will be to facilitate the clearinghouse mechanism for the transfer and exchange of licenses, fee collection, dispute resolutions and scientific research. This clearinghouse will be connected to the regional network which in turn, will be connected to the international network. Each connector (networks and clearinghouses) will maintain their own patent database as well as have selective access to certain elements of each other's databases. Through this system there is an envisaged continued flow of information from the inventor of upstream patents to the commercial companies who concern themselves with downstream patents. This continued flow of information will promote and encourage stem cell research and will ideally create a surge in the research and development that can lead to a safe marketable stem cell therapy treatment for consumers.

One cannot merely propose a standalone clearinghouse mechanism because the subject matter is an area of science, ethics and law that affects everyone across the world, whether negatively or positively. Therefore this proposed intricate system of management is the ideal solution for the current stem cell patent thicket because it will hack away at the dense overlapping intellectual property rights surrounding stem cell patents. Once this access and movement of innovation is facilitated for, there will be a renewed motivation for scientists and researchers to actively pursue this area of science without having to face financial constraints as Dr Loring had experienced in her endeavours. In the scenario where countries do not ratify the treaty, it is hoped that this proposal can be employed independently by countries or as collective action by private organizations. The system is designed to operate on a national overnmental level but its basic principles can be employed in a similar organisational structure. If this system were to be employed at a private level, the biggest challenge would have been to convince WARF and Geron to participate in this collaboration. However, if the system is employed at a national level and it is supported by national policies

these companies will have no option but to collaborate and participate in this initiative. They will come to see that it will be advantageous to participate in a system where members can readily obtain access to information on other patents, where the research and development periods for stem cell based products are shortened due to the increased knowledge brought about by sharing information – thus leading to a shorter time frame from laboratory to shelf for downstream products. Therefore if they were to participate, the loss in revenue as a result of the compulsory open licensing involving patents 780 and 806 can be regained in the profits for downstream consumer products.

Stem cell research has not progressed in the manner previously thought because of the ethical constraints and legal uncertainties. This proposal attempts to address the ethical concerns and proposes a way of coming together to first openly discuss, not debate, the issues surrounding stem cell research. There has to be a dispelling of myths surrounding stem cell biology and early human development and concurrently a commitment by scientists to explore alternative derivation methods which preserves the embryo if need be. Every year thousands and in some cases millions of IVF embryos are discarded by fertility clinics – it could be argued that this destruction is no different to the destruction of the embryo to derive stem cells. The difference is that in the former scenario there will be no benefit out of the loss but in the latter, the destruction of the embryo can mean the saving of hundreds of lives if a stem cell therapy could be developed as a result of that research.

The more openness is involved in this management solution the less suspicious and negative society might be to stem cell research. In the same manner, if scientists and researchers were to understand the gist of the ethical concerns, there might be a higher regard and consideration for the embryo through their support of the 14 day rule and the adoption of guidelines that has to be adhered to. If everyone is held to the same standards and held accountable for their actions within this system, there could be a shift in society's approach and attitude towards stem cell research. This shift is vital to the progress and continuance of stem cell research because ethics, science and law in this context are all linked and bears great influence on each other.

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