RESEARCH ETHICS AND POLICY IMPLICATIONS FOR STEM CELL TECHNOLOGY IN MALAYSIA

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RESEARCH ETHICS AND POLICY IMPLICATIONS FOR STEM CELL TECHNOLOGY IN MALAYSIA

ABSTRACT

Stem cell research and technologies are revolutionizing regenerative medicine tremendously. In Malaysia, the research has improved in the last decade resulting in significant publications and clinical trials, but merely overseen by the Guideline for Stem Cell Research and Therapy 2009 which was formulated originally in 2006. There is no legislation or regulatory policies enacted to regulate the whole subject area. While previous studies in Malaysia highlighted the ethical issues of stem cell research from a religious viewpoint, this study focuses on the ethical aspect and policy implication of stem cell technology in Malaysia. It aims to study the status and the current regulatory processes of the Malaysian stem cell research and technologies, to discuss the needs and implications of the stem cell policy and, to explore the ethical perspectives of the international and Malaysian authors. This study is significant as it emphasizes the primary issue of stem cell research and its technologies that is, the absence of an effective policy to regulate its practices. Data for this study were obtained through in-depth interviews with relevant experts including scientists, ethicists, and policymakers as well as library research to analyze both international and Malaysian authored publications. This study found that stem cell research is unregulated in Malaysia and this caused worries among scientists to conduct research more efficiently, formally and openly, which in turn delaying the progress of this field as a whole. The current stem cell guideline is insufficient to prevent the unethical conducts which notably involves the private sector of stem cell technologies, identified in this study as grey area or regulatory loopholes. Without a legal stature, it is ineffective in capturing non-compliances, formal complaints or whistleblowing, unlike a regulatory policy. The study also reveals red-tape

bureaucracies, interchanging directors with different instructions and religious issues are the main challenges faced by the Malaysian policymakers in devising a permanent regulatory framework for better management of stem cell technologies in Malaysia. Since Malaysian experts are accustomed to incorporate religious norms into their ethical inquiries and policymaking, it is vital to devise a framework that suits multi-religious setting, or significantly improve any globally available model they hope to adopt. The formulation of research and development (R&D) regulatory policies is very important in terms of its effectiveness in regulating and managing the national stem cell technology and other similar innovations in the future.

Keywords: ethics, stem cell technology, regenerative medicine, regulatory policy, clinical trials

ETIKA PENYELIDIKAN DAN IMPLIKASI POLISI BERKAITAN TEKNOLOGI SEL STEM DI MALAYSIA

ABSTRAK

Penyelidikan dan teknologi sel stem sedang giat memajukan bidang perubatan regeneratif. Di Malaysia, walaupun penyelidikan sel stem menunjukkan peningkatan sejak sedekad yang lalu berdasarkan penerbitan and percubaan klinikal, ia hanya dikawalselia oleh Garis Panduan Penyelidikan dan Terapi Sel Stem 2009 yang dibentuk pada tahun 2006. Tiada undang-undang atau peraturan polisi yang digubal untuk mengawal selia keseluruhan bidang sel stem dengan lebih baik. Sementara kajian-kajian terdahulu di Malaysia menekankan isu etika penyelidikan sel stem daripada sudut pandangan agama, kajian ini pula menekankan aspek etika dan implikasi polisi terhadap teknologi sel stem di Malaysia. Ia bertujuan mengkaji status dan proses pengawalseliaan semasa penyelidikan dan teknologi sel stem di Malaysia, membincangkan keperluan dan implikasi polisi sel stem serta meneroka perspektif etika antara penulis-penulis antarabangsa dan Malaysia. Kajian ini penting kerana ia menonjolkan isu utama dalam penyelidikan sel stem dan teknologi iaitu, ketiadaan polisi berkesan bagi mengawaselia amalannya. Data kajian ini diperolehi melalui temuramah yang mendalam melibatkan pakar-pakar berkaitan termasuk saintis, ahli etika, dan pembuat dasar dilengkapi oleh kajian perpustakaan untuk menganalisa penerbitan antarabangsa dan Malaysia. Kajian ini mendapati penyelidikan sel stem adalah tidak terkawal di Malaysia dan ini menimbulkan kerisauan di kalangan para saintis untuk melibatkan diri dalam penyelidikan sel stem secara mendalam dan terbuka seterusnya melewatkan tahap kemajuan bidang ini secara keseluruhannya. Garis panduan sel stem semasa tidak berkesan dalam membasmi amalan-amalan tidak beretika, kebanyakannya melibatkan sektor teknologi sel stem swasta, yang dikenalpasti dalam kajian ini sebagai kawasan kelabu ataupun kelemahan-kelemahan peraturan. Tanpa ketegasan undang-undang, garispanduan sel stem tidak berkesan dalam mengenalpasti sebarang isu berkenaan dengan ketidakpatuhan, aduan

rasmi atau pemberian maklumat, tidak seperti polisi kawal selia. Kajian juga mendedahkan karenah birokrasi, pernukaran pengarah berserta dengan variasi arahan antara mereka dan isu-isu agama antara cabaran utama yang dihadapi oleh pembuat polisi Malaysia dalam membangunkan rangkakerja pengawalseliaan yang kekal supaya teknologi sel stem boleh diurus dengan lebih baik di Malaysia. Oleh kerana pakar-pakar di Malaysia lazimnya mempertimbangkan norma-norma keagamaan dalam penyelidikan etika dan penghasilan polisi, adalah penting untuk sama ada membentuk rangka kerja yang paling sesuai melibatkan perduduk berbilang agama atau menambahbaik model global yang tersedia. Penghasilan polisi kawal selia penyelidikan dan pembangunan (R&D) adalah sangat penting dari segi keberkesanannya dalam mengawalselia dan menguruskan teknologi sel stem negara dan juga inovasi lain yang sama jenisnya pada masa akan datang.

Kata kunci: etika, teknologi sel stem, perubatan regeneratif, polisi kawal selia, ujian klinikal

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I am also grateful to my best friend and my husband, Kavin Jayaram for his love, continual support, understanding and patience. Without him and our daughter Kashaani, I would be completely lost.

"You may encounter many defeats, but you must not be defeated. In fact, it may be necessary to encounter the defeats, so you can know who you are, what you can rise from, how you can still come out of it." – Maya Angelou

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LIST OF ABBREVIATIONS

ART	artificial reproductive technology
ASC	adult stem Cell
ASM	Academy of Sciences Malaysia
BAC	Bioethics Advisory Committee
B. C. E	Before Common Era
BCRO	Bio-Cellular Research Organization
BFPK	*Biro Pengawalan Farmaseutikal Kebangsaan*
CRC	Clinical Research Centre
DHEW	Department of Health, Education and Welfare
DHHS	Department of Health and Human Services
ELSI	ethical, legal and social implication
EC	embryonic carcinoma cells
EG	embryonic germ cells
ESC	embryonic stem cells
ESI	ES Cell International
EU	European Union
FS	foreign scientists
FE	foreign ethicists
GCP	good clinical practices
GERD	domestic expenditure on R&D
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
GvHD	graft vs host disease
hESC	human embryonic stem cells
HFEA	Human Fertilization and Embryology Authority
HKL	Hospital Kuala Lumpur
HLA	human leucocyte antigen
HSCT	Haemopoietic Stem Cell Therapy
HSR	Human Stem Cell Research
IEC	institutional ethics committee
IDI	in-depth interview
IIUM	International Islamic University Malaysia
ICM	inner cell mass

IMR	Institute of Medical Research
iPSC	induced pluripotent stem cell
IRB	institutional review board
IVF	*in vitro* fertilization
JAKIM	Department of Islamic Development Malaysia
KKM	Kementerian Kesihatan Malaysia
LS	local scientists
LE	local ethicists
MAKNA	National Cancer Council
MBChB	Bachelor of Medicine and Surgery
MCCBCHT	Consultative Councils of Buddhism, Christianity, Hinduism, Sikhism and Taoism
MOH	Ministry of Health
MREC	National Medical Research & Ethics Committee
MSCR	Malaysian Stem Cell Registry
NCI	National Cancer Institute
NBAC	National Bioethics Advisory Commission
NHI	National Heart Institute
NHMRC	National Health and Medical Research Council
NIH	National Institute of Health
NGOs	non-governmental organization
NMRR	National Medical Research Registry
NMEC	National Medical Ethics Committee
NPCB	National Pharmaceutical Control Bureau
NPRA	National Pharmaceutical Regulatory Agency
NSCERT	National Stem Cell Research and Ethics Sub-Committee
NUS	National University of Singapore
NYU	New York University
PGD	Preimplantation genetic diagnostics
PHFS	Private Healthcare Facilities and Services
PM	local policy makers
PTR	Pahang Technology Resources
R&D	research and development
RIKEN	Rikagaku Kenkyusho, Institute of Physical and Chemical Research
SC	stem cell

SCMG	Stem Cells and Molecular Group
SCNT	somatic cell nuclear transfer
UH	University of Malaya Hospital
UiTM	University Technology MARA
UKM	National University of Malaysia
UM	University of Malaya
UMMC	University of Malaya Medical Centre
UPM	University Putra Malaysia
USM	University of Science Malaysia
WHO	World Health Organization
WMA	World Medical Association
WoS	Web of Science

LIST OF APPENDICES

CHAPTER 1: INTRODUCTION

1.1 Introduction

Stem cell research is well acknowledged for its potential in medical science, with many discoveries and emerging technologies offering potential cure and treatment for debilitating diseases. However several concerning issues such as (1) the use and destruction of human embryos, (2) the creation of viable embryos through somatic cell nuclear transfer (SCNT) solely for research purpose which is also known as therapeutic cloning, (3) the modification of these embryos, (4) the premature publicizing of clinical trials and (5) the use of unproven stem cell therapies have led to many ethical controversies and policy challenges (Kimmelman et al., 2016; McLaren, 2001). The growing research combined with the ethical implications have driven many governments to undertake regulative measures to oversee stem cell research including its funding aspects. The diverse viewpoints and cultural beliefs brought in varying intentions and angle in governing the entire stem cell research and its technologies. This denotes that no universal policy or well-suited set of rules that can be applied across the globe (Dhar & Hsi-en Ho, 2009).

For that reason, this study began by looking at the various position and policies of stem cell research and technologies available around the world. The World Stem Cell Policies Map presented by Figure 1.1 displays the diverse positions of nations within regions namely Europe, Africa, and Asia (Hoffman, 2009). A detailed description of several pioneering stem cell countries, such as the United States, United Kingdom, Australia, and Singapore due to the extensive review of their stem cell regulation were included. The dark brown tone denotes the countries with permissive and liberal approach that allows various stem cell techniques, such as the United Kingdom, Singapore, India, China, South Korea, Japan, Sweden, Belgium, Finland, and Australia. Among these

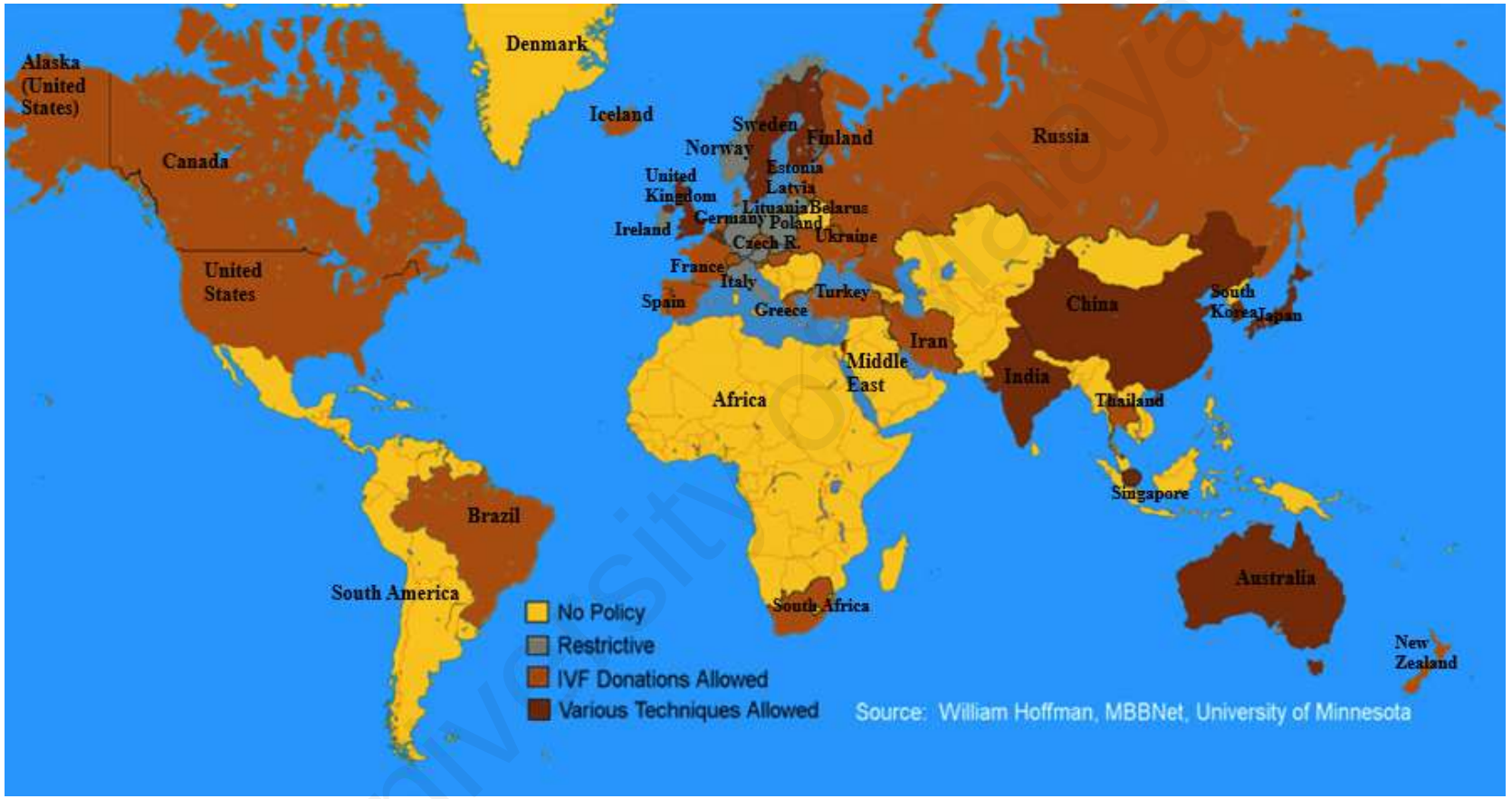


Figure 1.1: The world stem cell policies map (2009)

[Source: Image reproduced with permission from Hoffman (2009).]

countries, only India and China do not have legislation enacted to regulate its stem cell research. The others adopted a permissive approach with the help of a comprehensive policy and law that promotes research while safeguarding what is necessary such as stakeholders' rights and clinical trials.

The light brown tone represents countries that allows stem cell research but only on surplus *in vitro* fertilization (IVF) embryos donated by fertility clinics such as, Brazil, South Africa, Canada, Thailand, Russia, Spain, France, Switzerland (located between France and Czech Republic), Czech Republic, Slovenia, Hungary, Turkey, Iran, Ukraine, Latvia, and Estonia. South Africa has the 'National Health Act' (2003) that included provision on stem cell (Parliament of the Republic of South Africa, 2003), Canada has the 'Assisted Human Reproduction Act' (2004) (Parliament of Canada, 2004), Brazil has the 'Biosafety Law' enacted in 2005 (Civil Cabinet, 2005) and Russia introduced recently their 'On Biomedical Cell Procedures Act' in 2017 (Gromov, 2017; The Federal Assembly of the Federation of Russia, 2017).

In countries represented by the grey tone like Norway, Ireland, Italy, Lithuania, Germany, Austria, Slovakia (located just below the Czech Republic), and Poland, stem cell research is completely restricted with specific laws established on the subject matter (Hoffman, 2009). Slovakia has one of the most strict laws on human embryonic stem cell (hESC) research which includes 12-year imprisonment including other penalties for violation (The Witherspoon Council on Ethics and the Integrity of Science, 2012). Although there are many positions on stem cell research regulation, the pioneering stem cell countries like the United States and the United Kingdom are often reviewed by many to study and make exemplary of the origins of such regulations for the benefit of their own nations.

In the 2009 map, the United States is represented by a light brown toned country, which only allows stem cell research on excess IVF embryos. This represents the policy

position of the former President Bush who banned the use of federal funds on hESC but allowed its research on existing cell lines that is prior to 1st August 2009 (Wertz, 2002). Unlike the United States, the United Kingdom is presented by the dark brown tone that displays a more permissive approach considering stem cell research. Their 'Human Fertilization and Embryology Act' (HFEA) established originally in 1990 under the Human Fertilization and Embryology Authority allows stem cell research on embryos less than 14 days old and derived from surplus IVF embryos and those created specifically for research purpose either using IVF and SCNT (United Kingdom Parliament, 1990). Although 'Human Reproductive Cloning Act' enacted in 2001 bans all reproductive cloning while ensuring embryos created for research purpose are never implanted in a woman's womb. However, the Human Reproductive Cloning Act was repealed when the HFEA underwent an amendment in 2008 to update its provisions concerning assisted reproduction (HFEA, 2008).

In Asia, Singapore is known to be a country that has adopted a permissive approach regarding stem cell research similar to the United Kingdom, which is represented in the dark brown tone in the map. It is considered as one of the Asian countries apart from China and Japan, that is involved extensively in stem cell research. It is considered widely as the 'Asia's Stem Cell Centre" with more than 40 research groups in the country (Dhar & Hsi-en Ho, 2009). Its stem cell research is regulated and overseen by the Bioethics Advisory Committee (BAC) formed in 2000 (BAC, 2016; Lim & Ho, 2003). Besides developing and recommending policies, it also aims to protect the welfare of the public, especially research subjects ensuring the biomedical research progress ethically. The BAC announced the release of the 'Ethics Guidelines for Human Biomedical Research', which aims to guide the ethical, legal and social rights of all the stakeholders in human biomedical research mainly the research subjects (BAC, 2015).

While countries with yellow tone are those without any known stem cell policy or laws as of 2009 based on Figure 1.1 which includes Malaysia, Mexico, Indonesia, most African countries, some South American countries, most Middle Eastern countries as well as others (Hoffman, 2009). According to the map, a majority of the countries that have figured out their regulative positions concerning the stem cell research and technologies are developed countries, ranging from being restrictive to completely liberal. While only a handful of developing countries have adopted some positions concerning the subject topic with China in this list as an exceptional case despite its significant contribution in stem cell research standing next to the United States.

Generated in 2009, the map did not capture the Malaysian National 'Guideline on Stem Cell Research' published originally in 2006 or the revised 'Guideline on Stem Cell Research and Therapy' (2009) (MOH, 2006, 2009a). The World Stem Cell Policies Map in Figure 1.1 is informative but it required some updating as there are nations that have adopted new laws and policies since 2009. Therefore, for the purpose of this study, Chapter 2 will present the Global Stem Cell Laws and Policies that will highlight the latest stem cell laws and policies of nations around the world as they are revisited individually to ensure that they are up-to-date. The Figure 2.1 in Chapter 2 represents the new map of Global Stem Cell Laws and Policies as of 2017.

1.2 Overview of the chapter

This chapter presents an overview of the study by setting the general tone or context for this thesis while highlighting the many areas of this study. The focus and rationale of this study revolves around, (1) the status of stem cell research and development in Malaysia, (2) the current regulation of stem cell research and its technologies in Malaysia, and (3) the debate of ethical controversy concerning stem cell research and therapy based on the international authored literatures and those written by Malaysian authors. This chapter will also include the problem statement, the objectives and the research questions of this study. The significance of the study will be discussed with an outline of the study at the end of this chapter.

1.2.1 Status of stem cell research & development in Malaysia

Identifying and evaluating the three different areas involving stem cell in Malaysia such as, (1) the stem cell transplantation, (2) the establishment of public and private stem cell facilities and entities and (3) the number of stem cell related articles written by Malaysian scientists or those affiliated with Malaysian based facilities, ultimately allows us to gauge the status of stem cell research and its development in Malaysia. The following section will present these reviews in detail for an improved assessment.

1.2.1.1 Stem cell transplantations

Reviewing the status of stem cell research and development in Malaysia identified that the stem cell transplantation conducted as clinical trials as the beginning of stem cell research in Malaysia. The first documentation of stem cell research was the hematopoietic stem cell transplantation performed by the University of Malaya Medical Centre (UMMC) formerly known as the University of Malaya Hospital (UH) back in the 1987

(NTR, 2004). It was the first bone marrow transplantation, a form of hematopoietic stem cell performed on a paediatric patient with acute leukaemia. It was also the first allogeneic hematopoietic stem cell transplantation, whereby the marrow is retrieved from a non-related donor. Several years later in 1993, the UH performed its first allogeneic hematopoietic stem cell transplantation to an adult patient (Gan et al., 2008).

Umbilical cord blood was another clinically useful source of hematopoietic stem cell and in 1997, Malaysia began the high-risk umbilical cord blood transplantation using cord blood obtained from overseas cord blood banks on a small scale (NTR, 2004; Rocha & Gluckman, 2006). Subsequently, in the 1999 UH performed its first autologous hematopoietic stem cell transplantation to a 25-month old boy with beta-thalassemia major. Doctors diagnosed his unborn sibling in utero to be a beta-thalassemia carrier and also with compatible human leucocyte antigen (HLA), making it possible to retrieve the cord blood for transplantation (Chan et al., 1999). With that, the progress and number of transplantations performed in Malaysia will add in as one part the evaluation of the status of stem cell research and development in Malaysia. According to the National Transplant Registry (NTR) (2014) a total of 336 transplants were reported in 2014 alone, despite starting with only eight cases in 1987 as shown in Table 1.1 By October 2014, there was a total of 13 transplant units authorized to perform transplantation in 11 hospitals with a new unit established in Likas Hospital in Kota Kinabalu, Sabah. Out of the 13 transplant units, Ampang Hospital performs the greatest number of transplantations.

Table 1.1: Blood & bone marrow transplantation in Malaysia

Year	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
New transplant patients	8	6	22	5	12	21	19	25	30	28	33	49	62	94	108
New transplant rate pmp	1	0	1	0	1	1	1	1	1	1	2	2	3	4	5

Year	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
New transplant patients	114	128	140	148	136	149	181	213	262	271	303	312	336
New transplant rate pmp	5	5	5	6	5	5	7	8	9	9	10	10	11

[Source: Image reproduced with permission from NTR (2014).]

Although allogeneic stem cell transplantations were performed on a larger scale since it began in 1987, autologous stem cell transplantation exceeded the allogeneic since 2011 as illustrated by Table 1.2 The initial autologous transplants utilized bone marrow as stem cell source, but peripheral blood stem cell was later identified as the preferred choice (NTR, 2014).

Table 1.2: Allogeneic & autologous transplantation in Malaysia

Year	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996
Type of transplant	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Allogeneic + Syngeneic	8 (100)	6 (100)	21 (95)	5 (100)	12 (100)	20 (95)	18 (95)	24 (96)	29 (97)	26 (93)
Autologous	0 (0)	0 (0)	1 (5)	0	0	1 (5)	1 (5)	1 (4)	1 (3)	2 (7)
TOTAL	8 (100)	6 (100)	22 (100)	5 (100)	12 (100)	21 (100)	19 (100)	25 (100)	30 (100)	28 (100)

Year	1997	1998	1999	2000	2001	2002	2003	2004	2005
Type of transplant	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Allogeneic + Syngeneic	27 (82)	32 (65)	44 (71)	56 (60)	75 (69)	75 (66)	83 (65)	90 (64)	91 (61)
Autologous	6 (18)	17 (35)	18 (29)	38 (40)	33 (31)	39 (34)	45 (35)	50 (36)	57 (39)
TOTAL	33 (100)	49 (100)	62 (100)	94 (100)	108 (100)	114 (100)	128 (100)	140 (100)	148 (100)

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	Total
Type of transplant	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Allogeneic + Syngeneic	87 (64)	75 (50)	115 (64)	110 (52)	137 (52)	129 (48)	117 (39)	128 (41)	153 (45)	1793 (56)
Autologous	49 (36)	74 (50)	66 (36)	103 (48)	125 (48)	142 (52)	186 (61)	184 (59)	183 (55)	1422 (44)
TOTAL	136	149 (100)	181 (100)	213 (100)	262 (100)	271 (100)	303 (100)	312 (100)	336 (100)	3215 (100)

[Source: Image reproduced with permission from NTR (2014).]

Besides the well-established hematopoietic stem cell transplantations performed by the transplant units, several other stem cell transplantations, including those under research such as embryonic stem cell (ESC) and induced pluripotent stem cell (iPSC) are also conducted in the form of clinical trials by many public research laboratories, including the laboratories and hospitals of the public institution of higher learnings (UM, UKM, USM, UPM), the Clinical Research Centres (CRC) established within the public hospitals, the Institute of Medical Research (IMR), the National Cancer Institute (NCI) and the National Heart Institute (NHI).

1.2.1.2 Public & private stem cell facilities

The growing number of transplantations initiated the establishments of several private and public cord blood and tissue banks in Malaysia. It is mainly to allow parents to collect, process and store their newborns' umbilical cord blood and tissues for future medical use. The public cord blood and tissue banks were established within the public hospitals and the National Blood Centre (*Pusat Darah Negara*). According to the Transplantation Unit & National Transplant Resources Centre, developed by the Medical Development Division of the Ministry of Health (MOH), there are many umbilical cord blood collection centres established in numerous public hospitals such as the Kuala Lumpur Hospital (HKL), Selayang Hospital, Serdang Hospital, Ampang Hospital, Sultanah Bahiyah Hospital in Alor Setar, Kedah, Sultan Abdul Halim Hospital in Sungai Petani, Kedah, and Tunku Fauziah Hospital in Perlis (NTR, 2014).

The IMR together with the National Cancer Council (MAKNA) and MOH set up a registry, known as the Malaysian Stem Cell Registry (MSCR) as a joint project in December 2000. It is basically to allow those who wanted to donate their stem cells to register in the MSCR registry for easy location and screening of potential donors, maximising chances of successful transplantations. In 2013, it was identified that 18,000

people in Malaysia were registered as volunteers willing to donate their stem cell. The number greatly expanded but still nowhere close to their target of 40,000 people but it definitely encourages more people to join in the good course given appropriate publicity.

Along with the public sector, there are also the establishment of the private stem cell research entities offering stem cell therapies along with several cord blood and tissue banks, namely Stem Life Berhad, CryoCord Sdn Bhd, Nichi-Asia Center for Stem Cell & Regenerative Medicine (NiSCELL), Cellsafe International Sdn Bhd, and Stempeutics Research Malaysia Sdn Bhd. These entities practically launched the private sector of stem cell research and therapy as illustrated by Table 1.3 (Medical Practicing Division (MOH), 2016a).

Table 1.3: Private stem cell cord blood & tissue banks in Malaysia

Organization	Licensing	Established
Stem Life Berhad	(MOH), Private Healthcare Facilities and Services (PHFS) Act 1998	2001
CryoCord Sdn Bhd	(MOH), Private Healthcare Facilities and Services (PHFS) Act 1998	2002
Nichi-Asia Center for Stem Cell & Regenerative Medicien (NiSCELL)	(MOH), Private Healthcare Facilities and Services (PHFS) Act 1998	2007
Stempeutics Research Malaysia Sdn Bhd,	(MOH), National Pharmaceutical Regulatory Agency (NPRA)	2007
Cellsafe International Sdn Bhd	(MOH), Private Healthcare Facilities and Services (PHFS) Act 1998	2014

[Source: The Lists of Licensed Private Healthcare Facilities and Services as of 30th June 2016]

The Academy of Sciences Malaysia (ASM) identified eight companies offering stem cell services in their advisory report published in 2013, out of which three was not even captured by the list published by the Medical Practicing Division, which are Cytopeutics Sdn Bhd, EmCell, and StemTech International (ASM, 2013; Medical Practicing Division (MOH), 2016c). All the private companies are licensed and

authorized based on the 'Private Healthcare Facilities and Services (PHFS) Act' (1998) within the Medical Practicing Division of MOH Malaysia, except for Stempeutics Research Malaysia Sdn Bhd which is licensed to carry out stem cell research and clinical trial according to the National Pharmaceutical Regulatory Agency (NPRA) formerly known as National Pharmaceutical Control Bureau (National Pharmaceutical Control Bureau (NPCB)) or *Biro Pengawalan Farmaseutikal Kebangsaan* (BFPK).[1]

1.2.1.3 Stem cell publications

The status of stem cell research and development in Malaysia can also be assessed from the number of publications involving stem cell research. A keyword search conducted in 6th October 2016 using the Web of Science (WoS) Core Collection database using keywords, 'stem cells', appropriate symbols (asterisks, which captures variation of spelling or misspelling and double prime) and Boolean terms ('NOT' to exclude irrelevant keywords such as religion and ethics) resulted in 67,309 total stem cell articles published between 1980 and 2016 (up to 6th October 2016). Out of this, only 195 were Malaysian authored articles, and this does not include Malaysian authors studying abroad or affiliated with foreign universities. 6,843 articles from 67,309 were written on human embryonic stem cell while only 18 were Malaysian authored articles (WoS, 2016)

A similar search was conducted by the ASM in 2012 using Medline database, resulted in 100 articles for the span of 10 years (ASM, 2013). Although the resulting number is significantly low, it clearly indicates growth, that is expected to progress as long as stem cell research is considered potential and valuable as envisioned by the MOH Malaysia whereby extensive research is required to warrant discovery.

[1] This information is verified during my conversation with the participants. Chapter 4 presents description of the participants.

1.2.2 Current regulation of stem cell technologies in Malaysia

The stem cell research and its technologies in Malaysia are greatly improving with many research and transplantations, but it is currently unregulated and uncovered by any existing legislation.[2] Since the first transplantation in 1987, the Medical Development Services Section within the Medical Development Division of MOH Malaysia only formulated the Guidelines on Stem Cell Research in 2006. It was meant as standard practice for all stem cell research ensuring they are ethically conducted without violation. The guideline underwent a revision in 2009 to add overlooked aspects and was published as the Guidelines for Stem Cell Research and Therapy (2009) (MOH, 2009a).

Currently any research involving stem cells, clinical trials using human subjects or any public research facilities including IMR, NCI, NHI and those carried out by scientists attached with the institutions of higher learnings (universities), doctors affiliated with public hospitals or CRC are all required to first gain the appropriate authorization, second to follow standard protocols while carrying out their research without any violations. All such researches need to initially register in the National Medical Research Registry (NMRR) accessed online and apply for the ethical approval from the National Medical Research & Ethics Committee (MREC) (MREC, 2012; NMRR, 2017).

MREC was established in 2002 within the MOH to protect the welfare and rights of human participants in research. It aims to offer independent guidance, advice, and recommendations on health research, the specific protocol involving human subjects which are conducted by officers affiliated with and using the MOH facilities (MREC, 2012).

[2] This information is verified during my conversation with the participants. Chapter 5 presents further description on the topic

Figure 1.2 displays the review path of research submitted to the MREC before they gain the approval necessary to proceed.

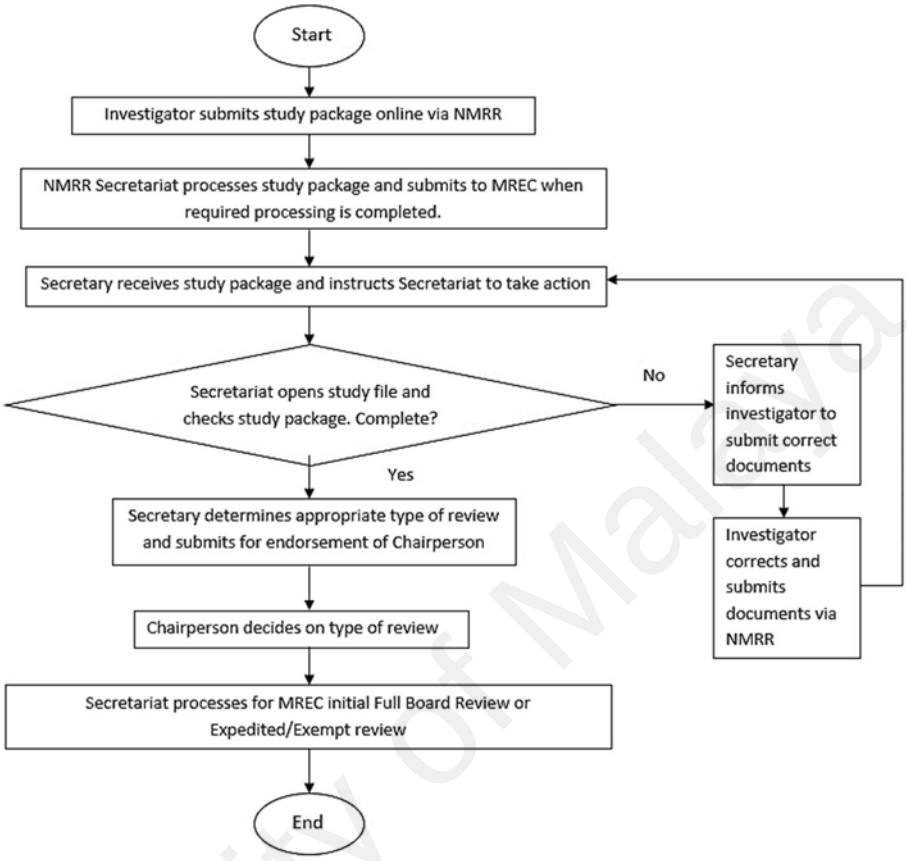


Figure 1.2: National Medical Research & Ethics Committee's (MREC) reviews & approvals

[Source: Image reproduced with permission from MREC (2012).]

According to the standard protocol, relevant stem cell research is first required to register in the NMRR and second gain the ethical approval from the MREC and the institutional review board (IRB) and institutional ethics committee (IEC) for those institutions of higher learnings and universities before they can proceed (MOH, 2009a). Following the formulation of the Guideline on Stem Cell Research (2006), the Medical Development Division of MOH established the National Stem Cell Research and Ethics Sub-Committee (NSCERT) to review all stem cell-related research for approval in accordance to their checklist which all institutional review boards and national and IEC required to follow. This means, all board and committees required to review stem cell-

related research proposals such as the MREC, the IEC and IRB will review each stem cell research based on the NSCERT checklist inclusive of their routine review procedure (MOH, 2009a).

Most of the non-hematopoietic stem cell therapy and transplantations in Malaysia are conducted as a clinical trial at the moment, and goes through series of approval beginning with (1) the NMRRR registration, (2) the ethical clearance from MREC (with the NSCERT checklist), (3) the IRB and IEC based on the checklist if it is carried out as academic research by institute of higher learnings or universities, and finally (4) the review of the NSCERT. The NPRA have yet to commence its position to regulate the stem cell therapy as an end product. They verified that they will assume their regulatory position fully only when the nation begins to introduce stem cell therapy as a routine form of treatment across all healthcare facilities.[3]

1.2.3 Research ethics and the diverse ethical debate

It is important to note that the term research ethics can be broadly interpreted with varied focus. It can be looked as a philosophical standard that guides and enlightens researchers concerning the many research conducts such as involving human participants, plagiarism, personal interests, including misconducts. In the context of this study, research ethics concerns the human subjects which includes both the clinical patients and the human embryos which cells are extracted from, the ethical conduct of the research which serves the interests of different stakeholders, and the ethical soundness of the research activities, which includes the topic of risks and informed consent, which is looked from a broader perspective (Duncan, 2014). Bioethicist, Resnik (2015), believe that research ethics can facilitate the understanding of the ethical standard, including the issues involved and the decision-making process for policies and ethical judgement

[3] This information is verified during my conversation with the participants. Chapter 5 presents further description on the topic

similar to this study.

With that, it is important to acknowledge that stem cell research is recognized greatly not only for its potential alone but also for the various ethical controversy it brought due to the embryo destruction during human embryonic stem cell (hESC) extraction. Although there are many types of stem cells, the hESC that unintentionally destroys human embryos in the course of stem cell extraction is considered as the most unethical form of stem cell and against many religious beliefs and moral principles (Fischbach & Fischbach, 2004). The ethical deliberations of hESC research often begin by laying the foundation of 'when life begins'? It is a slippery slope argument that perceived important to illustrate the unique value of embryos and the justification of when embryos are recognized as an individual and no longer as cells (Wert & Mummery, 2003). These ethical arguments include the moral status of the embryo (Doerflinger, 2010), the rights of the embryos and the personhood theory (Brock, 2006; Doerflinger, 2010), and the potentiality of embryos (Brock, 2006; Wert & Mummery, 2003).

Judging by previous studies, it is fair to conclude that there are various opinions and perspectives concerning the ethical inquiry of stem cell research ranging from those that discuss from religious fundamentals to those that set a universal tone in their judgements based on various bioethical principles that are greatly explored by ancient to contemporary scholars. This does not end with the moral status of embryos alone, it includes various discussion touching on the matters of donor exploitations, informed consent, research fraud, stem cell tourism, and others related. Chapter 3 will include a comprehensive review of many kinds of literature highlighting the ethical concerns of stem cell research.

1.3 The problem statement

Stem cell research in Malaysia has developed tremendously over the last 30 years, judging from the research publications, the clinical trials, the transplantations and the establishment of many private and public stem cell research facilities. In 2006, almost 20 years since the first bone marrow transplantation, the Medical Development Division of the MOH published the Guideline on Stem Cell Research (MOH, 2006). Since then, the Malaysian stem cell research and therapy are overlooked by the guideline which underwent a revision and was published as the Guideline for Stem Cell Research and Therapy (2009). There is no legislation or regulatory policy formulated to regulate stem cell research despite the growing research and development.

According to the Director General of the MOH, Tan Sri Datuk Dr. Hj Mohd Ismail Merican, the Guideline on Stem Cell Research 2006 is meant as a standard for the medical practitioners in both public and private hospitals to conduct stem cell research ethically and in accordance to the established legislation, which is yet to formulate. He also added that with the provision of the guideline, the Ministry of Health (MOH) hopes to improve the quality of research in the field of stem cells while assisting the researchers to use any available facilities as outlined by the regulations for the benefit of the public and patients in particular (MOH, 2006).

In 2008, two years after the guideline was published, a Czechoslovakian company, known as Bio-Cellular Research Organization (BCRO) tried to set up an unauthorized rabbit farm in Janda Baik, Pahang. The founder, Michael E. Molnar moved the base of the company several times, from the United Kingdom to the United States and finally to Malaysia (Nelson, 2008). It teamed up with the state-owned unit, Pahang Technology Resources (PTR) Sdn Bhd in the hope of leasing the 81 hectares of land to establish the country's largest rabbit breeding farm from which stem cell will be extracted and cultured to treat various human diseases (Mohamad, 2008). The project brought forward many

challenges, first the endorsement of the state officials of a technology neither approved nor licensed by the appropriate authority such as the MOH, second the use of animal (rabbits) stem cells as means of therapy for human diseases (*xenotransplantation*) without considering the cross-species effect and finally *xenotransplantation* that was not covered by any stipulations in the stem cell guideline at the time.

Besides BCRO, there are many other private entities identified marketing approval pending or unproven stem cell products ranging from food-based, cosmetics to healthcare. The Cytopeutics Sdn Bhd, EmCell, StemTech International and even Stempeutics Research Sdn Bhd were not listed as a private healthcare facilities or services (within the Medical Practicing Division) (Medical Practicing Division (MOH), 2016b). This is because they are involved in the manufacturing of stem cell products and therapy services and not a healthcare provider or cord blood and tissue bank. StemTech International is the only company with several products listed in the NPRA database (NPRA, 2014).[4] Stempeutics Research Sdn Bhd and Cytopeutics Sdn Bhd, both have stem cell research registered in the NMRR authenticating their nature of business and status. While EmCell's products or projects are not listed anywhere simply because they are simply marketing imported stem cell products.

The fact that some of these products are listed in one platform but not in another, creates doubt and confusion. Public including patients depend on firstly, the authority to ensure that the stem cell therapies and products are regulated and secondly, the platforms within the regulators offer straight-forward insight regarding the products and services but unclear jurisdiction makes it uncertain. The matter of what information is available and where may not be within my research interest, but it only indicates inconsistency within the authorities although they are largely governed by the same entity, which is the

[4] Chapter 5 presents the discussion on implication of private sector of stem cell research and development in Malaysia

MOH Malaysia which practice a strict and comprehensive oversight. This makes the process of determining the total number of licensed entities hard to confirm since there are different authorities involved in the process.

The Medical Practicing Division of the MOH is in-charge of the licensing of all private healthcare facilities and services based on the PHFS Act 1998. While the NPRA within the jurisdiction of the MOH is in-charge of the registration of cell and gene therapy products (NPCB, 2015). Apart from the products, all stem cell research, both within the public and private sector is required to be registered under the NMRR as standard protocol. Subsequently, these registrations will be reviewed by the NSCERT to ensure they follow the Guideline for Stem Cell Research and Therapy (2009) and the MREC should they involve human subjects. There is clearly a case of jurisdiction overlaps especially with stem cell. There is even an overlap of function involving license and registration of private stem cell companies and their products between Medical Practicing Division and the NPRA. Although some companies are registered within the Medical Practicing Division as a healthcare facility, such as some private hospitals and aesthetic clinics, they are not forthcoming of the stem cell therapy or products offered within their facilities. They also failed to have them registered as a product in the NPRA or in the NMRR as a clinical trial (NMRR, 2017; NPRA, 2017).

This includes, (1) a private medical facility that holds a United States patent for a stem cell therapy known as neochondrogenesis, which is induced by peripheral blood stem cell combined with hyaluronic acid to treat cartilage injury by regenerating the articular cartilage, as a licensed as a healthcare provider but the clinical trials are not captured in the NMRR (Saw et al., 2011), (2) several aesthetic clinics established which offer stem cell therapy to treat anti-aging conditions like skin pigmentation, skin lightening and hair loss also have registered their establishment as aesthetic clinic but failed to register their stem cell products or therapy and (3) foreign companies such as

those from China, Korea or Switzerland exporting their plant and animal based stem cells products worldwide in the form of capsule or drinks and sold by Malaysian marketing companies. Although the products may be harmless to some degree, however the risk towards customers is yet to be determine without product testing by the proper authority for endorsement which is a regular step in attaining license and approval. According to the MOH, without a formal complaint filed by the general public or whistle-blowing they are unable to intervene or take the necessary actions. [5]

There are many concerns regarding the regulatory deficiency of stem cell research and technology here in Malaysia. Aside from the unlicensed entities, Malaysian scientists are hesitant in pursuing extensive research within the field as they are unclear of the regulatory aspects. They fear that the uncertainties, regarding what is lawful and not, will reflect in their research proposal considering the cell lines, technology or method used that could result in rejected proposals leading to wasted time, energy and resources.[6] This often leads to unnecessary anxiety and concern that some scientists refuse to sign on the stem cell research journey. Stem cell research is at a phase where by it requires extensive research to warrant discovery, however the refusal of some Malaysian scientists to work on stem cell is identified as research hindrance, which is clearly a problem.

The guideline has sustained for the last 11 years but not without any consequences. In fact, it brought forward several issues such as, first, the fact that the stem cell research and therapy is only overlooked by a guideline without legal stature, second, the case of illegally operating entities like BCRO without conforming the proper authority or regulation, third, the matter of overlapping jurisdictions managing stem cell oversight, fourth, the issue of accountability which is not captured by the guideline in the form of non-compliance or penalty, fifth the need for formal complaints whenever the authorities are required to intervene pertaining illegal entities, unproven products, and

[5, 6] This information is verified during my conversation with the participants. Chapter 5 presents further description on the topic

other unethical conducts, sixth the guideline that obviously lacking transparency and finally the unintentional research hindrance triggered by unclear regulation which creates anxiety and uncertainty among scientists.

The revision of the guideline was well-timed not to mention necessary to accommodate the many exceptional cases such as plastic surgery, cancer and xenotransplantation that was outside the hematopoietic stem cell and uncovered in the original version. It requested the feedbacks of many religious experts in Malaysia, namely the Department of Islamic Advancement of Malaysia also known as *'Jabatan Kemajuan Islam'* Malaysia (JAKIM), the Islamic Medical Association of Malaysia (*Persatuan Perubatan Islam Malaysia*), the Consultative Councils of Buddhism, Christianity, Hinduism, Sikhism and Taoism (MCCBCHT) and some non-governmental organizations (NGOs). The revision also claimed to have included the 'Brainstorming Workshop' feedback conducted in May 2008 and the 'Public Forum on Stem Cell Research' conducted in Ampang Hospital on 18th October 2008 (MOH, 2009a). It is difficult to determine how they reflected in the revised guideline but it is necessary to identify the improvements made.

Therefore, this study is vital as it presents the many shortcomings of the current regulation of stem cell research and technology based in its long-term regulatory implications. The assessment of the current status of stem cell research and development and the technicalities of what the guideline is and is not, together with the insight of the experts directly involved in stem cell topic will help in the understanding of the factors involved.

1.4 Objectives of study

The objectives of this study are:

(a) To study the status and the regulatory processes of the current stem cell research and therapy in Malaysia

(b) To explore the ethics of stem cell research as presented by international and Malaysian authors

(c) To discuss the implications of allowing Malaysian stem cell research to be guided by the present regulatory policies and its limitations

1.5 Research questions

(a) What is the current status of stem cell research and therapy in Malaysia? [Objective 1]

(b) How are stem cell research and therapy are currently regulated in Malaysia? [Objective 1]

(c) What are the perspectives of ethical inquiry involving the stem cell research and therapy? [Objective 2]

(d) What are the trends of international and Malaysian publications in terms of the ethical inquiry of stem cell research and therapy? [Objective 2]

(e) What are the implications of the current regulative measures concerning stem cell technologies in Malaysia? [Objective 3]

(f) Is the current Malaysian stem cell guideline adequate in regulating the stem cell research and therapy? [Objective 3]

(g) How and where can the current regulatory measures be compromised due to continuous development of stem cell technologies? [Objective 3]

1.6 Significance of study

The significance of a study ought to reveal the range of contributions made by that study to expand our understanding, to modify concept or to endorse new theories in a particular field of research (Maillard, 2013). This study proved to be valuable because the cumulative knowledge gathered involving the ethics and regulation of stem cell research and technology in Malaysia are able to aid in a number of areas across expertise such as ethical, social, and policymaking.

In Malaysia, the stem cell research and technology are growing tremendously as verified by the increasing research, transplantation and publication, but because it is unregulated, there are many hidden consequences within the field. This study is significant as it will be useful in urging the authority for the development of a regulatory policy of stem cell research and therapy. Policymakers or regulatory experts in Malaysia, which is made up of qualified experts or personnel attached within the Medical Development Division, the Medical Practicing Division of the MOH, the NPRA and the NSCERT will be able to gain valuable insight from this study as it offers a clear and comprehensive documentation of the ethical, legal and social implication (ELSI) of stem cell research and technology. They can utilize the gathered data in their many deliberations among experts saving time and resources achieving the desired outcome promptly.

Since there is only the Guidelines for Stem Cell Research and Therapy (2009) in Malaysia at the moment which is not legally binding it is important to study the implication of not having a proper regulatory policy or an act which carries more mandate. The assessment would prove worthy for policy experts to understand the actual scenario of the public and private stem cell sector which has clear issues needing immediate attention. One of such issue is the research hindrance which policymakers are unaware off as it is acquired from directly corresponding with stem cell research experts. Apart

from that it hopes to initiate the long overdue assessment of the matter of negligence and non-compliance and its implication which is not captured by the stem cell guideline as it lacks formal mandate.

This study revealed many repercussions of the private sector of stem cell research and therapy which the regulators and policymakers are unaware of. It is unquestionably valuable in assisting regulators and policymakers understanding the area where sound oversight is a miss. This includes (1) the aesthetic clinics which do not follow the stem cell guideline as they have their very own guidelines to follow and are not forthcoming about their stem cell therapies and (2) the overlapping authorities and platforms that confuse private entities as to the flow of regulative protocol, which include identifying the category of their products and services and registering (while acquiring licensing) within the necessary authority or platform. Failure to follow through the regulatory steps by some of these stem cell companies results in their illegal and unproven therapies and products marketed to the general public failing to factor in risks and side-effects. This is highly unacceptable as it violates their general welfare and rights.

This study can urge the MOH to re-assess their online platforms including other available documents within their jurisdiction to ensure there is consensus among them all. It is necessary to make them accessible by everyone, linking them based on the type of services or products (in this case a novel technology such as stem cell) and updating them regularly to safeguard the welfare of anyone requiring product and service verification. This study also contributes towards the general public, including patients and their families by promoting the need to ensure quality management of healthcare services which puts the patients and society in central importance while suggesting necessary protocols that gives due importance to the safety of individuals. It will also present the need for adequate consideration concerning ethical issues surrounding stem cell research and therapy for both the general public as well as scientists.

All research begins with the notion for further investigation on the previous studies. It is a never-ending cycle of justification, verification and more insight to what is unknown. This study is the further reflection of the previous studies done on stem cell research particularly the ethical and regulative perspective. Previous studies conducted in Malaysia were more preliminary, they answered inquiries about the deficiency of the current stem cell guideline but strictly from a legal perspective and ethical impact of hESC research from a religious perspective mostly. Globally there are many extensive studies done but none captured the situation in Malaysia specifically. This study is important therefore to fill the gap of what is not known in the current regulative measures of stem cell in Malaysia in respects to the many setbacks due to the unregulated setting. It may help in building more comprehensive bioethical debates in Malaysia.

1.7 Scope of the study

This study mainly focuses on the issues of growing stem cell research and technology in Malaysia along with the regulative repercussions, owing to the absence of policies and legal framework. The researcher began by investigating the earliest stem cell research and therapy beginning with the bone marrow and cord blood transplantations and moved towards the most current state-of-the-art therapies including the cardiovascular stem cell transplantation to the aesthetic medicine in which it is applied. This will provide us with the fundamental overview of the research and development of stem cell in Malaysia.

The regulatory impact of stem cell will be highlighting both the public and private sectors of stem cell research and therapy. It includes probing of the regulatory measures of all public research and healthcare facilities conducting stem cell research and clinical trials, the private entities conducting research and clinical trials and other healthcare facilities (medical centres and hospitals) offering stem cell therapies. Although, both the

public and private sectors of stem cell research are investigated, however, due to the matters of copyrights, privacy, confidentiality it is impossible to actually gather the type of information the researcher is seeking, especially involving regulative compliance. The public sectors are required to be apparent and detailed in their documentation without having to conceal data, but the same could not be said for the private sector especially since it involves delicate matter such as exploitations and non-compliance.

This study will also concentrate on the matters of ethical inquiry concerning stem cell research which is examined from an international perspective and compared with that of the Malaysian perspective to further understand and assess the significance if any. The data will be gathered based on what is recorded, documented and that is readily available on the many platforms such as journals, official webpages, the annual reports, and governmental publications (journal articles, policies, and legal documents). Apart from that, this study will exclusively seek the perspectives of (1) the research experts within the public research healthcare facilities, (2) the ethical deliberators who often debate on the many ethical concerns of stem cell research and therapies, and (3) the regulators or policymakers, mainly those attached to the MOH Malaysia. The respondents chosen for this study represented the different area of expertise. Their experience and direct involvement in stem cell research and policymaking are highly valuable.

There will be no attempts made to conduct any assessment of the lay people perspective as it requires large sampling and plus it is beyond the scope of my study. Public engagement regarding stem cell research and its technologies are still largely in the initial stages or infancy that their insight may not be exclusive considering that stem cell research is in early development. The study will not be inquiring the perspectives of any religious experts regarding their opinion on stem cell research. It is beyond this study to look into the viewpoint of any religious figures as they have been well discussed in

previous studies. Moreover, the aim of this study has been to examine the viewpoint of scientists, ethicists, and policymakers.

It is beyond the scope of this study to:

(i) examine the ethical concerns of embryo destruction in the extraction of stem cell

(ii) debate the many religious or metaphysical elements of 'when life begins'

(iii) deliberate which stem cell (embryonic, adult, induced pluripotent) is superior

(iv) evaluate if the public and private stem cell research laboratories and healthcare facilities are operating within the boundaries

(v) devise a policy or a legal framework which is appropriate to regulate the stem cell research and therapy

1.8 Limitation of the study

This study focuses mainly on three significant perspectives involving stem cell research and therapies in Malaysia. Firstly, the view of the scientists working directly on stem cell research not specifying on the type of cells worked with. In order to obtain a much holistic insight, both foreign and Malaysian scientists were interviewed. The foreign scientists researching stem cells (both embryonic and non-embryonic) presented their view of the matter judging from their personal experiences and based on the progress of their country (namely the United States, Australia, and United Kingdom), while the Malaysian scientists presented their own views of the research and ethics of stem cell in Malaysia.

Secondly, the view of the ethicists identified as frequent deliberators or experts on all ethical matters of stem cells and its many technologies. The identified ethicists are from foreign countries (namely the United States and Canada) and Malaysia. Since

Malaysia is a multicultural country with high regards of religion and multiethnicity, most of the ethical issues or concerns regarding stem cell research and technologies are currently viewed largely from a religious perspective narrowing the whole approach as a religious view. Therefore, the Malaysian ethicists perspective will combine both the interview conducted and their publications (Malaysian and international) as Malaysia is still in its early stages of such study and this would provide the necessary viewpoint, which proved useful for this study.

Finally, the views of the Malaysian policymakers who are in-charge of regulating the stem cell research and therapy in Malaysia, attached to the MOH Malaysia within the many divisions such as the Medical Development Division, the Medical Practise Division and the members of the NSCERT. Each of them is in-charge of the different sectors of stem cell such as public and private sector, therefore allowed me to gather the whole insight into one holistic approach.

These different perspectives deserve extensive attention as there is limited study done as of now, especially one that combines these perspectives for a more comprehensive review regarding the topic. The international scientists and ethicists involving the matters of stem cells were approached via emails and so were their agreements. The type of correspondence limited the number of respondents gathered as only selected few displayed interest and support while the rest were not. The Malaysian experts, both the ethicists and policymakers were approached firstly through phone calls and emails to confirm their willingness and availability, then they were visited in their offices to conduct the interview. The researcher had no intention to interview any religious experts or certain religious figures for their perspective on the ethical issues of stem cell research and technologies. I strongly believe there is already sufficient study done regarding the matters of the religious perspective of stem cell research.

Apart from the interviews conducted for data collections, there were also literature searches performed using the University of Malaya's library portal. The articles identified and retrieved was based on the available database subscriptions of the library and therefore could have easily disregarded the other relevant articles within other databases, which is being taken as a limitation of this study. In regards of the main data which is acquired through the interviews of experts, being a qualitative study, it is inevitable to have a sense of reflection of the moral reasoning and personal positions of respondents due to their religious conviction. It is necessary to take the appropriate care to identify and exclude them as 'expert perspective'.

As this study is mainly addressing the stem cell research and therapies' regulative issues the international comparison only includes the pioneering stem cell countries such as United States, United Kingdom, Australia as pioneering countries and Singapore for its geographical and ethnicity closest. Although it is useful to study the regulative progress of the developing countries, however, it is not within the objective of this study. Hopefully, regardless of these limits, this study could bring a more holistic approach to the ethical discourse in Malaysia especially relating to the matters of stem cell research and therapy.

1.9 Stem cell & its research

The study of ethics and regulation of stem cell research and therapy requires one to first to understand the details concerning stem cell research beginning with its derivation that triggered ethical controversy, which is briefly described in this section. Stem cell research first became popular when Gail R. Martin extracted embryonic stem cell (ESC) from mice in 1981 (Martin, 1981). The ethical controversy began with James Thomson and his colleagues extracting stem cell from human embryos in 1998 (Thomson et al., 1998). Figure 1.3 presents the discoveries and historical events involving stem cell

research towards understanding the progressive concerns and ethical debates. The research began early and involved bone marrow and hematopoietic stem cells. After 1998, they focused on embryonic stem cell (ESC) which raised serious ethical and political debates due to the use of human embryos (Wert & Mummery, 2003).

Stem cells are precursor cell which is undifferentiated with the ability to renew themselves through many mitotic divisions and capable of generating numerous mature cells (Cogle et al., 2003). There are three types of stem cells which are totipotent, pluripotent, and multipotent. In the human body, the totipotent and pluripotent stem cell is extracted from embryos while the multipotent stem cells are extracted from non-embryonic sources such as umbilical cord, foetal tissue and adult stem cells making them the ethical alternative (Fischbach & Fischbach, 2004). The extraction of the ESC from embryos often considered unethical because the process leads unintentional destruction of the embryo (Lo & Parham, 2009). In 2006, Shinya Yamanaka and Kazutoshi Takahashi generated iPSC from adult mouse fibroblast, which closely resembles the ESC (Takahashi & Yamanaka, 2006). In 2012, Shinya Yamanaka and John B. Gurdon were jointly awarded the Nobel Prize in Physiology or Medicine, "for the discovery of that mature cells can be reprogrammed to become pluripotent" (The Nobel Prize in Physiology or Medicine, 2012).

Even though there are known available sources of pluripotent stem cells such as (1) IVF surplus embryos from the many fertility clinics, (2) genetically 'abnormal' or 'dead' embryos (3) single cell biopsy method, and (4) the embryos with carcinomas which consented patients readily donate for research, some scientists still believe they need to generate more pluripotent stem cells due to its limited sources.

Figure 1.3: The historical timeline of stem cell research discoveries

1.9.1 Stem cell transplantation as therapy

This section intends to describe the preliminary stem cell research and its development that translated into transplantation that is also known as stem cell therapy similar to solid organ transplantation treating the many haematological disorders (López-Larrea et al., 2012). Stem cell transplantation is a broad term including techniques in the process of restoring or replacing damaged or diseased cells, tissues or organs for a therapeutic purpose to resume normal function of the body using many sources of stem cells (Trounson & McDonald, 2015).

Although to this date there are many techniques reported available, however, hematopoietic stem cells transplantation was developed over 50 years ago, to provide autoimmunity from common chemoradiation (Henig & Zuckerman, 2014). Eventually, it was applied in treating hematologic and malignant and non-malignant lymphoid cancers, including many other disorders. In the 1970s and early 1980s, the hematopoietic stem cells used stem cell isolated from the marrow of close human leukocyte antigen (HLA) matched from related donors (López-Larrea et al., 2012; Thomas, 2004). There are two types of stem cell transplantation, which are autologous and allogeneic. When patients receive their own stem cell (bone marrow, peripheral blood, umbilical cord) they are identified as autologous transplantations. In many cases, autologous transplantations are preferred as they minimize the risk of rejection or graft vs host disease (GVHD). The allogeneic transplantations, however, receives stem cells from closely matched donors either identical twins, siblings, family members or even unrelated donors. It also includes the umbilical cord blood of siblings that have been saved in cord blood banks for future use. Unlike autologous transplantations, allogeneic carries risks of rejection and GVHD (van Besien et al., 2003).

Although stem cell transplantation involving adult stem cells is well established, however pluripotent stem cells including ESC and iPSC still have a long way to go.

Despite, the controversies and ethical issues due to the use of human embryos for stem cell extraction, several pieces of researches have progressed towards clinical trials (Lo & Parham, 2009). The iPSC discovered a decade ago equally valuable in medical research creating an ethical alternative compared to using human embryo (Wright et al., 2014)

1.10 Organization of thesis

Chapter 1 offers the overview of this study. It began by highlighting the world stem cell policies and laws based on the map created in 2009. It then provides the background, the problem statement, the research objectives, and research questions of this study based on the current stem cell research and development in Malaysia. It explains the importance of the study and its significance. It also outlines the scope of study including its limitation, before offering some description concerning the definition, the history of stem cell research and the transplantation as the stem cell therapy.

Chapter 2 presents the Global Stem Cell Laws and Policies originally meant to bring up-to-date the 2009 World Stem Cell Map in Chapter 1. This chapter describes the variety of stem cell regulation specifically concerning the use of human embryos, that is adopted by countries around the world depending on their need. They are reviewed based on their regions such as North American, South American, European, African, Middle Eastern, Australasia, and Asian. It also included a trend review concerning the diverse laws and policies concerning stem cell research and its technologies at the end of this chapter.

Chapter 3 focuses on the literature review of this study which is evaluated first from the international standpoint by looking at previous studies done on the policy and regulatory aspects of stem cell research and its technologies. It also includes the ethical inquiry of the international authored publications. Then, it moves towards the Malaysian standpoint by evaluating the previous studies done on the Malaysian stem cell regulation. With that, the review of the publications written by Malaysian authors concerning stem cell research and its technologies to evaluate its ethical inquiry was carried out. The international stem cell research regulation and its oversight were studied and presented thematically while the Malaysian stem cell research regulation was examined chronologically beginning with the concerns raised by Malaysian scholars regarding stem

cell research in Malaysia. This made the search for the research gap straightforward and simple. At the end of Chapter 3, the research framework of this study is presented that describes the course of this study.

Chapter 4 presents the methodology chosen for this research which is presented in two parts. Part I concentrates on conducting interviews of experts involved in stem cell research and its regulatory aspects, while part II incorporates the ethical inquiry of the international and Malaysian publications written pertaining the ethics of stem cell research and its technologies. This chapter also describes that both quantitative and qualitative research method were deemed appropriate and narrowed down to the in-depth interview as the chosen method utilizing semi-structured interview of respondents chosen based on purposive sampling. It justifies the in-depth interview as the chosen method and explains the criteria applied for selection of respondents including the sample size. The interview guide is also presented within this section which correlates closely with the research objectives and research question. The profiles of the selected respondents for this study is presented in this chapter, together with the method of analysis which uses thematic analysis. The second part focused on the method involved in searching for the relevant international and Malaysian publications including literature review as the method of analysis. This section used both quantitative and qualitative analysis.

Chapter 5 offers empirical proof and the research finding of this study. The chapter began with the presentation of the status of stem cell development in Malaysia which was previously established as research problem in Chapter 1. Then followed by the analysis of verbatim transcripts of the in-depth interviews within its respective categories (i.e. foreign scientists, Malaysian scientists, foreign ethicists, Malaysian ethicist and Malaysian policymakers) which was used to derive the appropriate sub-codes, codes, and themes. Besides explaining how the themes were derived, it also presents the thematic map of the data *corpus* generated based on the inductive thematic analysis. The result also

includes the origin of stem cell regulation with the formulation guideline as revealed by the policymakers and a study of the interrelationship of the different experts, namely scientists, ethicists and policymaker, which was performed by first summarizing the sub-codes of similar experts and then presenting them in a Venn diagram for a better review. This is followed by the final result, that incorporated the publication search result compared between international and Malaysian publication from their ethical inquiry perspective. The results and findings intend to address the three objectives of this study.

Chapter 6 brings in the key discussion of the result being the vital element of the study. It begins by outlining the research findings and its relation to the research objectives and research questions of this study. It includes a detailed discussion to interpret the research findings and its impact, gathered from the in-depth interview of scientists, ethicists, and policymakers. It presents the significance and relevance of the themes chosen including several concerns identified such as grey area. It also includes a preliminary analysis of the international and Malaysian publications which is presented together with an evaluation of the nature of their ethical inquiry. This chapter fulfilled the three objectives of this study.

Chapter 7 concludes the study by relating the major findings of the study to the three research objectives and the research framework established since the beginning of this study. It includes the concluding remarks with a brief description of the research contribution with relevant recommendations. The chapter ended with some suggestion for future research in the field of stem cell research ethics and its regulatory aspects.

CHAPTER 2: GLOBAL STEM CELL LAWS & POLICIES

2.1 Introduction

This chapter will look into the current regulation and policies involving stem cell research and its technologies concerning countries around the world. The World Stem Cell Policies Map in Chapter 1 presented by Figure 1.1 was published eight years ago and definitely requires an update. Since 2009, some of the countries around the world have made progress changing their previous policies or adopting new ones to improve their stem cell oversight. Therefore, for the purpose of this study, the stem cell laws and policies of some of the countries around the world were revisited to update the previous 2009 map. The countries are visited based on their continent and geographical location, namely the North American region, South American region, the European region, the African region, the Middle Eastern region, the Australasian region and the Asian region. Apart from that, the stem cell laws and policies of the United States, the United Kingdom and Singapore are also examined in much detail within their respective region for a better understanding of their well-established regulation.

Figure 2.1 presents the new Global Human Embryonic Stem Cell Laws and Policies Map as of 2017, with a zoom in of the European region in Figure 2.2 for a clearer view. In the new map the colours represent several positions considering their human embryonic stem cell (hESC) research beginning with countries with complete restriction, countries that have strictly regulated its stem cell research with laws, countries with liberal approach but with laws on stem cells, countries without stem cell law but have some regulation and finally countries without stem cell laws and are unregulated. This is different compared to the Hoffman (2009) World Stem Cell Map but it is more comprehensive as it captures all the different approaches and positions efficiently.

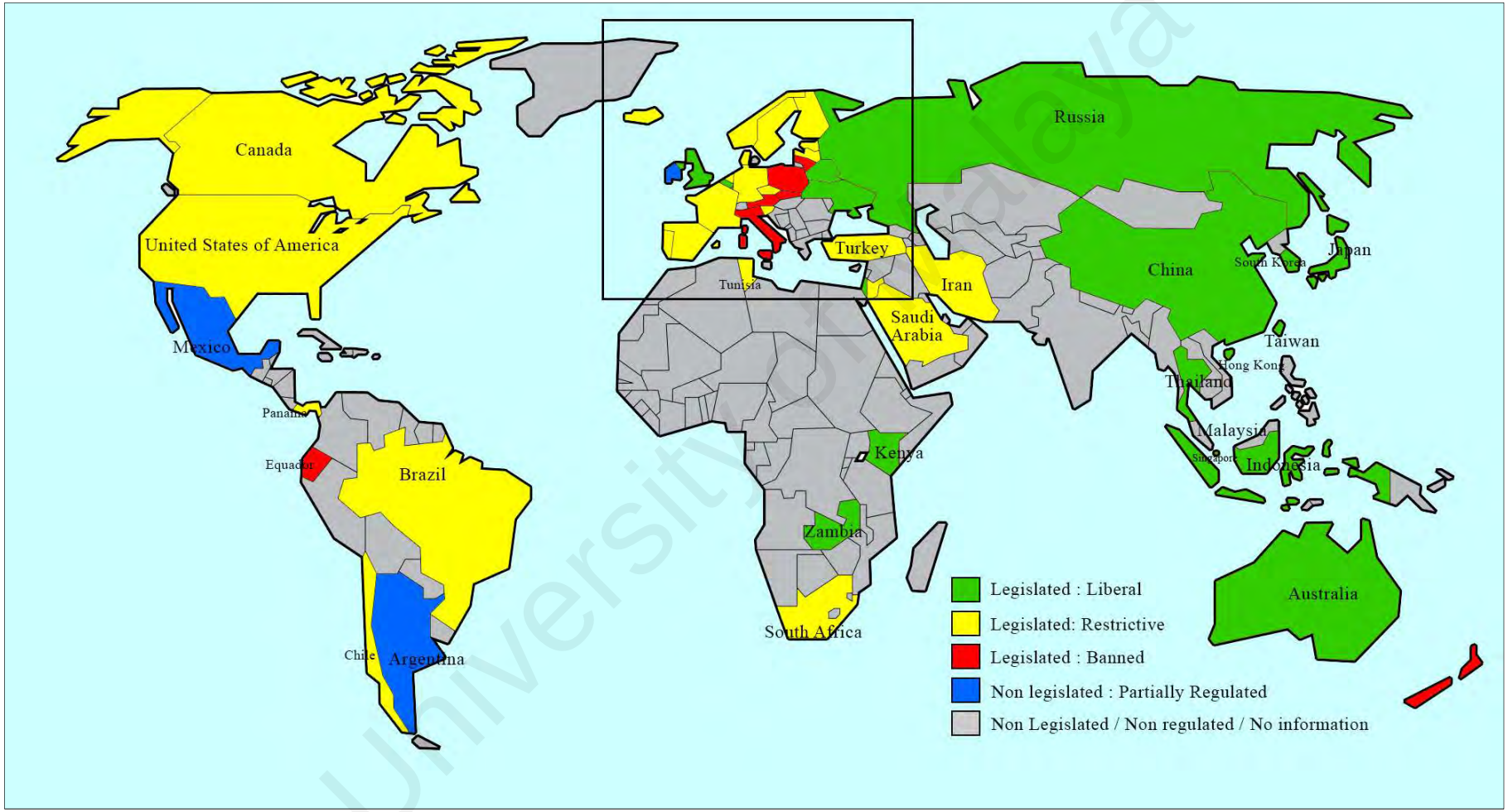


Figure 2.1: The global human embryonic stem cell laws & policies 2017.

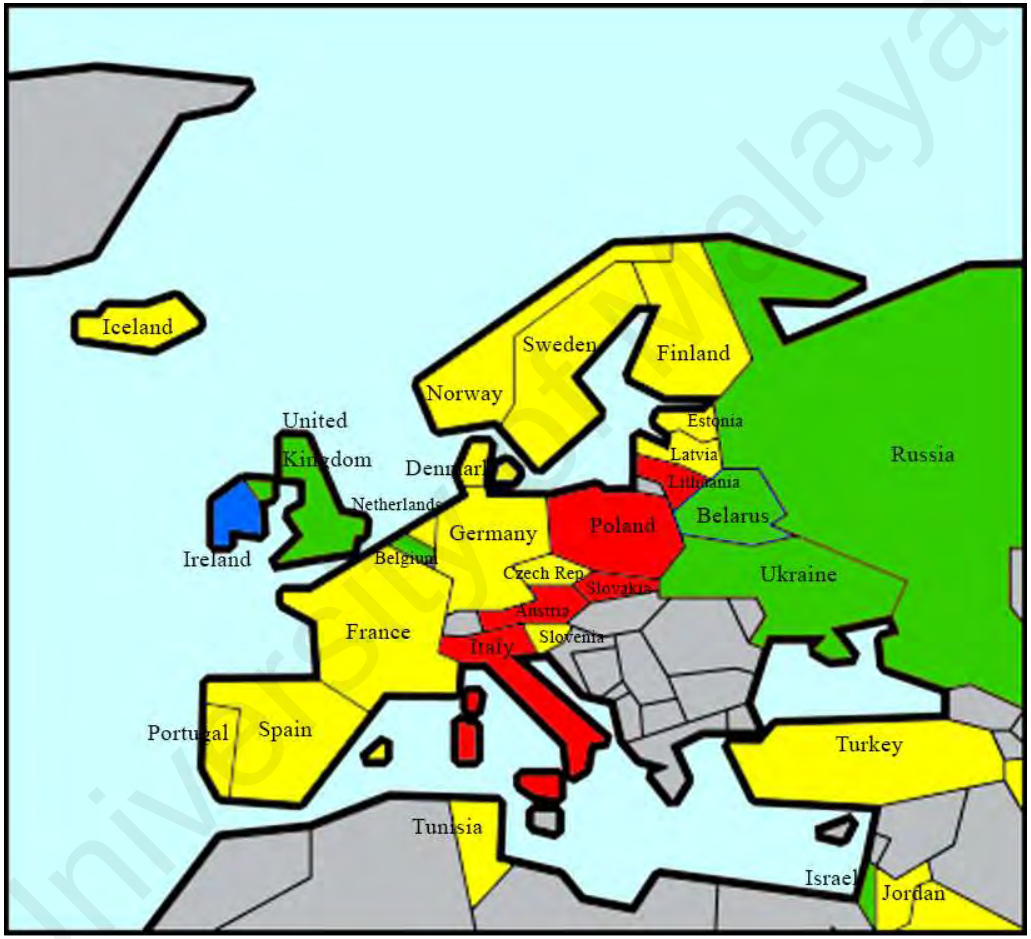


Figure 2.2: The zoom-in of the European region of the global human embryonic stem cell laws & policies 2017.

(Follow the legend in Figure 2.1)

2.1.1 North America

This region includes countries such as the United States of America, Canada, Mexico, Costa Rica, Honduras, Cuba, and Panama. The majority of the North American countries including Costa Rica, have banned both reproductive and therapeutic cloning but only recognized *in vitro* fertilization (IVF) for procreation purposes as allowed when considering research involving gametes (Palma et al., 2015: Svendsen & Ebert, 2008: Wheat & Matthews, 2004).

According to the 'International Compilation of Human Research Standard' released by the DHHS (2017) of the United States, Honduras has the 'Decree No.65-91' that covers some matters of research involving human subjects within its Article 175 and 176, while Costa Rica introduced its 'Regulatory Law of Biomedical Research No.9234' which underwent a revision in 2016 to regulate its biomedical research involving human subjects but both had no provision concerning stem cells or its research (Republic of Costa Rica, 2014; Republic of Honduras, 1996). While Cuba has no law or policies concerning stem cell, Panama has a few laws to manage their bioethical concerns including stem cells such as the 'Resolution No.390 Adopting the Operational Guide for Research Bioethics' in 2003, the 'Executive Decree Nº 1843' in 2014 on the 'National Research Ethics Committee of Panama', and the 'Executive Decree No.2' on stem cell in 2013 (DHHS, 2017; Republic of Panama, 2013, 2014). Although, there are some distinct regulative changes within the smaller North American countries compared to the previous 2009 map, however some of them are just within their initiation stage going through law making process and yet to result in enacted law.

In the 2009 map in Figure 1.1, the United States is represented as a light brown toned country, which only allows stem cell research on excess IVF embryos. This represents the policy position in 2009 during President Bush's administration, when he restricted federal funds for only research using cell lines extracted prior to August 2009.

However, when President Barrack Obama took office, he issued the Executive Order 13505 titled, "Removing Barriers to Responsible Scientific Research It Involving Human Stem Cells" that was signed on March 9th 2009 displaying support allowing all forms of stem cells that are permitted by law (NIH, 2016b). The new position allows research on hESC as long as they are within ethical borders as guided by the stem cell guideline issued by the National Institute of Health (NIH) in 2009 which remains up-to-date (NIH, 2016b).

The congress involved in stem cell policy as early as 1974 in the United States, when the Supreme Court decided that decisions about abortions are private, and between a woman and her doctor based on the case Roe v Wade in 1973 that ultimately legalized abortion ("Roe vs Wade," 1973). The case created large, political anti-abortion movement that is against research on embryos, because it became pivotal to all research involving human embryos. Members of the Congress were concern about the fate of the aborted embryos and foetuses and the research exploitations that may rise. The DHHS formerly known as the Department of Health, Education and Welfare (DHEW) placed moratorium on research involving living embryos (Wertz, 2002). In 1996 during Clinton's administration, the first major amendment associated with the use of federal funds for embryonic stem cell (ESC) research took place. The Dickey-Wicker Amendment authored by Representatives, Jay Dickey and Roger Wicker, was meant to restrict federal funds for the creation of human embryo(s) for research purposes or research in which a human embryo(s) are knowingly destroyed, discarded or subjected to risk of injury or death (Dickey & Wicker, 1996).

In 2001 President George W. Bush prohibited all federal funding of any research involving ESC which are derived after August 9th 2001. According to Bush, there are close to 71 ESC lines readily available for funding and thus there is no need for the creation of new stem cell lines. He also ascertained that research on adult stem cell (ASC) are not affected by this executive order (Murugan, 2009). When Barrack Obama became

the President in 2009, he revoked former President Bush's 2001 executive order and retained the Dickey-Wicker Amendment and introduced the Guidelines for Human Stem Cell Research in 2009. During Obama's administration, the NIH expanded the federal funding for stem cell lines meeting certain ethical requirements, such as discarded IVF surplus embryos, obtained from donors with informed consent, couples who did not receive financial aid or medical benefit or are forced or threatened (Dhar & Hsi-en Ho, 2009). The federal scrutiny of stem cell research began in 1996 which is mostly to address the funding issue but the administration change relaxed some of the imposed restriction to moderately permissive.

There are no federal laws enacted to either regulate human cloning or the hESC research in the United States up to now. The human cloning matter was brought into discussion many times through the bill 'Human Cloning Prohibition Act' introduced twice in the House but they were never passed (United States Senate, 2003, 2007). In 2002, President Bush in his speech for the United Nations made aware of his commitment to human dignity and human rights by re-joining the UNESCO reaffirming his position against human cloning (Bush, 2002). Although there is no federal law, but there are various position considering human cloning and hESC within the 50 individual states ranging from completely banned to a liberal approach (Gledhill, 2006; The Witherspoon Council on Ethics and the Integrity of Science, 2015; Vestal, 2008). Based on the The Witherspoon Council on Ethics and the Integrity of Science (2015) there are seven states that clearly forbids reproductive and therapeutic cloning (Arizona, Arkansas, Michigan, North Dakota, Oklahoma, South Dakota, and Virginia), ten states that forbids reproductive cloning but allows therapeutic cloning (California, Connecticut, Illinois, Iowa, Maryland, Massachusetts, Missouri, Montana, New Jersey, and Rhode Island) and one state that did not address the topic of reproductive cloning but have a legal decree concerning therapeutic cloning that forbids them which is Minnesota. While other states

addressed them indirectly by either restricting funding or by supporting and protecting doctors who oppose human cloning for ethical reasons (The Witherspoon Council on Ethics and the Integrity of Science, 2015). In 2013 the Supreme Court dismissed the request by scientists to block funding on stem cell research that uses human embryos that indicated immediate support by the federal government (Mears, 2013). In 2016, the NIH established the National Human Embryonic Stem Cell Registry to list out all the available cell lines that are entitled a for research fund by the NIH (NIH, 2016). Just before President-Elect Trump took office in 2016, Obama signed '21st Century Cures Act' into law the which includes stipulation to ensure the timely regulatory review of regenerative therapies including the cell therapies made possible by stem cell therapy research (United States Congress, 2016).

While in Canada, the growing stem cell research urged the Canadian Institute of Health Research (CIHR) to form the 'Ad Hoc Working Group on Stem Cell Research' in 2000 comprised of professionals from a range of expertise to guide the CIHR regarding funding issues. They released a report which later became the basis of the 'Guideline for Human Pluripotent Stem Cell Research' which was published in March 2002 to make sure that stem cell research is conducted ethically. All stem cell research applications are reviewed by the Stem Cell Oversight Committee (SCOC) within the CIHR (CIHR, 2014). The stem cell guideline was reviewed several times such as in 2005, 2006, 2007 and 2010, before it was combined into the second edition of the 'Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans' in 2014 (DHHS, 2017; The Witherspoon Council on Ethics and the Integrity of Science, 2012).

In March 2014, the Canadian government enacted the 'Assisted Human Reproduction Act' that addresses the matter of stem cell derivation and human cloning (Parliament of Canada, 2017). According to the act, both reproductive and therapeutic cloning are banned while hESC are allowed only on surplus IVF embryos. The act

underwent several revisions since and it up-to-date as of 2017. The CIHR launched the national registry of hESC to list all the available cell lines retrieved from human embryos using government funding consistent with the 'Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans' (2014) or before the December 18th 2014 to reduce the urgency to create new cell lines (The Witherspoon Council on Ethics and the Integrity of Science, 2012).

Mexico's General Health law introduced originally in 1983 did indirectly address two major concerns of stem cell research which partially regulates its stem cell research and therapies. First, the use of human organs, tissues, and cells but only the hematopoietic stem cell leaving out the embryonic stem cell (Palma et al., 2015). Second, the issue of false advertising of treatments and clinical interventions that do not have valid proof or that conforms with the five Mexican standards. Although this law prevents private entities from prematurely publicizing their stem cell therapies that exploit patients, and oversee the hematopoietic stem cell research, there is very little effective oversight. (Arellano, 2012; Council et al., 2014). They require formal complaint filed on the particular entity to take action (Palma et al., 2015).

The independent regulatory body of the Mexican MOH known as COFEPRIS (Federal Commission for the Protection against Sanitary Risk) has the exclusive right to oversee and regulate stem cell research and have the guideline NOM-253-SSA1-2012 that focuses on the use of human blood and its components for research purpose, but no standard guideline for their pluripotent stem cell. Their lack of funding and qualified experts was identified as the main challenges. The law underwent a revision in 2013 to add the provision that all procedures which include treatment using cells will bear a recovery fee without cost to patients but it remains incomplete. Accepting their regulatory deficiency, Palma et al. (2015) suggested the United Kingdom's Human Fertilization and Embryology Act (HFEA) be the best benchmark for the Mexicans to follow.

2.1.2 South America

The South American countries, such as Argentina, Uruguay, Peru, Columbia, Ecuador, Bolivia, Venezuela, Trinidad and Tobago, and Chile do not have any laws or act enacted specifically to overlook their stem cell research but research in these countries are not explicitly banned. This concurs with the map in Figure 1.1 and is accurate as of 2017, but several nations have taken step towards regulating their stem cell technologies such as Chile and Uruguay. Most of them have banned both reproductive and therapeutic cloning but only recognized IVF for reproductive purposes as allowed when considering research involving gametes (Palma et al., 2015; Svendsen & Ebert, 2008; Wheat & Matthews, 2004). However, individually some nations have begun addressing some of the issues related to stem cell through small changes in their current regulations which will be reviewed in this section.

In Chile, therapeutic and reproductive cloning and funding of its research is prohibited by the Bill No. 1993-11 'On Scientific Research on the Human Being, Its Genome, and Prohibit Human Cloning' introduced originally by the MOH in 2006 and amended last in 2013 (Congress of Chile, 2013; UNESCO, 2004). Based on the bill, the creation of hESC lines or even organs will be allowed to continue if they are meant for therapeutic diagnosis and scientific purpose. The creation of new embryos specifically for research purpose to extract stem cell is forbidden (The Witherspoon Council on Ethics and the Integrity of Science, 2012). In 2005 the Brazilian House of Representatives sanctioned the 'Biosafety Act' that legalized hESC using nonviable and surplus IVF embryos that have been stored three or more years (Leite, 2006). Although, the decision was contested through a legal suit, the Federal Supreme Court ruled in favour of the continuation of the research as long as they use frozen embryos of three years or longer since the fertility clinics will be discarded them anyway (Zorzanelli et al., 2017). The

Biosafety Act also banned both the reproductive and therapeutic cloning (Civil Cabinet, 2005)

In Uruguay, the National Ethics Committee for Human Research and the Ethics Committee of the Medical College jointly working to regulate their stem cell research since 2014 but have yet to result in anything permanent (Palma et al., 2015). While Argentina has its Transplant Act (1993) partially regulating its stem cell aspects. The act which has some provisions on cellular therapies but mostly on hematopoietic stem cell. Realizing that their current regulation's shortcomings, the Argentinian MOH passed an internal regulation within the jurisdiction of the act by issuing Resolution 610/2007 (supplemented by Regulatory Decree 512/95). It established the National Regulatory Authority on organ, tissue and cell transplantation (INCUCAI) as the governing body on cell therapy and all actions that involve human cells for therapy or transplantation in humans that is outside of hematopoietic stem cell which will be recognized as "experimental practice" until it is reviewed as harmless and potent. The INCUCAI also introduced a standard protocol or Guideline based on the Resolution 19/2012 considering the conditions and techniques for cellular products that agree with the international standards of Good Laboratory and Manufacturing Practices (de Arzuaga, 2013; Palma et al., 2015).

Stem cell research in Peru is regulated by the 'General Health Law No.26842' allows IVF for reproductive purposes but prohibits reproductive and therapeutic cloning based on its Article 7. Except for forbidding the creation of human embryos for stem cell extraction, there are no other specific provision concerning stem cell (DHHS, 2017). While Jamaica, Grenada and Guyana have no laws or policies enacted to regulate their stem cell research, Ecuador introduced the 'Organic Law of Donation and Transplantation of Organs, Tissues and Cells' in 2012 which regulated the hematopoietic stem cell and non-embryonic stem cell research (Republic of Ecuador, 2012). Research that involves

human embryos are completely against the Ecuador Constitution whereby their second provision of the Article 45 states, “the state shall recognize and guarantee life, including care and protection from the time of conception” protecting them from any form of exploitation including research (DHHS, 2017; Republic of Ecuador, 2008).

2.1.3 European Region

In the European region, all nations have banned reproductive cloning but not all of them have laws specifically enacted to regulate stem cell research. Countries like Denmark, Iceland, Norway, Latvia, Slovakia, Slovenia, Estonia, Germany and Netherlands do not specifically prohibit hESC research but they definitely banned both therapeutic and reproductive cloning (Svendsen & Ebert, 2008). The Nordic countries Norway, Denmark, Iceland, Sweden, and Finland all have a somewhat similar approach to regulating stem cell research, which began with regulating artificial fertilization and indirectly addressing research involving human embryos.

Norway is one of the first countries to introduce legislation on the matters concerning assisted reproductive technology through its 1987 ‘Act on Artificial Insemination and Fertilization’ after the Norwegian Parliamentary Committee of Health and Social Affairs recommended the government to legislate appropriate law on the matter a year after Norway’s first test tube baby in 1984 (Nordisk Ministerråd, Nordisk Råd, & Nordic Committee on Bioethics, 2006). The 1987 Act added some restrictions on assisted reproduction in Norway. In 1994, the ‘Act Relating to the Application of Biotechnology in Medicine’, was introduced based on the two reports by the Ethics Committee and the Labour government in 1993 (Norwegian Government, 1994). The 1994 Act underwent two revisions separately to include restriction on therapeutic cloning and stem cell research using IVF embryos in 2003 (Norwegian Government, 2004) and to lift the ban previously imposed making research on surplus IVF embryos including the

importation of stem cell lines legal as of January 1st 2008 (Francis & Ziebertz, 2011). In 2008, the Norwegian government also passed the 'Act on Medical and Health Research' which came into force in 2009. The purpose of the Act is stated in the purpose provision in Section 1 of the Act: "The purpose of the Act is to promote good and ethically sound medical and health research" that includes provision concerning respect to human dignity especially on research involving human material and subjects" (Norwegian Government, 2009).

While Iceland first introduced the 'Act on Artificial Fertilization' in 1996 that banned both therapeutic and reproductive cloning in its Article 12 but allowed some research on human embryos as long as they are within the reproductive subject area with the provision in Article 11 (Icelandic Ministry of Welfare, 1996). However, in 2008 they amended the 1996 Act relaxing the restriction on human embryonic stem cell research by allowing the use of surplus *in vitro* embryos as long as approved by a Bioethics Committee. It also permits Minister licensed scientists to create stem cell lines using somatic cell nuclear transfer (SCNT) only for therapeutic purpose with strict compliance to the standard outlined by the Minister and must not be over fourteen days old. It clearly stated that reproductive cloning using SCNT is prohibited (Icelandic Ministry of Welfare, 2008).

Denmark originally does not have laws on stem cell specifically but they enacted the 'Act on a Scientific Ethical Committee System and the Handling of Biomedical Research Projects' in 1992, which banned all forms of cloning (Danish Parliament, 1992). The regulation involving embryo research meant for reproduction was then moved to the 'Act on Medically Assisted Procreation in Connection with Medical Treatment, Diagnosis and Research' in 1997. The 1997 the Act underwent its first amendment in 2003 relaxing the previous law, allowing embryonic stem cell research using only

consented surplus IVF embryos. Since then, it is regularly revised with 2017 being the most recent (Ariff & Hin, 2005; Danish Parliament, 1997).

Sweden is the first country to legislate an act to regulate the infertility treatment through their 'Insemination Act' introduced in 1985 (Swedish Government, 1985). Subsequent to that, in 1989, they introduced the 'In Vitro Fertilization Act' (Swedish Government, 1988). Their stem cell research was never banned. In the absence of a law, stem cell research was permissive. The first law that was enacted to specifically regulate embryonic research, was the 'Activities Involving Human Eggs for Research or Treatment Purpose Act' 1991 which permitted research using human embryos that are not over fourteen days old (Swedish Government, 1991). Their liberal outlook also brought in the 'Biobanks Health Care Act' in 2002 to manage biobanks in healthcare considering human biological material and their storage (Swedish Government, 2002). The 1985 'Insemination Act' then underwent revision in 2002 and 2005 only to be repealed by the 'Genetic Integrity Act' introduced in 2005 (Swedish Government, 2005). The 2005 Genetic Integrity Act is to "protect the integrity of human beings" and restrict particular development in biotechnology meant for healthcare purpose. It includes a provision concerning matters of artificial fertilization, cloning, genetic engineering as well as stem cell. According to the 2005 Act, scientists are permitted to create embryos using SCNT. Sweden also has the 'Act Concerning the Ethical Review of Research Involving Humans' (2003:460) that is meant to offer guidelines for research that involves human subjects and their biological material (Swedish Government, 2003).

Unlike Norway, Sweden, and Iceland, Finland's regulation did not begin by addressing the artificial fertilization, instead, they enacted the 'Medical Research Act' in 1999 that applied to the medical research with some provisions on embryo research. Based on the Act, Section 13 of Chapter 3, the creation of embryos strictly for research purposes is banned. According to the 2005 report by the Finnish National Ethics

Committees (2005) embryos created using SCNT does not qualify based on the definition of embryo in the 1999 Act, “an embryo resulting from fertilization living cell mass that has not implanted in a woman's body” making them permitted. However, research on surplus IVF human embryos is allowed but should not be more than fourteen days old. This only includes embryos that have been stored up to 15 years and those passed that point are to be destroyed (Finnish Government, 1999). The 1999 Medical Research Act underwent several amendments in 2004, 2009, 2010, and 2015 with 2015 being the most recent adding provision regarding consent withdrawal (Finnish Government, 2015). The ‘Act on the Medical Use of Organs and Tissues’ 2001 states that “Embryos can only be used for fertility treatment or medical research” as stipulated in Section 6, Chapter 3. The Act also outlines restrictions considering the collection, storage and testing of human tissues and cells which includes hematopoietic stem cells and embryonic stem cells (Finnish Government, 2001).

Unlike the United States, the United Kingdom has taken a permissive approach which allow stem cell research using the many sources of stem cell including surplus embryos produced through IVF and those created using SCNT but within the 14-days old rule. The HFEA established in 1990 under the Human Fertilization and Embryology Authority and the Human Reproductive Cloning Act of 2001 are the current governing policies regarding stem cell in the United Kingdom. The HFEA (1990) was sanctioned originally to regulate the practice of IVF including monitoring and licensing of the fertility clinics in the United Kingdom and the creation, use and storing or disposal of embryos produced *in vitro*. However, it underwent several amendments since then, to finally result in the Human Fertilization and Embryology Act (2008).

In 1991, the amendments which does not extend to the Northern Ireland, the application for licenses, and relaxing the requirement relating to consent of the storage (gametes and embryos) already in store; 1994, the expedition sanctions relating to

abortion (not exceeding 24 weeks) and the application of parental order in the case of surrogacy; 2001: the Human Fertilization and Embryology (Research Purpose) Regulations which extend reasons for permissible research involving stem cells and cell nuclear replacement; 2003: the Human Fertilization and Embryology (Deceased Father) Act came into force which allows deceased man to be registered as father or children born through artificial reproduction technique (ART) after; 2007: the major review of the Human Fertilization and Embryology Act 1990, updating and amending the original act" (United Kingdom Parliament, 2008).

In Ireland, research involving human embryonic stem cell, both reproductive and therapeutic cloning which includes SCNT were all prohibited originally, prior to 2009. It was banned based on the proposed Article 40.3.3 during the 8th Amendment of the 1983 Irish Constitution, that stated, "The State acknowledges the right to life of the unborn and, with due regard to the equal right to life of the mother, guarantees in its laws to respect, and, as far as practicable, by its laws to defend and vindicate that right" which indirectly protected the right of all unborn child. The action was a result of the Irish pro-life believers that feared the famous American case, Roe v Wade in 1973 ("Roe vs Wade," 1973) that allowed abortion in the United States, would also seep into the Irish population in the future. Therefore, they proposed the 8th Amendment of the Irish Constitution. The provision made abortion as illegal (Ireland, 1983). The Attorney General questioned the integrity of the term 'unborn' used in the proposed article claiming it to be unclear and flawed (O'Carroll, 2013).

The 1992 case 'X' that involved a 14-year-old rape victim wanting to abort her pregnancy as a result of the rape shined some light into the issue of the unborn. The Supreme Court ruled in favour of the girl, taking into consideration of the health of the mother, despite the High Court ruling against her. The case questioned the right of the unborn and made clear that it was not absolute (Staunton, 2013b). The Constitution

Review Report in the 1996 also agreed that there are complications regarding the Article 40.3.3 and it was unclear if it actually protected the rights of *in vitro* embryos (Department of Health, 2005; Staunton, 2013a). The unclear regulation was addressed by the Irish Department of Health (2005) in their report on 'The Commission on Assisted Human Reproduction' with suggestion of an appropriate legislation within the subject area of cloning and stem cell. It included a detailed outline of the proposed legislation with specific recommendations (Staunton, 2013b). Coincidently, the courts were left to establish the grounds on the matter of Article 40.3.3 especially through the case Roche v Roche involving a divorced wife seeking to implant her previously created *in vitro* embryos against her divorced husband's wishes. The Irish High Court and the Supreme Court both ruled out the argument that the Article 40.3.3 of the Irish Constitution protected the embryos *in vitro* ("Roche v Roche," 2006; "Roche v Roche," 2009). The 2009 Supreme Court ruling evidently revealed that there is no legal restriction on embryonic stem cell research (Staunton, 2013b).

The gap in the Irish regulatory aspects especially regarding the importation of stem cell lines led to their scientists and scholars to find their own way for the sake of research. These scientists and their university were left to formulate their very own stem cell guidelines. This led to two established institution of higher learning in Ireland, the University College of Cork and Trinity Dublin College, to establish their very own stem cell guideline as recommended by their governing body (Irish Stem Cell Foundation, 2010). Right now, the human embryonic stem cell research as well as cloning in Ireland is not prohibited. The gap in the regulation continue to permit the research until specific law and legislation is devised to better regulate the technology involving embryos.

In Belgium, stem cell research regulation began in 2003 with the introduction of 'Act on Research on Embryos in Vitro' (2003) which permits research with therapeutic purpose that is meant to increase medical knowledge. Based on the Act, embryonic

research is allowed as long as they involve IVF surplus embryos that are not more than fourteen days old. However, it does not specifically forbid creating embryos for research purpose, permitting therapeutic cloning including SCNT (Belgian Parliament, 2004). It is a case of 'everything that is not forbidden is allowed'. Reproductive cloning is clearly banned. Their regulation on embryonic stem cell research made them very liberal considering human embryonic stem cell research (Pennings, 2003; Wheat & Matthews, 2004).

Netherlands introduced the 'Embryo Act' (*Embryowet*) on 20th June 2002 to restrict therapeutic and reproductive cloning, the use of embryos over fourteen days old, creating chimera or human-animal hybrids and to outline standard guideline regarding embryonic research. The Act came with a five-year moratorium on embryos created specifically for research purpose that require re-evaluation to confirm the status at the end of the tenure. In 2007, the evaluation by the Dutch cabinet resulted in no change. In 2013, the Embryo Act was revised to acknowledge that only excess embryos donated from IVF are permitted for research, making SCNT completely forbidden (Dutch Government, 2013; NRC Media, 2013). All research that involves human material or subject are required to be reviewed by the Medical Research Ethics Committee or the Central Committee on Research Involving Human Subjects (CCMO) for approval. The clinical trials involving human subjects are regulated by the 'Medical Research Involving Human Subject Act (WMO)' that was first introduced in 1999 (Dutch Government, 2006). It was revised in 2006 to ensure it follows the European Unions (EU) Clinical Trial Directives (2001/20/EC) which mostly to address the issue of drug trials in the Netherlands (Van Doorn et al., 2015).

In the European region nations with very restrictive regulation considering human embryonic stem cell research are Lithuania, Germany, Austria, Poland and Slovakia. Lithuania banned all human embryonic stem cell (HESC) research including all

forms of cloning. Their 'Ethics in Biomedical Research No. VIII-1679 Act' is extremely strict considering embryonic research. It was first introduced in 2000 and had undergone several amendments since (2004, 2007 and 2015) but remains the most restricted nations on the matters of stem cell research (Seimas of the Republic of Lithuania, 2015). Similar to Lithuania, Germany also imposes heavy restriction on research involving embryos. According to the paragraph 2, Article 2 of their Constitution (*Grundgesetz*) embryos have legal status and their rights are inviolable ultimately protecting them. It still gives freedom to scientists to carry out research within restrictions. The 'Embryo Protection Act' (*Embryonenschutzgesetz)* introduced in 1991 considers embryonic stem cell extraction a punishable crime (Bundestag of Republic of Germany, 2011). The 'Stem Cell Act' (*Stammzellgesetz*) introduced in 2002 prioritises ASC while ESC research is only permitted on imported cell lines based on conditions approved by the German parliament. In 2008, the Stem Cell Act was amended to remove the 'cut-off' date that recognized only cell lines retrieved between 1st January 2002 and 1st May 2007. The amendment accepted that German scientists working on hESC abroad will no longer be considered as crime and outlined that the hESC lines will 'only be used for research' especially if they prove useful in improving medical and scientific knowledge (Bundestag of Republic of Germany, 2017; The Witherspoon Council on Ethics and the Integrity of Science, 2012).

Unlike Germany, hESC research, therapeutic and reproductive cloning are all banned in Austria. The 'Reproductive Medicine Act' (*Fortpflanzungsmedizingesetz*) introduced first in 1992 forbids stem cell extraction for research purpose but research on imported cell lines is permitted since it was not addressed by the Austrian legislation. The Act underwent several amendments, with 2015 being the most recent to add provision regarding artificial insemination for lesbian couples. According to the Act, procedures involving embryos are only applicable to heterosexual and married couples for only

reproductive purpose making embryo donation for other reason completely banned (Austrian Parliament, 2015; Busardo et al., 2014).

In Poland, hESC research and reproductive cloning are banned. They have the 'Medical Profession Act' (1996) which has provision on the regulation concerning medical experiments on human among its Articles 21 to 29. Its Article 26 actually 'conceived children' or embryos are not allowed to be experimented scientifically, which ultimately makes embryonic stem cell creation completely against the Act (Polish Government, 2003). Human cloning is also prohibited in Poland since they signed in the European Council's Additional Protocol on the 'Convention on Human Rights and Biomedicine' and the Prohibition of Cloning Human Beings in 1999 (Busardo et al., 2014). Ultimately, research involving human embryos were deemed violation to the Polish penal and medical ethics code (The Witherspoon Council on Ethics and the Integrity of Science, 2012).

Slovakia's 'Law on Healthcare No. 277/1994' bans all research involving embryos which is not meant therapeutically for their own betterment. Therefore, technically any research involving embryos with 'therapeutic purpose' should be permitted considering other requirements. The law also clearly forbids therapeutic and reproductive cloning (Busardo et al., 2014; Slovakian Goverment, 1994). This make human cloning a crime based on the 1991 Slovakian Penal Code amended in 2003 that reads, "Any person who performs any intervention seeking to create a human being in any stage of development genetically identical to another human being, whether living or dead, shall be sentenced from 3 to 8 years of imprisonment or shall be punished by a prohibition of activity or by a pecuniary penalty" (Slovakian Goverment, 2003). Specifically, there are no stem cell laws in Slovakia but being a member of the European Union, they made the necessary amendment on the European Council's Additional Protocol on the Convention on Human Rights and Biomedicine and the Prohibition of

Cloning Human Beings banning all human cloning. Slovenia however, forbids both cloning techniques but permits embryonic stem cell research but only on surplus IVF embryos that are within fourteen days old as legislated by the 'Law on Biomedically Assisted Fertilization' in 2000. The law also bans creation of embryos for research purpose (Slovenian Government, 2000).

Ukraine and Russia have adopted a liberal position regarding stem cell research. In both this countries, reproductive cloning is banned but in Ukraine embryonic stem cell research and therapeutic cloning are not explicitly banned (Ukraine Parliament, 2004). Stem cell treatment is recognized and legal in Ukraine (Dario Siniscalco, 2015). It is regulated by the Ministry of Health Protection of Ukraine Order (Ukraine Parliament, 2012). Effective since 2012, the Order is mostly to regulate licensing conditions for cord blood and tissue banks. Brown (2012) implicated Ukraine as a nation that promotes stem cell tourism by actively marketing stem cell therapies. In Ukraine, stem cell therapies using cord blood, bone marrow and foetal stem cell is allowed providing each treatment acquires informed consent from its patients. Their law on 'Organ and Other Human Material Transplantology', No. 1007-XIV introduced originally in 2007 (updated in 2014) outlines the condition and regulation concerning transplantation and stem cell therapies (Ukraine Parliament, 2014). In Russia, therapeutic cloning is forbidden but not embryonic stem cell research. They placed a five-year temporary cloning ban in 2002 through the 'Law on Temporary Prohibition of Human Reproductive Cloning' (2002) which includes importation and exportation of cloned embryos (The Federal Assembly of the Federation of Russia, 2002). Although the ban expired in 2007 and the suspension was lifted, there were no authorized research involving cloning. In 2009, the Russian Ministry of Health Care and Social Services announced that they will extend the cloning ban for five more years (Gazeta.Ru, 2009). In 2016 the Russian Federation introduced a new legislation, the 'Biomedical Cell Products' which came into force on 1st of January

2017. It regulates biomedical cell products and their research including clinical trials and important and exportation of these products (The Federal Assembly of the Federation of Russia, 2017). Similar to Ukraine, C. B. Cohen and Cohen (2010) also implicated Russia as a nation that supports stem cell tourism with a discussion of its repercussion involving several cases that gone wrong.

Spain did not ban embryonic stem cell research or therapeutic cloning but it banned reproductive cloning. Based on the Spanish Law 35/1988 on assisted reproductive technology, between 1988 and 2003, research on embryos were only permitted on 'non-viable' ones (Spanish Government, 1988). In November 2003, the Law 35/1988 was amended and introduced as the Law 45/2003, which permitted research on surplus IVF embryos (Government., 2003). In 2006, the Law 35/1988 and its amended version Law 45/2003 were both repealed when they brought in the Law 14/2006 on 'Techniques of Assisted Human Reproduction'. The new 2006 law outlined the general requirement for assisted reproduction and added provisions on using germ cells for research purpose, informed consent, the use of embryos of up to fourteen days old, and that all research project involving embryos need prior approval of the National Committee of Assisted Human Reproduction (Spanish Government, 2006). They also introduced the Law 14/2007 on 'Biomedical Research' to allow SCNT in its Article 33, Chapter 1 (Spanish Government, 2007).

France passed its first legislation on bioethics in 1994 that bestowed a legal status to the human body while outlining civil and public health code that guarantees the respect of human body (The Witherspoon Council on Ethics and the Integrity of Science, 2012). The law prohibited research on human embryos. The Bioethics law underwent an amendment in 2004 to add provisions on research involving embryos and embryonic cells. According to the Bioethics Law 2004, reproductive cloning is forbidden just as creating embryo for research or therapeutic purpose using SCNT. It also bans all research

using human embryos, but allows research on donated surplus IVF embryos within 8 days old as approved by the France's Agency of Biomedicine (France Government, 2004). The compromise between protecting embryo right and allowing research on surplus embryos were focused by the French government hoping to liberalize the law considering embryonic stem cell research, but the review in 2011 resulted in preserving the 2004 law (France Government, 2017).

Estonia has its 'Artificial Insemination and Embryo Protection Act' first introduced in 1997. It allows embryonic stem cell research but only on surplus IVF embryos within fourteen days donated by consented couple. Creation of embryos solely for research through SCNT is forbidden (Estonian Government, 2014). Latvia does not have specific law on human embryonic stem cell research but it has the 'Law on Sexual and Reproductive Health' introduced in 2002 (amended in 2004) that allows ESC research while prohibits both therapeutic and reproductive cloning ((Saeima) Parliament of Republic of Latvia, 2004). Similarly, Portugal also allows embryonic stem cell research but banned reproductive and therapeutic cloning. Their 'Law on Assisted Reproductive Technologies' No. 32/2006 states that research on embryos is permitted if it is considered as beneficial to mankind as agreed by the National Council of Medically Assisted Procreation. It also forbidden to create embryos for research purpose however, research using 'non-viable' embryos and those surplus IVF embryos donated by consented couples are permitted (Portugese Government, 2006).

Belarus has no law specifically formulated on stem cell but it permits stem cell research with its international center for stem cell technologies and stem cell therapy clinics being established (Republic of Belarus, 2014). They also have the 'Law No.341-3 on Assisted Reproductive Technology (ART)' introduced in January 2012 that allows embryos used for research purpose but no other details considering the conduct (Republic of Belarus, 2012). ESC research in Czech Republic is only allowed using IVF surplus

embryos and imported cell lines. It is clearly stated in their 'Act on Research on Human Embryonic Stem Cells and Related Activities' formulated in 2006. Although, the Act banned reproductive cloning but it had no clear provision on therapeutic cloning. Unlike most nation that adopted the 'not more than fourteen days old embryo' Czech Republic adopted a seven day as mention in Section 8 of Chapter 3 of the Act (Parliamentary of the Czech Republic, 2006).

2.1.4 African Region

In the African region, only four countries enacted laws meant to regulate stem cell research specifically or with some provision on the subject matter, namely South Africa, Tunisia, Kenya and Zambia. The rest such as Sudan, Nigeria, Ghana, Zimbabwe, Mozambique, and Ethiopia have yet to work on adopting any legal framework concerning the technology. South Africa introduced the National Health Act 2003 that repealed the 1983 Law on Human Tissue which originally banned human cloning (Parliament of the Republic of South Africa, 2003; Republic of South Africa Parliament, 1983). According to the National Health Act, reproductive cloning is prohibited but therapeutic cloning is permitted subject to the minister's approval. The importation and exportation of ESC line are only allowed if authorized by the minister. The Act also permits research on ESC provided they are within fourteen days old (Parliament of the Republic of South Africa, 2003; Pepper & Slabbert, 2015). Kenya introduced its Health Bill in 2016 while Zambia introduced its National Health Research Act in 2013 which can be seen as an initiative towards regulating public healthcare with some acknowledgement of cloning, human tissue including stem cell (Parliament of Kenya, 2016; Parliament of Zambia, 2013).

Tunisia does not ban hESC research specifically but both reproductive and therapeutic cloning is banned. They introduced the Law 01-93 of 2001 on Reproductive Medicine that was meant mainly to regulate its ART similar to many European countries

(Tunisian Parliament, 2001). According to the Article 9 of the Reproductive Medicine law, it is banned to create embryos through IVF or other methods for research purposes. This provision ultimately banned derivation of hESC and therapeutic cloning using any method including SCNT (Van Pham, 2016b). It also means that research on imported cell lines is allowed. The Article 11, states that couples can store their embryos and gametes for therapeutic purposes only for reproductive reasons while Article 14 completely bans embryo or gamete donation (Tebourski & Ammar-Elgaaied, 2004).

2.1.5 Middle Eastern Region

The Middle Eastern region is made of many countries namely Syria, Turkey, Israel, Iran, Iraq, Saudi Arabia, Egypt and others, but only Israel, Iran, Saudi Arabia, and Jordan have some regulation concerning stem cell research. Israel allows ESC research but with some restrictions. Their introduced the 'Prohibition of Genetic Intervention (Human Cloning and Genetic Manipulation of Reproductive Cells' Law 5759-1999 which is meant to forbid reproductive cloning (Knesset (Israel Parliament), 1999). The 1999 law remained effective until 1st March 2009. It underwent a revision in 2016 and was known as the 'Prohibition on Genetic Intervention (Human Cloning and Genetic Change in Reproductive Cells)' 5776-2016 (Knesset (Israel Parliament), 2016). They have a national permissive stem cell research policy based on their Jewish law which supports the creation of embryos using IVF and the extraction and use of stem cell specifically for research purpose as also reported by the Bioethics Advisory Committee of the Israel Academy of Sciences and Humanities in 2001 (Bioethics Advisory Committee of the Israel Academy of Science and Humanities, 2001; Cherry, 2013; Flynn & Matthews, 2010; Holland et al., 2001).

hESC research in Iran is permitted as the Supreme Leader, Ayatollah Khamenei released a 'stem cell *fatwa*' in 2002 which affirmed that research using human embryo is

acceptable based on the *Shia* practises. Although formal documents concerning stem cell legislation were unable to locate, several writings have confirmed Iran's position on stem cell research written such as Saniei (2013); Baharvand et al. (2004); Flynn and Matthews (2010). In 2003, Ayatollah Khamenei also congratulated several Iranian scientists that successfully created hESC that the Iranian government celebrated (Raman, 2006; Saniei, 2013; Walters, 2004).

Unlike Israel, Turkey does not have specific stem cell legislation but it has adopted the international 'Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine' also known as the 'Biomedicine Convention (Oviedo Convention)' and accepted several provisions in 2004 as published by the Council of Europe originally in 1997. Based on the Treaty signed, research on surplus IVF embryos are allowed but forbids creation of embryos specifically for research purpose (Council of Europe, 2004). Apart from that the Turkish Penal Code declares research on human subjects as unlawful according to its Article 90 (Turkish Parliament, 2016). However, it does not address the use of human embryos for research. Vatanoğlu-Lutz (2012) wrote that, "there is no direct legal regulation that prevents embryo research" in Turkey as of 2012. Turkish law on ART introduced in 1987 known as the 'Regulation of Assisted Reproductive Treatment Centers Act' which has undergone several amendments but mainly to regulate the aspects of reproductive technology and services with some provisions on supernumerary consented embryos (Vatanoğlu-Lutz, 2012).

In 2014, Dajani (2014) wrote in the Nature magazine that the Jordanian government after consulting the Ministry of Education, the National Committee for Science and Technology Ethics and the Jordanian Religious Council (*Majlis Al-Iftaa*) enacted a law that is meant to regulate the hESC research and therapy. It is known to be one of first of its kind within the Islamic region (Jordanian Parliament, 2014). According

to the 'Stem cell by-law SIDRA No.10' stem cell research using human embryos is allowed as long as it is meant for therapeutic purposes and only if they are within period allowed by the Islamic law. Dajani (2014) also wrote that most Islamic scholars consider 40-120days after conception as when embryonic life begins therefore five-day old embryos that do not have soul, lack the recognition as 'human life' making them permissible for research. The new law also prohibits private entities from using embryonic stem cells and outlines standard practices concerning stem cell research and its therapies (Ismail, 2015; Matsumoto et al., 2015).

Saudi Arabia introduced 'In-vitro Fertilization Act' (No. 2870/1/12) that outlined the regulation of fertility clinics including some provision indirectly concerning gametes and embryos such as prohibition of storing them without couples' consents and others (Fischer, 2009). The Saudi government also set up the National Committee of Bioethics by royal decree (No.7/B/9512) on 8th August 2001, which was in charge of formulating the stem cell guideline that rejected human reproductive cloning and all its applications saying that the risks exceed the benefit (No. 4/14/23). In 2003, the *fatwa* (Islamic legal ruling) released by the Muslim World's League's Islamic Jurisprudential Council in Saudi allowed adult stem cells research and therapy as outlined by the religious framework. According to the *fatwa*, it is allowed to derive, propagate and use stem cells for research and therapeutic purposes, which includes surplus IVF embryos. However, the committee banned therapeutic and reproductive cloning (El-Awady, 2008; Matsumoto et al., 2015).

2.1.6 Australasia

Australia made significant changes in its research policies when it passed the 'Prohibition of Human Cloning Act' 2002 and the 'Research Involving Human Embryos Act' 2002 based on the report released in 2001 by the House of Representatives Standing Committee on legal and Constitutional Affairs involving human cloning and stem cell research (Then, 2009). The Prohibition of Human Cloning Act 2002 underwent a few amendments, in 2005, 2006 and 2008, since its formulation in 2002 which prohibited varieties of human cloning irrespective of its purpose including IVF for other than reproduction (Australian Parliament, 2008). The 2006 amendment relaxed its provision allowing SCNT for research purposes as long as the embryos are within fourteen days old. While the Research Involving Human Embryos Act 2002 was amended several time in 2006, 2007, 2008, 2014, and 2016 but remains up-to-date (Parliamentary Counsel, 2016). In 2004 the Australian National Health and Medical Research Council introduced the 'Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research' which was revised in 2007 that was meant to cover the ART considering clinical practice and research to ensure ethical conduct. The guideline was withdrawn in 2017 with the Prohibition of Human Cloning Act 2002 and Research Involving Human Embryos Act 2002 revised and amended to be comprehensive and up-to-date (Australian Parliament, 2007).

Unlike Australia, the stem cell research in New Zealand is strictly regulated. According to their Ministry of Research, Science and Technology (MoRST), there are no hESC research conducted in New Zealand as of 2006 except for collaborations (New Zealand's Ministry of Research, 2006). The New Zealand Parliament introduced the 'Human Assisted Reproductive Technology (HART) Act No.92 (2004)' to impose restriction concerning ART. The Act has undergone several amendments, in 2009, 2010, 2012, 2013, and 2017and remains up-to-date (New Zealand Parliament, 2017). According

to the Human Assisted Reproductive Technology (HART) Act some practices involving human embryos are banned such as the creation of hybrid embryos as well as human embryos using IVF including reproductive cloning. It is also prohibited to allow the growth of human embryos outside of the human body past the fourteen-day period making storage of any unused IVF embryo completely unlawful. Those who violate these provisions are heavily penalised (New Zealand Parliament, 2017).

As required by the Act, the Advisory Committee on Assisted Reproductive Technology (ACART) and the Ethics Committee on Assisted Reproductive Technology (ECART) were set up separately to regulate any subject matter concerning to ART and its research. In 2006, the MOH of New Zealand published its 'Guidelines for Using Cells from Established Human Embryonic Stem Cell Lines for Research' to guide the use of hESC lines in research (New Zealand's Ministry of Health, 2006). Jones (2016) wrote that New Zealand is categorized as 'restrictive by default' based on the Annual Report 2012/2013 released by the Advisory Committee on Assisted Reproductive Technology (ACART) (Advisory Committee on Assisted Reproductive Technology (ACART), 2013).

2.1.7 Asian Region

The Asian continent is the largest in the world that spans across Europe and Africa, including the Middle Eastern countries (Mattern, 2002). The stem cell policies of the countries within the Northern Asia, Central Asia and the Western Asia were discussed previously as a part of the European region and Middle Eastern region. Therefore, for practicality reasons, the countries within the Southern, the South-Eastern and the Eastern Asia will be reviewed as the Asian region in this section. China, Japan, Korea, India, Singapore, Pakistan, Indonesia, and Thailand are some of the countries within this region.

Not all of the countries within this region have enacted laws specifically to regulate stem cell research similar to the other regions.

China has the largest stem cell research scene in Asia which has progressed over the years with their research volume is next to the United States. It has one of the most unrestrictive policies concerning stem cell research (Dhar & Hsi-en Ho, 2009). Stem cell research and therapeutic cloning is permitted in China while reproductive cloning is banned based on their 'Rules on Assisted Reproductive Technologies for Human Beings' brought into force in 2003 by the Ministry of Public Health (Wheat & Matthews, 2004). The Chinese Ministry of Science and Technology (MOST) and the MOH released the 'Guidelines for Research on Human Embryonic Stem Cells' as a joint effort in 2004. Many believed that the provisions within the guideline were unclear and short of implementation. The funding committee of the MOST is responsible for making sure that only projects funded by them conform to the guideline, while those minor projects funded by other sources remain unregulated (The Witherspoon Council on Ethics and the Integrity of Science, 2012). According to the guideline, embryonic stem cell research is allowed on cells retrieved from aborted foetuses, surplus IVF embryos as well as those created through SCNT (The Witherspoon Council on Ethics and the Integrity of Science, 2012). China did not enact a law specific for stem cell until 2015, when they introduced 'The Stem Cell Clinical Trials Management Approach' (trial) (draft) (People's Republic of China, 2015). The draft issued by the former Ministry of Health, the Chine National Health and Family Planning Commission (NHFPC) outlined standards protocols to conduct clinical trials involving stem cells making sure they are within lawful and ethical boundaries (Rosemann & Sleeboom-Faulkner, 2016).

In South Korea there were no laws or legislation enacted to regulate stem cell research prior to 2005. The South Korean government formulated the 'Bioethics and Biosafety Act' in 2003 which took effect in 2005 (South Korean Parliament, 2005).

Within this law, reproductive cloning is banned but permits embryonic stem cell research and therapeutic cloning (Wheat & Matthews, 2004). It was brought in to address the issue of human subjects in biotechnology research After Dolly was publicized in 1997, Dr Hwang became popular when he successfully cloned a cow, *Jini* in 1999. Soon he began moving from animal work to human triggered social controversy among concerned member of the government and public (Clay, 2013). In 2000, the MOST established the Korean Bioethics Advisory Commission to draw up the new bioethics law. In 2002, the MOST and the Ministry of Health and Welfare, combined their drafts which resulted in the Bioethics and Biosafety Act 2005. Under the Act, the National Bioethics Committee were established to regulate stem cell research in South Korea. However, the controversial case of the Seoul National University professor who extracted stem cells from astounding 242 embryos donated by his researchers and fabricated data in his published work due to work pressure pushed for the fourth revision of the Bioethics and Biosafety Act to amend their provisions concerning egg donors and their exploitation which came into effect in 2008. Since then the Act has undergone several revisions with 2014 being the most recent (Yoon et al., 2010).

In Japan, there were no law or legislation meant to regulate Japan's regenerative medicine including stem cell and other cellular and tissue-based research until 2014. They mostly depended on the 'Guideline on the Distribution and Utilization of Human Embryonic Stem Cells' introduced by the Ministry of Education, Culture, Sports, Science, and Technology in 2009. It was meant to offer standard practice on the matters concerning stem cell derivation, distribution and its clinical uses prior to 2014 (Japanese (MEXT) Ministry of Education, 2009). Unlike the European countries, Japan has a separate law on human cloning, known as the 'Act on Regulation of Human Cloning Techniques' (Act No.146 of 2000). It forbids transfer of embryos created through SCNT including chimeras and hybrids into a woman's or an animal's womb (UNESCO, 2004).

Although, reproductive cloning is banned, embryonic stem cell research and therapeutic cloning is permitted in Japan (Wheat & Matthews, 2004). In 2014, the Japanese government introduced the 'Act on the Safety of Regenerative Medicine (RM Act)' that was meant to outline the standard procedures and measures for entities and facilities involved in regenerative medicine to promote an ethical conduct including the use of stem cells. The RM Act that was promulgated in May 2013, applies to both public and private sector for a better oversight. They also brought in the 'Pharmaceuticals, Medical Devices, and Other Therapeutic Products Act (PMD Act)' in 2013 that regulated the products concerning regenerative medicine while overlooking the cell therapy approval as clinical trials (Konomi et al., 2015; Kusakabe, 2015; Tobita et al., 2016).

Under this Act, a new review time was introduced for the approval procedure which expedites the entire process. The nine-month review is coherent with the United States' Food and Drug Administration (FDA) and much shorter than what were common in Japan (Konomi et al., 2015). Apart from that, they also have other healthcare and medical acts that overlaps in its jurisdiction ultimately tying loose ends considering stem cells including establishing the Japan's Agency for Medical Research and Development (AMED) that basically overlooks Japan's research and development (R&D) to improve their medical services (Azuma, 2015).

Taiwan originally addressed regulative concerns of stem cell research in 2001 when scientists and researcher advised the government to formulate the necessary legislation that allows ethical derivation of stem cell and research. In 2002, Taiwan's Department of Health (DOH) enacted its first regulation on hESC. The South Korean controversy in 2005 also spilled over Taiwan to initiate more regulative efforts concerning stem cell research. The government formulated a cross-ministerial 'stem cell task force' which formed three commissions to handle separate issues (Rosemann, 2010). Commission one to formulate new law on the extraction and use of hESC, commission

two involving the Intellectual Property Office (TIPO) to handle patenting regulation pertaining to hESC and the third commission was in control of the future strategy and funding plan. In 2007, the TIPO passed the 'Patent Law' to manage the patenting issue, while the DOH brought in a conditional regulation in 2007 concerning stem cell known as the 'Policy Instructions on the Ethics of Human Embryo and Embryonic Stem Cell Research' that replaced the 2002 regulation (DOH, 2007). In 2008, the Executive Yuan, which is the policymaking branch in Taiwan introduced the 'Human Embryo and Embryonic Stem Cell Research Act' which meant to offer transparency concerning ethical conduct of stem cell research (DOH, 2008). Separately, the matters of gamete and embryo donation, some provision on hESC as well as SCNT are also included within their 2007 Artificial Reproductive Act, which is enacted by the DOH (Rosemann, 2010).

Many identify Singapore as Asia's stem cell center with its high stem cell research publication not to mention heavy investment in biomedical research (Barfoot et al., 2013; Dhar & Hsi-en Ho, 2009). It is considered as one of the Asian countries apart from China and Japan, that is involved in extensive stem cell research. Its Biopolis, a state-of-the-art research facility with its own stem cell bank is world renowned as a biomedical hub (Arnold, 2006). Similar to the United Kingdom, Singapore is known to be a country that has adopted a permissive approach regarding stem cell research. Their first step in regulating stem cell research was establishing the Bioethics Advisory Committee (BAC) in 2000 to tackle the ethical, legal and social issues (ELSI) concerning biomedical research in Singapore (Lim & Ho, 2003). Their 2002 report on the Ethical, Legal and Social Issues in 'Human Stem Cell Research, Reproductive and Therapeutic Cloning' was significant with recommendations made regarding policy matters to the government (BAC, 2002). It allows therapeutic cloning within strict regulation and called for complete ban on reproductive cloning (Wheat & Matthews, 2004).

In 2015, the 'Human Biomedical Research Act' was introduced (Singapore Parliament, 2015). It authorizes the use of embryos that is less than 14 days for research and therapeutic purposes. They announced the release of the 'Ethics Guidelines for Human Biomedical Research' in 2015, which offers transparency concerning ethical, legal and social rights of all the stakeholders in human biomedical research mainly the research subjects. It is also helpful as a public resource, while it summarizes the standard practices for an ethical conduct of human biomedical research (BAC, 2015).

Similar to Singapore, India is emerging as a key player in the stem cell research with substantial governmental investment resulting in derivation of new ESC lines and increased scientific publication (Tiwari & Raman, 2014). Along with its development, there have been several complaints of stem cell clinics not conforming to proper regulatory oversight (Jayaraman, 2005). In 2002, the Indian Council of Medical Research (ICMR) declared that therapeutic cloning is allowed promoting stem cell research. In previous year, the Department of Biotechnology had also issued a guideline to prevent clinical exploitation. There had been some dispute between the two bodies regarding who should regulate stem cell research (Jayaraman, 2005). However, in 2007, they released the 'Guidelines for Stem Cell Research and Therapy' as joint effort to deal with ethical and scientific concerns to promote proper conduct of stem cell research and its therapies (ICMR and Department of Biotechnology, 2007). The guideline called for the establishment of the National Apex Committee for Stem Cell Research and Therapy (NAC-SCRT) as the governing body to oversee the issues concerning stem cell research and therapies. According to the guideline, stem cell research is divided into three key categories, which are permissible, restricted and prohibited. Therapeutic cloning or the creation of embryos for research using SCNT comes within the restricted category which is reviewed on a case-by-case basis under strict regulation (ICMR and Department of Biotechnology, 2007). On a separate note, although hESC and therapeutic cloning are

allowed in India, reproductive cloning however, is banned, as it adopted the United Nation's Declaration of Human Cloning (United Nations, 2005b)

Since then, the stem cell guideline has undergone two revisions. The 2013 revision was to highlight the successful implementation of the NAC-SCRT and its overall standard protocol, while the 2017 revision was to consider the latest developments in the stem cell field, the stakeholders involved, and with clear provisions concerning stem cell protocols for both clinical and basic research (ICMR, 2013; ICMR and Department of Biotechnology, 2017). There is still no laws or legislation either specially enacted or has provisions meant to regulate stem cell research in India.

Thailand is identified as the Asian stem cell tourism hub with their national government recognizing stem cell research as a significant economic revenue of Thailand. Tourists from all over the world are still traveling to Thailand to seek treatments which is not available in their native countries However, its many revolutionary stem cell clinical trials reaching the mainframe without proper evidence or success, have brought in reports of horrifying side effects of these untested therapies resulting in deformity and even death of patients (Cohen & Cohen, 2010; Cohen, 2008; Lunt et al., 2010; Thai Law Forum, 2014). Prior to 2009, there were no oversight on stem cell therapies or research. Research institute and healthcare providers involved in stem cell research are left to manage and regulate on their own. The Medical Council of Thailand is responsible for managing stem cell research as they are the governing body in charge of medical practices. In 2009, the Thai Ministry of Public Health began regulating stem cell and its therapies as drugs as advised by the FDA, which includes oversight of false advertising (Thai Law Forum, 2014). The Thai Medical Council formulated a draft regulation concerning stem cell therapies (Treerutkuarkul, 2009). According to the law, the entities providing stem cell therapies are required to register their research within the Medical Council for some independent control. On November 23rd 2009 the 'Regulation of Medical Ethics

Regarding Stem Cell Research for Human Treatment', was passed and came into force in 2010 (Thai Medical Council, 2009). The induction of the law was criticized by many within the biomedical field stating this will eventually obstruct research progress. In 2015, the Thai National Research Council published their 'National Policy and Guidelines for Human Research' as their national guideline concerning human research despite the international guideline that is available in International Society of Stem Cell Research (ISSCR) (Thai National Research Council, 2015).

In Philippines, several initiatives are taken to properly regulate the issue of human cloning and stem cell research. Although, there are no formal legislation enacted in Philippines but that may not be for long. They began by addressing the issue of human cloning by introducing the bill 'Banning on Experiments on Cloning of Human Beings Act' which aims to prohibit all research involving human cloning in the Philippines. The bill was first introduced in the 13th Congress meeting and was passed. It was then introduced in the 14th, 15th, and the 16th Congress meetings respectively that was approved on all introductions. However, the bill is still pending in the committee and have yet to be passed into law as reported by the Philippines Senate (Senate of Philippines, 2017). The 'Intensifying of Stem Cell Research and Therapy Act' was first introduced by the Honorary Eufaranio 'Franny' Riguel, in the House of Representatives on 1st of July 2013. Although it was approved, it is currently pending with the committee of health as reported by the House of Representatives (Philippines House of Representatives, 2017).

Pakistan have not enacted any law or legislation to regulate its stem cell research. Their stem cell research is not comparable to their neighbouring India. The only law that has come close is the 'Human Organ and Transplantation Act (HOTA)' was passed into law in 2010 by the Pakistan Senate to address the issues concerning human organs and tissues for therapeutic purpose (Pakistan Senate (Majlis-e-Shoora), 2010). However, there are no specific provision on stem cells or its derivation, but was mentioned once in its

Article 8, no 2(e), that highlights the consideration of *xenotransplantation* and stem cell through international collaboration as a solution for shortages of available organs but under strict review by the Human Organ Transplant Authority (HOTA). Within the authority, the 'Protocol/Guideline for Stem Cell Research/Regulation' was introduced with the help of the National Bioethics Committee of Pakistan which has clear stipulations on the matter of stem cell derivations and the ethical conduct of its research. Under the guideline, both reproductive and therapeutic cloning is banned while embryonic stem cell research is allowed only on surplus embryos within sixteen days old with proper consent from donating couples (HOTA, 2010)

Just as Pakistan, Indonesia's stem cell research has a long way to go before it is recognized equally to their other Asian counterparts. Despite their low scientific publication in stem cell research, Indonesia has enacted four laws that covers its legal stature on stem cell research which are, (1) the 'Health Law No.36 of 2009' that repealed the 'Health Law No.23 of 1992', (2) the '833/MENKES/PER/IX/2009 Implementation of Stem Cell Services', (3) the 'Health Ministry Decree No.834/MENKES/SK/IX/ 2009 on Guidelines for the Implementation of Medical Stem Cell Services' and finally (4) the 'Regulation No.32/2014' within the Health Ministry introduced to regulate hospitals that are authorized to offer stem cell therapy (Rulistia, 2016; Utomo, 2012). The Health Law No. 36 of 2009 highlighted some oversight on stem cell, such the Article 64, 66 70, and 75 with clear stipulations on stem cell, while the Regulation No.833 focuses on the hospital and stem cell service providers offering stem cell treatment in their institution in accordance to the government standards including storing stem cells in tissue banks. The Regulation No.834/2009 is to establish clear instructions concerning stem cell uses by healthcare providers while the Regulation No.32/2014 is more to restrict the number of authorized stem cell providers for a much closer oversight (Prathivi, 2015; Utomo, 2012)

Vietnam, Cambodia and Myanmar are low incomed countries in Asia that has lower research and development (R&D) in stem cell even compared to Indonesia or Thailand. Vietnam's first hematopoietic stem cell transplantation was conducted in 1995 and between 2002 and 2007 several researches translated to clinical trials. They even established their first stem cell bank in 2002 (Van Pham, 2016a). There is no record of any legislation or law specifically introduced to regulate Vietnam's stem cell research. However, they did enact the 'Decree No.12/2003/ND-CP a Law on Childbirth by Scientific Methods', which banned both reproductive and therapeutic cloning including surrogacy (Pashigian, 2012; Vietnam Government, 2003). The Symposium organized by the Vietnam's Ministry of Health in 2007 highlighted several proceedings focusing on the topic of approval and review of clinical trials on human subjects, the ethical aspects of biomedical research, and others. Despite the list of regulation on its Appendix 3, none of them addressed the issue of stem cell or its research and therapies (Ministry of Health Vietnam, 2007). They also have the 'Decree No.87/2011/ND-CP the Law on Medical Examination and Treatment', mostly to regulate activities involving both the private and public healthcare (Vietnam Government, 2011). It did not highlight stem cell therapies or its research. Since then there has not been any updates (Van Pham, 2016a).

Similar to Vietnam, Myanmar and Cambodia, both do not have laws specifically enacted to regulate stem cell research or its therapies. Myanmar's position on human cloning is also unclear when their government abstained from signing in the United Nation's Declaration of Human Cloning in 2005 (United Nations, 2005a). Regulation of biomedical research assuming stem cell included, is within the jurisdiction of the Ethics Committee. They review the research proposals to protect human rights, dignity and their safety. At the moment the documents within the Ethics Committee appear to be within the institutional level instead of national level giving mixed impression (Kojima et al., 2005). Although it has the 'Blood and Blood Products Law' enacted in 2003 and the

'Body Organ Donation Law' enacted in 2004, none of them addresses stem cell technologies specifically (Myanmar Government, 2003, 2004). There were no stipulations on the hematopoietic stem cell or its transplantations. Their 'Health Policy' also do not have any laws or legislation listed to regulate stem cell related technologies (Myanmar Government, 2008).

Cambodia does not have specific law on stem cell research or human cloning, but unlike Myanmar, Cambodia chose to oppose human cloning according to the United Nation's Declaration of Human Cloning in 2005 (United Nations, 2005a). Cambodia introduced the 'Ethical Guidelines for Health Research Involving Human Subjects' in 2001 which covers a lot on the matter of informed consent and subject violations (Cambodian Goverment, 2001). The 'National Ethics Committee for Health Research (NECHR)' was established by the Cambodian MOH in 2002 based on a sub-decree No.592 to review all health-based research proposals for proper oversight. In November 2008, the 'Standard Operating Procedures (SOP)' was published by the NECHR within the MOH for an ethical operation of all biomedical research (Cambodian Ministry of Health, 2008). However, both the Standard Operating Procedures (SOP) and the Ethical Guidelines for Health Research Involving Human Subjects have no provision focusing on stem cell. They introduced the 'National Guidelines for Transfusion Practice' in 2013 which covers a little bit on the hematopoietic stem cell transplantation, but nothing on stem cell derivation or its research (Cambodian Goverment, 2014).

According to the 2009 map, Malaysia is represented by the yellow tone which denotes countries without any laws or policies on stem cell and it is true as of 2017. Unlike some nations with several aspects of its stem cell stipulated within somewhat relevant legislation, Malaysia had no existing laws or policies that incorporated stem cell research and its technologies. Although this fact is accurate, it is necessary to review the current

progress on Malaysian stem cell regulation to understand the challenges involved that made the process even tougher.

2.2 The trend of stem cell regulation

The attempt to map all the global stem cell laws and policies were mostly to update the World Stem Cell Policies map created by Hoffman (2009). However, mapping the new Global Stem Cell Laws and Policies as displayed in Figure 2.1 and 2.2 respectively, identified a trend in stem cell regulation. Many expect countries that introduce laws specifically on stem cell as the one that are actually regulating their stem cell research and its technologies, but there are other direction and angle to regulate or overlook the subject matter. Research involving ASC are mostly to ensure there are ethical conduct considering human subjects, donors and medical practitioners conducting the procedure which are a part of most nation's Good Clinical Practice (GOP) and their general health laws. The hESC research are more challenging with grey area that are unclear which requires regulation and laws managing the delicate subject topic involving human embryos.

Since stem cell research involves the use of human embryos and human subjects, countries around the world have tackled their stem cell regulation from various angles. Mostly began by incorporating the aspects of hESC within their IVF or ART laws as witnessed in the United Kingdom and Italy. While others incorporated it within a variety of laws such as biomedical laws, transplant laws, cloning laws, general health laws, bioethics or biosafety laws or even within their constitution and religious laws. In this study, eight different types of laws or angles were identified that covers stem cells, its research including therapies in their provisions. This determines that the regulation of stem cell is diverse with different countries adopting different sets of laws however they see fit. Table 2.1 presents the countries and the laws enacted for hESC.

It is inappropriate to declare countries that did not enact specific laws on stem cell as having no laws or legislation concerning stem cell research or its technologies. As long as any matter of stem cell is covered within any of the new or available laws it is considered regulated, lawful and with laws. With the range of stem cell policies and laws available enacted from different angles, countries that have yet to regulate them or without laws including Malaysia, can now review their countries' position on stem cell and adopt any of these laws and policies to ensure a more efficient oversight that is suited to their position.

Table 2.1: Countries & the types of laws that regulate stem cell 2017.

Types of Laws	Countries	Countries that Combined Laws
In vitro Fertilization (IVF) & Assisted Reproductive Laws	United Kingdom, Canada, Italy, Austria, Iceland, Slovenia, Estonia, Latvia, Portugal, Tunisia, Turkey, Belarus, New Zealand, Japan, & Hong Kong	Norway, Denmark, Saudi Arabia, Spain,
Biomedical Laws	Singapore & Russia	Denmark & Spain
Cloning Laws (embryo for research)	Chile, Finland, Netherlands, Israel, Australia & Belgium	Norway & Sweden
Transplant Laws	Ukraine, Thailand, & Argentina	-
General Health Laws	Poland, Slovakia, South Africa, Zambia, Kenya, & Mexico	Sweden & Indonesia
Bioethics Laws	France, Panama, Brazil & South Korea	
Constitutional & Religious Laws	Vatican City, Iran, Ecuador	Saudi Arabia,
Specific Stem Cell Laws	Germany, Czech Republic, Jordan, Taiwan, China	Indonesia
State Laws	United States	-

Mapping the current stem cell laws and policies only verified that stem cell regulation can be approached from various direction. Being a technology that improves public health with regenerative medicine, stem cell fits within any of the angles in Table 2.1. Countries around the world can now learn from the many available options and

approach their stem cell regulation with this information at their very disposal. Multi-religious nations like Malaysia with consideration for various religion can adopt more than one law to have a comprehensive approach on the matters of regulation and policymaking similar to Saudi Arabia who have adopted both the Islamic law and ART laws to ensure they are specific to their nations' welfare.

CHAPTER 3: LITERATURE REVIEW

3.1 Introduction

Literature review of prior studies conducted on specific topic or subject matter is essential in building the foundation of any study (Webster & Watson, 2002). In this study, the literature review revolves around the two main concerns of the study which are, first, the policy and regulatory aspects of stem cell research and technology and second, the ethics of stem cell research. Although, they are connected issue sometimes they are discussed separately by scholars both nationally and internationally. Hence it is necessary to review both the ethics and regulation of stem cell research and its technologies from different perspectives, in this case, internationally and locally as well as individually as separate topic, to have a comprehensive approach and understanding concerning these issues (Pautasso, 2013).

With that, important literature regarding stem cell research ethics and its regulative aspects following the discovery of human embryonic stem cell (hESC) by Dr. James Thomson and his colleague in 1998 were analyzed as a basis of this study (Thomson et al., 1998). Since objective 1 and 3 of this study is to look into the status and the regulatory protocols of stem cell research and therapy in Malaysia and its implications, previous studies concerning the subject were reviewed thematically from an international perspective as presented in Section 3.2. While objective 2 that addresses the ethics of stem cell research based on the publication review were conducted thematically and chronologically primarily from an international perspective as presented in Section 3.3. The Malaysia perspective is subsequently presented in Section 3.4 that combines both the ethics and the regulatory aspects to offer a better understanding of its research gap. Figure 3.1 illustrates the research framework of this study.

3.2 Stem cell research and technology

3.2.1 Global research status

Stem cell research is without a doubt remarkably promising in regenerative medicine. Scientists believe it could be the answer in treating a range of incurable diseases (Gearhart, 1998). This has led experts from all over the world to pursue the course extensively. The status of stem cell research is often investigated to evaluate the innovative development of nations of the world. It is basically to gauge the progress and advancement considering stem cell research and its technologies either from a specific nation's perspective or of the world in identifying the key contributors. This study aims to specifically evaluate Malaysia's stem cell research progress in order to determine where it stands development wise since the discovery of hESC. This type of evaluation is not rare or uncommon, as several publications were identified to have adopted the approach in understanding the global stem cell research development like the 'Global Stem Cell Research Trend: Bibliometric Analysis as a Tool for Mapping of Trends from 1991 to 2006' and the 'Stem Cell Research: Trends and Perspectives on the Evolving International Landscape' (Barfoot et al., 2013; Li et al., 2009).

Barfoot et al. (2013) published a report as a joint effort by the EuroStemCell, Kyoto University's Institute for Integrated Cell-Material Sciences (WPH-iCeMS) and Elsevier Journal to present the global development of stem cell research through publication review. In their Chapter 3, The International Landscape, the United States emerges as the top contributor to world stem cell research while China follows closely (Barfoot et al., 2013). The report outlined the several key developments in the global stem cell research like the first derivation of stem cells which is not top news anymore, but individually the timeline of respective countries is quite informative. This includes the International Stem Cell Forum set-up to support international collaboration and funding in the European Union and the Chinese Ministry of Science and Technology (MOST) that

initiated the independent stem cell 973 programs together with funding efforts (Barfoot et al., 2013). With that, Li et al. (2009) also identified the United States together with Canada, France, Germany, Italy, Japan, and the United Kingdom as the top contributors in stem cell research through their publication number between 1991 and 2006.

Separately, there are studies done to individually highlight the efforts taken by nations in supporting their stem cell research and development. In Australia, there are several progressive initiations related to stem cell research like the Australian Stem Cell Centre (ASCC) that began in 2003 which is a major collaboration that has united many Australia's leading scientists to develop innovative therapeutic products treating a range of conditions (Svendsen & Ebert, 2008). Stem Cell Australia is another such initiative by the Australian General Research Initiative that was designed as a seven-year effort partnering with reputable Australian universities such as University of Melbourne, Monash University, University of Queensland and others (Bouhassira, 2015).

In the United Kingdom, the success of Louise Brown as the world's first test-tube baby in 1978 marked the beginning of research involving human embryos. Despite the opposition of the general public, stem cell research carried on in the United Kingdom until the necessary regulatory actions were taken in 2002 (Koka, 2008). Several pieces of researches in the United Kingdom are either financially supported by their UK Stem Cell Foundation that was established in 2005 to speed up the development of stem cell research and therapy for patients or by the United Kingdom's Wellcome Trust. The chairman of the UK Stem Cell Foundation, Sir Richard Sykes confidently stated that the "United Kingdom is without a doubt a leader in stem cell research" (Furcht & Hoffman, 2011; Qadir, 2012).

While in the United States the funding restriction revoked by the former President Obama that was originally imposed by Bush marked the full support of the nation on stem cell research. Although, this is only for those surplus embryos created

through *in vitro* fertilization (IVF) and not through therapeutic cloning procedures (Vakili et al., 2015). Even then, the scholarly success prior to the funding support by Obama was noteworthy as shown by the global stem cell trend mapping articles earlier identifying the United States as the key contributor. The investment in stem cell research in Singapore began heavily with first, the establishment of the Agency for Science Technology and Research (A*STAR) in 2000 and second, with more than USD4 billion invested between 2001 and 2010 specifically for the building of their infrastructure and other areas for biomedical sciences (Colman, 2008).

These types of assessments normally do not capture Malaysia and other small developing countries with lower research and development (R&D) involving all scientific innovations. Therefore, it is necessary that respective nations such as Malaysia undertake similar approach to understand their nations contribution regardless of how insignificant they are globally. It would prove quite valuable in making the necessary decision in the case of Malaysia, its regulatory concerns regarding stem cell research and its technologies.

3.2.2 International regulation & oversight

In spite of its potential, there are challenging matters like the shocking stem cell scandal involving a South Korean scientist who fabricated research data and inappropriately obtained human eggs from his student graduates'. Clearly, the exploitation is questionable judging by his role as a scientist and author (Cho et al., 2006). Dr. Hwang violated the fundamental code of research integrity without any intellectual honesty or accuracy in presenting his research (International Stem Cell Forum Ethics Working Party, 2006). The unclear regulation in the absence of legal framework was identified as the main cause of this scandal in South Korea.

Several other stem cell scientists were also identified having committed fraud and had their papers retracted. These scandals include Japan's Yoshiki Sasai, who was the deputy director of RIKEN (Rikagaku Kenkyusho, Institute of Physical and Chemical Research), Kobe, Japan and his research student Haruko Obokata, a scientist at RIKEN, caught for using falsified and fabricated data in their research presented in published articles (Normile, 2014). This humiliating tragedy led to Yoshiki Sasai to commit suicide due to media bashing and the retracting of several of their papers (Rasko & Power, 2015). The stem cell research fraud cases are alarming, but to top it off, there are the other existing ethical issues concerning stem cells beginning with the source of cells used and the derivation method which also equally disturbing. There are many articles written concerning the need for appropriate regulation or oversight to administrate and maintain the continuous integrity and validity of stem cell research and its technologies.

The ethical issues and moral implications of stem cell research and its technologies specifically due to its substantial growth have become the basis of many regulatory discussions all over the world. It is greatly valued and not uncommon. In fact, there is various research done pertaining to the topic either explicitly on a specific country or simply to compare different policies and regulations of the world concerning stem cell research and its technologies. The debate triggered governments of many countries to take effort in regulating the various aspects of stem cell research and its technologies such as research practices and its funding. Hayes et al. (2012) and Taylor (2005) are two research that addressed the United States' jurisdiction and policies. It addressed the difference between state law and federal law and how it affected stem cell regulation in the United States. The issues of federal funds, the patent policy in the United States, the emerging various state laws without federal management highlights lack of consensus which prevent ethically sound stem cell research in the United States.

Regardless of the localized issue in the United States, Gottweis (2002) compared the policymaking between Germany and the United States. It acknowledged the controversies of research involving human subjects and insisted that such study is vital to help calculate the potential future development from different angle beginning with the various interpretations not to mention the consequences involved in hESC research. Ultimately it will assist in understanding the available strategies in regulation that may even be useful to the United States in improving their oversight. Lovell-Badge (2008) and Hammond-Browning (2009) are similar research written on the ethical and legal aspects of stem cell research in the United Kingdom. It verified that the United Kingdom is the first nation that passed a law on stem cell research, with Human Fertilization and Embryology Act (HFEA) (1990). Winston (2007) drew attention to the United Kingdom's regulation on stem cell declaring that it has had drawbacks and is inconsistent with bureaucracy. Despite that, it has undergone several revisions to properly incorporate the regulation of stem cell research and remains as the most comprehensive regulatory framework concerning stem cell to date.

With that, there are many articles that are written and published within this context, in fact several nations began addressing the issue from a very personal inquiry concerning the regulatory concerns of their own stem cell research such as India, Argentine, China, Iran, and others (de Arzuaga, 2013; Rosemann & Sleeboom-Faulkner, 2016; Saniei, 2013; Tiwari & Raman, 2014). It mainly highlighted the concern, the importance and the significance of having stem cell research effectively regulated preventing negative implication. Whether written based on a specific countries' policies or by comparing a range of regulatory framework or legislation from diversified countries, the main focus is to track their developmental origins and understand the reason for their enactment to evaluate the need for such oversight.

Indeed, the various religious perspectives, concerns, opinion relating to stem cell have resulted in the impediment of a single policy or law to be formulated with the aim to regulate stem cell research. This promoted each country to develop their very own policies and laws (Dhar & Hsi-en Ho, 2009). [7] According to Dhar and Hsi-en Ho (2009) there are four known major positions in stem cell research regulations, which are identified as (1) those that completely restrict the use of human embryos in research, (2) those that only allows embryonic stem cell (ESC) research on pre-existing embryos, (3) those that allow the use and continuous isolation of embryonic stem cells only from excess IVF embryos and finally those that have adopted a more liberal approach, whereby they not only allow the use and continuously isolate ESC from excess IVF embryos, but they also allow the creation of embryos exclusively for research purpose (Jones & Towns, 2006). [8,9] The countries that fit into a particular position based on the Jones and Towns (2006) article may not fit in the same position today nor does the list remain the same. Many of these countries including those that were not originally included as part of the regulatory assessment such as Malaysia have begun to re-assess their position, moving away from no regulation to developing stem cell guidelines to create some degree of oversight. Therefore, it is always important to review them closely to update the facts as we go on.

It is no surprise that many studies are done pertaining to stem cell research regulation especially concerning the use of human embryos in hESC research. Judging from an international scale, there are hundreds or even thousands written either to highlight their comprehensive regulation, the origin of their nations' stem cell regulation, the progressive development of their policymaking or lawmaking concerning stem cell regulation. It is important to note that, the pioneering countries like the United States,

[7] The different policies are illustrated by the Global Stem Cell Laws and Policies map presented in Chapter 2
[8] Embryos that are within a certain period as adopted by the United States during President Bush's administration
[9] Embryos that are within the 14-day limits as adopted internationally by most nations of the world

United Kingdom, and Australia have had their regulation reviewed by many scholars countless times to emphasize the process and their journey in regulating their very own stem cell research and technologies. Although they have been reviewed by others from their nations' perspective or concern, here, it is reviewed yet again because no such evaluation was ever made from a Malaysian perspective or concern. Therefore, it is relevant to review the legal framework of the United Kingdom, the United States, Australia and Singapore to first, identify the factors that triggered regulative measure concerning stem cell research, second, to learn the challenges and make the necessary recommendation towards Malaysia's very own stem cell research and technologies policymaking and lawmaking.

3.3 Stem cell research ethics

This section examines the publications written on the ethical inquiry regarding stem cell research and its technologies. It is about what is already known and well discussed relating to the topic which is from a range of perspectives. Some are written from a general viewpoint using bioethical principles and scientific rationalization, while some are written completely from a religious perspective. Most of the discussion begins after stem cell was first isolated by Gail Martin (1981) from mice, and became more controversial when Thomson et al. (1998) isolated stem cells from the human embryo, leading to the unintentional destruction of that embryo (Shand et al., 2012). Clearly, there are many studies done on the matters of stem cell research and its therapy up to now. Regardless, of those written concerning the many discoveries, there are those that focuses on the many implications of stem cell research, such as embryo destruction due to stem cell extraction which brought forward the issue of (1) the moral status of human embryos, that includes embryo rights, personhood and potential being, (2) the exploitation of many women as egg donors in both human embryonic stem cell and pluripotent stem cell

research, (3) the matter of informed consent of donors as well as research subjects, stem cell tourism and (4) the regulative policy of stem cell.

Robertson (1999) is one of the first articles questioned the concerns of the ethics and policy of hESC research. It debated if hESC equivalent to human embryos, which led to the justification of using the surplus IVF embryos. The discussion was extensive with the foundation built on the basis of the legality of abortion, therefore the national advisory committee of nations such as the United Kingdom, Canada, and the United States permitted the research without reservation. Despite that, well-known scholars such as Professor George Annas, Arthur Caplan, and Sherman Elias argued using a combination of deontology and consequentialism logic that exploiting women donors by compensating them for their egg contribution and the creation of embryos solely for research purpose were unethical and has negative consequences and morally wrong. This article eventually highlighted the need for regulation and policy (Robertson, 1999). According to Sperling (2008), the ethical controversies of stem cell research eventually became the basis for the regulative measures taken up by many nations similar to the Germans back in 2002 when they introduced their new stem cell law. The article also addressed the challenges of lawmaking and regulation identifying the shifting progress due to cultural reasons during their deliberation (Sperling, 2008).

Since then, there have been many writing and inquiries concerning the ethics of stem cell research and its technologies. The most prominent topic still remains to be the embryo destruction in hESC research and have triggered ethical inquiry in many countries within many communities. Scholars from both ethical and religious background have argued countless time that the extraction of stem cells from human embryos violates the rights and dignity of that embryo. No doubt, there are more to ethics than the usual religious debates. However, the ethical deliberations founded on religious faith are mostly based on the utilitarian concept as often defended in Hinduism and Buddhism (Knowles,

2009). Stem cell research is often debated on the fundamentals of 'the ends justifies the means'. The original concept was to conserve the absolute morality of human life however, the newer concept is crafted to suit the progressive technologies which put a relative value on human lives. The new ethics may not be as valuable as perceived with experimentations done on justified embryos that do not succeed or turn out unworthy as the utilitarian justification hence, the old ethics may preserve after all in pursuit of other alternatives (Doerflinger, 2010).

The utilitarian approach is quite common in supporting the stem cell research and even from certain religious beliefs, but the ethical deliberations on the moral status of the embryos, embryo rights, personhood, and potentiality have been invoked from a more general perception supported by scientific reasoning. Stem cell is greatly potentiated in the field of medicine, and it is important to continue extensive research to ensure it brings the intended result. Despite its challenges, stem cell scientists rationalize the research by questioning if the human embryo is equivalent to an organism. The genetic humanity criterion recognizes only human to possess full moral status and rights, therefore by questioning embryos of their genetic equivalence, scientists hope to change their morality and rights (Steinbock, 2007).

On a similar context, the question, 'when life begins' got some scholars believe that by pointing out the beginning of human life during fertilization and conception, they can justify how an embryo deserves the same recognition. Unfortunately, this justification is ruled-out as it also accepts embryos created through cloning process creating some prejudice. However, even if one manages to deliver a clever argument with the fertilization notion, there is complication in identifying the exact point of conception, and how it divides creating more cells (progress from 2-celled embryo to 32 cell blastocyst) which at this stage could possibly allow for the development of more human beings from a single cell. This is certainly ambiguous in its theory (Steinbock, 2007).

Since pinpointing the exact moment of conception or when life begins is considered impossible, some stem cell opponents justify that human embryos are full being or person, qualified to important moral rights similar to any human person, including the right not to be killed. Despite these claims, those supporting stem cells do not share the belief and declare that the human embryos are nothing like a full human, nor is it morally comparable to mere tissues, they still however, deserve some respect which is against intentionally destroying the embryo (Brock, 2006). There is a multitude of opinions regarding the moral status of the human embryo in hESC research, especially a distinction between fact and value (Master et al., 2008). It remained a central topic in some political and academic discussions, particularly the use of embryos as a resource for research. Identifying when an embryo is equivalent to a person, has created moral gridlocks which is difficult to resolve through ethical arguments or dialogue. The ongoing dispute is a result of lack of consensus regarding the moral status of the embryo.

Commonly, an individual is identified as a person when deserving and recognized for several fundamental human rights such as the right to life and freedom of speech. Personhood establishes boundaries between a person and non-person and has been used many times as explanation on debates about stem cell research permissibility (Master et al., 2008). The human embryos do not possess any qualifications granting it personhood (Brock, 2006). The definition of a person can be considered somewhat controversial but there is a range of conformity that a person should be 'rational' and 'self-conscious'. The rationality and self-consciousness allow a person to have experience and react accordingly having sentience, or known as 'sentient being' (Bortolotti & Harris, 2005). Embryos not older than 14 days, which consist of 64 cells is not conscious and incapable to feel pain or suffer, hence fails to qualify as a person, or a sentient being. They only feel any pain sensation when they are around 8 weeks old in gestation, making research on such embryos ethical (Singer, 1999).

Embryo destruction is greatly concerned, and it is among the issues argued in ethical debates and dialogues. However, the issue of which embryo can be used for research remains. Creating embryos to use them solely for research purposes makes people fearful as it adds an instrumental value to embryos which not only disrespects them but also violates human dignity (Devolder, 2005). The technique used is similar to reproductive cloning, such as somatic cell nuclear transfer (SCNT) or parthenogenesis which is also banned in most countries, forcing stem cell researchers to find other alternatives unlike their liberal counterparts (Isasi et al., 2004). Many individuals believe using surplus or excessive pre-implantation embryos created by IVF in many fertility clinics which often times remain frozen and unused after serving its original purpose, to be more ethical and accepted (Knowles, 2010).

Although using the IVF surplus embryos for stem cell extraction justified to some degree, however, there are other issues concerning them that some pro-life supporters argue, such as potentiality. They claim that these surplus embryos are potential person or people, however unless they are implanted into a woman's womb, these embryos will remain embryos, frozen indefinitely or worst, it may even be destroyed if anyone from the fertility clinics makes that decision (Blackford, 2006; Bortolotti & Harris, 2005; Lo & Parham, 2009). Therefore, the use of surplus embryos is well justified and accepted by many people, including scholars. Despite that, Cohen et al. (2008) highlighted that in Canada, fresh surplus embryos are highly considered for research instead of the common frozen ones stored in fertility clinics. Although they are not chosen due to their superiority nature, the use of fresh embryos created originally by means of IVF for reproductive purposes, for stem cell extraction resulted in significant ethical concerns such as the informed consent of donors, which on its own is quite serious in this case having to urge donors to act quickly on donating since they involve embryos between 3-5days old requiring immediate processing and the shortage of frozen embryos in storage for future

needs (Cohen et al., 2008). This only ascertains that the argument of surplus embryos is not straightforward instead there are other unique cases which require more studying.

Apart from the embryo destruction, exploitation of women egg donors is identified as a serious ethical concern indirectly involving ESC research. Stem cell research scientists depend mostly on fertility clinics for surplus embryo supplies creating a demand for egg donation. Women being the only sensible source of human eggs, are sorted for more egg donation to meet the demand of both reproduction and stem cell extraction. Some people doubt there are adequate surplus embryos available from fertility clinics donated for research, causing the scientists and their laboratories to sort alternatives (Brock, 2006), such as paying women large sums for donating their eggs directly creating a dilemma in the form of solicitation and exploitation of women. It seemed necessary to reimburse or compensate them since egg retrieval from donors has surgical risks like hemorrhage and pelvic injuries, it is also time-consuming not to mention painful (Foohey, 2010; Master et al., 2008). Although these donors may have consented, however, their personal finance could be the deciding factor.

Informed consent is an important stage of any research or study that involves human subject or donors. It is considered as a prerequisite, covered by several sets of ethical principles such as the Nuremberg Code and the Declaration of Helsinki (Escobedo et al., 2007; Lo & Parham, 2009). The purpose of the informed consent is first, to make sure the research subjects and participants are aware of their choice and understand the risks involved and second, to encourage researchers to act ethically (Escobedo et al., 2007; McGuire & Beskow, 2010). Any and all research involving human embryos that are retrieved from fertility clinics or hospitals are required to gain informed consent from the egg donors. These donors who have fulfilled their reproductive need can now decide to waive their rights allowing the eggs to be either discarded or used for research purposes protecting their privacy (Lo & Parham, 2009). In delicate research like stem cell which

uses a human embryo that leads to its destruction, there are challenges concerning informed consent. A major issue is the misunderstanding between research subjects and research donors and researchers. This misunderstanding is due to factors like language barriers, religious conflicts or false expectancy. In some rare cases, researchers may withhold research details and the fate of the eggs from donors when they approach for informed consent fearing donors would change their mind (Escobedo et al., 2007).

Ultimately there are several studies done very similar to the context of this study, such as Wert and Mummery (2003), Fischbach and Fischbach (2004), Isasi and Knoppers (2006), and Caulfield et al. (2015). These are just some that specifically began their inquiry from an ethical argument, addressing the controversies and issues surrounding the use of human embryos which are slippery slope argument with varying opinion among people without any consensus, and concluding them with the significance of regulation and effective oversight. They are written from a specific nation's viewpoint or by comparing several to evaluate their comprehensiveness while acknowledging the various policies and positions that exist (Caulfield et al., 2015).

Since this study intends to look into the ethical issues of stem cell research and its technologies globally and locally, it is important to also identify and assess the ethical inquiry of Malaysian scholars concerning stem cell research.

3.4 Malaysian stem cell research ethics & regulation

Stem cell research in Malaysia was first documented 30 years ago in 1987 with its first bone marrow transplantation (NTR, 2014) but the research progress brought forward several ethical inquiries concerning stem cell only in the last decade. In order to fully understand the concern of stem cell research ethics and regulation in Malaysia, it is vital to explore all the relevant studies done in relation to that specifically by Malaysian scholars to identify the research gap. One of the first writings that ever mentioned stem cell was Majeed (2002). He wrote that Malaysia recognized stem cell research as a part of the biotechnology development and often discuss the ethical and legal issues involving biotechnology revolution which includes stem cell research. According to Majeed (2002), scholars believe that with the advances in these fields, there are implications which require careful oversight (Majeed, 2002). With that, stem cell research with the use of human embryos began generating many ethical debates based on a variety of bioethical principles such as autonomy beneficence, non-maleficence and justice and the necessity of public policy.

The first article published that discussed the matters of stem cell regulation by Malaysian author was written by Islam et al. (2005) titled, "Spare embryos and human embryonic stem cell research: ethics of different public policies in the western world". Although written by Malaysians, it did not specifically address the issue of Malaysian regulation instead it reviewed and identified major policies adopted by the Western countries concerning their ethical soundness. The authors identified and assessed the major policies accepted by the Western world hoping that it will prove valuable when Malaysia decides on similar system or plan (Islam et al., 2005).

In 2007, the only writing that came closes to highlighting the regulative matter of Malaysian stem cell was Fadilah et al. (2007), who introduced the development of the 'National Policy for Organ, Tissue and Cell Transplantation', the 'National Standards for

Cord Blood Banking and Transplantation', the 'National Guideline for Heamopoietic Stem Cell Therapy', the 'National Guidelines for Stem Cell Research and Therapy (2009)' and the 'Stem Cell Oversight Committee' by the Ministry of Health (MOH) as part of the initiative effort towards regulating Malaysian stem cell research and its technologies (Fadilah et al., 2007). It was one of the earliest articles that reviewed the initial hematopoietic stem cell transplantation conducted as autologous bone marrow transplantation which evolved into the allogenic bone marrow transplantation highlighting its benefit and potential. The authors identified the shortcomings of stem cell research due to creating embryonic cells, connecting the matters of human cloning, that stirred social, ethical and religious controversies, making this article relevant and valid for this study (Fadilah et al., 2007).

Fadilah et al. (2007) also described the beginning and progress of stem cell transplantation mostly involving the bone marrow and umbilical cord blood which are the hematopoietic stem cell. Despite the broad description of the slow progress of the stem cell transplantation in the public hospitals in Malaysia, they also discussed challenges in stem cell due to the social, ethical and religious controversies of using embryos in embryonic stem cell research which called for the formulation of stem cell guideline and policy by the MOH to ensure the stem cell transplantations are pursued ethically within boundaries. A 'Stem Cell Oversight Committee' was called for establishment to safeguard the ethical and scientific standards of stem cell research, which plan to comprise of representatives from a range of expertise which includes stem cell biology, law, ethics, public and religious figures (Fadilah et al., 2007).

The stem cell research growth in Malaysia, especially the increased use of human embryos in research triggered several discussions in Malaysia and one of such discussion specifically addressed the Malaysian stem cell research regulation written by Foong (2012) that focused on the assessment of the hESC research regulations in Malaysia. The

author considered the Guideline on Stem Cell Research and Therapy (2009) deficient and suggested that Malaysia should implement a regulatory framework, which is broad, wide-ranged and effective in governing its stem cell research, recommending the Braithwaite's Theory (Foong, 2012). Although some part of the study was relevant and valid it only addressed one issue which is the adequacies of the Malaysian stem cell guideline as a legal framework.

One of the most significant issues in Malaysia concerning stem cell is that it is a multi-religious country with various religious beliefs. The diverse religious background means Malaysia has certain reservation regarding the use of human embryos in research. It is expected that their diverse population brings about a various discussion that is greatly influenced by religious practices and norms. In the case of stem cell research and technologies, this is noticeable judging by the stem cell guideline formulation in Malaysia as well as the publications written on stem cell research. The Guideline for Stem Cell Research (2006) originally formulated with the advice and recommendation of the Malaysian *Fatwa* Council, which is the Islamic legislative body that decides on the practices suitable for the Muslim community. The revision it underwent in 2009 requested the inputs of several religious experts meant to evaluate the religious consideration of other than the Islam. Religious figures representing different faiths and beliefs such as Islam, Hinduism, Buddhism, Christianity, and Sikhism are often approached in Malaysia to learn and understand the justification of human life including the moral status of the embryo. This led to a variety of opinion founded on religious teachings, which clearly illustrates the challenges in reaching consensus in a pluralistic society such as Malaysia.

Separately, several articles highlighted the significance of religious consideration due to Malaysia's multi-religious population such as Majeed (2002), Foong (2011), Olawale (2013) and Sivaraman and Noor (2014, 2015). Foong (2011) reviewed the multi-religious beliefs and their perspective concerning the use of human embryos for stem cell

research. Using the expert opinions, the author explored the various challenges and viewpoint regarding hESC research in Malaysia. Soon other scholars followed, sharing similar concerns and perspective. Olawale (2013) wrote about the influence of Islamic law and its principles regarding stem cell research regulation in his article titled, "Islamic ethics and stem cell research" published in 2013. He believed that there is a link between Islamic law and Islamic ethics, whereby the traditional Islamic ethics justifies the embryonic stem cell research, recognizing its potential as long as it is within limitations (Olawale, 2013). Soon Sivaraman and Noor (2014, 2015) wrote about the significance of approaching multi-religious figures similar to Foong (2011). According to the published articles titled, 'Ethics of embryonic stem cell research according to Buddhist, Hindu, Catholic, and Islamic religions: perspective from Malaysia' asserted that the embryonic stem cell (ESC) research is permissible in Hindu, Buddhism, and Islam based on the "end justifies the means" notion, while the Catholics clearly against it (Sivaraman & Noor, 2014). The common dilemmas that surfaced concerning this topic are the sanctity of life, do no harm and the motive of research (Sivaraman & Noor, 2015). Despite tackling the ethical aspects of hESC first from a religious perspective, it highlighted the value of including public consultation in all discussion concerning stem cell regulation (Foong, 2011; Sivaraman & Noor, 2014)

The regulative discussion concerning stem cell in Malaysia brought forward the matters of patenting stem cell innovation specifically those that emerged from the hESC research but from an ethical and religious angle (Azmi & Zawawi, 2015), and the considerations of *halal* which implies permissible in Islamic law or *Shari'ah* law regarding stem cell therapies (Rahman, 2015). Since then, there have been several articles written in Malaysia regarding other matters concerning stem cell, like knowledge, attitude and awareness surrounding the entire pursuit. Although the ethical and religious angle plays a significant role and it is greatly discussed, however the regulatory matters of stem

cell research and its technologies has yet to reach a similar height and could be greatly improved to encourage the Malaysian stem cell policymakers and regulators to consider the endeavor.

The articles identified for this study were mostly preliminary addressing the various issues within the ethical discourse such as *halal* patenting, the justification of human embryos for research and religious position considering the hESC research, but none focused specifically on the issue of stem cell regulation in Malaysia or its implications. Although, the international concerns like the federal funding matters highlighted by the United States are not that relevant in Malaysia, the topic of patenting stem cell innovation has its merits, but on a completely different tone involving Islamic perspective. Globally, the slow growth of stem cell research in Malaysia and the absence of law and policies regulating them have not captured anyone's attention. It is clear that there is a huge gap concerning studies done on the topic of stem cell regulation in Malaysia.

Regarding the publications written by Malaysians, it is clear that there are currently very few writings that are exclusively focused on the ethics and regulation on stem cell research and its technologies, especially when compared to those written by international authors. The foundation of the international authored inquiries is based on either a general or personal view of the authors while the Malaysian ethics displays diverse discussion reflected on their regional distribution and cultural exposure. There is a clear difference in the approach of their ethical inquiry which is often left unexplored. Therefore, this study will weigh the ethical debates in fulfillment of one of the research objectives of this study, while bringing about the long overdue discussion of Malaysian stem cell regulation in fulfillment of two of the research objectives of this study.

3.5 The research framework

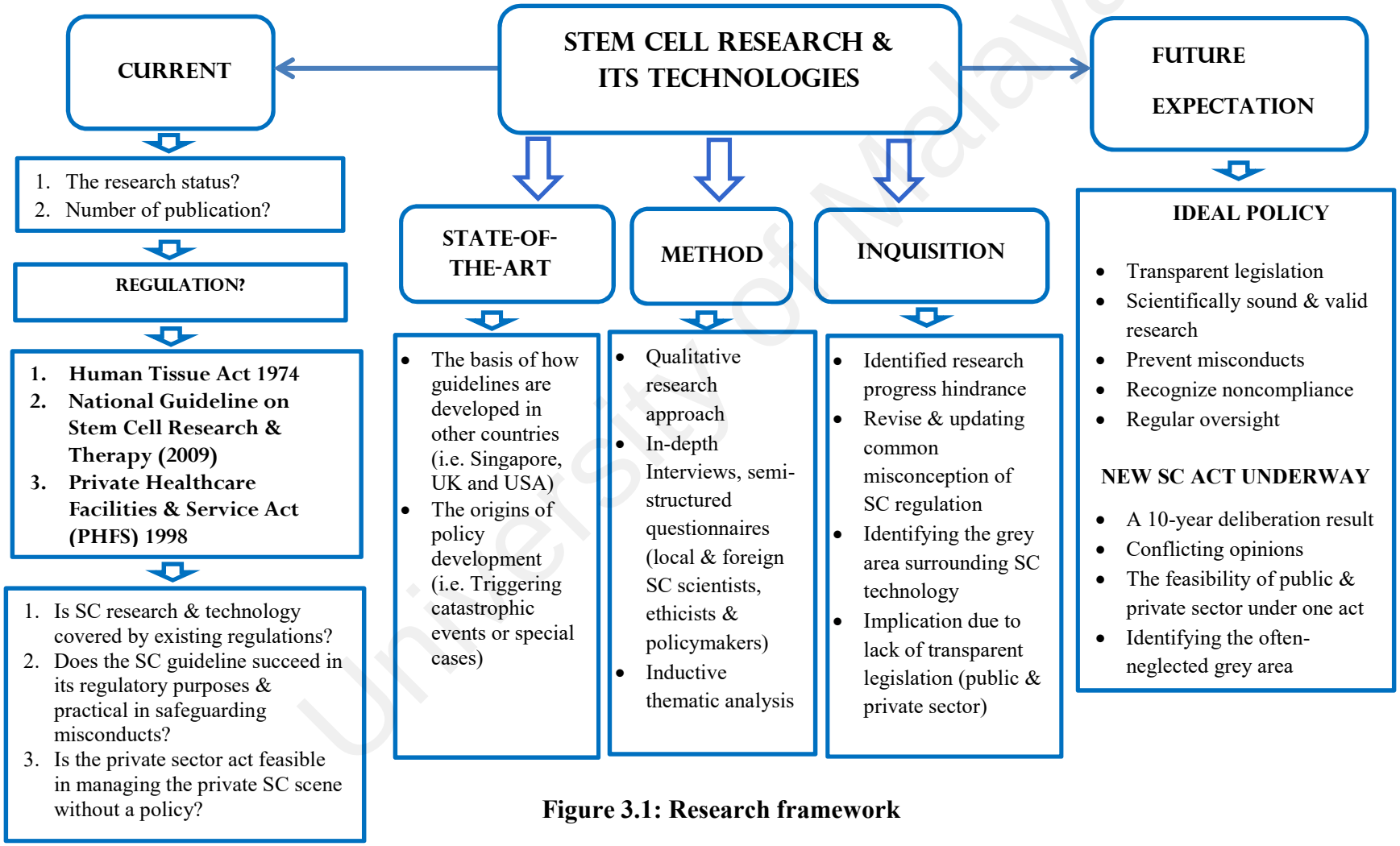


Figure 3.1: Research framework

CHAPTER 4: METHODOLOGY

4.1 Introduction

This chapter justifies the motives of the methods employed in this study, which is presented in two parts. Part I is to conduct in-depth interviews with experts involved in stem cell research including its regulative affairs and part II is to search for publications focusing on the ethical concerns of stem cell research and technology. This study largely constitutes as a qualitative research but incorporated some quantitative methodology. This chapter explains the rationale for the qualitative and quantitative methodologies, the in-depth interview as the chosen method including a description of the selection of interviewees, the data analysis and finally the limitation of the selected methods.

The qualitative research method was suitable for this study as it provided comprehensive answers to the research questions. Qualitative research method is appropriate in answering the 'whys' and the 'hows' of the human behavior including opinions, attitudes, and experiences which this study involve mostly (Guest et al., 2012). Primarily the qualitative research method is descriptive in nature and concentrates on the procedures which includes understanding the dynamics and explaining it. This makes the qualitative research method appropriate for this study in discussing the regulatory development and policy making of stem cell in Malaysia. It is a method that is more exploratory and implicated with explanations of social phenomena, which is gathered from variety of fieldworks ranging from observations to in-depth interviews.

According to Patton (1990), the qualitative research method prevents fieldwork to be limited by predestined classifications, instead it contributes greatly to the depth, openness and details of qualitative inquiry which is what all researchers look for. The qualitative research is considered to be inductive as it does not begin with sets of hypothesis or intent to test models, but simply uses inductive analysis of the collected

data to study the themes, interrelationships in the phenomenon. Therefore, in this study the qualitative research permits a more holistic perspective, as it manages to take up a whole phenomenon under study through triangulation of different perspectives which allows a thorough examinations of the topic in study (Miles & Huberman, 1994; Patton, 1990).

The quantitative methodology was devised in the physical sciences, especially in chemistry and physics, whereby the researchers employed mathematical calculations for data analysis (Creswell, 2005). Aliaga and Gunderson (2006) defined quantitative research as 'explaining phenomena by collecting numerical data that are analyzed using mathematically based methods'. In this study, a quantitative method was employed on a very minimal scale in two separate areas. At first, as mentioned by Creswell (2005), it was used to describe the research problem by offering a description of the stem cell development in Malaysia by identifying the statistics of the stem cell transplantations, the stem cell entities and stem cell publications that became the basis of the problem statement that was established previously in Chapter 1 but will be also contribute as research finding in Chapter 5 as an assessment of impact (Creswell, 2005). It is also used to identify and evaluate the stem cell research ethics publications to explain its relationship and impact towards stem cell regulations in Malaysia.

Part I: Malaysian stem cell regulation

4.2 In-depth interviews

In a qualitative research, there are many types of interviews available such as focused interviews, unstructured interviews, non-directive interviews, open-ended interviews, active interviews and semi-structured interviews. Interviews are often one-to-one, between the interviewer and the respondent, but they can be in groups or in person intercepted in shopping malls or the park or through telephone or via electronic

correspondence like emails and fax, however these are not commonly restricted (Fontana & Frey, 1994). Figure 4.1 presents the elements that are important to consider when choosing interview as a research method.

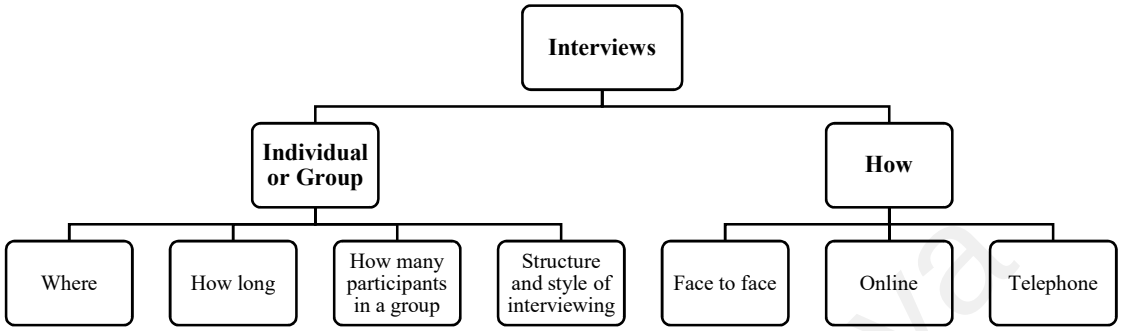


Figure 4.1: The classification of interviews based on methodological features.

[Source: Image reproduced with permission from Styśko-Kunkowska (2014) from pg.46.]

This study employed semi-structured interviews that entailed vital questions that help define the unknown that require further exploration. The interviews of local experts were conducted face-to-face involving one person while the foreign experts were interviewed through email. The nature of the semi-structured interview allows it to be scheduled at any specified time and location in advance. The semi-structured interviews allow the interviewer to freely probe the respondents to comment expanding the original chain of question in a conversational manner without any restriction, which lasts for 30minutes to a few hours. It often used in the study of ethics and policy research such as this, which enables the tracking of ethical opinion, legislative and regulative changes (DiCicco-Bloom & Crabtree, 2006; Hancock et al., 2009).

The interviewer need to have certain skills and training prior to the interview session to help maximize the validity and reliability of the interview data (Fontana & Frey, 1994). The relevant interview skills are, (1) the interviewer to be knowledgeable and familiar with the topic in discussion, (2) the ability to actively listen to the respondents' answers while staying quiet, (3) the right amount of probing to extend the answer for a clearer explanation and (4) to stick within the topic in discussion and not

stray away off topic causing confusion and wasted time. It is equally important to practice the technique of interview and keep track of all the other necessary aspects of the interview such as the interview schedule, body language, dress code (Gill et al., 2008; Harrell & Bradley, 2009; Whiting, 2008). It proved valuable to audio record the interviews sessions as it creates a more casual and relaxed environment and avoid note taking distraction. Plus, digital voices act as permanent record that is much easier to use and is less repulsive than tape recorders. It also allows the verbatim transcription of the audio recorded interviews to prevent bias and protect the authenticity of the original data (Liamputtong & Ezzy, 2005; Whiting, 2008).

Finally, the matters of the ethical conduct of this research, which includes, first the approval of the appropriate ethical committees regarding the involvement of respondents as human subjects in this study and second, the informed consent of the respondents. It is mandatory for all the respondents of the interviews to consent freely their willingness to take part in this study without feeling pressurized or coerced. Therefore, it is the interviewer's duty to well-inform the respondents regarding the study, the objective and finally to assure that their identity will remain private and confidential to protect their rights, while guaranteeing their decline or refusal will not affect in any way (Bricki & Green, 2007).

4.3 In-depth interview as the selected method

This part explains the reason why in-depth interview (IDI) was chosen as the appropriate method of study of the ethical and regulatory aspects of stem cell research and technologies in Malaysia. The in-depth interviews involve focused conversation with respondents to investigate the perspectives on specific idea or situation. It is useful in exploring the respondents' participations, their experiences and expectations concerning the idea or situation as well as their opinions on that matter (Boyce & Neale, 2006).

Interviews are used commonly in many qualitative researches as data collection method and one such study is the Wainwright et al. (2006) which studied the 'Ethical Boundary-Work In The Embryonic Stem Cell Laboratory' comprised of interviews involving 15 biomedical scientists working in laboratories aims directly to draw a rhetorical boundary between science and non-science.

The article written by Zarzeczny and Clark (2014) titled, 'Unproven Stem Cell-Based Interventions & Physicians' Professional Obligations; A Qualitative Study With Medical Regulatory Authorities In Canada' also employed semi-structured telephone interviews of six representative of different provincial Colleges of Physicians and Surgeons in Canada, which aimed to study the experiences, involvement and viewpoints concerning stem cell tourism (Zarzeczny & Clark, 2014). Following that, the article written by Saniei (2013) entitled, 'Human embryonic stem cell science and policy: The case of Iran' was written to describe the views of the Iranian scientists, embryologist and the members of their ethical committee concerning the current human embryonic stem cell (hESC) policy as well as to explore their view on the mater.

Joshi et al. (2015) wrote the article, 'Awareness and Attitude of Physicians in Academia towards Human Stem Cell Research (HSCR) and Related Policies in Rajasthan, India' by analyzing data retrieved from the semi-structured interviews conducted with 200 doctors from three different public medical colleges in Rajasthan, India to gain insight of their attitudes and awareness regarding the use of stem cell research including the matters of international and ethical policy of stem cell. It has proved that in-depth, semi-structured interview would be the most appropriate and effective to study the ethical concerns and the implication of regulatory policy involving stem cell research and technologies in Malaysia.

4.4 Interview guide

The interviews have proven as an important method of qualitative research but it requires extensive preparation which entails developing the interview guide. The interview guide steers the conversation within the subject and focus of the study. It guides in the development and sequence of the questions, while deciding which information requires further perusal (Patton, 1990). It consists of a list of questions with certain degree of freedom and adaptability, which varies from being greatly scripted to being reasonably loose that is well framed by the research objectives.

This study adopted the semi-structured interview that permits the line of questioning to flow effortlessly without a strict order, with some freedom to go 'off-script' for probing and follow-ups whenever necessary. This would enable the interviewer to build conversation, and ask questions freely within the predetermined topic of interest (Boyce & Neale, 2006; Patton, 1990). The research question of this study was developed based on the available literatures, such as books and journal articles especially on the topic concerning stem cell research ethics and policy implication. Figure 4.2 displays the development process of the interview guide, which will safeguard the data collection objective.

Figure 4.2: The development of interview guide.

[Source: Image reproduced with permission from Styśko-Kunkowska (2014) from pg.88.]

The interview was organized and developed based on two key area of the research inquiry that was deemed important which are: (1) the ethical inquiry of stem cell research

and (2) the regulation of stem cell research and technologies. Within these two areas, the interview questions were then designed and formulated considering all the identified issues concerning them from available sources, such as the destruction of embryo in embryonic stem cell (ESC), the public and private sector management of stem cell and the implication of the current regulation of stem cell in Malaysia.

The interview guide (attached as Appendix D) was developed and finalized early Jan 2013. The interview was conducted beginning of March 2013 which was divided into two sections, (1) the email corresponded interviews and (2) the face-to-face interviews. Table 4.1, presents the interview guide which is aligned with the research objectives and the research questions of this study. The preliminary interview comprises of the interviews of stem cell research experts, whom are actively involved in stem cell research (not restricting to a particular derivative of stem cell) and the ethical experts of stem cell research and its technologies, whom regularly engage in stem cell debates. The specific policy interview involves interviewing the stem cell policy makers (research and therapies), whom are governmental officers in charge of regulating stem cell research and its technologies in Malaysia, which includes more detailed questions regarding the current stem cell oversight in Malaysia.

Table 4.1: The interview guide/question based on the research objectives & research questions.

Research Objectives	Research Questions	Interview Questions
(a) To study the status and the regulatory processes of the current stem cell research and therapy in Malaysia	(a) What is the current status of stem cell research and therapy in Malaysia? (b) How is stem cell research and therapy currently regulated in Malaysia? (c) What are the implications of the current regulative measures concerning stem cell technologies in Malaysia? (e) Is the current stem cell guideline adequate in regulating the entire stem cell research and therapy?	**The Preliminary Interview** 2. As a scientist do you believe there are enough law/legislation/guidelines regulating proper SC research? 11. Do you think it is necessary for the world to work together to ensure the regulations of SC research as a whole? **The Specific Policy Interview** **[Questions: 1-6, 8, 10, 14, 16]** 1. When the Malaysian government did first start looking into the issue of stem cell research and therapy? 2. We have a Research and therapy, which was established in 2009, what was its original intention? 3. Do you believe the guideline succeeds in its aims up to now? 4. In your opinion, how is stem cell research regulated in Malaysia? 5. Apart from the institutional review board (IRB) and institutional ethics committee (IEC) which help monitor stem cell research pursued by local academicians, students affiliated with local institutions of higher learnings, how else are/can we regulate stem cell research? 6. Is there an oversight committee assigned to help with the regulation of stem cell research and therapy? 8. In April 2014, Health Ministry's Medical Development Director Datuk Dr Azmi Shapie said to The Star News that they have set up a National Stem Cell Coordinating Centre, that commenced operations in March. Besides assisting with the search for a suitable donor in Malaysia, what is its objective/function? 10.What are the legal, ethically approved procurement of stem cells? 14. Looking at the original 2006 Stem Cell Guideline, it mentions that research on 14th day and older embryos are prohibited based on the justification of human life, as accordance to the Malaysia's National Fatwa Law. However, in the 2009 Guideline although it said to have valuable feedbacks from other religious groups/experts (namely Buddhism, Hinduism, Sikhism, Taosim & Christiany) but it still and only reflected the Fatwa Law. Why? 16. How did the religious input used otherwise?

Table 4.1, continued

(b) To explore the ethics of stem cell research as presented by international and Malaysian authors	(d) What are the perspectives of ethical inquiry involving the stem cell research and therapy? (e) How are the internationally published and Malaysian publications reflect in terms of the ethical inquiry of stem cell research and therapy	**The Preliminary Interview** 1. In your personal opinion, what is the main potential of SC that makes it a gold-mine as some people believe? 2. As a scientist, when do you think 'life' begins? At conception or at foetal stage? Why? 3. Do your think a blastocyst (5-day old embryo) should be given the same respect and right to life as a living human adult? Why? 4. What is the ethical debate over human embryonic stem cell (heSC) research? 5. Are you against heSC research? 6. I hear some scientists are more comfortable to use Preimplantation genetic diagnostics (PGD) embryos compared to IVF embryos. What are your opinions on the matter? 7. Using heSC to save one's life would be the beginning of a "slippery slope" which could end in the unnecessary killing of embryos for people who hunt SC merely for cosmetic purposes. Your thoughts on the matter.

Table 4.1, continued

(c) To discuss the implications of allowing Malaysian stem cell research to be guided by the present regulatory policies and its limitations	(e) Is the current stem cell guideline adequate in regulating the entire stem cell research and therapy? (f) How and where can the current regulatory measures be compromised due to continuous development of stem cell technologies.	**The Preliminary Interview** 12. How do you believe we can help in monitoring SC research without violation of human rights? 13. In your expert opinion, is it important for countries with SC research and therapy to regulate the research with a legal framework (policy or law) to protect the research subjects (embryo) and to prevent unethical issues? **The Specific Policy Interview** **[Questions: 7, 9, 11, 12, 13, 17]** 7. In 2012, our former Health Minister Dr Liow speaking to the press in China, said "so far the ministry has no interest in pushing for a stem cell act". Is that still how the ministry sees the stem cell research now or has the opinion changed with the new minister? Why? 9. In your opinion, has the stem cell research field improved over the last decade or two? So, how has these advancements contributed to the Malaysian public? Policy wise, has there been any improvements too? Why or why not? 11.Hypothetically speaking, let's say one researcher in a public university wanted to pursue human embryonic stem cell research. First, he got to secure approval from the IRB and IEC. Then, we might need to justify once more to secure grant or fund, but after that, how are the authorities monitoring the continuous progress of his work? Once all the necessary approvals are attained, is there any way to capture any wrong-doing such as creating more embryos through somatic cell nuclear transfer (SCNT) although originally, they claim to only use IVF surplus embryo from fertility centre? 12. How about the private laboratories? There are several labs such as Stempeutics, Stem Life, CryoCord and others. Some of them are licensed and are trading legal products, but there are also non-licensed (illegal) companies selling un-tested, un-approved products to the public. Do you agree? 13. Since whistle-blowing is not practical in Malaysia (despite the Whistleblowing Protection Act 2010), how can we safe-guard the welfare of subjects (embryos), the principles written in the Guideline and ultimately the welfare of user (public) from un-necessary harm and wrong-doings? 17. In your expert opinion, since there is no use of local human embryonic cell lines, there is no need for regulation or policy?

4.5 Validity & reliability

In any research reliability and validity are fundamental requirements which help differentiate between a good research and a poorly conducted one. Reliability applies to the consistency of the research finding and its reproducibility by other researchers. Validity refers to the accuracy or the investigative capability of the selected method and its appropriateness in investigating what intended (Brink, 1993; Kvale, 2008). Qualitative studies are subjective due to the wide interpretations of its researchers leading to questionable finding. Therefore, it is important to enable researchers and scientists decide which research and findings to be credible and trustworthy (Brink, 1993).

Lincoln and Guba (1985) believe that the element of reliability is irrelevant in a qualitative study. They claim that a qualitative study can be objective only when they employ objective instrumentations between the researcher and the object of study. However, when the researcher is the chief instrument of the study then objectivity is said to have dissolved. Lincoln and Guba (1985) also said that, a study is reliable when it is stable and is reproducible but that is not possible in most qualitative study due to a wide range of designs which researchers can easily modify according to their research aims making the methodology impossible to replicate with unaccounted variables. This led researchers to create specific concepts and adopt terms like rigor, quality, and trustworthiness, which they consider appropriate (Lincoln & Guba, 1985).

The reliability and validity of this study greatly improved with the consistent interviewing skills and the integrity displayed by the interviewer, who is the key instrument of this qualitative study. Several actions were taken to ensure that this study is reliable and valid through the conventional and modern approach, which are, (1) to ensure the interview questions are open-ended, to minimize pre-determined responses, (2) the careful wording of the interview questions, which will increase reliability of its answers, (3) recording the interview session to prevent data losses, that ultimately reduce

inconsistency, (4) to take-down notes during interview sessions to ensure high consistency between the recorded data and the written notes, (5) to organize and file the interview sessions (details of interview such as time, date, venue, informed consent) including the transcripts to minimize mix up, and finally (6) to employ data triangulation to further increase the validity of the study by incorporating several viewpoints or perspectives. Patton (2001) encourages researchers to use triangulation to strengthen their study, which according to Denzin (1978) there are four basic types of triangulation, which are (1) data triangulations, (2) investigator triangulations, (3) theory triangulations and (4) methodological triangulations. In this study, data triangulations, was employed, whereby evidence was obtained from a wide range of 'experts' or subjects (scientists, ethicists, and policy experts) and comparing the findings proved valuable not to mention highly valid (Denzin, 1978; Patton, 2001).

The mentioned measures were treated as controlled variables, which would help other researchers in repeating the study to a certain degree. It definitely helped making this a reliable and a sound research without bias.

4.6 Purposeful sampling

This section explains the sampling of the suitable respondents for this study. In a qualitative study, the sampling of interviewees or research subjects needs to be homogenous with some critical similarities depending on the research questions, its objective and available resources (DiCicco-Bloom & Crabtree, 2006). Purposeful sampling was employed in this study to identify and select respondents, which is considered as a common method in a qualitative study. According to Patton (1990), the logic and the strength of the purposeful sampling depends greatly in selecting 'information-rich' cases from which interviewer can learn from in-depth. The individuals were selected based on their background knowledge or expertise which fit best with the

purpose of this study. The active stem cell researchers and scientists, the ethicists actively engaging in stem cell related debates and the Malaysian stem cell research and technology regulators, were selected as participants of this study. Their experiences, knowledge and direct involvement in the research, controversial debates and the regulative matters of stem cell research and technologies deemed them highly suitable.

Firstly, Google (and other relevant databases) were used to search for (1) foreign and Malaysian stem cell scientists whom are involved in stem cell research, especially on embryonic stem (ES) cell as their insight would be comprehensive, (2) foreign and Malaysian ethical experts or ethicists, actively debating on the many ethical discussions related stem cell whom have published many valuable articles both locally and internationally and finally (3) public service officers attached to the Ministry of Health (MOH) Malaysia whom are in charge of overseeing and regulating stem cell research and its technologies. Although the search resulted in many potential participants, a small number of them responded positively when contacted via email and by telephone to reconfirm their willingness in participating in this study. The foreign experts corresponded strictly via email from the beginning while the Malaysian experts responding the initial emails was contacted further through phone calls for formality and to discuss availability.

A total of 17 respondents were selected, out of which eight (8) of whom are from Australia, the United Kingdom, the United States and Canada and were interviewed through email while nine (9) Malaysian experts were interviewed face-to-face. The first email correspondence began on 8th September 2013 for the foreign experts and carried on to the first face-to-face interview on 1st August 2016 involving Malaysian experts.

4.6.1 Sample size

According to Patton (1990), there is no rule for sample size in any qualitative study. It is subjected largely to what one wants to know, the objectives of the study, what's at stake, what proves valuable and credible within the accessible time and resources. Therefore, what represents a satisfactory sample size? In a qualitative study, sample sizes can be relatively small. The interviewer carries out interviews until it reaches empirical saturation, which is when the data stop generating new facts (Baker & Edwards, 2012; Bricki & Green, 2007). However, the concept of saturation cannot offer practical guidance for approximating a healthy sample size prior to data collection (Guest et al., 2006). Therefore, in this study considering the limited time and resources, only experts that responded positively were confirmed as respondents for this study, despite the many that were contacted.

Since this study intended to seek the perspectives of different experts concerning stem cell research and it incorporated purposeful sampling which relies on 'information-rich' cases, therefore in-depth information from a smaller number of people still proved valuable and significant. There is a range of factors that can affect the extent of data a researcher collects, but it definitely is not measured solely by the number of interviews conducted (Baker & Edwards, 2012). Altogether, 17 respondents were interviewed, eight were foreign experts and scholars affiliated with universities abroad, while nine are Malaysian experts affiliated with Malaysian institutions. They are stem cell scientists, ethicists debating on stem cell issues and stem cell regulators and policymakers.

4.6.2 Basic profile of respondents

The scientists conducting stem cell research, the ethicists engaging in numerous stem cell related debates and the stem cell research and technologies regulators were identified as suitable participants for this study who are also known as interviewees or respondents. The basic profile of these respondents is given below consistent with their position and career at the time of the interview. The detailed biography of these respondents is available in the Appendix for an extended reading. However, some respondents will be labeled "anonymous" with respect to their request to remain anonymous, hence they will only be described in general based on their expertise, experience, and position.

4.6.2.1 Stem cell scientists

The stem cell scientists are from the United States, Australia, the United Kingdom and Malaysia respectively. They are, in no particular order:

1. Professor Dr. Martin Pera [Australia]

Dr. Pera was a professor of Stem Cell Sciences at the University of Melbourne at the time of the interview. He was a part of the group that pioneered the isolation and characterization of the human pluripotent stem cell in Australia which helped in understanding embryonic stem cell (ESC) and its development. His advanced knowledge and experience in stem cell, having authored over 100 peer-reviewed articles and holding 14 patents, he has proven as an expert of stem cell research and a participant for this study.

2. Professor Dr. Dan Kaufman [United States]

Professor Dr. Dan Kaufman was a Professor of Medicine and an Associate Director of the Stem Cell Institute at the University of Minnesota at the time of interview. He has over 14 years of experience and more than 80 publication concerning stem cell, making his input valuable and significant as a stem cell scientist.

3. Associate Professor Dr. Megan Munsie [Australia]

Associate Professor Dr. Megan Munsie is the Head of the Education, Ethics, Law and Community Awareness Unit, a joint effort by the University of Melbourne and Monash University. Involved in stem cell research since 1995 and have co-authored many educational resources and have extensive linkages with Australian patients' advocacy groups, media regulators, politicians, and policymakers, that made her knowledge and experience valuable for this study.

4. Professor Dr. Peter W. Andrews [United Kingdom]

Professor Dr. Peter W. Andrews, has a long-standing research with human embryonic stem (hESC) cells and human embryonal carcinoma cells, having worked on pluripotent stem cell since 1974. He is currently the Arthur Jackson Professor of Biomedical Sciences at the University of Sheffield, United Kingdom and an editorial member of various journals. His knowledge and experience are considered a huge addition to our study.

5. Associate Professor Dr. Rajesh Ramasamy [Malaysia]

Dr. Rajesh is an Associate Professor at the Department of Pathology, Faculty of Medical and Health Sciences in the University Putra Malaysia (UPM) since 2006. He has written over 86 publications related to immunology and stem cell. He is also the current Head of Stem Cell and Immunity Group as well as the Head of Regenerative Medicine

Research Program in UPM. His fast track in stem cell research was the reason why he was chosen for this study.

6. Associate Professor Dr. Thilakavathy Karuppiah [Malaysia]

Associate Professor Dr. Thilakavathy is currently an Associate Professor at the Department of Biomedical Science, Faculty of Medicine and Health Sciences of the University Putra Malaysia (UPM). She is also a member of the Stem Cells and Molecular Group (SCMG) in the UPM. She has over 20 publications and have some work done on mouse embryonic stem (ES) cell. Dr. Thilakavathy's experience is considered valuable in learning all the level of research in Malaysia.

7. Dr. Norshariza Nordin [Malaysia]

Dr. Norshariza Nordin is a Senior Lecturer at the Department of Biomedical Science, Faculty of Medicine and Health Sciences, University Putra Malaysia (UPM). Her stem cell research in Malaysia includes amniotic fluid stem cell studies, the mechanism of differentiation process of stem cell using mouse embryonic stem (ES) cells and the *in vitro* model study of Alzheimer. Dr. Norshariza has over 30 publications in stem cell research, making her input useful in this study.

4.6.2.2 Stem cell ethicists

Stem cell ethicists are experts that have discussed and debated the matter of ethics and controversies involving stem cell research and its technologies. They are from the United States, Canada, and Malaysia. In no particular order they are;

1. Dr. Arthur Caplan [USA]

Dr. Arthur Caplan is the Drs. William F. and Virginia Connolly Mitty Professor of Bioethics at the New York University (NYU) and the founding Director of the Division of Medical Ethics launched in 2012. He was the first person in NYU interested in the issue of medical ethics and engaged in the issues related to the use of fetal tissues from abortions around the 1980s, cloning and the embryonic stem cell research in late 1990s. Dr. Arthur Caplan has written close to 600 articles on research and medical ethics and holds seven honorary degrees from colleges and medical schools. His experiences and active engagement in the ethical debate concerning medical ethics especially in embryonic stem (ES) cells, prove to be valuable for this study.

2. Anonymous [Canada]

Respondent is one of the few assistant professors at the Alden March Bioethics Institute, Albany Medical College and a Research Associate at the University of Alberta, Canada. The respondent's research interest includes ethics, the policy of embryo, stem cell research, genetics, the ethics and governance of research concerning humans. Published many articles on subjects such as stem cell tourism, translation and commercialization of stem cell research, bio-banking, informed consent and many others.

3. Professor Dato' Dr. Abu Bakar Abdul Majeed [Malaysia]

He is currently the Deputy Vice Chancellor of the University Technology Mara (UiTM) Sungai Buloh and Selayang campus, executing the duties of a UiTM Selangor campus Rector. He's research interest includes neuroscience, drug delivery and bioethics. He is also the current Chairman of the National Bioethics Council of Malaysia or the *Majlis Bioetika Negera*. Professor Dato' Dr. Abu Bakar Abdul Majeed has published over 360 articles on topic concerning his expertise making his input a valuable asset.

4.6.2.3 Stem cell policymakers

Stem cell policymakers are public service officers attached to the relevant division within the Ministry of Health (MOH) Malaysia. They were involved in the formulation of the stem cell guideline and other policy related deliberation since. Since this study is about the regulative aspect of stem cell in Malaysia, no foreign policy experts were contacted. They are in no particular order;

1. Senior Chief Director of Obstetrics & Gynecology Pediatrics Service Unit, Medical Development Division, Ministry of Health (MOH) Malaysia [In-Charge of Public Sector]

A medical doctor by qualification, the respondent is currently the Senior Chief Director, in the Obstetrics & Gynecology Pediatrics Services Unit of the Medical Development Division, within the Ministry of Health (MOH) Malaysia, located in Putrajaya. Apart from the Drafting Committee for the Guideline on Stem Cell Research, the respondent is also a member of the National Stem Cell Research and Ethics Sub-Committee (NSCERT). The respondent's involvement in the stem cell guideline formulation from the very beginning made the respondent valuable for this study.

2. Senior Pediatric Consultant, Medical Development Division, Ministry of Health (MOH) [In Charge of Public Sector]

The respondent is a medical doctor by qualification, currently the Head of the Department of Pediatric Medicine, of the Kuala Lumpur Hospital (HKL). The respondent has offered numerous consultations including for stem cell guideline formulation and as a member of the National Stem Cell Research and Ethics Sub-Committee (NSCERT). The respondent was a pioneering stem cell researcher in Malaysia with over 50 publications making him an asset for this study.

3. Deputy Director of the Private Medical Practicing Control Section, Medical Practicing Division, Ministry of Health (MOH) Malaysia [In Charge of Private Sector]

The respondent is a medical doctor by qualification and is currently the Deputy Director of the Private Medical Practicing Control Section within the Medical Practicing Division of the Ministry of Health (MOH) Malaysia, located in Putrajaya. The respondent's division is one of the four divisions within the Medical Program, headed by Deputy Director General of Health (Medical). The respondent is also in charge of overlooking the private healthcare sector by enforcing the Private Healthcare Facilities Services Act 1998 [Act 586].

4. Deputy Director for the Centre for Investigational New Product, National Pharmaceutical Regulatory Agency (NPRA) [In Charge of Private Stem Cell Product]

Respondent is the Deputy Director of the Centre for Investigational New Product at the National Pharmaceutical Regulatory Agency (NPRA) formerly known as National Pharmaceutical Control Bureau (NPCB) in-charge of overlooking the stem cell products, i.e. stem cell therapies once introduced commonly, and was a participant of the

'Brainstorming Workshop – Scientific Meeting on Stem Cell Research' held in Kota Bharu between 4 – 6 May 2008 as published by the National Guidelines for Stem Cell Research and Therapy 2009.

4.7 Method of analysis

This section explains the method of analysis used for this study. According to Merriam (1998), the data analysis should incorporate either inductive and deductive reasoning and presented in different degree of analysis. Bogdan and Biklen (1982) described qualitative data analysis as examining the data, classifying and deciphering it into manageable bits, combing and harmonizing it, studying for patterns, uncovering what is critical and finally determining what to disclose. According to Patton (1987), there are three distinct stages in data analyzing, which are classifying data, summarizing and cataloging and finally identifying patterns and themes from them. The qualitative analysis is challenging and needs accurate processing and classification of respondents' response for these reasons.

This study closely followed the six critical steps listed by Braun and Clarke (2006), in thematic analysis, which are (1) data familiarization, (2) initial code generation, (3) themes searching, (4) themes reviewing, (5) defining and naming themes and (6) production of report. In this study, the data collected in the form of in-depth interview response was analyzed to understand the respondents' opinions and feedbacks which will be examined for patterns and themes and finally integrating them as theory (Patton, 1990). The collected data in the form of quality audio recorded interviews are transcribed manually, verbatim into text form to ensure no data loss by the researcher while gaining familiarity of the data based on prior knowledge, which is also known as an interpretative process. The transcription process includes careful examination of data through repeated listening which took an average between an hour to several (close to ten) depending on

the intensity of probing and questions-and-answers within the recorded sessions (Bailey, 2008).

The transcripts are categorized into stem cell scientists (Malaysian and foreign) and ethicists (Malaysian and foreign) engaged in stem cell debates and stem cell policymakers or regulators (Malaysian). Each category of transcripts is then carefully read line by line by applying a label or more accurately a 'code' which represents the key points within the passage (Miles & Huberman, 1994). The coding of transcribed interview data is an essential process, and Strauss and Corbin (1998) defined 'open coding' a part of the analytical process where concepts are inductively identified recognized and located from the data. Although coding could represent independent things such as behaviors, incidents, emotion, however in this study, the codes were based on the more intricate aspects concerning the ethics of stem cell research, its regulation, and its pre-determined concepts. The long list of collated codes then helps generate a broader unit of analysis known as themes, which are more data-driven (Boyatzis, 1998). The reason the analysis is approached from a specified angle like scientist, ethicists, and policymakers within a similar broad theme is to study and distinguish the link between them.

In this study, the codes, sub-themes and themes were inductively identified from the respondents' transcripts (Guest et al., 2006). The identified themes are carefully reviewed to better refine them removing the incompatible ones which resulted in eight themes altogether, however, they do not emerge in all category. Braun and Clarke (2006) claim that themes present the significant part of the data corresponding to the research question which symbolizes a certain degree of patterned response of the transcript. Although thematic analysis is a part of the original grounded theory, however it is important to understand that grounded theory involves iterations which is moving back and forth between data collections and analyses unlike thematic analysis which only

initiates analysis once data collection is complete (Glaser & Strauss, 1967; Strauss & Corbin, 1990). The refined themes facilitate in generating a satisfactory thematic map of this data, which then defined and specify the themes that represent as the final analysis, which is clearly presented in Chapter 4.

The flexibility and its accessibility made thematic analysis a suitable method to summarize key aspects involving participatory research model with concentrated data, which recognized for its unanticipated insights and informing policy development (Braun & Clarke, 2006).

Part II: Stem cell research ethics

4.8 The publication searches

One of the research objectives of this study is to evaluate the perspectives of the ethical inquiry of stem cell research between publications written by international authors and Malaysian authors. In order to carry out the literature review, it is necessary to conduct the search of the respective publications. The search was divided into the international publication search and the Malaysian publication search. This part includes both quantitative and qualitative analysis of data.

4.8.1 International publication

The international publication search was carried out in the form of a keyword search using several databases accessed through the University of Malaya library portal. There are many available databases such as PubMed, Scholar Google, Web of Science (WoS) (Core Collection), but combination of databases (Embase, JSTOR, MEDLINE, ScienceDirect and BioMed Central) was chosen as the others resulted in less publication with limitation in online software making the combination of databases as most adequate. The keyword search using combination of databases resulted in more articles compared to using any one larger database.

The search was conducted in 2013 using appropriate keyword and Boolean terms. The keyword stem cell and ethic, accompanied with the asterisk and inverted comma symbols, (“stem cell*” AND “ethic*”) in the title section allow the databases to recognize and identify many variations of spelling (even misspelling). The resulting publications were further refined to embryo destruction to capture only relevant publications. Only journal articles were considered while other types of publications like review paper, conference papers and other were not. In order to prevent Malaysian authored articles

being captured during the search, the country Malaysia was excluded. The search period includes from 1980 to 2013.

4.8.2 Malaysian publication

The search for the Malaysian authored publications on the ethical inquiry of stem cell research combined two parts, which are (1) internet search engine (Google) and published books and (2) the database search using Web of Science (Core Collection). The Google search resulted in conference papers, proceedings, and newspaper article, while the locally published books resulted in several book chapters. The Web of Science (WoS) (Core Collection) database was used to search for this publication by employing similar keywords as the international publication search, for example ("stem cell*" AND "ethic*"). However, the country was refined to only Malaysia, which captures international publications written by Malaysian authors affiliated with Malaysian institution and not those affiliated with a foreign institution. The Malaysian authored publication included all types of publication, unlike the internationally authored articles. This is mainly because the ethical discussion involving stem cell is relatively new in Malaysia and limited, therefore it is vital to include all publications ensuring a comprehensive review. The search period is from 1980 to 2016.

4.9 Stem cell research ethics publication review

The purpose of this review is mainly as a method of analysis. The full articles are read and reviewed to specifically learn the research focus, the main points, and the arguments used in the resulting articles which will help in identifying the basis of the ethical inquiry of the retrieved publications (Hewitt, 2007; Jesson & Lacey, 2006). The emerging perspective based on the review will constitute as research finding which is presented in Chapter 5.

CHAPTER 5: RESULT & ANALYSIS

This chapter presents the results and the analysis process of this study. It is divided into two parts for clear presentation since it addresses two distinct topics which are the ethics and the regulation of stem cell research and its technologies in Malaysia. Part I presents the results of the in-depth interview, its transcription and analysis that addresses the first and the third objectives of this study focused on the regulative aspects answering five of the research questions defined in Chapter 1. While part II presents the international and local, Malaysian publication search and analysis that concentrated on the matters of stem cell research ethics that addresses the second objective of this study answering two of the research questions defined in Chapter 1.

Part I: Malaysian stem cell regulation

5.1. Status of stem cell research and development in Malaysia

The current status of stem cell research and development in Malaysia was previously established in Chapter 1 as the basis of the research problem of this study. It was used to demonstrate the progress of stem cell research and technology in Malaysia in the last three decades. This was necessary to prove that there is definite progress instead of mere assumptions. However, since it is also the objective of this research, 'to study the status and the regulatory processes of the current stem cell research and therapy in Malaysia', this section will summarize the current status of stem cell research and development in Malaysia. In the last three decades, stem cell research and technology have progressed tremendously in Malaysia. This was established based on the number of stem cell transplantation conducted, the number of public and private stem cell facilities set up and finally the number of stem cell articles published. Since the first stem cell transplantation conducted in 1987, there is a steady increase in the number of transplantations as reported by the National Transplant Registry (NTR). In 2014 alone,

there was 336 transplantations reported as previously presented in Table 1.1 (NTR, 2014). This includes both allogeneic and autologous stem cell transplantation.

The growing number of transplantations led to the establishment of several private and public cord blood and tissue banks in Malaysia. Table 5.1 presents some of the private and public facilities and entities established involving stem cell research and technology in Malaysia. Apart from the new entities and facilities there are existing ones that have extended their research by working on stem cell such as the laboratories in public institute of higher learning, Institute of Medical Research (IMR), National Cancer Institute (NCI), National Heart Institute (NHI), National Cancer Council (MAKNA) and Clinical Research Centre (CRC) established within the public hospitals.

Table 5.1: The public & private stem cell facilities

Sector	Stem Cell Facilities & Entities
Public	Transplantation Unit & National Transplant Resources Centre
	Umbilical Cord Blood Collection Centre (within some public hospitals)
	Malaysian Stem Cell Registry (MSCR)
Private	Stem Life Berhad
	CryoCord Sdn Bhd
	Nichi-Asia Center for Stem Cell & Regenerative Medicien (NISCELL)
	Stempeutics Research Malaysia Sdn Bhd
	Cellsafe International Sdn Bhd

Aside from the stem cell transplantations and the stem cell facilities, based on the keyword search conducted on 6th October 2016 using Web of Science (WoS) Core Collection resulted in a total of 67,309 articles as presented by Table 5.2. Out of which only 195 were Malaysian authored, among which 18 were the human embryonic stem cell (hESC) based. Although this is a very small number, there is definitely growth compared to the search conducted by Academy of Science Malaysia (ASM) in 2012 which only presented a total of 100 articles for the span of ten years (ASM, 2013).

Table 5.2: The keyword search

Keyword	Database	Result	
"stem cell" NOT "religio*" NOT "ethic*"	Web of Science (WoS) Core Collection	Total	637,309 articles
		Malaysian Authored	195 articles

Although there is significant growth, stem cell research and technology remain unregulated with only a guideline, known as the Guideline for Stem Cell Research and Therapy (2009). There is no law or policy specifically devised to better regulate the subject area. All stem cell research is required to follow protocol as presented previously in Chapter 1 as Figure 1.2. Apart from registering in National Medical Research Registry (NMRR), they need to gain approval from National Medical Research Ethics Committee (MREC), the National Stem Cell Research and Ethics Sub-committee (NSCERT) and respective institutional review and ethics board. Both public and private sector need to conform to the guideline, while the private sector needs to conform to the Private Healthcare Facilities and Services (PHFS) Act 1998 as well (Ministry of Health (MOH), 2009a; MREC, 2012; NMRR, 2017).

5.2. In-depth interview: Deriving sub-codes, codes & themes

The method of analysis for this study comprised of managing the collected in-depth interview data 'by-hand'. Utilizing the three stages of data analysis as mentioned by Patton (1987), the verbatim transcripts of the respondents were first, categorized based on their respective questions, second, generating overarching sub-codes and codes which summarizes the verbatim quotes and finally identifying the patterns and themes from the codes. Tabulating the verbatim quotes extracted from data transcripts help simplify the reviewal process which allows accessible analysis especially for a much easier coding process considering the larger datasets. The coding process basically involves several steps beginning with familiarizing with the data, reviewing their meaning and category

and finally labeling them with a relevant sub-codes and codes, which fits many of the verbatim quotes. It ultimately functions as an overall summary of the verbatim quotes (Braun & Clarke, 2006). In this study, repetition whereby words that are mentioned repeatedly often perceived as significant or noticeable in the minds of the respondents. Therefore, these repetitions are considered as the most straightforward and simplest method to identify sub-codes, codes, and themes (Ryan & Bernard, 2003).

In order, to ensure these codes are suitable and appropriate, respondents' quotes need to be reviewed several times to maximize comprehensiveness. Once, the sub-codes are satisfactory then, the next step involves reviewing process of the sub-codes to assign relevant codes and finally themes that cover the topic (Burnard et al., 2008). The key factor here is to ensure that the sub-codes, codes, and the themes reflect and capture the issues debated regarding stem cell research ethics and its policy implication which is also easily elaborated with the assigned codes, making it more acceptable globally.

5.1.1 Initial coding framework

The initial coding framework will highlight the sub-codes and codes in respect to the specific categories. For the purpose of analysis, the Malaysian experts will be known henceforth as local scientists (LS), local ethicists (LE) and local policymakers (PM), while the foreign experts will be known as foreign scientists (FS) and foreign ethicists (FE). The foreign and local scientists and the foreign and local ethicists responded to the same set of questions, but the policymakers were questioned specifically regarding their explicit duties, role, experience, and knowledge being in regulative management. Therefore, the policymakers' data consist of long, extended answers and comments which was analyzed for common sub-codes and codes. This is followed by the final framework in the following section. Table 5.3 (A) to (E) presents the categories of respondents and their particular sub-codes and codes.

Table 5.3 (A): The initial coding framework for foreign scientist (FS).

Questions	Respondents				Sub-Codes	Codes
	FS1	FS2	FS3	FS4		
1.	*…therapies for intractable, new platform, understand human biology, study functional genomics, disease modeling & drug discovery, important new platform….*	*…revolutionize medical treatment can fix all ailments limited, valuable to learn greater understanding development disease progression identification of other therapeutics…*	*…test new and existing drugs for toxicities therapeutic potential study human developmental biology study genetic disease derive novel therapies cure untreatable disease…*	*…capacity to differentiate regenerative medicine disease modeling drug discovery toxicology…*		• future therapy • broaden knowledge • clinical test • unique
2.	*…no bright line scientifically, in biological terms, trace uniqueness, epigenetic influences, discriminate between life & moral status, conflating leads to controversy…*	*…as a scientist: pre-implantation stage, embryo is not yet a life, as a mother: acknowledged pregnancy at conception…*	*-not my area of expertise-*	*…sometime after gastrulation…*	• conception • gastrulation • no clear line scientifically	• scientific ambiguity
3.	*…termination of pregnancy legalized, does not have the same moral status as an adult, body yet to emerge, impossible predict the ability to develop to term...*	*…blastocyst not equivalent to adult, has potential, not an absolute certainty, without a womb, the blastocysts may not continue…*	*…No, no consciousness, routinely discarded as part of IVF…*	*…not a person, has the potential, right circumstances, it cannot by itself…*	• lack moral status • lack consciousness • not a person	• embryonic
4.	*…the destruction of the embryo, zygote the moral equivalent of a child, less relevant to the field today, there's already many cell line available, alternative iPSC*	*…sanctity of life, destruction of embryos, objectionable, exploitation of women, differing opinions,*	*…hesc comes from excess IVF embryos, will be destroyed once fulfilled, donated by IVF couples, otherwise wasted valuable embryos, useful in development potentially life-saving therapies, imperative to pursue all promising areas…*	*destruction of early embryo*	• sanctity • right to personhood • retain resources • informed consent •exploitation →	•embryos destruction • utility •eggsploitation

Table 5.3 (A), continued

5.	*...No...*	*...No, long term supporter, ethically review & approved...*	*...No, ethical, essential, key advances in biomedical research...*	*...No...*	• PGD vs IVF embryos •PGD weak argument •uncertain success in iPSC • do not supersede • trivial use	•ambiguous claims
6.	*...not a strong argument, downgrading status, value potential, a weak argument, ethically unacceptable to interfere deliberately normal embryo...*	*...surprised, its ethical to biopsy embryo, ridiculous to question the fate of a single cell or blastomere, there's excessive embryos in fertility clinics, couples welcome donating embryos than discarding...*	*...no difference, IVF embryos successfully used, couples prefer donating for research than discarding them...*	*...red herring topic, the discarded PGD embryos can be used for research than wasting, IVF creates more than implantable embryos, excessive IVF embryos will be discarded anyway, not clear if the argument helps...*		
7.	*...invoked but has little merit, development & use rigorous oversight, scientific & ethical viewpoint, decision made by national & local regulatory bodies, ethical committee, considering purpose...*	*...any 'approved' medical treatment, donors understood & consented...*	*...unfortunate predisposition, no one is doing it for cosmetic purpose, not a serious reason against hesc...*	*...red herring topic, hesc benefit, maintained and expanded indefinitely, could possibly be used for cosmetic purposes, not interfere with original aim for research, impression of trivial reasons but some cosmetic surgery aren't trivial...*	• decent • deceptive • broaden knowledge • unproven • less ethical controversy •there are concerns	• alternatives
8.	*...some avoid research using embryos, majority agree...*	*...some might agree, depending on their research requirements, can learn from the different types of stem cells, iPSC from hesc...*	*...majority support doing all avenues, for different purposes....*	*...One should not class all scientists together, some may favour asc without embryo destruction, can produce a wide range of tissues, it's a matter of opinion, in some circumstances, not solution for all....*		
9.	*...less ethical controversy, too early in our understanding, prove safe, treatment for range of conditions, not yet know if iPSC are biologically equivalent, there are many concerns around iPS cells, the iPSC ethical challenges...*	*...support, don't believe it completely replaces, but the number of embryos used likely reduced...*	*...not a replacement, no ethical hesc research, best use all viable approaches...*	*...principle, in the idealized scenario, are equivalent to hesc, not clear if can program completely, unlike hesc with restricted and uncertainty remains, may well replace the need for ES cells, to understand the mechanisms, do not then eliminate all ethical concerns...*		

Table 5.3 (A), continued

10.	*…in most jurisdictions, there are sufficient regulations in use of embryos, concern today is the proliferation of clinics offering unproven stem cell, outside the context of a proper clinical trial, regulatory loopholes, loopholes need to be addressed, use of stem cells from embryos is subject to very rigorous oversight by review boards...*	*…the laws in Australia strike balance, permissive yet strict set of conditions, ethics approval and obtaining a license, would seriously hamper research more than caused by the lack of uniformity of regulation. …*	*…Yes…*	*…country specific, UK balance struck well, with appropriate laws and regulation, pragmatic and permissive, different in other countries, wide range…*	• transparent • judicial review • pragmatic • balanced • oversight • flexible • clear boundaries • guidelines • hinder research • informed consent	•ideal • legal framework
11.	*…very important, international harmonization, goal that requires constant effort, not always achievable…*	*…transparency essential, in jurisdictional regulations, understanding what is possible, would be ideal a common global position, not be feasible…*	*…not sure if very feasible, ISSCR does work to standardize…*	*…an ideal case, science is an international activity, free interaction and collaboration, common standards and rules, are invaluable, worldwide set of regulations, lack of uniformity of regulation….*	•gain approval → •loopholes →	• prevent misconduct • grey area
12.	*-respondent overlooked the question-*	*…essential to protect donor, done through carefully crafted, overseen regulatory framework, process of ethical review and approval embryos, do not need protecting….*	*…research subjects do need legal protection, embryos do not really have legal status…*	*…important to respect views of others…*	•wide range •country specific •harmonization •collaborations •international activity •common global standard •not feasible	• scientific community
13.	*…important to regulate, research where appropriate, should not be too proscriptive, should be flexible…*	*…clear regulatory boundaries are essential, research progress, clinical application, conduct are existing guidelines ISSCR, reflected in local laws…*	*…research subjects do need legal protection, US, embryos do not really have legal status…*	*…is a clear legal framework, decision as what's acceptable and what is not is a matter for opinion, cannot be prescriptive, helpful to have clarity, with clear rules controlling work, there is no clear national regulation…*		

Table 5.3 (B): The initial coding framework for local scientists (LS).

Questions	Respondents			Sub-Codes	Codes
	LS1	LS2	LS3		
1.	*..it's very new, used in many hematopoietic disorders, become the peak esthetic medicine for self-enhancement, regenerative disease, shows its potential…*	*…therapeutic regenerative diagnostic, regenerative of organs…*	*…not as potential, there's still a long way to go, still in its infancy, a lot of gaps to fill…*	•future therapy •unique •infancy	
2.	*…did not research embryonic stem cell…*	*…more after the fetal, when the brain is developed consciousness…*	*…muslim, believe life begins not at conception, 120days, some believe after it got implanted, explain by Quran, difficult to pin point…*	• conception • brain develops • 120-day • no clear line scientifically	•scientific ambiguity
3.	*…shouldn't be given same respect as adult, they aren't conscious, need the human body to develop, brains need to develop…*	*… dividing and undifferentiated that is difficult to say that there's life, they are just cells, can be yes or no, yes, if the purpose is to have a child, no, considered as cells, developing, not yet a human…*	*…difficult to identify, considered as a clump of sell, without a soul, not a person yet, do not deserve the same right, might be discarded…*	• lack moral status • lack consciousness • no assurance without womb • not a person	• embryonic

Table 5.3 (B), continued

4.	*…on religious beliefs, scientists have sense of awareness, have a global perspective, consequentialism approach…*	*…involves embryos, the destruction of embryos…*	*…considered embryos deserve the same respect…*	•sanctity •right to personhood	•embryo destruction
5.	*…Not against, depends on motives…*	*…not against…*	*…not against, need proper justification…*	• consequentialism • religious • inform consent	• motives
6.	*…depends on the couple are willing to consent...*	*….it depends on the purpose, should pursue to extract accordingly….*	*…depends on the individual…*	• trivial use • disrespecting embryo	•ambiguous claims
7.	*…the product from China, using placenta would be discarded anyway, much bigger motives…*	*…against it, not worth it, enhance your features for trivial purpose, against to restore damages, its ok…*	*…against the idea, not respecting the embryos…*		
8.	*…no ethical issues, Easier to obtain compared…*	*…depends on the research, ethical securitization as far as hesc might take longer…*	*…Depends on objectives, source should fit appropriately, fill in the gaps, are no such priorities or superiority…*	• decent • easier • objectives • do not supersede • broaden knowledge • deceptive • less ethical controversy	•alternatives
9.	*…bright promise, without ethical issues, genetic stability, formation of teratomas, fragile field, long way to go…*	*…do not favor, genetic manipulation of somatic cells feels fake, seems to imitate the cells….*	*…is a easier choice isn't true, may sound simple but it's difficult, less ethical issues, there are a lot of hurdles in reprogramming…*		

Table 5.3 (B), continued

10.	*…no legal laws/act in Malaysia, only a guideline, no such prosecution for wrongdoers, go through right pathway, approval of IRB and IEC….*	*…clinical tests/research, they are really strict, policymaker need sc experts on it not incompetent members, no law only a guideline, have a board that regulates, good to have a law…*	*…no law yet, need one, created by the right authority, no law to prevent misconduct, only a guideline, we cannot persecute, need a law, need to appoint the right people….*	•guideline •no law yet •competent authority •proper standard	• legal framework
11.	*…good to be able to synchronize legislation, every country there's too many ideas, might not seem possible, depends on the political and intellectual….*	*…Yes…*	*…should be working together, fill in all the gaps…*	•prosecution →	• prevent misconduct
12.	*…can be done, researchers should be well matured…*	*…Yes, with/by attaining consent…*	*…everyone's doing their part, ultimately do it right….*	• wide range • country specific • not feasible • harmonization	•scientific community
13.	*…Yes…*	*…Yes…*	*…Yes...*		

Table 5.3 (C): The initial coding framework for foreign ethicists (FE).

Question	Respondents		Sub-Codes	Codes
	FE1	FE2		
1.	*,..the ability to modify cells, to treat disease, overcome immunologic problems, gene editing…*	*…has the potential, to treat a range of debilitating diseases…*		• future therapy • unique
2.	*…begins at conception, fetal life has moral standing…*	*…even before conception, cells are living, early-stage embryo does not deserve more protection, can be used for socially valuable goals…*	• conception • no clear line scientifically	•scientific ambiguity
3.	*…No, Only potential life…*	*…No, early embryo do not have moral status….*	• lack moral status • not a person	•embryonic
4.	*…destruction of embryo, time to start clinical trials…*	*…about the moral status of embryos, potential harm to women, the translation and commercialization of stem cell research, stem cell tourism…*	•moral status	•embryo destruction
5.	*…No…*	*…. No….*	•time •clinical trial	•translation
6.	*…supports excessive IVF embryos, its ethical to use abandoned IVF embryos, there are many…*	*…specifically, for research, instead of creating new lines appropriate sometimes to create an embryo….*	•exploitation	•eggsploitation
7.	*…if no funding, it won't happen, no need, there's enough abandoned embryos….*	*…cosmetics?*	•retain resources •funding •commercialization •stem cell tourism	•utility
			• PGD vs IVF embryos	•ambiguous claims

Table 5.3 (C), continued

8.	*...yes, easier to control….*	*….no comment…*	• decent • simple • may fail •less ethical controversy	•alternatives
9.	*...No, iPSC may not work….*	*...less ethical issue….*		
10.	*...No, need better international standards…*	*...Yes…*	•imperative •sufficient oversight	•legal framework
11.	*---absolutely yes…*	*...No…*		
12.	*...require reporting in standardized template, no publication without attestation of authors, follow ethical standard….*	*...is done sufficiently, no violations of rights…*	• author attestation • follow standard regulation	•prevent misconduct
13.	*...need laws, professional standard, ethical standard, set by journal, religious opinion & commercial companies….*	*...Yes…*	•country specific •international standard •ethical & professional standard	• scientific community

Table 5.3 (D): The initial coding framework for local ethicist (LE).

Question	Respondents	Sub-Codes	Codes
	LE1		
1.	*...scientific endeavors, the idea is to try to find solutions in improving the health of patience, potential maybe in some areas, certain areas there maybe usefulness of stem cell but we cannot for example expect stem cells to solve everything, There is also concerns about stem cell the hype in providing solution to many if not all health-related complications in life ....*	• future therapy • broaden knowledge	
2.	*...as scientists, life begins at conception, cells are living, both male & female, and formation of gamete, religiously, 120 days at the point of primitive streak...*	• Conception • 120-day • primitive streak	• scientific ambiguity
3.	*...all cells should be given equal respects, because of the potential of becoming adult, to stop development that's terminating a life, need to give respect in all stages, as they have developed...*	• equal respect • potential life • no terminating life	• embryonic
4.	*...whether if we can make use of the cells, experiments & manipulations, tinkering of the cells, understanding how the growth, manipulations done early stages, I would think for experimentation you can deal with only cells which are not functional normally, or has problem with., The cells which are functioning normally should be touched, shouldn't be bothered....*	• committed to develop • not temper	• embryo destruction
5.	*...No, as long as done in early stage, when not fully developed, and dealing with dysfunctional cells...*	• practicality • no tinkering • future possibility • only dysfunctional cells • not fully developed	• utility
6.	*...PGD is preferred, it's against using healthy cells, excess IVF embryos should have better fate, instead of destroying...*		
7.	*... Frankly, I do not know of any possibilities or any situation when stem cells can save ones' life, as least at this point of time, practically haven't reached that stage yet, it's a future possibility, no concrete proves it can safe life, not for cosmetics, If you it can improve certain diseases or symptoms that I say fine, but stem cell is not yet there as super-duper therapeutic solution ...*	• PGD vs IVF embryos • IVF deserve better fate • no absolute success • trivial use	• ambiguous claims

Table 5.3 (D), continued

8.	*…yes, a better option, but need to make ASC work 1st, as long as you are not meddling with beginning of life, its safe…*	• decent • less ethical controversy • no tinkering • deceptive • simple • retain resources	• Alternatives
9.	*…yes, as long as not meddling with beginning of life, more comfortable, less ethical objection, there is success with dolly, plus there's plenty of somatic cells…*		
10.	*…no specific law yet, guideline already in place, no law for clinical trial for example people not following standard procedure, no prohibition of misconduct, don't think people in private sector are abusing…*	• no law/act • guideline • lack compliance • sufficient	• Regulation
11.	*…yes, there are effort towards that WHO and other regional bodies, about ethics, formulation of ethical guidelines, Helsinki Declaration, need proper code of practice…*	• starting point • need legal framework	• SC guideline
12.	*…Yes, the guideline is a starting point, try include into existing laws, add/embed new stipulations, a new law would take long, future depends on ethical subscription and consensus…*	• directed effort • WHO a& regional bodies • Helsinki Declaration • code of practice	• Scientific community
13.	*…yes, important to have law, it's an ongoing experiment, proper act will oversee the proper operations of sc in certain countries…*	• need consensus • intricate & extensive • imperative • need legal framework • oversight	• Ideal

Table 5.3 (E): The initial coding framework for local policymakers (PM).

Question	Respondents			Sub-Codes	Codes
	PM1	PM2	PM3		
1.	*…something happened, due to urgency, stem cell therapy, clinical trial-basis…*	*…who should address the SC transplantation, people were talking about embryonic SC, hematopoietic SC, adult SC that was the reason when come to clinical trial it falls under the Medical division, newer forms of SC falls under clinical trial…*	*…established for the hematopoietic SC, it is conform already, another choice to treat leukemia, evidence based medicine, different criteria required to put it into existing law…*	•trigger •urgency •clinical trial •transplantation	
2.	*…yes, there's a lot of advancements, sprouting privatized companies out there, I understand there are many products out there,*	*…newer forms of SC, there are many new marketing of cord blood…*	*…. i think yes, in principle there is improvement, because a lot of budget pumped to do research, people of CRC and NIH, both are actually quite active up to, still have a lot to do…*	•advancement •state-of-the-art •different characteristic •improved	• future therapy • unique
3.	*…heard about SC, SC therapy, still unregulated, don't have, you need an act, BPFK they are (unknown statues) producing an act, as for the guideline, it is deemed still adequate…*	*…we don't have any statute or any aspect of our that that handle SC research/transplantation, who should address the SC transplantation, it's about transplantation but no transplantation act…*	*……the idea of the politicians, his opinion and does not reflect the entire ministry, no formal bill created or established, the direction is there….*	•transplant matters •no law/act •unregulated •guideline •supremacy	• state affairs
4.	*…guideline is still counted as good enough to overlook everything, guideline itself is sufficient, NSCERT whereby the committee convene and discuss ethical issues, originally they were stringent in their screening process but then eventually they became a bit lenient due to sprouting privatized companies, yes the NSCERT, it needs to be through the IRB and IEC which will still be advised by NSCERT and MREC, submit in phases and the IEC should also be strict, however informed consent which is a part of our checklist….*	*….and now it is formalized as the National SC Ethics and Research and Therapy Committee (NSCERT), the committee that looks into all aspects of SC, MREC the ethical committee that reviews all the Ministry of Health hospital research, by law that circular is actually binding, all researcher from institutional higher learnings comes under IRB and IEC, they all go through NSCERT…*	*….you can download the Director General's directives, there are two things, one we mention about circulars, only applicable to the government sector, the private sector we have the PHFS act 1998, so when we want to enforce it to the private sector as well we need to put in into Director General's directives, it is a lot depend on the ethical committee …..*	•guideline •NSCERT Committee •Director General's Directive •Circulars •PHFS Act •MREC •informed consent •IRB & IEC •lenient review •approvals in phases	•standard protocol

Table 5.3 (E), continued

5.	*…but without any formal complains, there's nothing the NSCERT can do about it, they need whistleblowers to take action, at the moment the alarming issue is the misconducts…*	*…and before the ministry can do anything or take action against any malpractice there need to be a complain, we all know this happening without complains we are tied and cannot do anything, unless there's a whistleblower saying that there's something happening there, how else to catch these people…*	*….. whistleblowing act is good, But there is issue on implementation, it is not practical but because we are not focusing how to implement it, sometimes we don't have enough evidence, everybody have to play their role, if people know something, they need to complain to the ministry, to the right department cause otherwise they will keep it because nothing to do with them, you can put in anonymous but then you need to tell me details ….*	•lack implementation •formal complaints •reach right venue •misconducts & noncompliance •go undetected •anonymous	•Whistle Blowing
6.	*…but without any formal complains, there's nothing the NSCERT can do about it, then there's public need to be responsible, the companies want to advertise must ask for MOH's approval to protect the public due to their lack of knowledge ….*	*…we even had a public kinda discussion and circulated the draft to the public and there was even a public engagement on the website, getting their feedback, companies want to advertise they need to get it looked through by the ministry of health and get their approval, emotional blackmail, in order to tighten the regulation we decided to inform the public so we did some roadshows, to create awareness, actually there was a public engagement done for…*	*… so need input actually, we need feedback from the public, if we have input we have information then easier, we really need feedback actually from people, because otherwise they mislead the public, that is why we need people to come forward….*	•public engagement •formal complaints •misleading ad	•Public awareness
7.	*… yes we had engaged them prior the launch, but the feedback wasn't that positive cause there are those that did oppose and it was captured but the 14th day justification only reflects the Muslims….*	*….we tried to get the religious authority on board, Malaysia being an Islamic country we need to get the Fatwa sorted out, BCRO at the time tried to get Halal certification just to brand the product, they went to see the Jakkim to get the Halal cert and being naiive Jakim was entertaining, fatwa 2011 there was 67 seating, datwa says that the therapeutic cloning 'harus' meaning permissible, cloning of individual is 'haram' meaning not allowed, to use them beyong the 'alaqah; stage, fatwa is not legally binding, when we had the feedback session, those from the religious bodies/group tend to speak a lot about their own religion, going into detail…*	*…for me this one in my opinion regarding the religious aspect as well, under federal constitution we have rights to belief in god, if you look into the 'Rukun Neagara', we have religious bodies, they should look into these issues as well, religion is not federal law, we can get their input, call them together, they need to give input to the technical people, we have to respect all religion, religious people ask them to quote with their reference, not about your opinion….*	•all religions •religious inputs not baseless •not federal law •not mere opinion •lack consensus •lack technical understanding •confuse treatment with food based	•Religious affair

Table 5.3 (E), continued

8.	*…even the MOH does such conduct audit/inspection to those who apply for approval (the resources, the facilities, their certifications, good beneficiary product license, evidence), but if private hospital want to offer SC therapy they need to apply from MOH first for approval and MOH need to go inspect to ensure everything is ok before agree….*	*…of course, whatever happens in the private sector is bound by the private sector act, the private healthcare facilities and services act…*	*….we are not talking about the product, the product is under pharmacy division, because when we license, we license the facility, the service in accordance to the pro-healthcare, if the contravene the requirement to be approved or licensed then we can take them to court, we are going into the renewal of license, audits are done only for renewal of license…*	•establishments & service only •licensing audits •renewal of licenses •SC products licensing (NPRA)	•PHFS Act
9.	*…. there are many products are put there and they are unlicensed and we hear of many bizarre cases like SC treating down syndrome, beauty saloon that offer SC based facial treatment but it's not directly under the MOH…*	*…they called themselves BCRO, he got the Pahang state government to give a piece of land for the establishment of a rabbit farm, they have been working under the radar, actually unapproved study, it's far-fetched, and if you want to open up an aesthetic establishment even then you need to have some aesthetic inside your license for every kind of service, they can't put embryonic SC in their license, that's why there's abit of an overlap between function of MREC and the running of NSCERT*	*…..Because here we don't actually go specific into the practice, what we do actually we ensure they have the facilities they have the service, they have the right personnel that is my role, so but then if they want to talk about product then it is under the pharmacy division,* *so sometimes when we don't have enough evidence, proof we cannot take action, aesthetic clinic, yes, KLMSC is under our control but we hope you complain to us, because we wrote to them they denied, I have mentioned in many meetings they are not actually licensed for that purpose…*	• jurisdiction overlaps • BCRO • endorsement of official w/o proof • aesthetic clinics • lack proof, lack action • exceptional cases • marketing of unapproved products	•Grey area/loopholes
10.	*…BPFK they are producing an act on the advance cell therapy (inclusive of everything), the BPFK's act is still what is eagerly awaited, to set up an act it takes very long..*	*…. create such a law or act would take at least 10 years, we had this committee to look into the tissue act, drafted a few, there was a lot of discussion about separating the solid organ transplant and SC transplant, the solid organ group says it would be easier to get act passed that do not include, if we get it this new transplant act passes it would replace the tissue act and cover what was missing in the private healthcare act…*	*…they want to put it under ART bill, the assisted reproductive technology, under the human tissue act, under the organ transplant act, we encourage for one standard …..*	• exceptional SC • committee lack consensus • ongoing deliberation • combines all • intricate & extensive 10years	• new act

Table 5.3 (E), continued

11.	*….in terms of the guidelines, we believe and hope they will adhere, as for the guideline, it is deemed still adequate, well the guideline itself is sufficient, that the guideline is deemed as merely a recommended practice…*	*…. because guideline has no legal standing, it's an ad hoc measure…*	*…this is everything about guideline to do research for research purpose…*	•interim measure •recommended practice •no statute •sufficient	•stem cell guideline
12.	*--perhaps the BPFK working on will prove useful, we are now going towards the vision of a policy as a legal framework which will cover all private and public sector, submit in phases….*	*…that is why when we wanted to actually formulate the transplant act, don't have an act but the circulars by the ministry is quite tight and the private healthcare facilities act quite comprehensive, we just need to rely on a few strategies starting now to existing regulation…*	*…because if you prepare guideline not linked to act, need to make it connected to law, it is specified under the law we have to comply. We encourage for one standard, we look into other country, learn from the developed country who are success…*	•comprehensive •need legal framework •guideline connected to law •acquire designated approvals •apply across nation •comply to available law •one standard •learn from developed country	•Ideal

5.1.2 Final coding framework

The final coding framework of this study involves the process of deriving significant themes from the sub-codes and codes which is presented in Table 5.4 (A) up to (E). The themes will then be illustrated in a thematic map, which aims to conceptualize the pattern and relationship emerging from the data transcripts as described by Braun and Clarke (2006).

Table 5.4 (A): The final coding framework for foreign scientists.

Foreign Scientists		
Sub-Codes	**Codes**	**Themes**
	• future therapy • broaden knowledge • clinical test • unique	**Revolutionary Medicine**
• conception • gastrulation • no clear line scientifically	• scientific ambiguity	**Right to Personhood**
• lack moral status • no certainty • lack consciousness • not a person	• embryonic	
• sanctity • right to personhood	• embryos destruction	**Conflict**
• retain resources • informed consent	• utility	
• PGD vs IVF embryos • PGD weak argument • uncertain success in iPSC • do not supersede • trivial use	• ambiguous claims	
• exploitation	• eggsploitation	
• decent • deceptive • broaden knowledge • unproven • less ethical controversy • there are concern	• alternatives	

Table 5.4 (A), continued

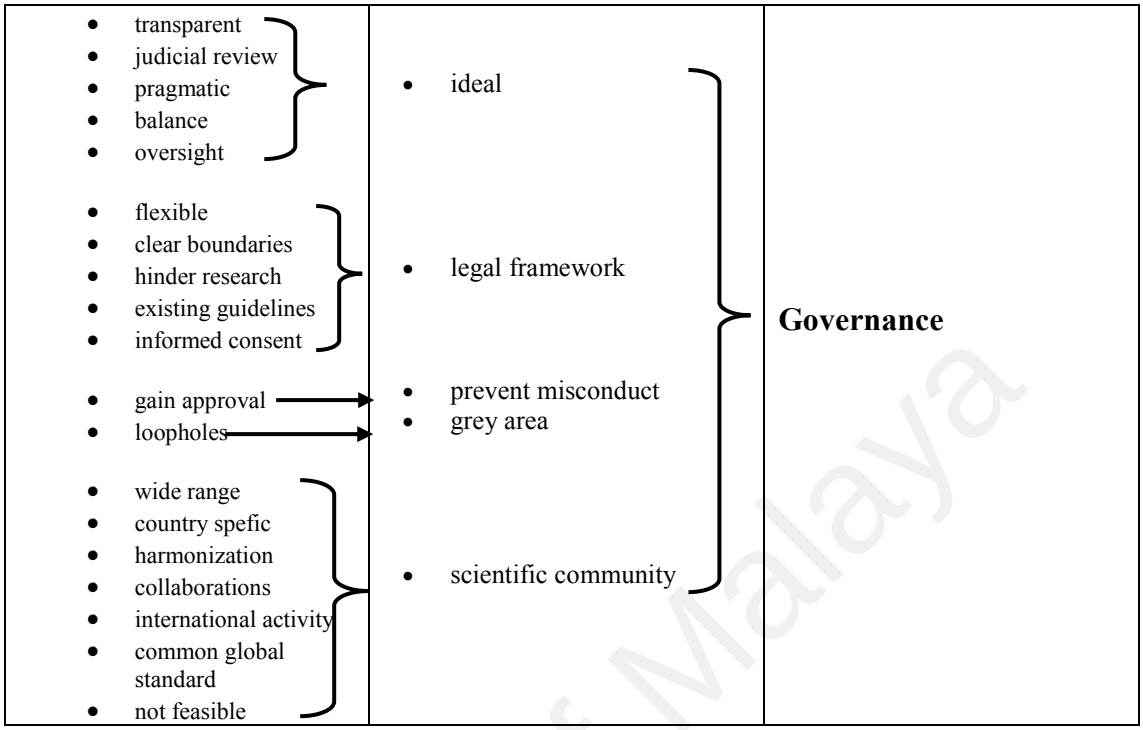


Table 5.4 (B) The final coding framework for local scientists.

Local Scientists		
Sub-Codes	**Codes**	**Themes**
	•future therapy •unique •infancy	**Revolutionary Medicine**
• conception • brain develops • 120 day • no clear line scientifically	• scientific ambiguity	**Right to personhood**
• lack moral status • lack consciousness • no assurance without womb • not a person	• embryonic	

Table 5.4 (B), continued

• sanctity • right to personhood • consequentialism • religious • inform consent • trivial use • disrespecting embryo • decent • easier • objectives • do not supersede • broaden knowledge • deceptive	• embryo destruction • motives • ambiguous claims • alternatives	**Conflict**
• guideline • no law yet • competent authority • proper standard • prosecution • wide range • country specific • not feasible • harmonization	• legal framework • prevent misconduct • scientific community	**Governance**

Table 5.4 (C) The final coding framework for foreign ethicists.

Foreign Ethicists		
Sub-Codes	**Codes**	**Themes**
	• future therapy • unique	**Revolutionary Medicine**
• conception • no clear line scientifically • lack moral status • not a person	• scientific ambiguity • embryonic	**Right to personhood**
• moral status • time • clinical trial • retain resource • commercialization • funding • stem cell tourism • exploitation • PGD vs IVF embryos • decent • less ethical controversy • simple • may fail	• embryo destruction • translation • utility • eggsploitation • ambiguous claims • alternatives	**Conflict**
• imperative • sufficient oversight • author attestation • follow standard regulation • country specific international standard • ethical & professional standard	• legal framework • prevent misconduct • scientific community	**Governance**

Table 5.4 (D) The final coding framework for local ethicist.

Local Ethicists		
Sub-Codes	**Codes**	**Themes**
	• future therapy • broaden knowledge	**Revolutionary Medicine**
• conception • 120 day • primitive streak • equal respect • potential life • no terminating life	• scientific ambiguity • embryonic	**Right to personhood**
• committed to develop • not temper • practicality • no tinkering • future possibility • only dysfunctional cells • not fully developed • PGD vs IVF embryos • IVF deserve better fate • no absolute success • decent • less ethical controversy • no tinkering • deceptive • trivial use	• embryo destruction • utility • ambiguous claims • alternatives	**Conflict**
• no law/act • guideline • lack compliance • sufficient • starting point • need legal framework • directed effort • WHO & regional bodies • Helsinki Declaration • code of practice • need consensus • intricate & extensive • imperative • need legal framework • oversight	• legal framework • SC guideline • scientific community • Ideal	**Governance**

Table 5.4 (E) The final coding framework for local policymakers.

Local Policymaker		
Sub-Codes	**Codes**	**Themes**
	• trigger • urgency • clinical trial • transplantation	**Origin**
• advancement • state-of-the-art • different characteristic • improved	• future therapy • unique	**Revolutionary Medicine**
• transplant matters • no law/act • unregulated • guideline • supremacy • guideline • NSCERT Committee • Director General's Directive • Circulars • PHFS Act • MREC • informed consent • IRB & IEC • lenient review • approvals in phases	• state affairs • standard protocol	**Regulation**
• lack implementation • formal complaints • reach right venue • misconducts & noncompliance • go undetected • anonymous • public engagement • formal complaints • misleading ad • all religions • religious inputs not baseless • not federal law • not mere opinion • lack consensus • lack technical understanding • confuse treatment with food based	• whistle Blowing • public awareness • religious affair	**Social Intervention**

Table 5.4 (E), continued

• establishments & service only • licensing audits • renewal of licenses • SC products licensing (NPRA) • jurisdiction overlaps • BCRO • endorsement of official w/o proof • aesthetic clinics • lack proof, lack action • exceptional cases • marketing of unapproved products	• PHFS Act • Grey Area/loopholes	**Private Sector**
• exceptional SC • committee lack consensus • ongoing deliberation • combines all • intricate & extensive 10years • interim measure • recommended practice • no statute • sufficient • comprehensive • need legal framework • guideline connected to law • acquire designated approvals • apply across nation • comply to available law • one standard • learn from developed country	• new act • stem cell guideline • ideal	**New Bill**

5.3 Thematic map

Figure 5.1 (A)-(E) illustrates the thematic maps generated based on the relationships between themes, codes and sub-codes from Table 5.3 (A)-(E) and Table 5.4 (A)–(E), derived from the review and analysis of the verbatim quotes of the original data gathered from a range of respondents. These thematic maps were created based on respondents' categories such as foreign scientists, local scientists, foreign ethicists, local ethicists and local policymakers.

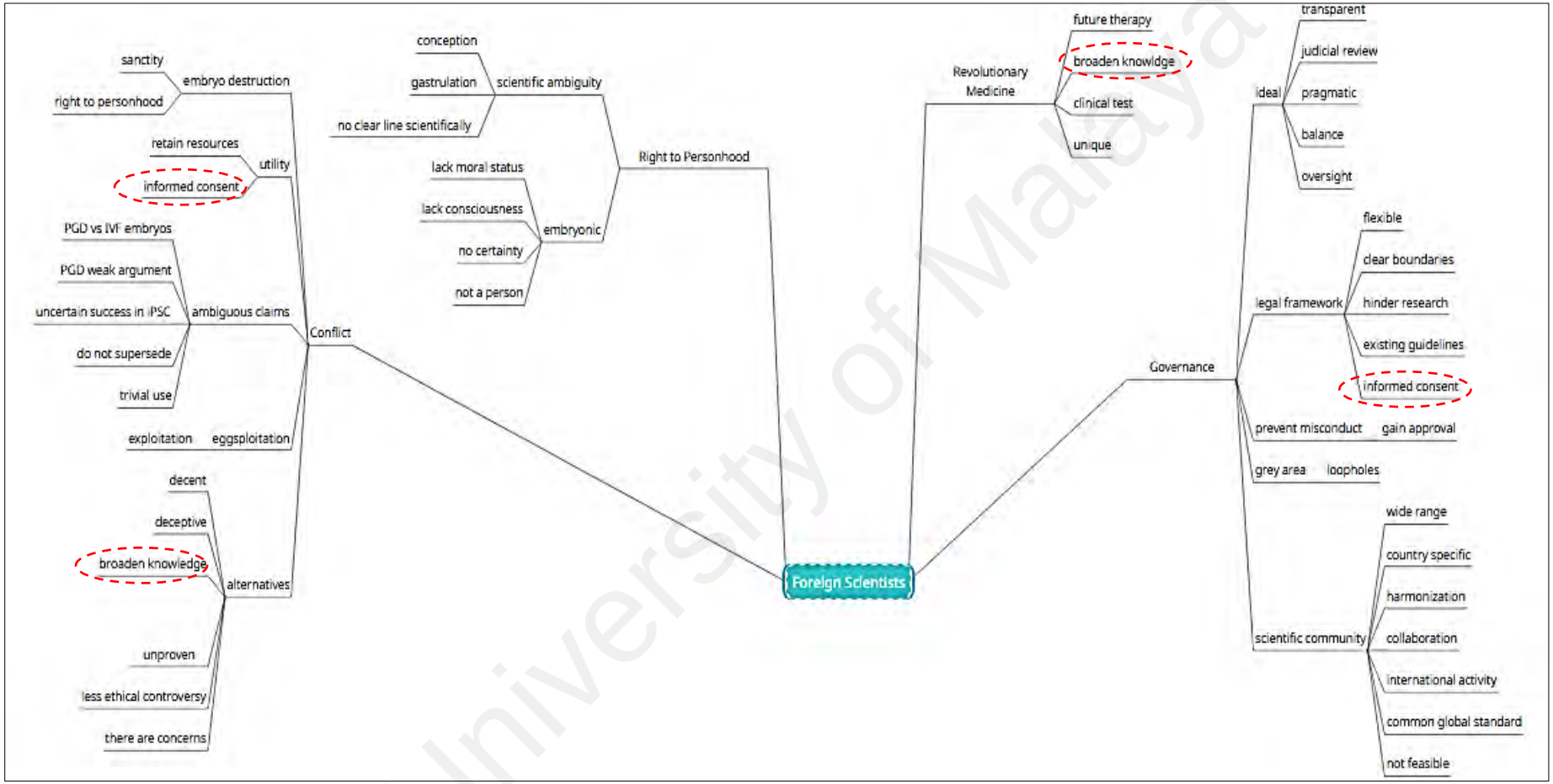


Figure 5.1 (A): Thematic map of foreign scientists.

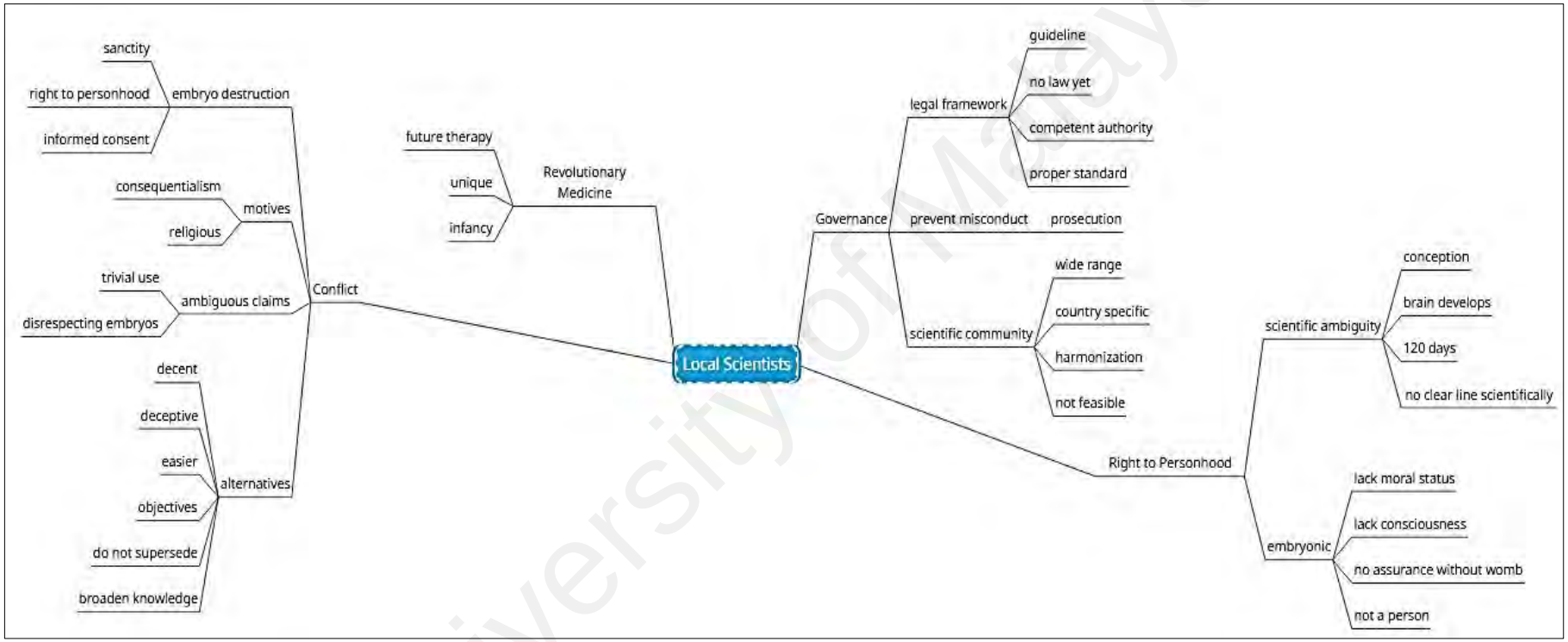


Figure 5.1 (B): Thematic map of local scientists.

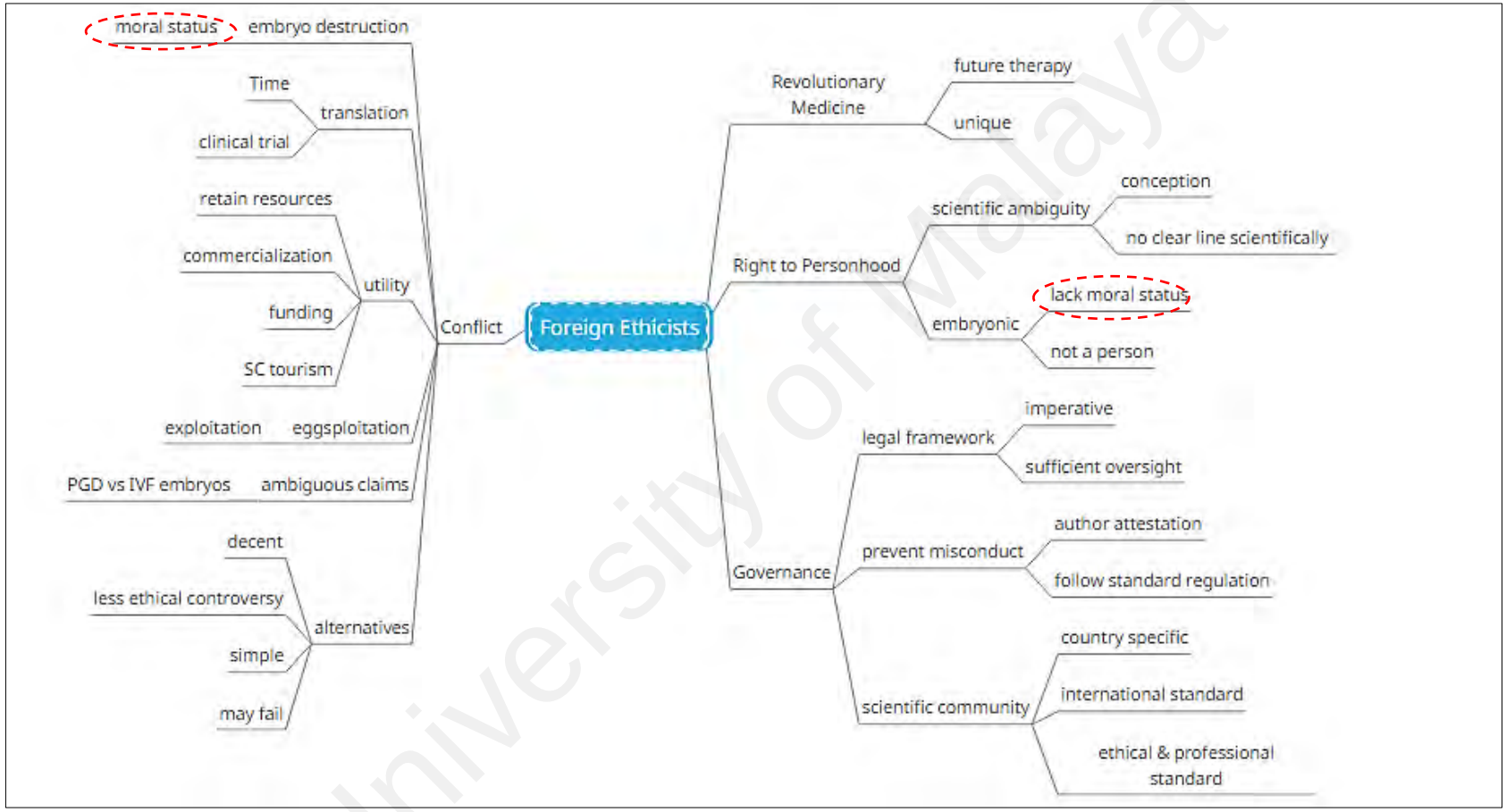


Figure 5.1 (C): Thematic map of foreign ethicists.

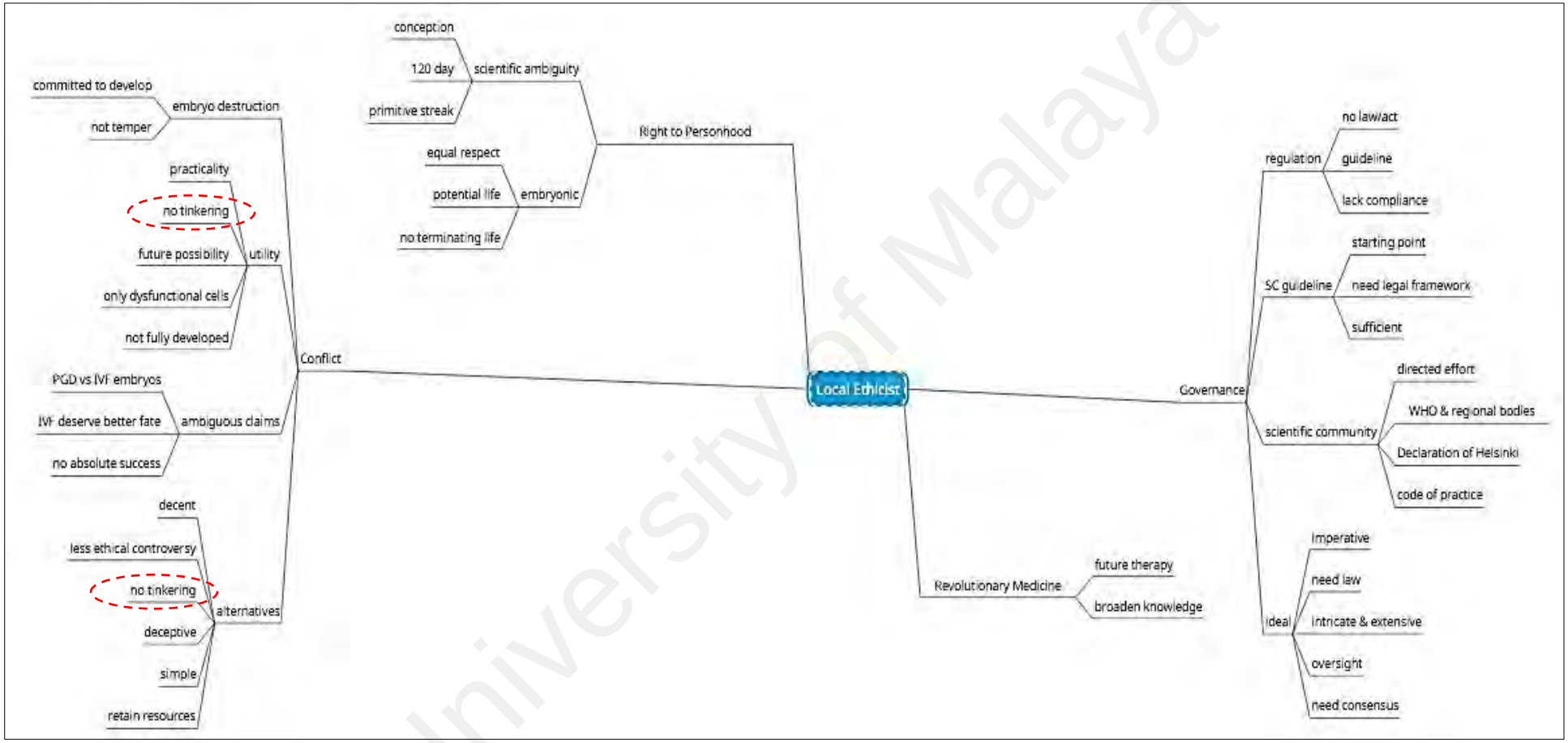


Figure 5.1 (D): Thematic map of local ethicist.

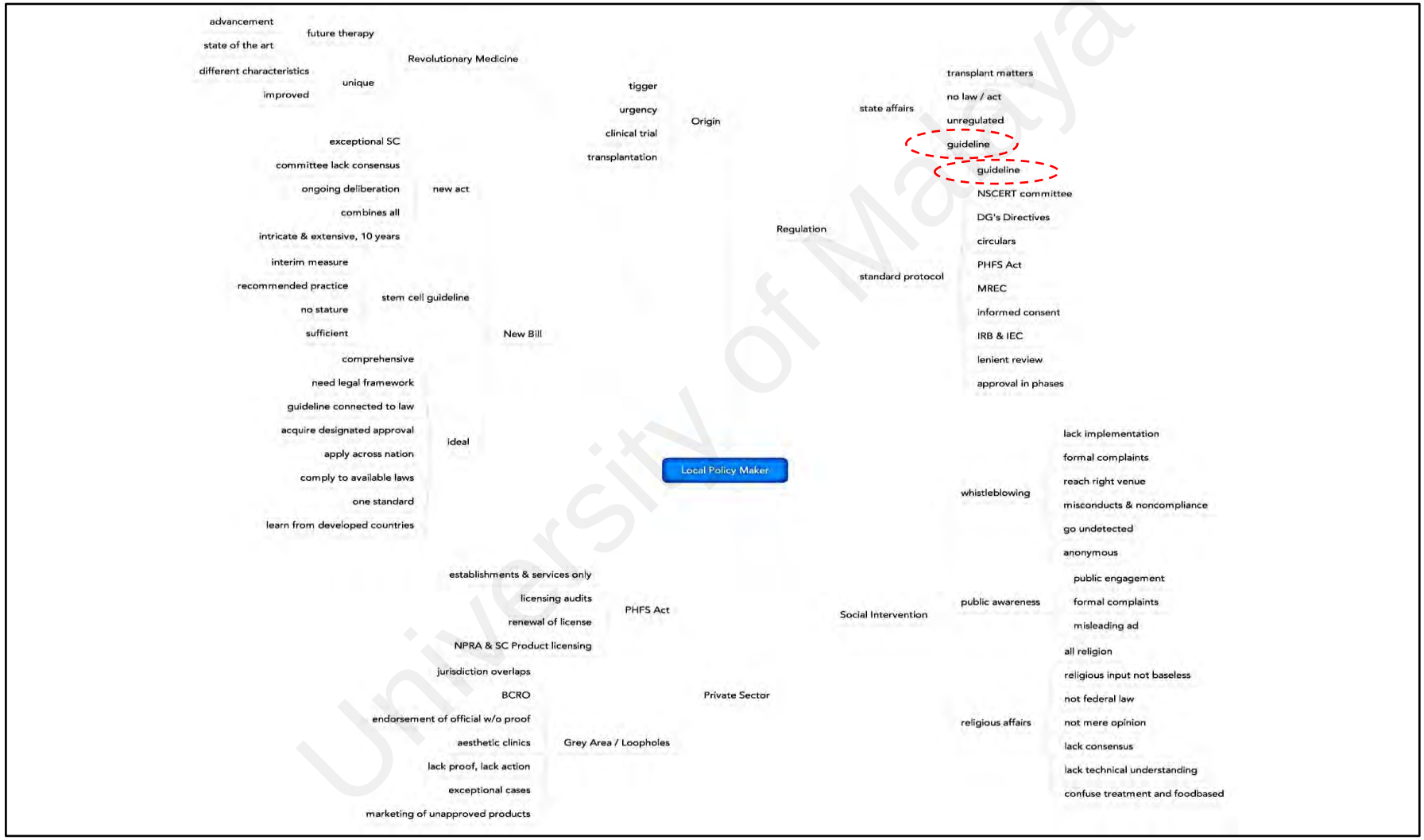


Figure 5.1 (E): Thematic map of local policymaker.

5.4 Thematic map revealed

The resulting thematic maps were analyzed and reviewed as a collective representation of the data from different expertise or angle, by only using the sub-codes which are more detailed and self-explanatory clearly presented by the Tables 5.4 (A) – (E). The sub-codes are summarized within their categories based on their significance.

The analysis of the thematic maps of the different experts displayed by the Figure 5.1 (A) – (E), disclosed that there are some overlapping sub-codes within the same map indicated by the red loop. The overlaps basically mean that a particular sub-code is important and significant across one or two themes. There were two overlapping sub-codes within the foreign scientist thematic map which is, 'broaden knowledge' and 'informed consent'. According to the foreign scientists, stem cell research is mainly to broaden knowledge regarding what is known and the unknown. Similarly, the idea to uncover the ethical source of stem cell results in the discovery of alternative forms of stem cell or other derivatives of stem cell. The pursuit of finding an ethical source of pluripotent stem cell is fundamental with respect to broaden knowledge. The sub-code informed consent is an important principle especially since the embryos (oocytes) are retrieved from donors hence, it is a required protocol to obtain informed consent prior to retrieving them. Therefore, informed consent is recognized as a standard protocol and a part of stem cell regulations or legal framework.

The foreign ethicist's thematic map identified 'moral status' as an overlapping sub-code within an interconnecting issue, which is the theme 'right to personhood' and the 'conflict' related to the code embryo destruction. The topic of justification of human life, the question of when life begins or when an embryo is deemed a person brings in the topic of the moral status of the embryo. Therefore, the use of human embryos in hESC research which unintentionally destroys them brings in the same justification and debate, hence the moral status is an overlapping topic. The local ethicists thematic map identified

'no tinkering' as an overlapping sub-code within the same theme, conflict but in two different area or codes known as utility and alternatives. Manipulation of embryos for research purposes is considered unethical but alternative cells that do not require such manipulation makes them an ethical choice. Therefore, the sub-code 'no tinkering' act as a baseline deciding which ones are ethical and which ones are not. Finally, the policymakers thematic map identified 'guideline' as an overlapping sub-code within the regulation theme, but it is distinguished as a state affair and as an important standard protocol involving stem cell research and its technologies in Malaysia since it is the only available documentation concerning stem cell. The thematic map of the local scientist detected no overlaps of sub-codes.

5.4.1 Foreign scientists

The foreign scientists described a wide range of strong prospect and potential of stem cell research that can improve medical healthcare just as reported by many. They justified the use of human embryos for research by unanimously agreeing that embryo is not a person and that it lacked the moral status equivalent of an adult completely supporting hESC research. One of them further explained that there is no clear point scientifically to mark the actual point when an embryo is distinguished as alive. They also agreed that blastocysts are not equivalent to an adult as they depend greatly on the womb to continue growth without which they cannot survive completely ruling out their moral status of a person.

Despite acknowledging the potential, they unanimously identified the use of human embryos for stem cell extraction as the most debated ethical issue but explained how excess *in vitro* fertilization (IVF) embryos can be useful for stem cell research instead of being discarded once served its purpose. The argument that preimplantation genetic diagnosis (PGD) embryos that are extracted for diagnostic purpose can also be

used for stem cell extraction to ensure maximum utilization preventing wastage was identified as a red herring argument that is weak by foreign scientists. This is due to the nature of these embryos that already have issues, to begin with, and unless they are specifically required they may not be as valuable as a normal healthy embryo. The use of hESC for cosmetic purpose is also distinguished as a tricky topic with very little merit as some cosmetic procedures are not as trivial as they made to believe.

Although adult stem cell (ASC) can be an ethical alternative preventing the use of human embryos, the foreign scientists explained that ASC are chosen based on the research requirement using all avenues but it is not an overall solution. Similarly, induced pluripotent stem cell (iPSC) is another ethical alternative without the use of human embryo but being in an early stage there is much to understand and it is unsure if they are biologically identical to the hESC. Although it is proved safe and ethical it does not completely replace the hESC as there is restriction. Ultimately, both ASC and iPSC do not supersede the need for hESC or its research.

All the foreign scientists consider the regulation of stem cell research in their country are well-balanced and sufficient. These experts are from the United Kingdom, the United States, and Australia. As their stem cell laws and policies were reviewed and acknowledged to be quite comprehensive and pragmatic promoting its research excellence as described in detail in Chapter 2 it is fair to agree that it is true. Only one of the experts from Australia acknowledged the presence of regulatory loopholes involving clinical trial that require attention. According to them, harmonizing stem cell regulation globally is ideal but it may not be feasible. The expert from the United Kingdom supported the idea as research is considered as an international activity involving collaboration among scientists around the world. Currently, there is no uniformity concerning stem cell regulation as they are country specific. He believed that having such global standard and rule would be invaluable.

Foreign scientists agreed that stem cell regulation is important to prevent violation but they are more to protecting donors and research subjects but not the embryos from which stem cells are extracted from. They unanimously agreed that legal framework regulating stem cell research and its technologies are vital to ensure no violation but it needs to be flexible to promote research while having clear boundaries to safeguard the welfare of those concerned.

5.4.2 Local, Malaysian scientists

Unlike the foreign scientists, the local, Malaysian stem cell scientists were not elaborative concerning the extensive potential of the stem cell research. They agreed that there is potential but they also unanimously believe that it is still in its early stages with much to learn. This is true as far as Malaysian stem cell research and development status are concerned as it is still in its infancy as believed by many locals. The question 'when life begins' to justify hESC research often lead to a variety of responses depending on their personal or scientific opinion and religious faith. In Malaysia, there are two justifications, first, from the scientific line when primitive streak develops marking brain development which happens at gastrulation, while second, is from a religious view especially the Islamic law based on the Qur'an which marks the 120th day after conception as when life begins. Although, they agreed with the foreign scientists that blastocysts do not have the same status as an adult and that they are the only clump of cells, but they also explained that it is not easy to distinguish, agreeing to the foreign scientist view of 'no clear line scientifically'.

The local scientists also agreed that the most debatable issue concerning stem cell research is the use of human embryos which leads to its destruction as infringing its respect. One of them strongly believes that these arguments are mostly founded from a religious viewpoint but also acknowledged the sense of duty of scientists from a

consequentialist approach. Although they are not against hESC research they expect scientists working on hESC to have a valid motive and proper justification. The PGD embryos argument was not ruled-out, instead, they think it depends on the purpose of the research conducted and the individual involved to consent the use. Similarly, using stem cell for cosmetic purposes resulted in varied responses from local scientists. One of them explained that some products are extracted from the placenta which is acceptable since they are often disposed of anyway. While the remaining experts felt the use of stem cell for trivial cosmetic purpose would be unethical and disrespecting the embryos if they were extracted from hESC. If they are used specifically to restore damage such as facial reconstruction it is well justified.

Among the local scientists, one of them explained that researchers choose ASC as they are ethical and are much easier to obtain compared to hESC. Although, this is true, the others explained that it mostly depends on research requirement and objective agreeing to the foreign scientists. There are no priorities or superiorities compared to ASC or hESC agreeing with the foreign scientists. The iPSC is often debated as an alternative replacing hESC, but it is not completely true. Despite, the bright promise of a much ethical alternative the iPSC has a long way to go before they can replace hESC as they have their constraints. One of the local scientists were bold to express her view that iPSC was not original with a sense of imitation, while the other was explaining the inaccurate presumption that it is an 'easier' choice as the reprogramming of somatic cells to behave as a pluripotent stem cell is challenging.

The local scientists are well-aware that there is no law on stem cell research and its technologies in Malaysia and that they are relying on the Guideline for Stem Cell Research and Therapy (2009). They are also well-aware that the guideline is not legally binding and unable to prosecute any wrongdoers. They concurred that Malaysia needs a law to regulate its stem cell research and technologies but clarified further that it must be

formulated by qualified experts with relevant skill sets to ensure that the new law is comprehensive and practical to the nation's needs. They also urged that it should be broad specifically intended to regulate all matters concerning stem cells. Similar to the foreign scientists, the local scientists also agreed that harmonizing stem cells regulation globally is ideal as it would fill in the gaps by working together but it may not be feasible.

5.4.3 Foreign ethicists

The foreign ethicists involved in this study are from the United States and Canada. They acknowledged the potential of stem cell research ranging from treating debilitating diseases to overcome an immunologic problem and modifying cells. When asked about 'when life begins' they identified conception as the point when life begins unlike the scientists marking gastrulation as the point. According to these ethicists, fetal life has moral standing as cells are living entities which is against the belief of scientists. However, the foreign ethicists unanimously agreed that blastocysts do not have the moral respects equal to an adult supporting the hESC research. According to their view, it is not the use of human embryos but the period when it is used specifically that is justifiable, giving it merit. The extraction of stem cell leading to embryo destruction which revolves around the issue of moral status of human embryos, the right time to translate from preclinical to clinical stage, the commercialization of stem cell research and the exploitation of women donors are a few issues concerning stem cell research and its technologies. It is quite apparent that the foreign ethicists are more experienced and knowledgeable on the ethical issues concerning stem cell compared the local and foreign scientists.

The foreign ethicists explained that it is ethical to use the excess IVF embryos dismissing the odds of using PGD embryos. They explained that the issue of using hESC for cosmetic purpose is not concerning as its funding requirement will call for its review

but even then, since there are plenty of excess IVF embryos it is reasonable to use them. The foreign scientists shared the same thought but not the local scientists. Between the two ethicists, there is distinction in their opinion considering several issues. While one of them agree that ASC is favored by scientist compared to the hESC, the other refrained from commenting. Regarding the iPSC being a better choice ethically, one of them believes that it still has a long way to go and may not work completely while the other disagreed. This varied opinion based on personal conviction can be captured better with more respondents in the future study.

Between the two foreign ethicists, the expert from the United States believes there is insufficient regulation concerning stem cell which can be addressed with better international standards supporting the need for nations to work together in harmonizing the global stem cell regulation. Incidentally, the Canadian ethicists disagreeing with his neighboring expert concerning the international standard is pleased with their current stem cell regulation. However, both experts are certain that stem cell regulation should be sufficiently managed which a legal framework is able to provide. It is necessary to impose some restrictions considering ethical standards by consulting religious experts and commercial entities to ensure no violation of human rights. The regulation should also prevent research article without author attestation does not get published.

5.4.4 Local, Malaysian ethicist

The local, Malaysian ethicist has a completely different view compared to the foreign counterparts. He shared his view considering the potential of stem cell research which is to ease symptoms and improve a medical condition. He also believes stem cell to be a valuable scientific endeavor that will provide a solution for all. However, his opinion is conflicted between his faith and being a scientist. The ultimate debate of 'when life begins' which is commonly used to justify the hESC research resulted in two

opposing views as described by the sole local ethicists. Although his faith recognizes life at 120th day after conception that marks the 'ensoulment' process which is the point when primitive streak develops, he asserts that his scientific knowledge that all cells are living, compels him to also accept that life begins at conception. His opinion recognizes blastocysts as equivalent to adults and deserving equal respects as they are potential to becoming adults. This is incompatible compared to the opinion by both local and foreign scientists as well as the foreign ethicists, all of whom unanimously identified that gastrulation being the point that marks beginning of life in embryos further justifying their lack of moral status.

The local ethicist briefly identified the issue of stem cells utilization and its experimentation including manipulation as the ethical issues concerning stem cell. Although he is not completely against hESC, he is strict in his view that they should only involve dysfunctional cells and done earlier on (early stages). His view also accepts the argument that PGD embryos as suitable for research compared to IVF embryos which should expect a better fate instead of being sacrificed for research. In respect to that, he strongly supports both the ASC and iPSC research. He believes they are plenty and easily available without any interference with 'life'. However, he still not convinced that both sources of stem cells are fully mastered by experts.

As a Malaysian, the local ethicist is familiar with the fact that there is currently no law regulating Malaysian stem cell research or its technologies. He concurred that legal framework is effective as it provides a better oversight considering stem cell research and its technologies. Although stem cell guideline is a good starting point, he doubts that people are following the standard procedure. He is convinced that private stem cell entities are not abusing their privileges or the ethical conduct. In the absence of law, the local ethicist has reservation concerning medical practitioners approaching authority for approvals concerning their clinical trials since authorities have not made public these

sanctions. He urges the authority to embed stem cell related provisions within the existing laws by adding new stipulations or modifying older ones instead of working towards formulating a new law as it will take much longer than anticipated. Although specifically, stem cell regulation in Malaysia is challenging, he agrees that the world should work together to harmonize global stem cell regulation for a proper code of practice. The existing effort was taken up by the World Health Organization (WHO) and other regional bodies qualify in his opinion.

5.4.5 Local, Malaysian policymakers

The stem cell policymakers are members of the Ministry of Health (MOH) of Malaysian within several divisions and units in charge of regulating stem cell research and its technologies. Being qualified doctors, these policymakers are quite knowledgeable and experienced responding to the regulative aspects of stem cell research and its technologies. They described stem cell potential as means of advancement and future therapy treating all sorts of conditions. The many varying aspects of their responses regarding the regulation of stem cell research and its technologies are further discussed in detail in several sections beginning with Section 5.5 all the way to 5.7

The policymakers identified the origins of stem cell guideline identifying the specific case that triggered the effort, which is discussed in detail in Section 5.5. They verified that stem cell research and its technologies are unregulated in Malaysia and that currently there is no law or legislation meant to offer oversight regarding the subject matter. The Malaysian stem cell policymaking process and its progress up to now (the time of writing) are discussed in detail in Section 5.6 and 5.7 respectively. They concurred that there are many areas without sound oversight which are identified as a grey area for the purpose of this study. The critical truth revealed by the policymakers is that whistleblowing is strictly necessary especially reaching the rightful venue. Without

formal complaints, the authorities are unable to take any necessary action. This may be practiced in many countries, but the public need to be informed regarding their civic duty to ensure effective regulation. In most cases, being unaware the public refrain from getting involved not knowing it will further obstruct the proper flow of regulation especially involving misconducts and noncompliance.

Comparing all the four different expert categories, it was evident that all of them approved that stem cell and its research will revolutionize medicine with its future therapy. All of them except Malaysians, were quite satisfied with their own countries' state of stem cell regulation claiming them to have reached the balance they need. Aside from the Malaysian policymakers, the local experts although are aware of the lack of regulation in stem cell research and its technologies, they do not acknowledge it to be an immediate threat or problem due to the infancy of the research status. Although, only a few experts involved in this research within their respective categories, they still resulted invaluable insights. However, a single expert's view is insufficient to capture a more consistent response as seen in local ethicist category, but it did capture the intended outcome effectively, whereby the religious diversity and personal conviction gives out a multitude of responses that are easily contradictory in Malaysia. This is already clear with the opinions gathered from local Malaysian scientists who have also shared their opinion. Therefore, to improve this study, more experts can be engaged to gather more data and can be pursued further as a future study.

5.5 Evaluating the perspectives of experts

The resulting thematic maps were further analyzed and reviewed using themes, codes, and sub-codes which are more detailed and self-explanatory. It is necessary to evaluate the perspectives of the experts especially based on their opinions and answers. First, they are compared between different regions but within the same expert group and secondly, they are compared to the same region but different expert groups mostly to understand the interrelationship if any.

5.5.1 The foreign scientist vs local scientists

This section will briefly elaborate the differences between foreign and local scientists. The Figure 5.2 shows that both foreign and local scientists shared very similar viewpoints with similar worries based on their expert knowledge, qualification and experience. However, their regional position did play a role as their individual judgements reflected their own countries' developmental state and their vast growth concerning stem cell research development, its technologies and regulation. The local scientists' viewpoint that have stem cell research is still in its infancy is a localized view, which foreign scientists did not share. The foreign scientists stated that majority of the stem cell research have reached clinical trials unlike Malaysia. While Malaysian scientists use religious motives as what drives them to embark on the controversial hESC research, and expressed that ASC and iPSC as a simpler alternative that still constitute as stem cell research, whereas the foreign scientists explained the versatility of stem cell lines in respect of available alternative and highlighted the issue of donor exploitations unlike Malaysian scientists. It is clear that their contrasting viewpoints represent their nations status and position not only on hESC research but also overall on an economic and financial standpoint.

5.5.2 The foreign ethicists vs local ethicist

This section elaborates briefly the comparison of foreign and local ethicists. Figure 5.3 shows that foreign and local ethicists have contradicting viewpoints. The foreign ethicists addressed the ethical matters largely from a general perspective, while the local ethicist's opinions were based on religious fundamentals. The local ethicist elaborated greatly on the matters of stem cell research based on his religious practices. According to the Malaysian ethicists, the use of human embryo in research is unethical, in fact, urged that IVF surplus embryos should still fulfill their primary aim, unlike the foreign ethicists who denies human embryo having any moral status justifying their effective use. The foreign ethicists explain that the ethical issues of hESC involves very specific but extended concerns such as translation and informed consent, but local, Malaysian ethicist being a single person, had a very opposing hESC viewpoint insisting that human embryos deserve better fate overall. This proved that regional position which is defined by their developmental state, their experiences, resources, and knowledge considering stem cell and religious inclination and diversity play a significant role regarding the experts' opinion on stem cell matters.

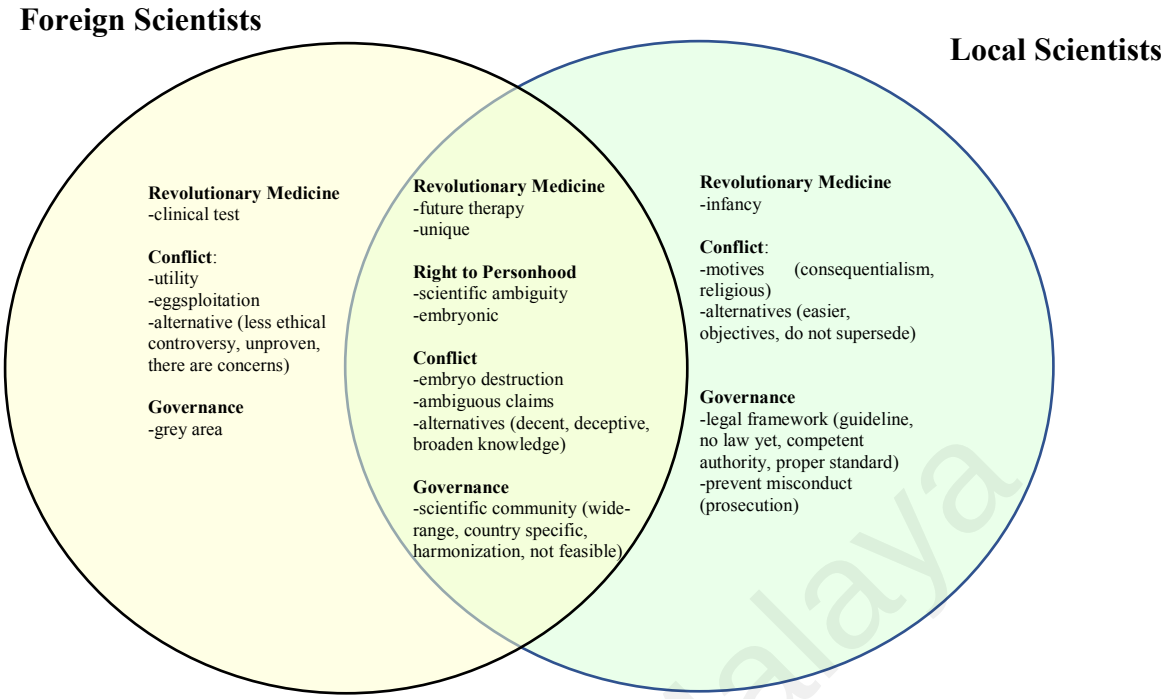


Figure 5.2: The evaluation of foreign scientists & local scientists.

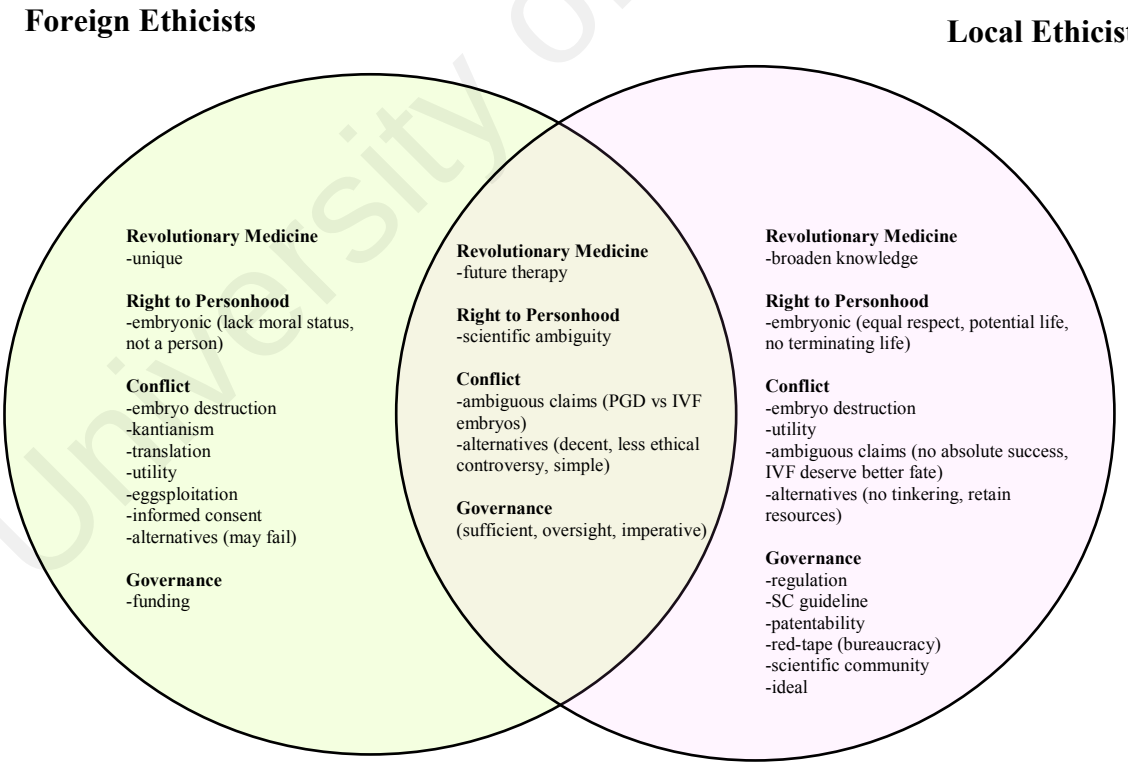


Figure 5.3: The evaluation of foreign ethicists & local ethicist.

5.5.3 The inter-perspective of local, Malaysian experts

The local experts of different categories namely scientists, ethicist and policymakers were analyzed within their cohort to study their perspectives. The review resulted in Figure 5.4. According to the Venn diagram:

1. All the experts are well aware of the potential of stem cell research and the current regulation state of stem cell research and its technologies.
2. Several scientists acknowledged that human embryos are justified alive at the point of conception, while one of them acknowledged the point of primitive streak development at the120th day to be more accurate similar to the ethicist.
3. The scientists and ethicist have opposing view regarding the use of human embryos to extract stem cell. The scientist based on their scientific knowledge accepted that early embryos are not person and lack consciousness warranting their use, while the ethicist although a qualified doctor was completely against the idea.
4. The scientists and the policymakers agreed that informed consent plays an important role especially in retrieving embryos from donors for stem cell extraction and as a part of standard protocol. They acknowledged that guidelines are necessary and that all the researchers and scientists working on stem cells should comply to prevent an ethical breach or violation.
5. The policymakers and the ethicists both declared that Malaysia needs a legal framework and law to complete the existing guideline. However, they both still believe that currently, the guideline is sufficient as the policy or lawmaking being an intricate and extensive process.

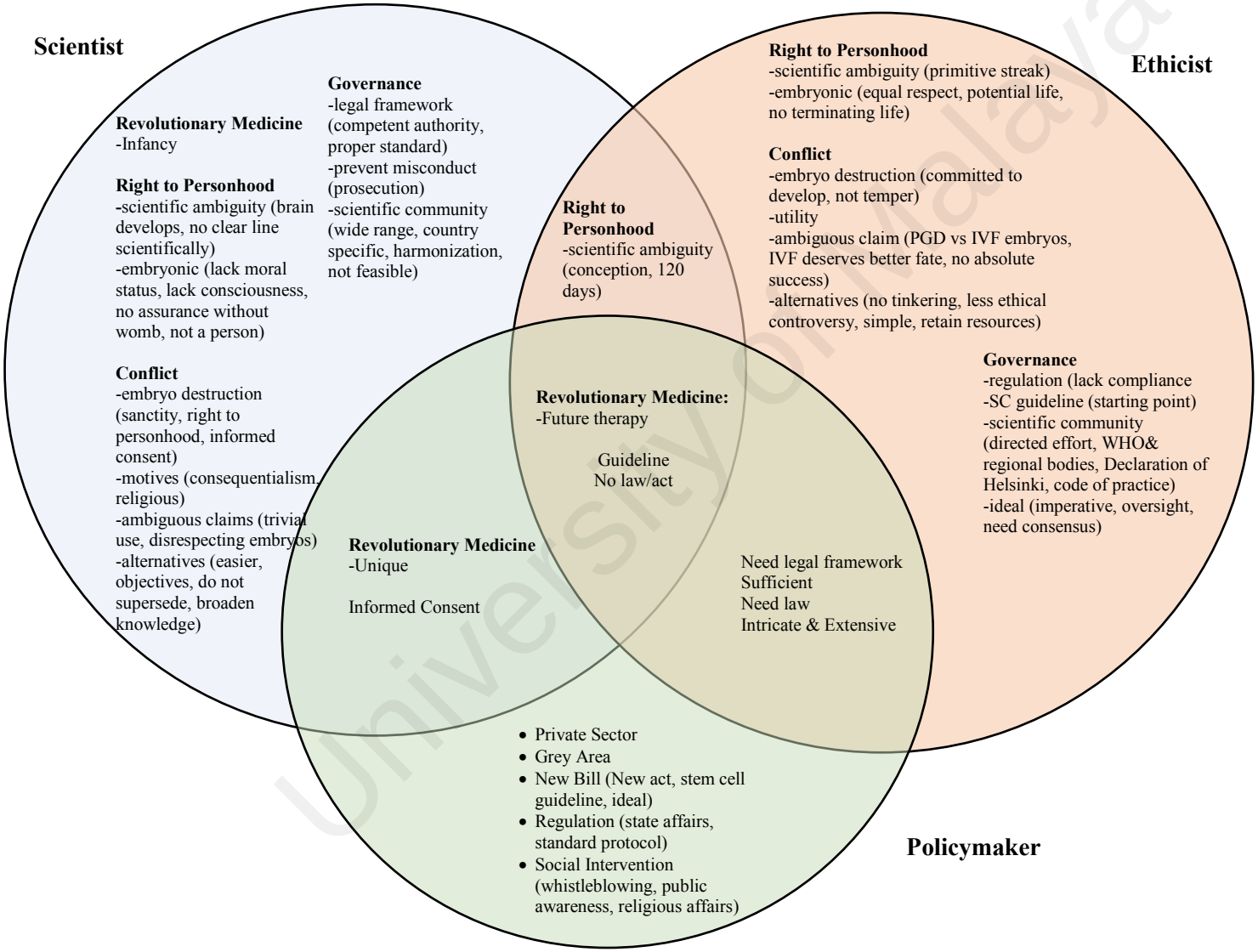


Figure 5.4: The inter-perspective of local experts.

5.6 The Malaysian stem cell guideline

The Guideline on Stem Cell Research and Therapy (2009) is the only form of regulation available in Malaysia which acts as a standard code of practice for all institutions involved with stem cell, though it does not hold any wrongdoers accountable (MOH, 2009a). The policymakers verified that the guideline is only a recommended practice devoid of a legal mandate and only meant to act as an interim measure, while a more permanent solution was achieved.[10]

It was originally formulated in 2006 as the Guideline on Stem Cell Research by the Medical Development Division of the MOH. They formed the Drafting Committee for the Guidelines on Stem Cell Research within the Technical Committee on Stem Cell Research in order to accommodate the emerging number of stem cell transplantations including a particular case involving a civil servant in 2003. The Technical Committee on Stem Cell Research was actually a subcommittee under the National Committee on Human Cloning as shown by Figure 5.5 (MOH, 2006).

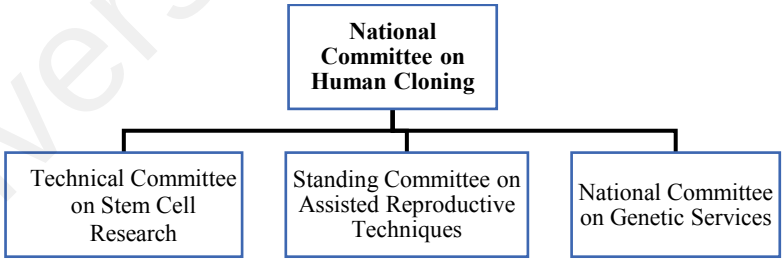


Figure 5.5: The subcommittees within the National Committee on Human Cloning.

[Source: Image reproduced with permission from the Guideline on Stem Cell Research (2006) (MOH, 2006).]

[10] This information was verified by the local policymakers during the in-depth interview session

In 2003, the National University of Malaysia (UKM) and the NHI approached the Deputy Director General of MOH to review their very first cardiovascular stem cell transplantation as a clinical trial. The review brought forward continuous deliberation on drawing up the guideline by the Drafting Committee for the Guidelines on Stem Cell Research whose members were largely from the Medical Development Division of the MOH with a few consultants from the Kuala Lumpur Hospital (HKL), IMR, Institute of Molecular Medicine of UKM and the Islamic Medical Association of Malaysia also known as *Persatuan Perubatan Islam Malaysia* (MOH, 2006).[11]

The case that triggered the guideline formulation received significant attention being the first of its kind in Malaysia as documented by major newspapers in Malaysia as displayed in Figure 5.6. Despite having visited NHI a total of 31 times for chest pains since his bypass surgery in 1997, Allagara Arumugam, a 60-year old cardiac patient was rendered incompatible for all other surgeries making him suitable for the very first cardiovascular stem cell transplantation (Lee, 2003). In order to approve the transplantation, the MOH decided they needed to design, formulate and publish the stem cell guideline to concede the procedure, and others alike as a clinical trial that may or may not succeed safeguarding the welfare of all parties.

On September 16th, 2003, 20 medical experts from HKL, NHI and the Kansai Medical University of Osaka collaborated by successfully performing the country's first cardiovascular stem cell transplantation which involved collecting marrow from the patient's hipbone and inserting it into his heart expecting to promote growth. It was one of the few of its kind in the world treating severe heart disease as displayed by Figure 5.6 (Lee, 2003).

[11] This information was verified by the local policymakers during the in-depth interview session

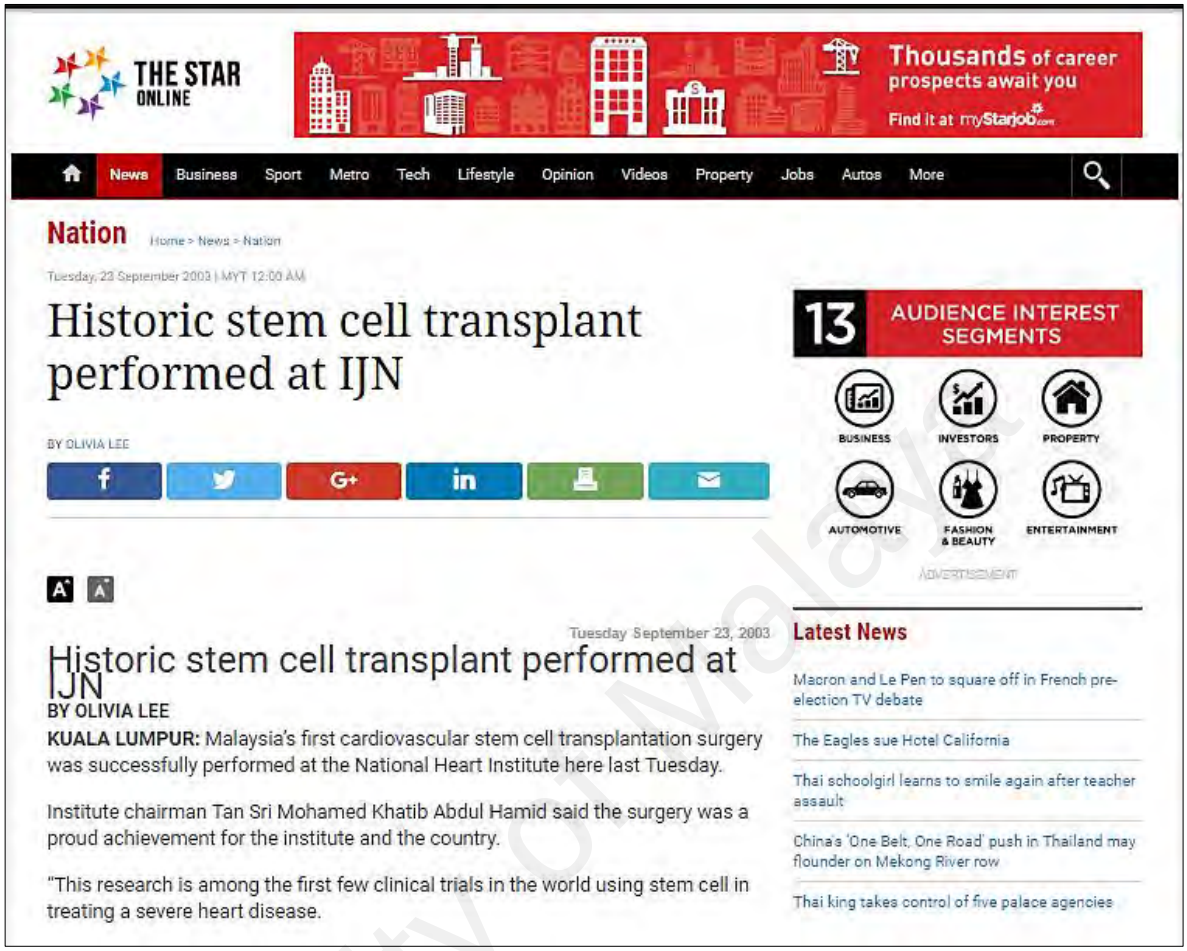


Figure 5.6: Malaysia's 1st Cardiovascular Stem Cell transplantation: The guideline trigger.

[Source: The Star Online Newspaper written by Lee (2003)]

Three year after the guideline was formulated it underwent a revision in 2009 to accommodate several aspects that were overlooked in the original version, such as the administration of animal cells to human patients (xenotransplantation) due to the BCRO case, the consideration of other religious beliefs regarding the use of human embryos in stem cell research apart from the Islamic *Fatwa*, and finally the unforeseen consequences of stem cell research and its technologies based on ongoing deliberations.[12]

The revised Guideline for Stem Cell Research and Therapy (2009) published by the MOH (2009a), included constructive comments from many religious bodies and the

[12] The issue with BCRO is discussed in detail in Chapter 1

non-governmental organizations (NGOs), as well as the valuable input and feedbacks of participants of the public forum and the resulting discussion of the brainstorming workshop that involved expert participations (MOH, 2009).[13] However, speaking to the policymakers the process is much harder than it looks.

5.6.1 The guideline: Before and after revision

The Guideline on Stem Cell Research (2006) is very limited in its directives not to mention its failure to address many elements of stem cell research and its technologies. Perhaps it is mainly due to the novelty of stem cell and the uncertainties of the technology including the minutes of its science and mechanism, which the policymakers were unable to fully grasp or comprehend. The revision, however, highlighted numerous issues that were originally overlooked to ensure the guideline to be more comprehensive and somewhat complete to address the standard practice.

Table 5.5 presents the modifications made in the Guideline for Stem Cell Research and Therapy (2009) after the revision in comparison to the original version. First of all, the 2006 version only addressed the issue concerning the research and not the transplantation of stem cell, unlike the revised 2009 version which included standard practices for both stem cell research and its transplantation clearly. It is quite comprehensive compared to the older version, addressing the private sector regarding licensing, procurement and processing of cells, as well as patient evaluation and the laboratory requirement (MOH, 2009).

[13] This information was gathered from the Guidelines for Stem Cell Research and Therapy (2009)

Table 5.5: The analysis of the stem cell guidelines: 2006 vs 2009.

Stipulations in 2006	Changes Made in 2009	Comment
1. *All stem cell research must passed through an institutional review board and a institutional ethics committee to prevent unethical research and unethical use of stem cells*	*-All stem cell research and applications must be reviewed by the respective Institutional Review Board (IRB) and/or the Institutional Ethics Committee (IEB) for approval to ensure ethical research and use of stem cells. The IRB and IEC must strictly adhere to the National Guidelines for Stem Cell Research and Therapy.* *- A copy of all research proposals must be submitted to* ***the National Stem Cell Research and Ethics Sub-Committee*** *which shall retain the rights to review any research proposal as and when required.*	Specified the terms as review and approval for a clearer understanding, and the establishment of the new committee to strictly review stem cell research is an update
2. *Use of non-human stem cell lines are also allowed (mice and primates)*	*- Use of non-human stem cell lines are also allowed*	Removed the specified species
3. *Use of embryonic stem cell lines (from 64 cell lines) for research and therapeutic purposes should be allowed*	*-Use of embryonic stem cell lines for research purposes is allowed.*	Removed the cell line count its only allowed for research and not therapeutic purpose
4. *The creation of embryos either from Assisted Reproductive Techniques / Somatic Cell Nuclear Transfer (SCNT) specifically for the purpose of scientific research is presently prohibited*	*-The creation of human embryos by any means including but not limited to assisted reproductive technology (ART) or somatic cell nuclear transfer (SCNT) specifically for the purpose of scientific research is prohibited*	Acknowledged all forms of human embryo creation that are presently available including those have yet to devise but within similar contaxt
5. *Use of sample or excess embryos either from assisted reproductive techniques requires further deliberations and guidance from the various religious authorities, although from the Islamic point of view this is allowed specifically for research cloning (refer to 'Keputusan Muzakarah Jawatankuasa Fatwa Majlis Kebangsaan Bagi Hal Ehwal Agama Islam Malaysia Berkaitan Pengklonan Dan ART' dated 22 February 2005 on page 11)*	*-Research on embryonic stem cells derived from surplus embryos is allowed. (Please refer to the Keputusan Muzakarah Jawatankuasa Fatwa Majlis Kebangsaan Bagi Hal Ehwal Agama Islam Malaysia berkaitan Pengklonan dan ART dated 22 February 2005)*	They considered the surplus embryos of IVF as allowed although previously it only reflected the Islamic point of view hence, unable to completely agree without considering the other religious beliefs and practices which were approached for the sake of the revision process

According to the Guideline for Stem Cell Research and Therapy (2009), any choice made by donors, human subjects and patients related to the creation of embryos for reproductive treatment should be independent without any manipulation by the investigators who plan to extract or use hESC. The decision made should be autonomous and free of conflict of interest. Therefore, "whenever it is practicable, the attending physician responsible for the infertility treatment and the investigator deriving or proposing to use hES cells should not be the same person" (MOH, 2009). Consent from the donors wanting to donate their excess embryos (blastocysts) for research purposes are obtained from every donor and when a specific research is being considered, these consented donors are approached again to give informed consent again depending on the nature or details of the research. They will not be paid in cash or offered any form of compensation, but they do have the right to either retain or withdraw their consent until the cells are actually being extracted.

At the moment as specified by the guideline, the following procedures are not permitted;

(1) research using *in vitro* culture of any intact human embryo, irrespective of its extraction method for older than 14 days or until primitive streak formation begins

(2) research involving human embryonic stem cell being introduced into non-human primate embryos, or any embryonic stem cell which is introduced into human embryos

(3) animals with introduced human embryonic stem cell are not allowed to breed

(4) any fusion of human stem cell or other non-human pluripotent cells should not be developed beyond 14 days or until the formation of the primitive streak, or whichever occurs first.

There are also the many requirements of the laboratories involved in stem cell research (including the private sectors) and its transplantation, which are (1) to conform with the guideline for Good Laboratory Practices (GLP) which is regulated by the National Pharmaceutical Control Bureau (NPCB), (2) are required to be Good Manufacturing Practices (GMP) compliant as required by the NPCB, (3) are those producing stem cells based or tissues products for profitmaking are required to be licensed as GMP compliant and (4) stem cell based products that are imported for clinical trials should be GMP certified and registered by the NPCB.

Therefore, it is clear that the laboratory aspects of stem cell research and its technologies are directly under the jurisdiction of the NPCB. Currently, it is known as the National Pharmaceutical Regulatory Agency (NPRA) as shown in Figure 5.7.

Figure 5.7: The Official Portal of the National Pharmaceutical Regulatory Agency (NPRA).

[Source: The NPRA (2017b)]

While the therapy should also be within their oversight, but since it is still reviewed individually, case-by-case basis as clinical trials and not completely offered as a routine therapy the NPRA have yet to offer license or regulate the stem cell therapy.[14] However, they have licensed certain stem cell products labelled as cosmetics, that is easily searched using their search engine available in their official portal. According to the Figure 5.8, a total of 326 stem cell-based products are currently licensed under the NPRA, although the figure only meant as a preliminary search.

Figure 5.8: The clipping of the stem cell products list: Based on the National Pharmaceutical Regulatory Agency (NPRA) product search engine.

[Source: The NPRA (2017b)]

[14] This information was verified by the local policymakers during the in-depth interview session

5.7 The ongoing deliberations

The policymakers verified that the establishment of the Guideline for Stem Cell Research and Therapy (2009) was as an interim measure while they continued to deliberate for a better but permanent solution. According to the policymakers, they were unable to figure out the complexities of stem cell at the time and wondered if they should deal with the research and transplantation separately. They decided to set up the Technical Committee on Stem Cell Research an *ad hoc* measure within the National Committee on Human Cloning originally established in 2002 (MOH, 2002).

The cloning issue has its own concerns, however in 2003 the committee in charge within the MOH held three meetings (11th Mac 2003, 29th August 2003 and 21st Mac 2003) for the groundworks of the Human Reproductive Cloning Bill which was presented to the Director General of Health but as of December 2003 the bill remains under drafting process despite what the former Health Minister Chua Jui Meng said in his statement in Malaysiakini news proving that under different administration, objectives and aims, the basis of what is appropriate at the time can change (MOH, 2003).

Although the matter of stem cell research has yet to settle, however, the MOH deliberated on the issue of stem cell transplantation which was initiated by Deputy Director General of Health (Medical), Datuk Dr. Noorimi Morad. Apart from the medical, there are two other Deputy Director Generals which are Deputy Director General of Health (Public Health), Deputy Director General (Research & Technical Support). In 2007, Datuk Dr. Nooriimi Morad was recognized for her initiative and her guidance in the development of the National Organ, Tissue and Cell Transplantation Policy, whilst being a part of the National Standards for Stem Cell Transplantation: Collection, Processing, Storage and Infusion of Hematopoietic Stem Cells and Therapeutic Cells that was published in 2009.

The emerging stem cell transplantation especially the bone marrow and the cord blood, Malaysia decided to address the matters of transplantation first, instead of the research. The Medical Development Division reviewed and handled other forms of stem cell such as embryonic, adult stem cell and the other hematopoietic stem cell as clinical trials. The former Deputy Director General (Research and Technical Support), Tan Sri Datuk Dr. Hj. Mohd Merican overlooked and managed certain characteristics of the embryonic stem cell research and other evolving technologies as Research Division, that was established eventually as the NSCERT in 2010. Formerly, these stem cell research projects were reviewed personally by the MREC, however the lack of qualified experts, they felt unfit to deal with the issues of stem cell and this urged for the formation of the committee.

At the time, the key interest was the issue of transplantation and the demand for legislation or an act that could better regulate not just the standard solid organ transplant but the newly emerging stem cell therapies and transplantation overall. Sadly, there is no governing act or a policy that could combine them all under one oversight. With the stem cell guideline acting as the interim measure, the NSCERT continued to deliberate to fit stem cell within any existing legislation such as Human Tissue Act 1974. The only existing legislation which has essentially some inclusion on the subject of human cells is Human Tissue Act 1974 and it is inadequate to integrate stem cell or its advanced therapies, thus creating a deficiency and the legislative gap which is not possible to unravel overnight, since the process of lawmaking would take close to ten years to accomplish.

In 2010, regardless of the stem cell issues, the MOH Malaysia instructed a committee to amend the inadequate Human Tissue Act 1974 to include other overlooked matters such as those concerning the standard solid organ transplantation. Jahn Kassim (2005) highlighted several issues concerning the Human Tissue Act 1974 such as, the

lack of clear definition of 'tissue' or 'person' that raised series of complex ethical questions. The deliberation to amend the act resulted in a few drafts, one of which was presented to the Director General of Health, but he rejected the draft suggesting that the solid organ transplantation and stem cell transplantation be combined.

The suggestion drove the committee to yield in the idea combining the two forms of transplantation under one act, rather than developing two separate acts or revising the present Human Tissue Act 1974. Even so, the committee was not entirely pleased and continued to deliberate extensively about separating the solid organ transplantation and stem cell transplantation. The members who supported the solid organ transplantation refused to combine stem cell in the act, despite the two-year deliberation as they felt strongly that the act had a higher possibility of passing without the elements of hemo-therapy and cell therapy. The unpleased Director-General questioned the future of stem cell research, its governance and the act that nobody interested to work on. Consequently, they formulated the act which finally combined the two elements, and presented to the Attorney General at the time Tan Sri Datuk Seri Panglima Abdul Gani Patail. However, the draft only led to more deliberations as the Attorney General had a completely different opinion regarding it. The ongoing deliberation led to more complication when a new Director General of Health was appointed in 2013, who brought in new opinions and suggestions. This proves that the formulation process may have started in 2010 but the long overdue, well-needed act is yet to emanate because of the existing bureaucracy.

Despite countless deliberations resulting in numerous proposals and drafts of the transplantation act, however, it is still unavailable for the last 10 years. The policymakers reckon that the development of the proposed policy or act is in progress anticipating for its ruling or statute, which targets to incorporate every type of transplantation including stem cell.

5.8 The 'new draft underway'

The exceptional characteristics of stem cell, its research and the transplantations together with the existing complexities of the solid organ transplantation policy making, resulted in extended delibrations involving several experts within the MOH for the past ten years. Despite the claim of being at its final drafting stage, it has yet to materialize proving lawmaking is an ongoing challenging process. Although have acquired their legal experts' approvals, the draft will only come into enactment once passed in the parliament. In order to reach the parliament, the draft should be presented and approved by the current Attorney General the Honorable Tan Sri Dato' Sri Hj. Mohamed Apandi Ali. The working draft or the 'new transplant act', aims at replacing the Human Tissue Act 1974 and incorporating the neglected and overlooked issues concerning PHFS Act 1998 as well.

The new act is definitely long awaited for, and may even be just what Malaysia need considering the deficiencies and insufficiency of the Guideline for Stem Cell Research and Therapy (2009) and PHFS Act 1998 regulating the stem cell research and its technologies. However, in the course of ten years, the stem cell science has improved with new discoveries.

The red-tape bureaucracy and the inability to reach coherence or homogeneity during challenging deliberations could easily delay the draft from being passed and legislated into the much-anticipated law even though it is at its final stage, and have taken a decade already. While awaiting for its statute, the stem cell research and its technologies will remain to be governed by the Guideline for Stem Cell Research and Therapy 2009, the NSCERT, the PHFS Act 1998 and the MOH formal circulars.

Part II: Stem cell research ethics

5.9 The stem cell ethics publication

This section presents part II of this study which is the research ethics of stem cell and technology based on written publications. The ethics of stem cell research and technology are well studied by national and international scholars, written to justify the many arguments concerning stem cell and its technologies. The publication search that was therefore divided into two, the international and the local, Malaysian. The resulting publications are presented in Table 5.6 and Table 5.7 respectively. The assessment of local, Malaysian experts and international experts displayed a distinct approach that is not documented enough based on ethical perspectives.

5.9.1 Publication written by international authors

The combination of databases (Embase, JSTOR, MEDLINE, ScienceDirect and BioMed Central) resulted in a total of 75 publications. Figure 5.9 illustrates the subsequent process after publication retrieval, which included the removal of duplicates, and exclusion based on, (1) types of publication (to focus only on journal articles), (2) abstract (topic of interest) and finally any Malaysian articles captured.

Figure 5.9: Database search & stages

The resulting publication that started originally with 75 articles, resulted at 31 at the end, with the duplicates removed and the irrelevant ones excluded. Table 5.6 presents a review of the 30 articles based on the focus area, angle and the main argument of the ethical inquiry.

Table 5.6: Publication written by international authors.

Author	Title	Journal	Aim	Conclusion	Focus Area	Ethical Perspective
Cahill, Lisa Sowle (2000)	Social ethics of embryo and stem cell research.	Women's Health Issues	To raise issues about ethics of SC research, the status of embryo and market context of biotechnology and the life science industry	US debates over SC often and takes the embryo status only as decisive ethical issue to show it cannot be shown as person. Even if SC should be banned but it needs control through funding policies, regulatory and oversight of all research.	Ethics (status of embryo, personhood) Policy (need regulation)	Universalist Ethics
Harris, Lisa H (2000)	Ethics and politics of embryo and stem cell research: reinscribing the abortion debate.	Women's Health Issues	To review the most recent iteration of the embryo research debate and explore ways the terms on the debate can further strengthen feminist claims of abortion.	If the embryo research supported by public policy, they would be making an important contribution to scientific research and abortion politics as well as policy.	Ethics (moral status, personhood, right to life) Abortion	Universalist Ethics
Macklin, Ruth (2000)	Ethics, politics and human embryo stem cell research.	Women's Health Issues	Aims to describe the differences between three reports made on the ethical aspects of HESC issued on 1999 in US.	Neither moral intuition nor linguistic maneuvers can substitute for ethical argument of using human embryos for SC. The consideration of moral status of embryo and fruits of research using embryos can then permit creation of embryos for SC research.	Ethics (moral status, personhood) Public Policy Federal Funding Oversight Process	Universalist Ethics

Table 5.6, continued

Ryan, Kenneth J (2000)	The politics and ethics of human embryo and stem cell research.	Women's Health Issues	To discuss the matter of the status of human embryo through addressing the history of regulations overseeing federal funded research on embryos and the ethical consideration of human embryos and SC research.	The argument based on principles of status of embryo life has not changed many people since it began. The benefit from carefully regulated research is undeniably great and doesn't convince many regarding abortion and immoral acts. Public policy therefore should approve governmental support for embryo and SC research.	Ethics (moral status) Policy (regulation) Abortion Federal Funding	Universalist Ethics
Ruiz-Canela, Miguel (2002)	Embryonic stem cell research: the relevance of ethics in the progress of science.	Medical Science Monitor	Aim to address ethical issues concerning ESC research which requires human embryo destruction and the implication of social and political debates of SC research. Also, to discuss alternative to ESC.	The moral status of human embryo can be justified from utilitarian perspective, as well as ontological and with internal value. There's varied political consequences with different laws. Even with the controversial ESC and alternatives of ASC, however researchers believe they are all necessary and should not be restricted.	Ethics (moral status) Policy (regulation)	Universalist Ethics

Table 5.6, continued

Oduncu, Fuat S. (2003)	Stem cell research in Germany: ethics of healing vs. human dignity.	Medicine, Health Care and Philosophy	It aims to present and evaluate many ethical debates which created on biological and medical data and their potential use of SC technologies and ultimately support the ASC instead of ESC.	Although the goals of medical research using human embryos has useful potential however author urge researchers to withdraw from using human embryos and use ASC instead.	Ethics (moral status, right to life, personhood) Policy (German regulations)	Universalist Ethics
O'Neill, Onora (2003)	Stem cells: ethics, legislation and regulation.	Comptes Rendus Biologies	To address some ethical issues with SC research and also to briefly describe the regulation in the UK, and moral debate results from advances in bio-medicine.	There's strong agreement that human reproductive cloning be banned. Author says UK have accepted IVF, have controlled embryo research and also control the ESC only when alternatives fail.	Ethics (personhood, right to life) Policy (regulation)	Universalist Ethics
Fischbach, Gerald D & Fischbach, Ruth, L (2004)	Stem cells: science, policy and ethics.	The Journal of Clinical Investigation	The article aims to address the issues of SC debate especially the moral status of embryos. Also to bring about the attention that the integrity of scientific process being independent without too much restriction.	Research is considered obstructed with regulations and thus HESC had not been positive enough to have cured any disease, as arguments reported. Believes that without federally funded research, SC research will remain within the state of ignorance.	Ethics Policy (regulation)	Universalist Ethics

Table 5.6, continued

Curzer, Howard J (2004)	The ethics of embryonic stem cell research.	Journal of Medicine and Philosophy	To rebut the conservative protest to the five phases of ESC. To argue that the scientist using existing ESC are not deceitful in the previous destruction of embryos.	There was no positive argument regarding the use of embryos in HESC, instead the argument was that the current objections fail. Objections to practices are often any, where you defend one, another spring up.	Ethics (right to life)	Universalist Ethics
Schmidt, Jotterand & Foppa (2004)	Neither convention nor constitution – what the debate on stem cell research tells us about the status of the common European ethics.	Journal of Medicine and Philosophy	Study that aims to discuss the issue of human embryos in SC research based on the geography of the debate in Europe.	That those who claim that all embryos despite being given the opportunity to become a human deserve protection and those who claim embryo has to become a human to receive protection would never and can be united. The philosophical and religious debate in Europe shows that the question of the status of the embryo is unavoidable.	Ethics (right to life, personhood, embryo moral, status of embryo) Policy (regulation)	Relativist Ethics
Towns, C.R & Jones, D.G (2003)	Stem cells, embryos, and the environment: a context for both science and ethics.	Journal of Medicine and Philosophy	Aim is to highlight the scientific understanding that may be relevant to the ethical debate.	Many of the disapproval to HESC rely on the fact that AS could offer similar benefit. The actual benefit of ASC still remains as a disputable and needs more experimentation. It is necessary to question if it is useful to continue thinking of the blastocysts as an independent being with moral status stemming from its potential.	Ethics	Universalist Ethics

Table 5.6, continued

Towns, C.R & Jones, G (2004)	Stem cells: public policy and ethics.	New Zealand Bioethics Journal	To assess some of the ethical and policy issue faced in regulating SC and also aims to demonstrate that the scientific point play little if any part in formulating policy.	Out of the many positions, the one which is found in the UK may be the most reliable position ethically and the most beneficial one scientifically.	Ethics (personhood, moral status) Policy (regulation)	Universalist Ethics
Shenfield, Francoise (2005)	Semantics and ethics of human embryonic stem-cell research	Lancet Neurology	To discuss the definition and ethical issues of HESC.	Conclude that many may consider SC from embryos generated by somatic-cell nuclear transfer a feminist issue, due to exploitation of women. However, this might be fair at a time when there's lack of equality between donation of and demand of oocyte everywhere.	Ethics Policy (regulation)	Universalist Ethics
Taylor, Patrick L (2005)	The gap between law and ethics in human embryonic stem cell research: overcoming the effect of US federal policy on research advances and public benefit.	Science and Engineering Ethics	The goal is to identify the key ethical and legal issues, their differences and connection as well as the federal position towards SC.	The relationship between law and ethics differs, and at its best the law explains the necessity of its time without over control. Limiting the governmental financial support, there are several consequences apart from absence of funds alone, which are, data and material sharing rule do not apply, absence of federal leadership, lack of agency guidance, and others. The need to design a legal system which is best ethically and logically supports SC and public benefit.	Ethics moral status, personhood, Policy (regulation) Oversight Intellectual Property	Universalist Ethics

Table 5.6, continued

Hamdy, Ronald.C (2006)	To condone or to condemn? On the ethics of stem cell research.	Southern Medical Journal	This study is to address the issue of support or oppose SC research based on its ethics.	The answer as to when human life start would offer the basis if we should proceed with it or not. The scientist would offer the facts and the religious figure would answer the issue of beginning of life	Ethics Policy (regulation)	Universalist Ethics
Giacomini, Baylis and Robert (2007)	Banking on it: public policy and the ethics of stem cell research and development.	Social Science & Medicine	Aim to propose a framework for ethical policy analysis of SC and to map ethical concerns about the welfare of the community and donors.	Need more attention to deal with the ethics of protecting healthy people from the unknown risk, giving a fair access to all, finally sustaining economic viability and the impartial health system. They have proposed an ethical framework which would evaluate options for SC research and development that looks past the welfare of the in vitro embryos or the ill patients but ultimately study the impact on the healthcare system.	Ethics Policy (regulation)	Universalist Ethics
Hurlbut, William B. (2007)	Ethics and embryonic stem cell research: altered nuclear transfer as a way forward	BioDrugs	To discuss the scientific foundation of altered nuclear transfer and the moral reasoning to investigate how it can sustain social consensus and open opportunities for progress in SC.	Altered nuclear transfer can provide relevant practical benefit for PSC research and its application while introducing direct path to social consensus. It will also introduce SC research to US federal funding with ethical oversight, wide public support and coordinated collaboration in all level.	Ethics Policy (regulation)	Universalist Ethics

Table 5.6, continued

McLaren Anne (2007)	A scientist's view of the ethics of human embryonic stem cell research.	Cell Stem Cell	To examine the ethics on HESC from the scientists' perspective.	Scientists are not ethicists and the hold little right to their opinion on the ethics of HESC research as the public. With the elaborate knowledge, scientists have an ethical duty to offer explanation to public what is the research about and its implication. However, education of the public is not enough, public understanding is depressingly insufficient therefore a dialogue between public and scientists would help both.	Ethics (moral status) Policy (regulation) Federal Funding	Universalist Ethics
Steinbock, Bonnie (2007)	The science, policy and ethics of stem cell.	Ethics, Law and Moral Philosophy of Reproductive Biomedicine	It examines the science behind the HESC research and explains three different approaches to moral status of the embryo.	Despite there's restriction human cloning, yet there have been reports of human cloning being done successfully by the British which questions the use of alternative form of SC such as somatic cell nuclear transfer. Human cloning for medical research raised a lot of concern even though legal in some parts of US it involves possible dangers and exploitations to women donors. The fact that moral status of embryo is deserves full status and right is also justified.	Ethics (moral status, personhood) Policy (regulation)	Universalist Ethics

Table 5.6, continued

Holm, Soren (2008)	'New Embryos' – New Challenges for the Ethics of Stem Cell Research	Cells Tissues Organs	To analyze how the issue of SC being ethically problematic because of embryo destruction and the kind of regulation embryo donor should have engaged in obtaining SC from anomalous embryos.	At the end, it might be worth considering why effort to avoid the main ethical issue in SC research may seem attractive but for similar reasons only.	Ethics (moral status)	Universalist Ethics
Solbakk J.H & Holm, S (2008)	The ethics of stem cell research: can the disagreements be resolved?	Journal of Medical Ethics	To briefly review the controversies motivating the debate and suggest some answers to a set of related questions.	Based on their three apparently reasonably realistic scenarios, they believe the use of ESC will continue to be essential for research but their use in therapies will be minimum would be the best and eventually the controversies will lessen in time.	Ethics (moral status,	Universalist Ethics
Solomon & Brockman -Lee (2008)	Embryonic stem cells in science and medicine, Part II: law, ethics and the continuing need for dialogue.	Gender Medicine	To address the most recent announcement and review the relevant history so that we can consider if the moral, ethical and social issues do vanish with these advancements.	Despite the fuss, nothing much has changed. If there are ethical concerns surrounding HESC, they remain as critical as it was previously. The medical and scientific communities continue to do harm by failing to create a solid governing body to address and make recommendations regarding the ethical, moral and social issues.	Ethics (moral status, Policy (regulation) Oversight	Universalist Ethics

Table 5.6, continued

Sugarman, Jeremy (2008)	Human stem cell ethics: beyond the embryo.	Cell Stem Cell	To describe some of the ethical issues relevant to SC research and therapy but is not concerning the embryo. To offer knowledge and ultimately navigation to those working in SC and oversight bodies. To urge the scientists to develop ethical guidelines and to follow them.	Even though HESC research has brought upon many ethical issues, however some are not related to the embryo destruction. These includes issues related to the source of cells used, the whole process of obtaining the cells, the in vivo use of the SC, intellectual property and finally the conflict of interest.	Ethics Policy (regulation) Oversight Intellectual Property	Universalist Ethics
Master *et al*., 2008	The ethics of human embryos and embryonic stem cell research.	Journal of Stem Cells	To review the many normative theories on the moral status of human embryos that captures issues from continuity to cognitive prerequisite for personhood including sentience and awareness. To discuss argument of the symbolic value of human embryos.	It might have enormous social and scientific benefit but the use of human embryos in HESC still raises a lot of arguments similar to abortion. The many available ethical viewpoints on the moral status of embryos, the exploitation to women and the value of ESC that influences the commercialization of SC in various jurisdictions. More consideration and debate by relevant parties are needed to decide how public can increase SC benefit but keep the harm to embryo and women low.	Ethics (moral status, personhood) Intellectual Property	Relativist Ethics

Table 5.6, continued

Kilner, J.F (2009)	An inclusive ethics for the twenty-first century: implication for stem cell research.	Journal of Religious Ethics	The main goal is to discuss the issue of inclusive ethics for the 21st century involving SC research, which is a religious viewpoint.	That Christian ethics is much better at explaining matters involving vulnerable people and inclusiveness compared to the modern ethics, as far as SC is concerned. Human rights, donor welfare, beneficiary of treatment and the moral imperatives can be explained using the inclusive ethics. The alternative form of SC like adult sources can also offer some form of advantage compared to HESC.	Ethics (moral status, personhood)	Relativist Ethics
Doerflinger, Richard M (2010)	Old and new ethics in the stem cell debate.	Journal of Law, Medicine and Ethics.	To outline a non-religious argument of this kind and compare it with the ethical approach often used to defend embryo destruction for HESC research and to explain the disagreement and the implication of future ethical dispute.	To acknowledge the moral status of embryo, and not simply committing a fallacy. The accepting of personhood claim to much re-evaluated and logical level. The endless dispute of the old and new ethics and while some might agree that the new ethics is more compatible but the old ethics continue to offer reasons why can't we take the next step.	Ethics (moral status, personhood) Policy (regulation)	Universalist Ethics
Klotzko, Arlene J (2011)	Regenerating a stem-cell ethics debate	New Scientist	To address the ethical issues concerning HESC and iPSC.	The destruction of human embryo in HESC might have found an alternative in the form of iPSC but with creation of cloned HESC revives some old moral issues. Using consequentialism theory, they can argue that the research is acceptable whole others might not support it.	Ethics	Universalist Ethics

Table 5.6, continued

Zacharias *et al*., (2011)	The science and ethics of induced pluripotency: what will become of embryonic stem cells?	Mayo Clinic Proceedings	To briefly review the current SC platform, especially the two existing pluripotent lines available for therapeutic use; HESC and iPSC.	Recognized iPSC technologies as a potential and as a superior alternative to HESC for future medical research as it is ethically acceptable. However, while it appears to be promising but there are recognized limitations and hence need a much clearer scientific goal.	Ethics Policy (regulation)	Universalist Ethics
Master, Z & Crozier, G.K.D (2011)	The ethics of moral compromise for stem cell research policy?	Health Care Analysis	To analyse many scientific proposals to obtain SC and to conclude that most of them are not scientifically practical and violates other moral standards.	Moral compromise offers a great deal of ethical outcome in current US debate regarding SC research. The bioethics troubled with the issue of morality with SC research should also consider the value of moral compromise as a realistic and reasonable solution to address the varied moral perspective of SC research.	Ethics (moral status, personhood) Policy (regulation	Universalist Ethics
Carvalho, A.S & Ramalho-Santos, J (2013)	How can ethics relate to science? The case of stem cell research.	European Journal of Human Genetics	To illustrate how taking bioethical belief to the scientific debate can become beneficial in both ethics and science, especially as narrative shift.	Presenting uncertainties and formulating challenges is an example of the beneficial act in both ethics and science. This strategy can be used in other controversial fields. The support imposed on these debates can generate speculative expectations as well as fears in society but how they are framed can eventually be useful and in the future.	Ethics Policy (regulation)	Universalist Ethics

5.9.2 Publications written by Malaysian authors

The publications written by local, Malaysian authors are presented in Table 5.7. Only 18 publications were identified. These publications include a range of publication types, unlike in international publication, which was only focused on the journal article. The reason for this is that the local publications are still new and the discussions have yet to research the mainstream like international publication, plus they are more localized in their discussion. Therefore, to show the current publications in Malaysia, it is only fair to include what is available since there are not many. The Malaysian publications are also reviewed based on the focus area, angle and the main argument of the ethical inquiry.

Table 5.7: Publications written by Malaysian authors.

Author	Title	Journal	Aim	Conclusion	Focus Area	Ethical Perspective
Abu Bakar Abdul Majeed (2002)	'Genetics' – Integrating ethical reasoning and scientific findings	Institute of Islamic Understanding [Book Chapter]	To discuss the many issues raised by the "biotech" revolution, including stem cell.	That the ethical and legal issues about biotechnology cannot be ignored. With the progress, there could be long-range implication which need to be carefully monitored.	Biotechnology Awareness	Relativist Ethics
Islam, S., Nordin, R., Ab Rani, S., & Mohd Nor, S. (2005)	Spare embryos and human embryonic stem cell research: ethics of different public policies in the western world.	The International Medical Journal Malaysia [Article]	To identify the major policy options which adopted by the Western world and to assess their policies being ethically sound. Finally, to illustrate the test of different Bioethical principles of Autonomy, Beneficence, Non-maleficence and Justice	That to properly deal with biomedical issues, morality need to be concomitant with law and public policy. hESC is not like other issue, in fact is multidisciplinary with great deal of views.	Multiview of hESC	Universalist Ethics
Fadilah, Leong & Cheong (2008)	Stem cell transplantation in Malaysia and future directions.	Medical Journal of Malaysia [Editorial Comment]	To highlight the stem cell transplantation from the beginning and its future direction in Malaysia.	That stem cell faces delay due to controversies while assuring it to have potential and further revealed the Malaysian transplantation policy 2007 that was introduced. The dogma of impossibility in medicine is being challenged.	Future direction of stem cell	Universalist Ethics
JHP, Hui., M. Azura., & EH, Lee. (2009)	Stem cell therapy in orthopedics surgery: current status and ethical considerations.	Malaysian Orthopaedic Journal [Article]	To offer a brief summary of the current status of stem cell research with emphasis on the clinical application of stem cell therapy.	The stem cell research is potential treating orthopedic related conditions. Acknowledged the issue of unproven stem cell therapies marketed focusing on the issue of ethics.	Feasibility of stem cell in orthopedic medicine	Universalist Ethics

Table 5.7, continued

Abu Bakar Abdul Majeed (2009)	Too clone or not to clone - and other ethical issues in pharmacy and medicine.	UiTM Publishing [Book]	To discuss about the advancement in biotechnology, pharmacy and medicine. To highlight the issue of stem cell (others) and they need judicious approach.	The advancements in biotechnology, pharmacy and medicine need to adopt applied ethics based on secular approach being not ideal. Religious principles need to be the foundation for such discussion.	Implication of research (cloning & stem cell)	Relativist Ethics
Foong (2011)	Human embryonic stem cell (HESC) research in Malaysia: multi-faith perspective.	Asian Bioethics Review [Article]	To investigate the many perspective regarding stem cell research especially human embryonic stem cell.	Malaysia being multi-religious have many controversies regarding human embryonic stem cell. The embryo can be respected with necessary controls, limitations and accountability through appropriate regulatory framework.	Multi-religious perspective on embryo rights	Relativist Ethics
Amin, L., Rezali, N.I., Samani, M.C., Hassan, Z., & Jusoff, K. (2011)	Ethical issues on Biotechnology in four mainstream newspaper.	World Applied Sciences Journal [Article]	To assess the ethical issues that are being address by the local media in relation to biotechnology.	That the ethical issues relating to biotechnology not reported frequently in Malaysia although the government had brought forward the importance of biotechnology as the stimulus for development.	Stem Cell Awareness	Relativist Ethics
Foong (2012)	The regulatory regime for human embryonic stem cell (HESC) research in Malaysia: a critique	Malaysian Journal of Law & Society [Article]	Aims to assess the current regulation of human embryonic stem cell research in Malaysia from the Guidelines perspective and to make policy recommendation.	That Malaysia need to consider adopting a regulatory framework, that is comprehensive and effective in monitoring stem cell research.	Stem Cell Regulation	Relativist Ethics

Table 5.7, continued

Abu Bakar Abdul Majeed (2013)	When cloning benefits mankind.	Institute of Islamic Understanding [News Article]	To address the issue of cloning and the moral status of the cloned organism.	Recognized somatic nuclear transfer as another method of cloning. The validation of Islamic scholar of the ensoulment of embryo linked to the nervous system development	Cloned Embryo	Relativist Ethics
Sivaraman, M.A.F., & Nor S.M. (2014)	Ethics of embryonic stem cell research according to Buddhist, Hindu, Catholic, and Islamic religions: perspective from Malaysia.	Asian Biomedicine [Article]	To study the ethical positions of the many faiths regarding the use of surplus' embryos and 'research embryos'.	Embryonic stem cell research allowed according to Hindu, Buddhist and Islamic perspective based on the greater benefit but with some reservations. The Catholics found embryonic stem cell research against their principle.	Embryo Status	Relativist Ethics
Sivaraman, M.A.F., & Nor S.M. (2015)	Human embryonic stem cell research: ethical views of Buddhist, Hindu, & Catholic leaders in Malaysia.	Science and Engineering Ethics [Article]	To investigate the multi-faith ethical viewpoints, in particular, those of Buddhists, Hindus and Catholics in Malaysia relating to embryonic stem cell research.	Based on the data, three ethical dilemmas emerged which are sanctity of life, do not harm and finally the intention of the research.	Embryo Status	Relativist Ethics
Lye, J.L., Soon,L.K., Wan Ahmad, W.N., & Tan, S.C. (2015)	Knowledge & attitude about stem cell and their application in medicine, among nursing students in University of Science of Malaysia.	Malaysian Journal of Medical Science [Article]	To examine the level of stem cell knowledge, attitude concerning stem cell application in medicine, and its link with years of education among University of Science undergraduate nursing students.	The result justifies a need to foster stem cell knowledge and its application in medical field to create awareness among undergraduate nursing students. Further assessment and effort is needed to cultivate the knowledge and positive attitude in these students.	Stem Cell Exposure	Universalist Ethics

Table 5.7, continued

Azmi, A.G., Madieha, I., & Zawawi, M. (2015)	Human stem cell research: ethical and religious concerns over patenting biotechnological invention in Malaysia.	Kluwer Law International [Article]	To examine the patentability of biotechnological inventions especially those from human embryonic stem cell research.	It proposes Malaysia to also adopt the UK and Europe's consideration in incorporating ethics and morality in patentability criteria, and with that Islamic position would be relied upon.	Patentability	Relativist Ethics
Abu Bakar Abdul Majeed (2015)	Research ethics: sharing and scaring.	Conference BioBorneo 2015 [Proceeding]	To highlight the ethical dilemma and the issue of right from wrong. The ethical imperative	The ethical imperative (origin of words) and what they mean. Introduced theories of ethics and acknowledged the bureaucracy and red-tape in government.	Ethics	Universalist Ethics.
Amin, L., & Hashim, H. (2015)	The role of religiosity and religious acceptance in influencing attitudes towards embryonic stem cell research.	The Proceeding of the 6th International Symposium on Islam, Civilization and Science [Proceeding]	To determine the role of religiosity and religious acceptance in influencing stakeholders' attitudes towards embryonic stem cells	There is no difference between the respondent's ethnic and religion. That the Chinese are most experienced against religious tolerance compared to others.	Religious Acceptance	Relativist Ethics
Abdul Rahman, S.H. (2015)	War 38 halal stem cell research and therapy: the Malaysian perspective.	World Academic and Research Congress 2015 [Proceeding]	To assess whether attempts to develop common halal standard nationally and internationally, harmonizing the process products release.	The public accessibility of stem cell therapies which increased requirement to incorporate halal status of such products. The existing halal standard should also be established for stem cell research therapy.	Halal Standard for Stem Cell	Relativist Ethics

Table 5.7, continued

Lai, D.P.K., Ramasamy, R.S., & Amini, F. (2016)	Knowledge, awareness, and perception of stem cell research amongst Malaysian medical students.	Tissue Engineering and Regenerative Medicine Society of Malaysia [Article]	To assess the knowledge, awareness and perception of medical students in Malaysia about stem cell research.	The depth of stem cell awareness amongst medical student is not subject to their education background. They were aware despite lack of exposure in their curriculum. Although not significant, religion did play a part in the respondents' view.	Stem Cell Awareness	Relativist Ethics
Amin, L., Hashim, H., Ibrahim, M., Che Ngah, A., & Sidik, N.M. (2016)	Effects of education level and religion on attitude to stem cells in Malaysia.	Akademika [Article]	To evaluate and compare the attitude level of Malaysian public (Klang Valley) about adult stem cell and human embryonic stem cell.	Concluded that Malaysia public attitude towards adult stem cell was more positive than human embryonic stem cell. They believed that adult stem cell had less moral concern compared and thus more acceptable by their religion.	Stem Cell Awareness	Relativist Ethics

5.10 The perspectives of ethical inquiry of stem cell research

The authors of the international articles are mainly from Western countries, like United States, United Kingdom, Canada, Germany, Portugal, Netherlands, Norway, Switzerland and even Spain. Some of the articles were written by multiple authors as collaborated work and they are from Western countries as well. By reviewing their names and their affiliated institutions, it is safe to conclude that none of the international authors are Malaysians. The publications written by Malaysian authors also included two internationally published articles written by the same Malaysian authors, Sivaraman and Noor (2014) and Sivaraman and Noor (2015). These articles represented a very significant point of view regarding stem cell research ethics in Malaysia, and their finding was recognized to have a worldwide impact from a multi-perspective viewpoint publishing in the international journal. All the Malaysian authored publications were written by Malaysians judging from their names and affiliated institutions. The Malaysian authored publications excluded (1) publications by foreign students studying within Malaysian institutions of higher learning and (2) publication by foreign authors presenting at Malaysian conferences.

The review and analysis of the international authored and Malaysian authored publications based on their research focus, angle and main arguments revealed two very common but strong perspectives in the ethical inquiry of stem cell research and technology which are the universalist ethics and the relativist ethics perspectives as presented by Table 5.6 and 5.7. Any discussion that was founded on the basis of culture and religion, were categorized as relativist ethics while those that discussed using a general tone that applies to everyone were categorized as universalist ethics.

The universalist ethics perspective is the ethical evaluation made based on universal principles of morality (Mepham, 2008). Based on Table 5.6, majority of the international authors discussed the many controversies surrounding the destruction of

human embryos for stem cell extraction and the implication of stem cell research predominantly using knowledge, rationality, and values that are accepted universally by all, despite very few of them engaging in the discussion from the relativist ethics perspectives. The relativist ethics strongly believe that '*there are no universally accepted standards'*(Mackinnon, 2004). Unlike the international authors, Table 5.7 showed that majority of the Malaysian authors' discussions were primarily from the relativist ethics perspectives. Their ethical deliberations and opinions regarding the use of human embryos in human embryonic stem cell research are relative to their culture and religious background. Only a few of them discussed the issues of stem cell research from a universal standpoint, highlighting topics such as public awareness and regulative challenges that carry a sense of universality in essence.

5.11 Conclusion

Part I of the result highlighted the in-depth interviews, its transcription, and the analysis of that transcripts. The finding is focused towards the context of this study by answering the Research Questions (a) 'What is the current status of stem cell research and therapy in Malaysia?', (b) 'How is stem cell research and therapy currently regulated in Malaysia?', (c) 'What are the implications of the current regulative measures concerning stem cell technologies in Malaysia?' and (f) 'Is the current stem cell guideline adequate in regulating the entire stem cell research and therapy?'.

While part II included the analysis of international publication and the local, Malaysian publication, which revealed that the internationally published articles are written from a universalist ethics perspectives that use a universal or a general approach to the subject matter, unlike the local, Malaysian publication. However, the local Malaysian authors tackled their concern of stem cell research from a relativist ethics perspective, that is relative to religious beliefs and their norms. This directly responds to

the Research Question (d) 'What are the perspectives of ethical inquiry involving the stem cell research and therapy?'. The completely opposite nature of assessment as far as the ethical inquiry of stem cell research is concerned between local, Malaysians and international authors as described in this section basically denotes how these culturally different people confront certain matters such as ethics and lawmaking based on what matters to them fundamentally. This subject matter will be further discussed in Chapter 6, which will answer the Research Question (e) 'How are the internationally published and Malaysian publications reflect in terms of the ethical inquiry of stem cell research and therapy?'.

The analysis of the in-depth interviews revealed that the international scientists have universal concerns which conform with the nature of how they tackle such topics based on the result in part II. The local, Malaysian scientists' concerns were lowered, fitting their country's stem cell research and development status and its regulatory statute. It represented a more personal opinion rather than what the nation as a unit may or may not offer. The analysis also revealed that the opinion of the local, Malaysian ethicist who represented all the ethicists in Malaysia being the chairperson of the Bioethics Council Malaysia regarding this issue were founded based on a religious foundation, unlike the foreign ethicists whose opinion were universal at its best, again conforming with the nature how foreign experts (including publications) have a tendency to look beyond their religious norms, based on the result in part II.

The result in part I demonstrates the thematic maps generated based on the transcripts of the in-depth interview of the experts. The individual maps in Figure 5.1 (A)-(E) signified the opinions and concerns of the respective experts ranging from scientists, to ethicists to policymakers which responds to the Research Question (a), (b), (c), and (f), while the Venn diagram in Figures 5.2, 5.3 and 5.4 displayed the inter-perspectives of respective experts. What constitutes a major finding is that (1) the local, Malaysian

experts, have accustomed to incorporate religion in all their decision-making processes, (2) their religious practices often influence their opinion and viewpoints, (3) the identification of the grey area due to regulatory loopholes or deficiency, (4) the extensive implication of the current stem cell regulation and (5) the presentation of a preliminary review of the original and revised stem cell guideline. These findings including others will be well discussed in Chapter 6. Finally, the local policymakers who are civil officers attached to the MOH disclosed many facts including the origins, the challenges and the hope for stem cell regulations in Malaysia which is not documented elsewhere, giving this study a sense of novelty.

In conclusion, based on this study, ethical inquiries of stem cell research and its technologies turned out to be based mainly on religion and its principles in Malaysia compared to the common international publication which is universal in perspective. In fact, this warrants the discovery of how religion is a part of decision-making even in regulatory deliberations as proved by the policymakers. Since Malaysia is a pluralistic society with many religious practices and norms, this has become a standard practice. Apart from religion, identifying the grey area as a deficiency and the origin of stem cell guideline formulation and much other implication are significant in understanding what is neglected in regulation and what needs reformation.

CHAPTER 6: DISCUSSION

6.1 Introduction

This chapter is important to discuss and interpret the research findings in regards to the research objective and research question of this study. It explains the implication of the research findings and to make recommendations concerning future study (Hess, 2004). This study highlighted that despite the growing stem cell research and technologies in Malaysia established by the increased stem cell transplantations, research publication and the increased number of private stem cell research entities including cord and tissue banks, there is no law or policies devised to effectively regulate the stem cell research and technologies in Malaysia. As a result, there are unproven stem cell therapies advertised and offered by unauthorized stem cell entities to the general public, which if not contained will promote uncontrolled stem cell tourism with serious repercussion involving tourists similar to Thailand (Arellano, 2012; Brown, 2012; Cohen, 2008).

The in-depth interview of stem cell scientists, ethicists and policymakers led to several discoveries that constitute as major findings of this study. They are, (1) the stem cell research and technologies in Malaysia is greatly unregulated despite its growth in the last three decades, (2) the formulated Guideline for Stem Cell Research and Therapy (2009) does not have any legal stature that warrants its purpose as a legal framework, (3) the unclear regulation is causing unintentional hindrance among Malaysian scientists, (4) the unproven stem cell therapies advertised and offered by unauthorized entities within the private sector such as the private medical health providers and aesthetic clinics due to ineffective oversight, (5) the red-tape bureaucracies and the absence of unified vision among policymakers and their directors that continue to severely extend the nature of their deliberation for something permanent, and (6) the ethical inquiry written by Malaysian authors concerning stem cell are largely from the relativist ethics perspective

which also adopted in law and policymaking in Malaysia, unlike the international authors whose writings are based on universalist ethics perspective.

The research findings immediately answered all the research questions of this study. The first two research findings answered the first two research question, "What is the current status of stem cell research and therapy in Malaysia?" And, "how is stem cell research and therapy currently regulated in Malaysia?" in fulfillment of the first objective which is to study the status and the regulatory processes of the current stem cell research and therapy in Malaysia. The research finding (2) up to (5) answered three research questions which are, "What are the implications of the current regulative measures concerning stem cell technologies in Malaysia?", "Is the current stem cell guideline adequate in regulating the entire stem cell research and therapy?" And, "how and where can the current regulatory measures be compromised due to the continuous development of stem cell technologies", in fulfillment of the third objective which is to discuss the implications of allowing Malaysian stem cell research to be guided by the present regulatory policies and its limitations. The remaining two research questions, which are, "What are the perspectives of ethical inquiry involving the stem cell research and therapy?" And, "how are the internationally published and Malaysian publications reflect in terms of the ethical inquiry of stem cell research and therapy?", fulfilled the second research objective which is to explore the ethics of stem cell research as presented by international authors and Malaysian authors. The research findings are discussed in detail in the following sections.

6.2 The in-depth interview revealed

6.2.1 The emerging themes

The thematic analysis of the in-depth interview begun by identifying and selecting significant phrases from the respondent's transcripts as sub-codes and using them to derive the relevant codes and themes representing a collective exemplification of the sub-codes (Braun & Clarke, 2006). Figure 6.1 presents the themes generated that are significant for this study. The themes 'conflict' and 'governance', were captured well as the main context of this study which concurs with the first and second research objectives which are related to ethics and regulation of stem cell research.

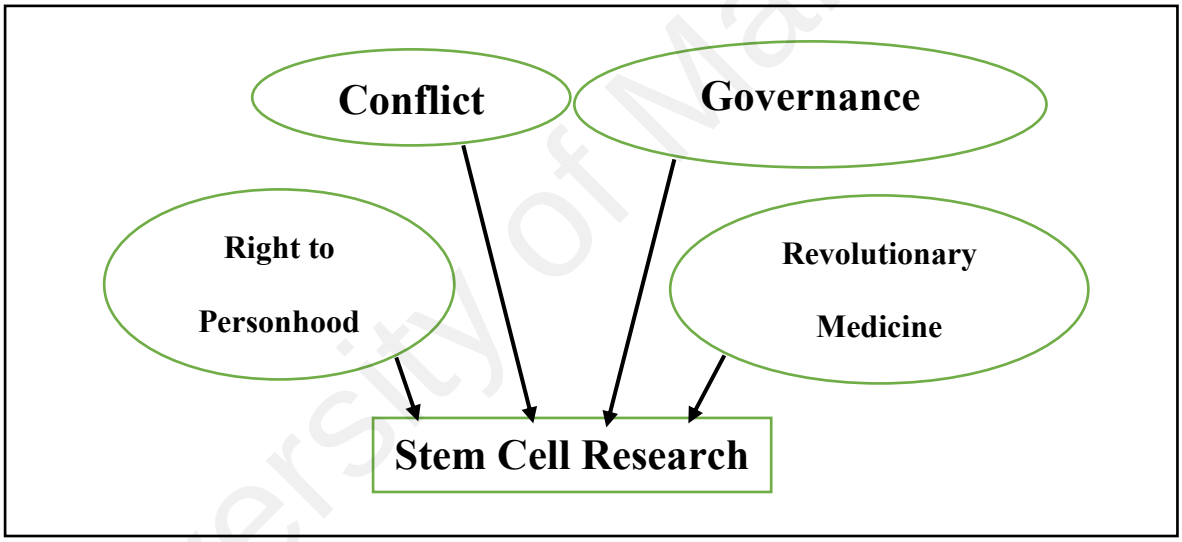


Figure 6.1: The significant themes generated.

In general, the resulting themes are not new or completely novel. In fact, the in-depth interview conducted managed to capture the themes which featured what stem cell research and its technologies are universally made famous for. The reality is that stem cell research is mainly pursued to broaden knowledge and to fill-in the gap between what is known and the unknown (Hyun, 2013; Panno, 2014). The continuous research which theorizes a new cell-based therapy translated into the state-of-the-art clinical trials revolutionizing the medical field (Mark et al., 2014). The theme 'revolutionary medicine' therefore, emerged from these sub-codes and codes. The codes, 'scientific ambiguity' and

'embryonic' represents many arguments focusing on the use of human embryos. There are several very common debates within these codes, with the justification of human life being the most popular. It identifies when life actually begins, either at conception or gastrulation. There is definitely inconsistency considering this topic mainly due to the impossibility to point a clear scientific line as to when life actually begins, and the argument that embryo is not a person. Therefore, the 'right to personhood' was chosen as the appropriate theme summarizing them into one very similar concept of discussion.

The theme 'conflict', pretty much sums up every controversies, debates, implication, and theories scholars have previously identified or argued about stem cell research and its technologies. This theme comprises of seven codes altogether, which are 'embryo destruction', 'utility', 'ambiguous claims', 'eggsploitation', 'alternatives', 'translations' and 'motives'. The embryo destruction discusses the moral status of human embryos with some correspondence to the right to personhood, while utility includes the discussion of surplus *in vitro* fertilization (IVF) embryos, the effective use of resources and the issue of informed consent as they are very much connected. The ambiguous claim explains several misleading or unclear claims or assertions such as the preimplantation genetic diagnosis (PGD) embryos being better ethically than surplus IVF embryos as a source for research or adult stem cell (ASC) and induced pluripotent stem cell (iPSC) being superior than human embryonic stem cell (hESC). Eggsploitation includes the discussion on the matter of women and donor exploitations, whereas alternatives argued about the matters concerning other available alternatives of pluripotent stem cell which are ASC and the iPSC and their superiority complex. The first five codes appeared within all the expert categories but the last two, which are translation and motives only appeared in the local scientist and foreign ethicists category. These two codes represented the discussion regarding the best time to conduct or begin clinical trials and the consequentialism theory on the pursuit of stem cell research.

The final theme ‘governance’, included all the matters of stem cell regulations beginning with what is ideal and necessary to what is unfortunately lacking. The imperative need for a law or legal framework, prevention of misconducts and addressing other noncompliance matters comes directly within the regulation of stem cell. The implication of stem cell commercialization and the pursuit of stem cell research as an international activity with global collaborations also insinuate the element of governance that should be within legal and ethical boundaries and well balanced. Hence, the theme governance deemed appropriate.

The four themes which are revolutionary medicine, right to personhood, conflict and governance were identified within all expert categories (foreign scientists, local scientists, foreign ethicists and local ethicist) but not the local policymakers. The policymakers have varied themes and codes, this is because the Malaysian policymakers were expected to be specialist with a range of expertise such as legal or public policy, hence they have their own set of questionnaires designed specifically to assess their knowledge and experience in policymaking. The four similar themes, enabled for an evaluation review among relevant categories such as between foreign and local scientists and ethicists. While, the resulting themes between all local experts, namely scientists, ethicist, and policymakers, still prompted an interrelationship study to identify common concerns and gaps among them. Overall, the in-depth interview managed to capture all the relevant sub-codes and codes generating significant themes focusing on matters concerning stem cell research, which will be discussed in detail in the next section. In this study, the identified themes are a large representation of what is important as far as stem cell research is concerned.

6.2.1.1 Revolutionary medicine

The pursuit of stem cell research is identified to extend the knowledge of cellular regeneration and to develop the effective therapy to help treat incurable diseases. The unique properties of stem cells to differentiate and self-renew managed to reshape the medical field using special therapeutic methodology (Watt & Driskell, 2010).[15,16] Currently, the stem cell research in Malaysia is still in its infancy (Ministry of Health (MOH), 2009a) unlike their stem cell pioneers verified by the foreign scientists. Malaysian scientists and researchers have undertaken several stem cell transplantations but mostly in the hematopoietic stem cells using bone marrow and umbilical cord blood (Fadilah et al., 2007).[17] The transplantation of other derivatives of stem cells like the hESC, ASC or iPSC are often conducted as clinical trials which still require extensive research before it can be offered as risk-free therapy (Sivaraman, 2016).[18]

6.2.1.2 The right to personhood

The use of human embryos in the hESC research have created controversy and often triggered ethical debates among people (Lo & Parham, 2009). Scholars focus on the point when human life deserve recognition, the point when they claim life begins in order to explain why it is acceptable to use early human embryos in research. The foreign scientists and the foreign ethicists, both agreed and were strong in their opinion that early embryos are not human being worth respect ultimately distinguishing their benefit in research. Although all the experts identified conception being the point when life begins, local experts disclosed that formation of primitive streak local experts disclosed that formation of primitive streak at gastrulation stage identifies the onset of brain development which occur around 120 day of embryo development based on the Islamic

[15] Verified by foreign scientists, foreign ethicists, local scientists, local ethicists, and policymaker
[16] Verified by foreign scientists, local scientists and foreign ethicists
[17] Verified by local scientists and policymakers
[18] Verified by foreign ethicists

law.[19] Brain development are distinctive, it is when embryos are considered as conscious being making them special and moral worthy (Goldstein & Schneider, 2010).[20] The local scientists also explained that early embryos are useful in research, but without a womb these embryos, especially those created through IVF, will not fulfill personhood.[21] Nevertheless, it is recognized an ambiguous claim since there are no clear line scientifically to identify when life actually begins (Devolder et al., 2007; Maehle, 2011).[22]

Whether it is the sanctity of human life principle, the right to personhood as the foreign and local scientists described or the moral status of the embryo claimed by the foreign ethicists, the fact that embryo deserves value and respect is well-acknowledged (Blackford, 2006). Branding embryos as not a person and lacking both moral status and consciousness are often how scientists and ethicists justify their function in research (Steinbock, 2007).[23] Unlike the scientists, the local ethicist is against terminating life even for therapeutic research as he considers embryos as potential life and should be allowed to continue living as fated.[24] He believes that these embryos that are committed to develop should not be tempered with, and suggested using dysfunctional embryos instead (Douglas & Savulescu, 2009; McMahan, 2007).[25] It may seem virtuous to protect the IVF embryos, however they are often created in excess which result in some being discarded either due to failing to implant or decreased viability, therefore bestowing them with purpose for stem cell research is actually commendable.

[19] Verified by foreign scientists, foreign ethicists, local scientists, local ethicists and policymaker.
[20] Verified by local scientists
[21] Verified by local scientists
[22,] Verified by foreign scientists, local scientists and foreign ethicists
[23] Verified by foreign scientists, foreign ethicists and local scientists
[24, 25] Verified by local ethicists

6.2.1.3 The conflict

The most significant conflict in stem cell research is still and will remain to be, the embryo destruction which all scientists and ethicists corroborated, just as claimed by the many internationally and locally published articles. The debate that early embryos do not have rights and that they are not a person as discussed in the right to personhood theme often justifies the use of excess or surplus IVF embryos in research. These embryos are often created in excess and the left-overs remain in storage indefinitely or are discarded after serving their purpose. According to Sher et al. (2013), about ten to 16 eggs (oocytes) are retrieved per retrieval attempt for the IVF process and believe they can successfully fertilize 70-80% of them, although it depends on the individual cases especially on the biopsies required (Sher et al., 2013). One or two healthy embryos which are in 5 or 6-day old developmental stage are then transferred to the uterus for successful implantation (Falcone & Hurd, 2013). The success rate of implantation that results in a pregnancy varied between women due to either age.

According to the Human Fertilization and Embryology Authority (HFEA) (2014), chances of a women less than 35 years of age resulting a successful pregnancy after an embryo transfer is 40% while women over 45 only have a 3.4% chance of resulting in a successful pregnancy. The left-over IVF embryos are then frozen within the viable cycle to transfer them for a later time (HFEA, 2014). The frozen embryos are viable only for about a decade provided that they are preserved properly without any technical errors in storage, allowing them to survive the thawing process for the next cycle (HFEA, 2014). With that in mind, many embryos may not fulfil their original aim and remain in storage. The idea of all these embryos reaching its goal being a person is unconceivable not to mention absurd. It is the decision made by donors (couples) who originally signed up for the procedure. The fear of allowing these embryos to fully develop even by donating them to other couples' trigger many social concerns ranging from the competence of the

new couple, to the possibility of unintentional incest between 'full siblings' regardless of the odds. Only few families willing to donate their frozen embryos to other couples, while majority of them are completely overwhelmed since they bare the financial, legal and medical liabilities during these processes (Nachtigall et al., 2009). Although, chances of all the IVF embryos fulfilling their objectives growing into a full human are scarce to impossible, the local ethicist asserted that these embryos created for the sole purpose of reproduction deserve to fulfil their original objective and grow into human beings without any tempering, despite some do waste away due to the screening process being unhealthy, or failure to implant in the uterus (HFEA, 2014).[26] Perhaps the embryos rejoicing personhood may not be achieved, however a particular local scientist believe that exploiting embryos to fulfill research purpose is directly disrespecting the embryos (Manninen, 2007; Pennings & Van Steirteghem, 2004).[27] On the contrary, both the foreign scientists and ethicists stated that these embryos should be retained as valuable resource which is significantly useful in stem cell research instead of wasting them or discarding them when they are no longer viable.[28] The validation of giving the surplus IVF embryos purpose other than reproduction profiting its viability recognizes its utility, potential and full value instead of discarding (Devolder, 2015; Scully et al., 2012). [29]

The ethical controversy surrounding human embryonic stem cell research compelled scientists and researchers to find alternative source of pluripotent stem cell similar to embryonic stem cell without destroying any embryos (Pennings & Van Steirteghem, 2004). The search led to the discovery of many derivatives of adult stem cells and the iPSC which are ethically decent alternatives compared to the human embryonic stem cell (Larrú, 2001; Mertes et al., 2006).[30] One of the identified methods is a technique known as somatic cell nuclear transfer (SCNT) long before Yamanaka and

[26] Verified by local ethicist
[27] Verified by local scientist
[28] Verified by foreign scientists and foreign ethicists
[29,30] Verified by foreign scientists, local scientists and foreign ethicists

Takahashi discovered iPSC in 2006.

The SCNT was actually discovered by Wilmut et al. (2002). The group of scientists led by Sir Ian Wilmut was the first to 'clone' a sheep made famous by the name Dolly. Using similar method, pluripotent embryonic stem cells can be recreated by removing the nucleus of a somatic cell and transferring it into an enucleated human egg (oocyte) creating an embryo. This is also known as 'therapeutic cloning' which is quite useful in stem cell research and regenerative medicine (Wilmut et al., 2002), but since cloning has its own ethical concerns and controversy the SCNT is banned in in several countries including Malaysia (Ministry of Health (MOH), 2009a). Despite his success, Sir Wilmut credits the rival method, iPSC as a better potential in producing more compatible embryonic stem cell using patients' own DNA (Highfield, 2007).

There are many other derivatives or forms of stem cell discovered but unlike the misconception, these alternatives are not substitutes or replacement of human embryos. According to the local scientist there are no absolute success in iPSC and they definitely do not supersede.[31] iPSC does not replace human embryonic stem cell just like ASC (Maienschein, 2014). In fact, these derivates of stem cell have many exceptional characteristics that makes them unique and each with their own set of research motives and advantage.[32] ASC and iPSC still require extensive research to learn everything, to broaden knowlegde.[33] These studies still incorporate hESC as a standard control when performing research and clinical tests, at least for the present time in attempt to copy the properties of human embryonic stem cell. Except for the easier isolation and extraction, nothing about these alternatives that makes them a simpler choice or an easier method.[34] In reality, they are unproven and may even fail.[35]

[31] Verified by foreign scientists and local scientists
[32, 33] Verified by foreign scientists and local ethicist
[34] Verified by foreign scientists, foreign ethicists and local scientists
[35] Verified by foreign scientists and foreign ethicists

The alternative sources of stem cells are not the only misleading discussion with ambiguity in their claims, there is also the use of human embryos in human embryonic stem cell for trivial reasons like developing cosmetics (Mertes et al., 2006).[36] Since embryos are valuable and it often symbolizes a person, using them for trivial research often get scrutinized. On a separate note, all the scientists and ethicist recognized several aspects of stem cell research which are ambiguous in its claims.[37] Using healthy IVF embryos for research purposes are often debated, and sharing the view of the local ethicist of using dysfunctional embryos, several scholars urge the use PGD embryos.[38] They suggested that the PGD embryos to be more resourceful and ethical. It was originally presented as a prenatal diagnosis prior to uterus implantation especially for couples affected by serious sex-linked genetic disorders (Sermon et al., 2004; Stephenson et al., 2009). Based on the diagnosis, the healthy embryos and those that are identified as only carriers (in the case of recessive disease) are either put back into the mother or stored for future use (Stephenson et al., 2009).

Since, stem cell has the ability to expand indefinitely, the remaining cells following the PGD embryos could still be useful for research as precious commodity (Boyle & Savulescu, 2001; Pickering, 2003). However, scientists believe that the source of cells depends largely on the objective of the research. The claim that PGD embryos are a source of human embryonic stem cell line is an ambiguous claim, as their limited availability and even if there are available they could be discarded for their genetic compromisation affected by genetic disease makes them impractical (Pickering, 2003). Hence, the debate that PGD embryos are better than the IVF embryos with no absolute in success is ambiguous in its claims. If the objective of the research is to study the disease, screen for drugs and to develop treatments for specific diseases, these cell lines with

[36] Verified by foreign scientists, local scientists, foreign ethicists and local ethicist
[37] Verified by foreign scientists and local ethicist
[38] Verified by foreign scientists, local scientists, foreign ethicists and local ethicist

genetic disorder would serve as an unlimited source, making them valuable. However, if the healthy embryos are the one sorted after, then PGD embryos would not be suitable at all (Aran et al., 2012; Stephenson et al., 2009). The motives and aims of the research decides which source of human embryonic stem cell lines would be more appropriate, and that PGD embryos would not replace or substitute the IVF embryos completely.

The issue of using surplus embryos brings into perspective, the matter of informed consent.[39] According to the foreign and local scientists, it is vital to gain necessary consent from the donors to ensure they are aware of the risk involved and prevent any conflict of interests. The Malaysian policymakers confirmed that it is often standard protocol to gain informed consent from donors and patients during any research involving human subjects. In some countries, the medical practitioner carrying out the IVF, the one retrieving the consent from donors and the one carrying out the stem cell research cannot be the same person (Caulfield et al., 2007).[40] This highlights the risk of enduring agonizing fertility procedures and the exploitation of women for eggs (oocytes) as a commodity (Shalev & Werner-Felmayer, 2012) known as eggsploitation (Baylis & McLeod, 2007).[41] The foreign scientists and ethicists both identified donor exploitation as an important issue apart from the embryo destruction.

The fact that, human embryonic stem cell research is permitted in some country while banned in some, displays the diverse viewpoint of people. According to the local scientists, the pursuit of stem cell research depends on the end-result that may benefit mankind with a therapy that treats or cures all diseases. It is a consequentialism theory that, morality should be evaluated exclusively on the merits of its consequences, instead of the action (Hyun, 2013).[42] Several religious beliefs such as Hinduism and Buddhism are founded by such motives of actions. Some also claim it is a sense of duty of the

[39] Verified by local scientists
[40] Verified by local policymakers
[41] Verified by foreign scientists, foreign ethicists, and local scientists
[42] Verified by local scientists

scientists to service the suffering people (Sivaraman & Noor, 2014).[43] The diverse legislation and liberal research protocols in some countries brought forward the issue of commercializing stem cell therapy, a phenomenon known as stem cell tourism[44]. Suffering patients are willing to travel from the United States, Canada and the United Kingdom to countries like China, Mexico, Thailand and even India where stem cell treatments are affordable, unproven and highly risky (Brown, 2012). Besides being ineffective, there are many other repercussions of traveling abroad for unproven novel treatment beginning with serious complications of the treatment not to mention contracting other regional bound infections like meningitis and dengue (Kolata, 2016).

No research is straight-forward, and stem cell research with its unique regenerative characteristics have many obstacles and challenges to resolve before it can translate into proper clinical trials. The issue of clinical translation of stem cell research is quite common lately, especially to distinguish the appropriate point to make the transition from pre-clinical to clinical trial.[45] Many scientists push for clinical trial with insufficient data concerning safety, long-term survival, differentiation and even efficacy that could prove risky to patients with formation of teratomas and graft rejection (Lindvall et al., 2012). Although it may be reasonable to feel that way or even to question every stem cell research simply to justify their objectives, either significant or just trivial, however even the use of stem cell in cosmetic can have a significant effect from the patients' point of view. The use of stem cell in cosmetology may offer hope to patients with skin disorders and accident and burn victims to help regenerate their skin to restore damages and heal wounds (Blanpain, 2010; Ojeh et al., 2015).

Apart from that, some turn to stem cell to restore or repair other conditions ranging from baldness to aging, but if they are trivial, it is hard to say.[46] These techniques

[46] Verified by foreign scientists and foreign ethicists
[43] Verified by local scientists
[44, 45] Verified by foreign ethicists

improve patients' emotional well-being and revive their confidence. I believe that they are not, unless if these treatments are drawn to enhance the already existing healthy features, conditions and overall beauty which is petty considering the other reasons. Many of these cases use other derivates of stem cell such as mesenchymal, epithelial and even hepatic stem cell instead of the controversial human embryonic stem cell (Wong et al., 2012). Basically, different field of medicine with different objectives may use stem cells to fulfil the many different research expectations and as foreign scientists claim, stem cell has wide potential and several cells from one source may still go into other research instead of the original research, making complete use of the valuable resources.

6.2.1.4 Governance

The theme 'governance' addressed and highlighted all the regulative aspects of stem cell research and technologies and corresponds with the research question (c) 'What are the implications of the current regulative measures concerning stem cell technologies in Malaysia?'. Beginning with the status of regulation in respondent's respective countries', to the ideal protocol considerations and ultimately the implications from the respondents' perspectives. The foreign scientists and ethicists whom are from the United States, the United Kingdom, Australia and Canada asserted that the stem cell regulation in their countries are well-balanced and quite pragmatic (Lauder, 2011; Mehrpisheh, 2015).[47] They insisted that transparency in judicial review is key approach in regulation, not to mention rigorous oversight as practiced by their country (Bianco et al., 2013).[48]

[47] Verified by foreign scientists
[48] Verified by foreign scientists and foreign ethicists

Despite the sufficient regulations, some strongly believe that there are still concerns.

The increase in clinics promoting unproven stem cell therapies beyond the context of proper clinical trial are among the concerns (Hyun, 2010). This is clearly a grey area which is also known as regulatory loophole.[49] Many articles have brought the issue to light either to alert the authority regarding these entities or to educate people considering the risks involved (Elder, 2015; Harvey et al., 2015; Metherell, 2016). According to a professor at the University of Sydney, there are about 19 clinics identified in Australia that are exploiting the regulatory gaps or loopholes by directly offering the public stem cell treatments that are still in clinical trial, despite being identified as a serious concern. This resulted in Australia being ranked as top five in the world for the operations of such clinics (Roy, 2016). Considering the major risks involved and the serious repercussions faced by victimized patients, concerned individuals are urging the authority to do the necessary to close the loopholes at once (Harvey et al., 2015; Roy, 2016).

It is quite common for foreign scientists from pioneering stem cell countries to have an elaborate thought about the regulations of stem cell, since they have been well exposed to the process and development longer than Malaysia or other developing countries. Unlike stem cell pioneers and the developed countries, Malaysia is yet to devise a law or an act to regulate the local, Malaysian stem cell research and its technologies (Rahman, 2015). [50] Equipped with only a guideline that entails the ethical protocols and proper standard practices regarding the use of human embryos and the dos and don'ts of stem cell research, it does not hold wrongdoers accountable or prosecute them (MOH, 2009a).[51] Local scientists pursuing stem cell research, both embryonic and non-embryonic are aware of the absence of a policy and legal framework regulating stem cell

[49] Verified by foreign scientist and local policymakers
[50] Verified by local scientists and local ethicists
[51] Verified by foreign scientist, local scientists and local ethicists

research. They believe not having competent regulatory officers or policymakers that are well-knowledged about the science of stem cell could be the cause, although several of the policy experts spoken to for this study were doctors by qualification.[52] It is also what Blanpain et al. (2012) explained when he agreed it is very important for lawmakers and policymakers to be 'well informed by most competent scientists' prior to any laws or acts passed on the matters of stem cell.

Experts with proficiency in stem cell will bring clarity in the subject matter while recognize the inadequacies (Blanpain et al., 2012). These experts are more capable initiating a better system in regulation that would result in an effective law and policy making process which would help prevent misconducts that goes undetected at the moment.[53] Local ethicists verified that there have not been any reports of abuse in the private sector of stem cell research in Malaysia, giving an impression of regulatory sufficiency. However, the absence of law regulating or overlooking the stem cell research and clinical trials can trigger certain lack of standard compliance which can go easily undetected which need addressing.[54] This brings our attention to legal framework, which the Translegal Dictionary (2017) defined as, 'a broad system of rules that governs and regulates decision making, agreements and laws'.[55] Legal framework or regulatory framework overseeing stem cell research and its technologies would help control cell and tissue based research and therapies to remain within the ethical borderline (von Tigerstrom, 2008). According to Barbara J. von Tigerstrom (2008) it is essential to have appropriate regulation on stem cell-based products to guarantee public safety and confidence but to ensure a coherence between the public safety and reducing unnecessary barrier in product development is more challenging but necessary. She strongly believes that the diversity of authorities and the ill-fitting of product categories and the innovative

[52] Verified by local scientists
[53] Verified by foreign scientists, local scientists, foreign ethicists and local policymakers
[54] Verified by local ethicist
[55] Verified by foreign scientists, local scientists, foreign ethicists and local ethicist

technologies are the weakness of current legal framework (von Tigerstrom, 2008).

These frameworks are meant to protect the people and to confirm the standards and guidelines which is largely based on sound ethical and scientific considerations (Blanpain et al., 2012). A flexible framework with clear boundaries would prove valuable and constructive to regulate novel innovations such as stem cell research. It will offer ethical protection to patients, doctors, donors and even the research subjects safeguarding their rights and welfare. Legal restrictions are necessary but some foreign scientists are concerned that the demand for transparency and accountability may impair or hinder research progress (Little et al., 2006). Nakatsuji (2007) wrote how the Japanese regulation on stem cell seemed irrational and its implementation were tedious that it deters the research progress.

Currently the laws and legislations formulated to regulate the stem cell research and its technologies are wide-ranged and country-specific as revealed in Chapter 1 and 2.[56, 57] These laws basically vary between countries but with some exceptions of universal rules, such as cloning ban, and in the case of human embryonic stem cell the 14 day rule (Blanpain et al., 2012). The variety of opinion across region regarding what is permissible, ethical and required are based on their beliefs and cultural viewpoints which have led to the design of such policy that largely represents the country (Blanpain et al., 2012; Dhar & Hsi-en Ho, 2009). Hence, it is now common for scholars to compare the regulations and policies of different countries. The article, "Regulations and guidelines governing stem cell based products: Clinical considerations" is one such study written to help recapitulate the current regulations and guidelines regarding stem cell based products and the importance on clinical aspects in the United States, the European Union (EU) and India (George, 2011). These sorts of reviews discovered that there are countries that offer stem cell-based therapies that are unavailable in other countries. This

[56] Verified by foreign scientist, local scientists, foreign ethicists and local ethicists.
[57] It is extensively described in Chapter 2

bring stem cell tourism into focus whereby stem cell therapies which have become a profitable business bringing positive impact in the economic growth of certain countries with patients travelling for hopeful therapeutic possibility (Council et al., 2014).

Stem cell tourism involves patients with incurable diseases that are willing to travel to countries where unproven stem cell therapies are available as treatment unlike their home countries. Countries like South Africa, China, Mexico and Thailand are often associated with stem cell tourism, with their lack of governance or weak implementation of regulation to having completely liberal policy, which led to these therapies reaching public without the necessary clearance by the relevant authorities (Meissner-Roloff & Pepper, 2013). There are many challenges and implications due to stem cell tourism and the chances or possibility of the phenomenon happening Malaysia is not impossible since there are some private medical healthcare providers offering such therapies currently in Malaysia. There is no telling if tourist have come to Malaysia seeking these treatment as they are clearly advertised within their web portal. In fact, Malaysia is often included as a common destination for stem cell tourism next to Thailand (Petersen et al., 2017; Slabbert & Pepper, 2015; Sleeboom-Faulkner et al., 2016). Despite, these red flags the Malaysia stem cell regulators and policymakers have yet to address them not because they are unware but mostly due to the lack of whistleblowing. However, without speaking to the relevant healthcare providers, it is difficult to assess the extent of the issue. Unfortunately, it is unlikely that these entities will come forth considering the delicate matter of noncompliance and regulation that would jeopardize their reputation and integrity as a private healthcare provider.

In some countries like Japan, Taiwan and South Korea, stem cell products include cosmetic stem cell therapy or some label it as holistic or aesthetic medicine. The terms or phrases used to brand or categorize these products despite major disagreement, somehow challenge an effective oversight. By labelling or classifying stem cell therapies simply as

'stem cell treatment' some companies in Thailand are marketing their unproven stem cell products without flagging criticism or acquiring the necessary authorization. This is because only those labelled as 'therapy' are recognized and required to gain authorization as proper stem cell therapy, while those that do not simply slips through the cracks (Sleeboom-Faulkner et al., 2016; von Tigerstrom, 2008). This is also occurring in Malaysia as the NPRA have several items listed in their registered products that are stem cell-based products.[58]

There are many challenges within the translation of stem cell research into therapy and some area within this concern are considered as grey area which often goes unaddressed due to regulative loopholes. Margaret Sleeboom-Faulkner et al. (2016) recognized the wide-ranged regulations across the globe. They addressed the issue as national home-keeping as an idea to identify policies created by countries that meant to underlay universal standards but were adopted from somewhere else, which is not conducive to the existing local policies. In explaining the theory, they identified Malaysia being a country that has invested billions through the Biotechnology Corporation to finance stem cell research but with presumably loose regulation, which led to the development of companies and clinics marketing unproven stem cell products. The stem cell products listed in Figure 6.2 are the only products permitted to market based on their analysis (Sleeboom-Faulkner et al., 2016). The implications of stem cell tourism, the unproven stem cell therapy reaching the public and the exploitations of donors and subjects are against international ethical standards. It is no longer just a national concern involving specific countries, but it has urged a larger focus since it affects everyone globally.

Just as stem cell research stirred the ethical pot, human cloning was also scrutinized for its controversy. But unlike the stem cell, the human cloning issue received

[58] There is an extended discussion on this topic in Section 6.4.4

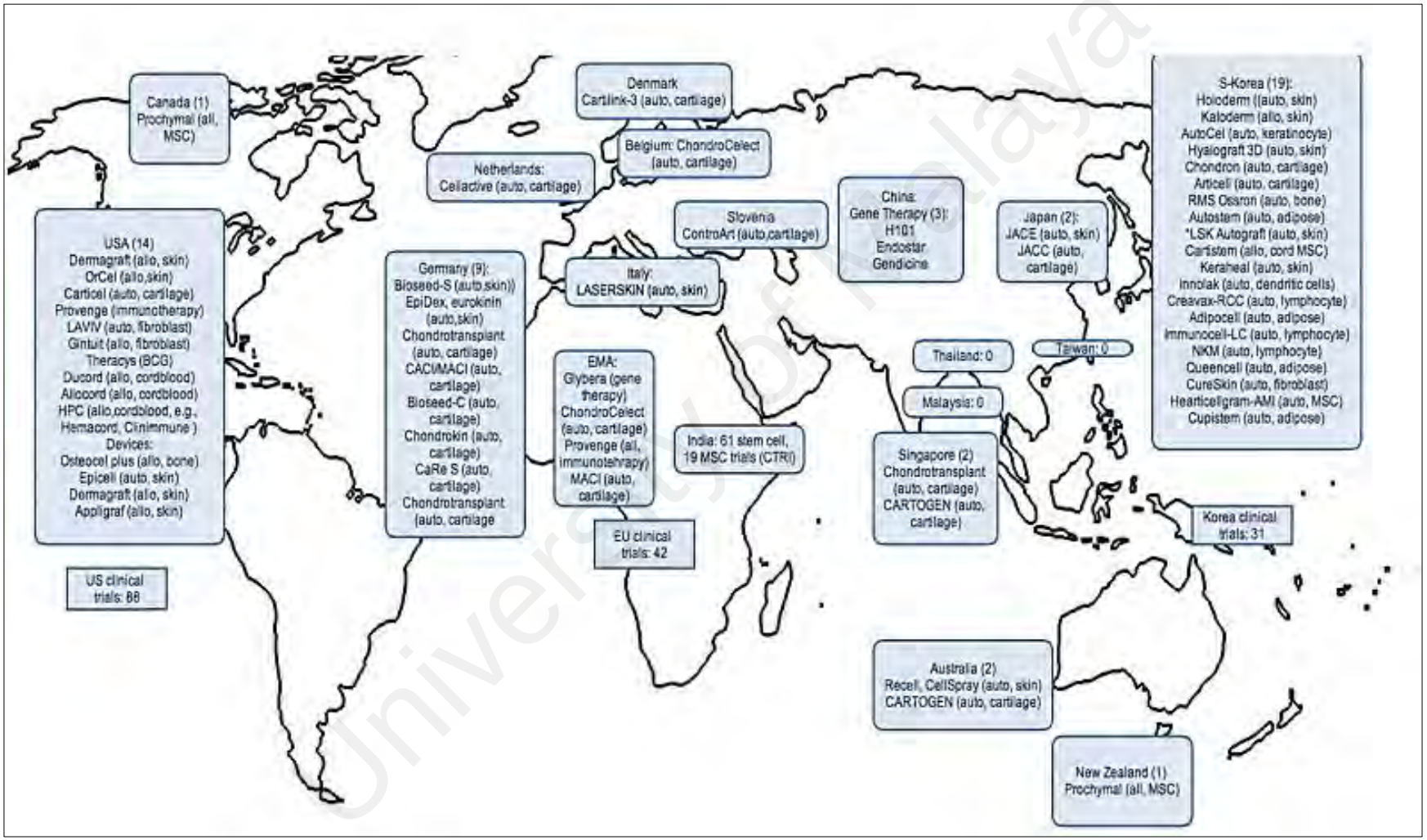


Figure 6.2: Permitted stem cell & genetic engineered products.
[Source: Image reproduced with permission from Sleeboom-Faulkner et al. (2016).]

significant attention at the United Nations' general assembly (Campbell & Nycum, 2005). On 8th March 2005, the United Nations called its member states to adopt the Declaration on Human Cloning, which bans all forms of human cloning with a vote of 84 in favor to 34 against, and 37 abstentions. The United Nations (2005) Declaration on Human Cloning was a result of a four-year debate in an attempt to prohibit any form of human cloning. Since countries like United Kingdom, Singapore, and China where SCNT as therapeutic cloning is allowed, they voted against the declaration. Countries with significant religious standing like Saudi Arabia, Italy, Philippines, even Australia and United States, have all voted in favor of the declaration.

Malaysia despite its against in SCNT with clear stipulation of its prohibition in the Guideline for Stem Cell Research and Therapy 2009 decided not to vote creating some perplexity (United Nations, 2005). The Health Minister at the time, Chua Jui Meng asserted that the Malaysian is against human cloning and despite not having a law governing the subject, it will support the United Nations' resolution forming the *ad hoc* committee on drafting the International Convention Against Reproductive Cloning of Human Beings together with other international declarations that bans cloning of humans. Although all said and done, the minister claimed that Malaysia will not oppose research on therapeutic cloning, in fact Malaysia encourages research on the subject (Mae, 2002).

Research is a scholarly activity, one of which that combines researchers and the community of scholars nationally, regionally and even internationally. It is basically recognized as international activity (Carek et al., 2011).[59] Scientific community that comprises of scientists specifically conducting research in a particular field of science, often engage in such activity.[60] Apart from the common publications, they also attend conferences and seminars worldwide presenting their findings and their thoughts about

[59] Verified by foreign scientists
[60] Verified by foreign scientist, local scientists, foreign ethicists and local ethicists

their research, which often inspire other scientists for collaborations (Michaut, 2011).[61] Stem cell research have also triggered many such collaborations. Scientists from greatly different policies and regulatory background are seen collaborating with each other. Although, this has been the practice for centuries however for the present time it calls for some harmonization in international policy the least, to ensure the ethical and international standard.[62] Harmonization entails a process that combines or modifies different elements to form one coherent unit while preserving their individuality (Isasi, 2009). Stem cell research that triggers international collaborations are not the only aspect of stem cell which could use some international harmonization, in fact the unproven stem cell therapies offered all over the world initiating stem cell tourism could definitely use some international policy that potentially eradicate the phenomenon.

According to Campbell and Nycum (2005) harmonization signifies formulation of laws and policies of diverse jurisdiction in a manner that makes them consistent with other jurisdiction. They also clarified that harmonization is not about coming up with one universal law that is identical, but instead ensuring that they are compatible with one another (Campbell & Nycum, 2005). When there so many policies and legislations as presented by Figure 1.1 in Chapter 1, Figure 2.1 in Chapter 2 and Figure 6.3 that are founded on the basis of their nations' cultural norms and beliefs, is harmonization in stem cell regulation achievable? The foreign and local scientists both believe the idea to harmonize international policies may sound ideal but it is definitely not feasible.[63]

The local ethicist however believes strongly that there are efforts directed towards harmonizing the regulation of stem cell research with the World Health Organization (WHO) joining forces with other regional bodies in similar objective. The WHO (2002) in its report titled, 'Genomics and World Health' mentioned that its Director-General

[61] Verified by foreign scientist
[62] Verified by foreign scientist, foreign ethicist, and local scientists
[63] Verified by foreign scientist and local scientists

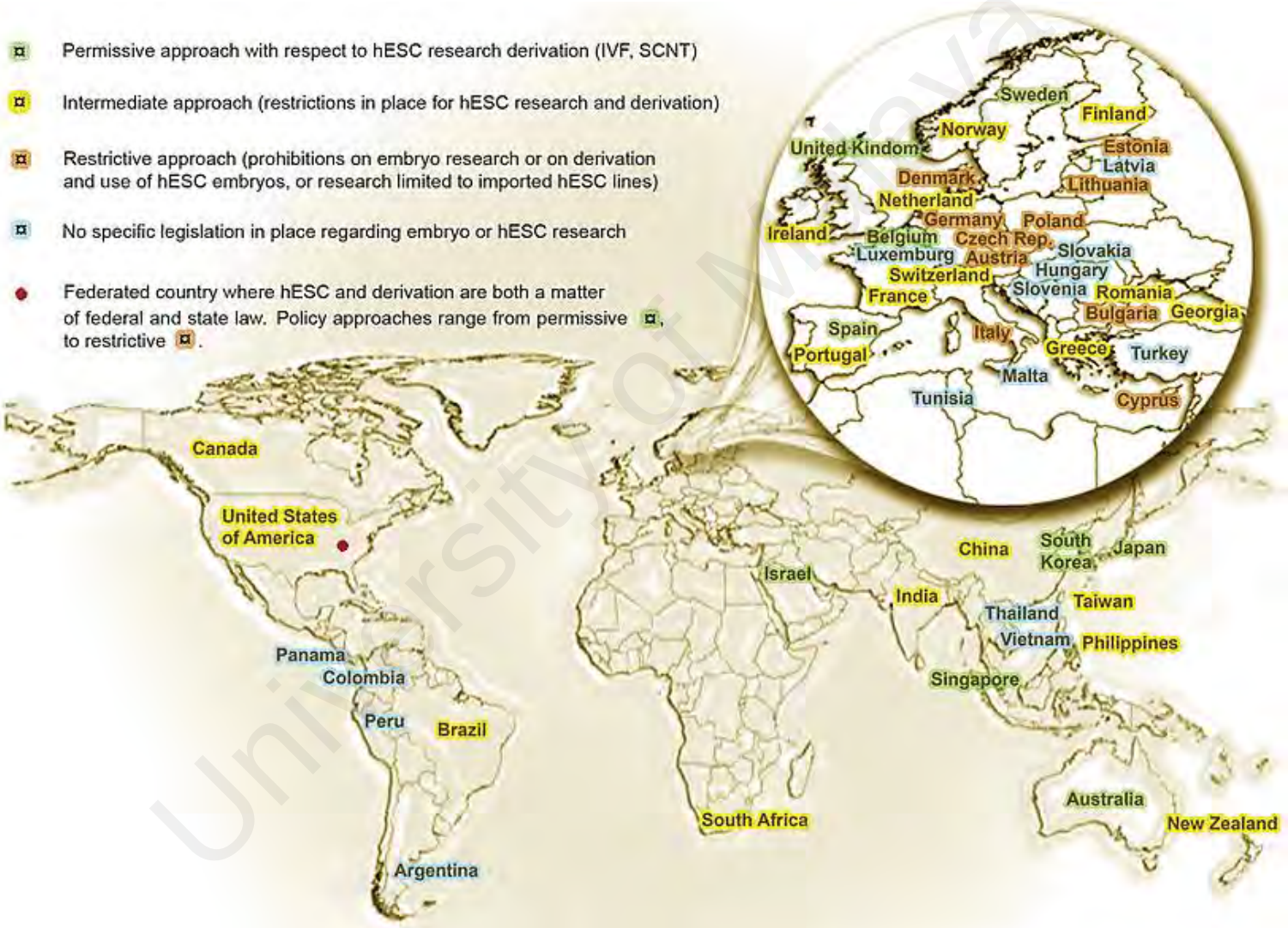


Figure 6.3: The diverse stem cell policies.
[Source: Image reproduced with permission from Isasi (2009).]

reported that "Strong international leadership is required to achieve these laudable aims. WHO is committed to facilitating this by promoting international partnerships and cooperation strategies to ensure that the fruits of the genomics revolution are equitably shared by all" this also included stem cell research and although it is yet to result in a formal declaration, we can accept this as prove there are similar objective as far as harmonization is concerned (WHO, 2002). They also made several recommendations after their 16th International Conference of Drug Regulatory Authorities (ICDRA) held in Rio de Janeiro, Brazil, on 26–29 August 2014 on many health-related matters, including stem cell therapies and the possibility of promoting harmonization of regulatory processes either with neighboring countries or among authorities that share similar interest with particular products (WHO, 2014).

The Declaration of Helsinki was developed by the World Medical Association (WMA), 'as a statement of ethical principle for medical research involving human subjects, including research on identifiable human material and data' (WMA, 2013). Given that the many aspects of stem cell research are reviewed or assessed indirectly beginning with therapeutic cloning with the development of the United Nations Declaration on Human Cloning, stem cell topic covered within WHO report and its other activities and finally with the Declaration of Helsinki that addresses the issue of human subjects in medical field. The statements largely comprise of recommendations involving the use of human subjects in medical research and clinical trials with a clear stipulation of the general principles, the risks and benefits involved and the scientific and research protocol It also acknowledged that all research with human subjects are required to acquire informed consent (donors specifically) and ethical approval before pursuing the research (WMA, 2013).

Although, the local ethicist's point is valid, however expecting the stakeholders to simply do the right thing, which entails the right code of practice may not be practical

or even wise. It is hard to guarantee they follow the ethical principles and work within boundaries, unless there are legislations in place with proper oversight. A columnist at Reuters, Saft (2009) wrote, 'Ethics without regulation won't cut it', in which he demanded guarantees and better safeguards. The demands rejected the ethical codes and self-regulation but insisted on stricter regulation, better oversight and terrible penalties (Saft, 2009).

At the moment, misconducts can be prevented if all parties gain the necessary authorization before embarking on any research, clinical trial or even marketing of cell-based therapies.[64] Foreign ethicists believe as long as scientists follow the standard regulation there would not be any issues concerning misconducts.[65] Local scientists strongly believe that wrongdoers and those exploit the legal deficiency should be prosecuted or penalized for their misconducts, but based on the current regulations in Malaysia, that is clearly unlikely.[66]

6.2.2 The evaluation of experts' input

The in-depth interview of the diverse experts involved in stem cell research have revealed many things. These experts' broad, high level knowledge concerning stem cell research and its regulation equipped with relevant training, exposure and experience in respective field have made them valuable assets. Their opinions and insights regarding the ethical, legal and social implications (ELSI) considering stem cell are valuable in regulative decision making (Klee, 1972; von Winterfeldt, 2013). Concurring with the research objectives one and two, the regulative matters and the ethical controversies involving stem cell research and its technologies were captured as the main concern among the experts during the in-depth interview. Despite their different primary concerns,

[64] Verified by foreign scientists, local scientist and foreign ethicist
[65] Verified by foreign ethicists
[66] Verified by local scientists

foreign experts and Malaysian experts proved that they also view things quite differently. The foreign scientists and ethicists are from developed countries, such as the United States, United Kingdom, Australia and Canada. It is fair to say that their responses directly reflect their countries' advanced research and development (R&D) which is comprised of qualified professionals and state-of-the-art facilities and resources. The judgements and opinions are therefore, based on their exposure to the topic and quite personal, unlike Malaysian experts. As far as stem cell research is concern, being highly qualified and with prolonged exposure to the topic founded on the idea of universalizability or to reach global consensus, made foreign experts' opinion directly proportional to their position as developed country (Cervellini & Vose, 1983; Sanford, 2003).

Malaysia is a developing country within its initial industrial development with low per capita income. Its R&D is not significant when compared to any developed countries. Their trained experts are definitely outstanding compared to 25 years ago (Cervellini & Vose, 1983), but they are still incomparable to their well-developed Western counterparts. Malaysia's low industrialization and low per capita income often result in them relying on developed countries for new discoveries and guidance. Judging from the gross domestic expenditure on R&D (GERD) presented in Figure 6.4 which is often used for international comparisons, the high incomed developed countries, have higher R&D expenditure compared to those from lower incomed developing countries like Malaysia (Spire Research and Consulting, 2002; The World Bank, 2017).

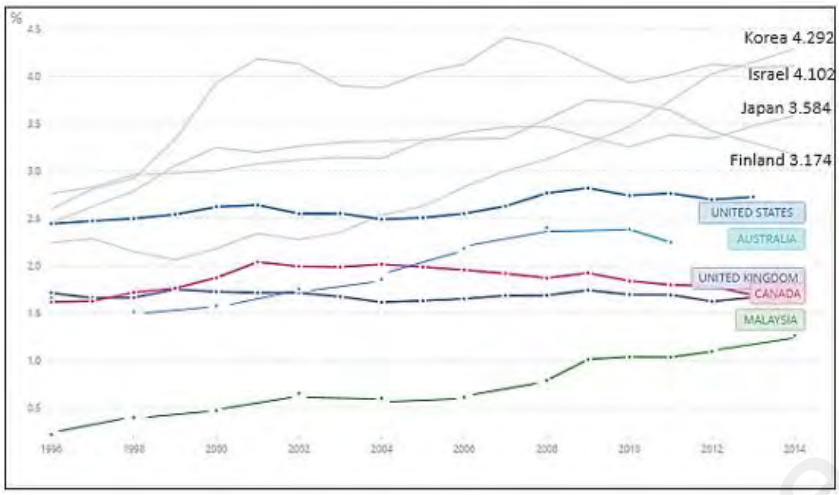


Figure 6.4: The gross expenditure for research & development (GERD) (1996-2014) (% of GDP).

[Source: The The World Bank (2017)]

The GERD expenditure reflects on the available resources of countries that promotes innovative research. This is quite true based on the significant discoveries involving pioneering stem cell countries, which is directly proportioned to their available skilled professionals and resources. In the chart in Figure 6,4, Malaysia as a low incomed developing country spends the lowest in R&D compared to developed countries. It is fair to conclude that Malaysia's GERD value is not substantial enough compared to developed countries to result in significant discoveries. Their consistent budget not to mention high volume of experienced scientists could have easily boost their innovative success unlike Malaysia whose slight increase in budget were only observed recently.

With that, the expert opinion of Malaysians inadvertently reflects on their country's position and their depth in R&D. This is equally evident with the Malaysian experts' responses which are relative to their current state of stem cell research, that is still in its infancy with more room for discoveries in both research and regulation. These experts' opinion therefore is very specific to Malaysia and relative to their standard and concerns, unlike the foreign experts, which judging by the responses regardless of their categories, they have grown accustomed to a wider ethical consideration concerning the

many aspects of stem cell and its technologies. They also displayed a sense of content and satisfaction regarding the regulative progress of stem cell, which is quite reasonable based on their own nations position as stem cell pioneer with a sense of balance in their regulative matters (Spire Research and Consulting, 2002).

There are similar studies done to demonstrate that experts' regional position influences their expert opinion. One of such study was Murray et al. (2009), and although the specific context of the study is different compared to this study, however the concluding fact is that regional differences do affect experts' opinions. Globalization and the case of developed vs developing countries are also factors that influences experts and their knowledge.

Despite the obvious difference between foreign experts and Malaysian experts, there is also the subtle but valuable interrelationship between Malaysian experts of different categories. Unexpectedly, all three experts, namely scientists, ethicist, and policymakers only agreed that (1) the potential of stem cell as a future therapy revolutionizing the medical field, and (2) Malaysia does not have law enacted to regulate stem cell instead it relies on the Guideline for Stem Cell Research and Therapy 2009. Between the Malaysian scientists and ethicist, they had some concern involving the issue of 'right to personhood' but on a contradicting degree. Although, the ethicist is a scientist by qualification, his religious faith compelled him to draw his ethical viewpoint opposing hESC research unlike the scientists whose opinion were largely motivated being a scientist regardless of their faith. The 'unique' nature of stem cell and its technology and the significance of informed consent is the only issue both the scientists and policymaker have some correlation on. While, both the ethicist and policymakers agreed that legal framework is essential to regulate stem cell research and its technologies. Despite that, the ethicist somehow believes that the Malaysian stem cell technologies are sufficiently regulated, at least for the time being. This is completely against the finding of this study

based on the input of the policymakers themselves. One thing that they did agree on is that policymaking or lawmaking involving stem cell technologies are extremely intricate and extensive.

It is necessary to note that there were very little overlaps between these experts, especially involving the policymakers which is nothing like expected. The experts' vested interest keeps them separated. There should be more connection especially involving the policymakers and the other experts, as a liaison would prove significantly valuable.

6.2.2.1 The scientists

The foreign scientists' opinions are broad and more universal in nature. While the local scientists' opinion is more specific to Malaysia with its current stem cell research status and its present regulatory aspects. The local, Malaysian scientists in certain occasion brought in the element of religion responding to the justification of life question, unlike the foreign scientists. Regardless of where they came from all scientists supported human embryonic stem cell research. Although, local, Malaysian scientists felt any research involving human embryos need proper justification and should warrant its motives, however foreign scientists were more tuned towards the nature of broadening knowledge.

The response to the question number seven, "Using hESC to save one's life would be the beginning of a 'slippery slope' which would end in unnecessary killings of embryos for people who hunt stem cell merely for cosmetic purposes. Your thoughts on the matter", was quite noteworthy. The argument that hESC used in cosmetics as trivial is not rare, but it has little merit. According to the foreign scientists, it is acceptable to use all available resources judging by the characteristic of stem cell to expand indefinitely. One of them in particular, preserved the idea that some cosmetic research is not trivial although it is customary to think so. Obtaining relevant informed consent equipped with

proper regulation and rigorous oversight there should not be any issue using stem cell in any type of research. Local, Malaysian scientists however had very different opinion regarding it. Since all the local scientists believe the use of human embryos for research require proper justification, they unanimously were against the use of human embryonic stem cell in cosmetology and felt that cosmetics especially those trivial do not fit as deserving research, instead they called for bigger motives. Although one of the local scientist did accept damage restoration as a worthy pursuit.

The element of religion ultimately becomes the basis of the local scientists' judgement. Malaysia being multi-religious country, it is quite normal to have many conflicting views regarding a particular topic, as to the use of human embryos in research. Although, local researchers are scientifically qualified, however they normally incorporate religious beliefs and norms to distinguish right from wrong and the dos and donts. Similarly, even the issue of stem cell regulation retrieved completely opposite response from the foreign and local scientists. The foreign scientists were pleased with their countries' current comprehensive legislation regulating stem cell research and its technologies. While the local Malaysian scientists acknowledged the lack of law and its implications such as issue of unable to prosecute wrongdoers or prevent misconducts. They suggested that a broad law formulated by the right and competent expert is imperative. However, both foreign and local scientists agreed that international harmonization is important and having a common global position that synchronizes legislation would be ideal. They believe that it would be good to synchronize legislation but with the variety of opinion across countries it may not be as feasible.

Being scientists, it is expected that their expert opinion is formed based on empirical knowledge and logic. However, their regional position and experience greatly influenced their opinion as far as this study is concerned. The foreign scientists are from countries such as United Kingdom, Australia, and United States with well-developed

legislation regulating stem cell research, unlike Malaysia. Therefore, it is acceptable to have a positive opinion regarding stem cell legislation, but since Malaysia currently has not regulated its stem cell research and technologies with any form of legislation the local scientists are concerned. In fact, they are urging the relevant authorities to consider the benefit of a law or an act in regulating novel innovation such as stem cell.

6.2.2.2 The ethicists

The responses retrieved from foreign ethicists were more general and universal similar to the foreign scientists. Apart from their regional position and their advanced R&D there were no other external factors such religion contributing to their views regarding the topic. However, since ethics have wide interpretation and opinion, between the foreign ethicists themselves there were disagreement especially in the matters of justification of human life, the status of regulation managing stem cell research and its technologies and the need for international harmonization of stem cell legislation. The ethicist from the United States urged for harmonization and better regulation, while the Canadian ethicist was convinced there is adequate oversight and that international harmonization is unnecessary or irrelevant. Perhaps, their political position and the professionalism in tackling the issue in hand is better projected within these responses.

Although, the responses of foreign and local scientist were compared to evaluated their opinions, the same cannot be done for ethicists due to the limited number of research participants. While, Figure 5.3 were included initially in Chapter 5, the review of the in-depth interview date did not capture anything significant. Therefore, the publications written by the international and Malaysian scholars were included to better capture the distinct differences in respect of their perspectives. The foreign ethicists had very different opinion when compared to the Malaysian ethicists. It is customary for Malaysians to incorporate their religious beliefs and principles as the foundation of their

rational thinking and decision-making as seen by the Malaysian ethicists, while the foreign ethicists were more universal in their viewpoint, although one or two tackled the stem cell research ethics from a Christian viewpoint.

Local, Malaysian scholars were not in full-support of the use of healthy human embryos for research, instead he was persuasive that these embryos should fulfil their original goal and any interference in its journey is unethical. They discussed their viewpoint largely from an Islamic perspective, as proved by the many Malaysian written publications since Islam being the predominant religion in Malaysia. This is definitely a complete opposite in opinion between local and foreign ethicists.

6.2.2.3 The policymakers

The local, Malaysian policymakers are well aware of the current stem cell research status and did not deny the present regulatory position involving stem cell. This reinstate two presumed notion which are, (1) the relevant authority is not aware of the extended implication of unregulated stem cell research and its technologies and (2) that the authorities are satisfied and confident with the existing protocols. In fact, it was clear that they were frustrated with factors beyond their control in fulfilling their primary directive of amending the Human Tissue Act 1974 or to incorporate stem cell innovation into existing legislation.

They described the challenges and the intricate details of law or policy making beginning with lengthy continuous deliberation to reaching consensus among diverse members. These policy experts are doing their best considering the many stakeholders involved. Reaching agreement among the varied committee members and attaining a go-ahead signal of all the different level of official with diverse background and intellect to enact a law or policy is not an easy task, in fact it is strenuous. External factors like these

impacts legislative decision-making and affects the deliberative committee indirectly despite their already challenging process.

Even the deliberation has several considerations that needs careful examination and discussion such as the element of religion, the opinion of the general public and the insights of other non-member experts. With that, the pluralistic society of Malaysia with many religions to consider and entails a tough job in reaching a middle ground or some form of agreement regarding a specific topic, such as stem cell. Approaching the public and getting the lay people involved in the discussion of the regulation of stem cell research and its technologies is often considered as an essential part of decision-making.

It is clear that policy and law making involves many experts and the deliberative committee regularly gage other experts to ensure they secure all venues. In the context of stem cell research regulation, the National Stem Cell Research and Ethics Sub-committee members comprises of officers of the Ministry of Health (MOH) Malaysia, the stem cell experts from various institutions of higher learnings and officers of the public laboratories within the National Institute of Health (NIH). Regrettably, ethical experts such as those from the National Medical Research and Ethics Committee (MREC) or any other field like political science or law were not included. In fact, they only gaged one law lecturer from the International Islamic University Dr. Ida Madieha who wrote an article pertaining to intellectual properties law on biomedical science and stem cell topic during the brainstorming workshop.[67] One of her article was included as a part of my local, Malaysian publication in the result chapter, 'Human stem cell research: ethical and religious concerns over patenting biotechnological invention in Malaysia'.

The regulatory deliberative committees are comprised of only subject experts within the medical field, however having other experts like ethicists included on regular basis could prove constructive judging from their knowledge and opinion of the matter

[67] This is a local Malaysian article assessed in Chapter 5

concerned. In another word, it is bridging the gap of the unknowns beginning with what the committee knows and aware based on their own expertise compared to what the other active experts (i.e. ethicists) perceive especially when there is diverse knowledge involved. These scientists and ethicists who have been working on the topic of stem cell actively are tremendously beneficial in gathering input improving the regulation of stem cell research and its technologies (Klee, 1972; von Winterfeldt, 2013).

The analysis of the thematic map, also revealed an interesting finding, which is the policymakers and the ethicists have some overlapping interest apart from recognizing the potential of stem cell research and its technologies. Although, the set of questionnaires of the two experts are different, however as excepted their intersecting expertise does have interrelating concerns beginning with acknowledging the current unregulated states of stem cell research and its technologies equipped with only a guideline as being sufficient. However, they both agreed that legal framework overlooking stem cell research and its technologies is imperative despite the process being intricate and extensive. The element of religion will always be a part of decision-making considering the ethical, social and legal matters in all Malaysian topics, which may delay the execution of a plan but it focuses on what is closes to the heart of Malaysians.

6.3 The progress of stem cell regulation of pioneering countries

6.3.1 United Kingdom

Majority of articles identified the United Kingdom as among the first countries that passed and introduced a law in regulating artificial reproduction and research involving human embryos, including stem cell (Denoon et al., 2015; Wert & Mummery, 2003; Winston, 2007). Their regulatory framework is considered well-established and quite comprehensive (Mehrpisheh, 2015). Although there were extensive research involving embryology, legislation was only devised in the 1990. The regulatory concern originally sparked after the birth of Louise Brown in 1978 through IVF that resulted in the 1984 report published by the Warnock Committee regarding the artificial reproductive technology (ART) that criticized the distinct status of human embryos recommending that animal models or other alternatives should be used (Warnock Committee, 1984).[68] The report became the basis for the United Kingdom's legislation on human embryo, which is the HFEA since the 1990 (HFEA, 2012; Matthews & Rowland, 2009)

According to Schechter (2010), prior to the formulation of the HFEA in 1990, the Interim (Voluntary) Licensing Authority was set up to regulate the human artificial reproductive research including IVF as a temporary standard until the government introduces a legislation based on suggestions in Warnock Report. Between that period, several 'Unborn Children (Protection) Bills', initiated first by Enoch Powell, were presented for consideration to forbid research involving embryos, but never passed (Schechter, 2010). The discussion of human embryonic regulation often brings in other topic such as surrogacy and cloning (Bleiklie et al., 2004; Deech, 2002; Hadaway, 2004; Holm, 2015).

[68] The Warnock Committee was established in 1982

In 1985, the 'Surrogacy Arrangements Act' was enacted into law in the United Kingdom, which prevented illegal surrogacy arrangements making it the first of its kind overseeing the surrogacy arrangements in the world (United Kingdom Parliament, 1985). The 'Human Fertilization and Embryology: A Framework for Legislation' was first introduced in 1987 which was published in 1990. The HFEA commenced officially beginning August 1st 1991 (HFEA, 2012; Matthews & Rowland, 2009).

Soon after, the HFEA underwent a partial revision in 2001 to extend its regulation on research using human embryos allowing hESC research. Originally, they were not clear about the fact that human embryos were not allowed to be created through cloning procedure (Agrawal, Burt, & Homburg, 2013). Following that, the 'Human Reproductive Cloning Act' was introduced in 2001 to prevent human cloning (Deech, 2002; Hadaway, 2004). In 2007, the HFEA begun its revision process by reviewing the legislation, updating and amending the original act by adding new provisions which came into force in 2009, with some additional changes made in April 2010. The new provisions which adopted a more liberal approach, repealed the Human Cloning Act 2001, allowing the creations of embryos for research purpose through whatever means or process permitted, including SCNT, IVF and even the creation of "admixed embryos" that are hybrid embryos containing various animal and human materials (HFEA, 2012).

The HFEA authority is the non-departmental public body of the Department of Health which implements the regulation of the HFEA and licensing of the IVF clinics as well as researchers working on human embryos in the United Kingdom. The HFEA authority expects all those licensed to gain approval from the Steering Committee for the United Kingdom Stem Cell Bank before they are able to pursue their research by placing the samples of the cell lines created in that bank (Deech, 2002; The Witherspoon Council on Ethics and the Integrity of Science, 2012). They are exceptionally attentive and a

reflective body that offers reasonable oversight of delicate research area such as genome editing which allows for its continual progress (Callaway, 2016).

6.3.2 Australia

They are equally many articles written about the Australian stem cell regulation just as the United Kingdom. The Australian Government did not enact any legislation for stem cell research or the use of human embryo before 2002, instead each of their states had varied laws and regulations. The state of Victoria in Australia passed world's first comprehensive legislation regulating ART in 1988 (Johnson, 2014). Then (2009) explained that the House of Representative Standing Committee on Legal and Constitutional Affairs released a report on cloning and stem cell research, which led to the passing of the 'Research Involving Human Embryos Act 2002' and the 'Prohibition of Human Cloning Act 2002', which underwent several amendments since (NHMRC, 2014).

The aim of Research Involving Human Embryos Act 2002 was to focus on certain matters including ethical concerns, the scientific progress in human reproduction and the permissible use of human embryos created by ART (Australian Parliament, 2002). The act was originally somewhat conservative, whereby it bans, first, the reproductive and therapeutic cloning procedures unless it is approved by the Embryo Research Licensing Committee of the National Health and Medical Research Council (NHMRC), second, the production of chimera embryos and third, trafficking of eggs or embryos. Moreover, the research using embryos resulting in their destruction, should be created prior to 5th April 2002 (Then, 2009).

The Research Involving Human Embryos Act 2002 and the Prohibition of Human Cloning Act 2002, both underwent several amendments in 2006 as Senator Patterson and the Australian Prime Minister John Howard, refused to ignore the recommendations made by the Legislation Review Committee, known as the Lockhart Review. The Lockhart

Review Report released on December 2005 made 54 recommendations based on their assessment of the Commonwealth legislation governing research using human embryos (Cooper, 2006; Then, 2009). The amended act was passed and enforced on 12th June 2007 and continued to ban reproductive cloning but permitted the creation of human embryos using SCNT as long as they are not more than 14 days old (Then, 2009). Following the amendment, various responses emerged from the states and territories. This resulted in states such as Victoria, New South Wales, Queensland, Tasmania, South Australia and the Capital Territory agreeing with the amendment and passing the law but Western Australia became the only state that rejected the amendment not allowing SCNT despite the federal support (Blackburn-Starza, 2008; Sinclair & Schofield, 2007).

According to the Research Involving Human Embryos Act 2002 and the Prohibition of Human Cloning Act 2002, all scientists pursing research using excess human IVF embryos as well as creating new embryonic stem cell lines through means of SCNT are required to gain license from the NHMRC Licensing Committee. On top of the licensed approval, these scientists are also required to follow relevant guidelines such as the NHMRC National Statement on the Ethical Conduct in Human Research 2007 not to mention complying their individual states legislation (Australian Parliament, 2008, 2016).

6.3.3 United States

Just like United Kingdom and Australia, the policy development of stem cell research in the United States was also triggered by a specific issue concerning reproduction, more specifically abortion as identified by several publications. In 1973, the Supreme Court decided to legalize abortion against strong opposition by the Roman Catholic Church. Based on the case Roe vs Wade abortions are a private matter involving a woman and her medical practitioner and a woman has rights to terminate her pregnancy within the stage where the embryo is not viable to survive outside the womb on its own.

The court alleged that a "fetus is not a person" due for Constitutional protection (Kiessling & Anderson, 2003; William L. Saunders, 2003). The ruling generated a huge anti-abortion movement which also opposed research on human embryos. Congress representatives were worried about the implication and exploitation of the aborted embryos and fetuses. The politically active movements soon led to the moratorium placed on federally funded research on living embryos by the Department of Health, Education and Welfare (DHEW), which later became Department of Health and Human Services (DHHS) (Wertz, 2002). Although the US Congress tried to override the moratorium by voting against it, however President Bush vetoed these votes (Kiessling & Anderson, 2003).

After President Clinton taking office, Donna Shalala, the Director of the DHHS lifted the moratorium and within that year the US Congress passed legislation known as the NIH Revitalization Act 1993 to allow funding for research involving human embryos and fetal tissue obtaining appropriate consent (United States Congress, 1993). In 1995, a few Congress members tried to include a new provision or rider forbidding funding on research using human embryos in the appropriation bill, which was passed into legislation. The rider is known as the Dickey-Wicker Amendment in honor of the Congressmen Jay Dickey and Roger Wicker, which signed by President Clinton, preventing the DHHS from using funds for the creation of human embryos specially for research purposes, or which result in death of that embryos (Patel & Rushefsky, 2015). The NIH based on the Dickey-Wicker Amendment, released a guideline as a standard to follow for research involving embryonic stem cell (Cummings, 2010). The Guidelines for Research Using Human Pluripotent Stem Cells published on 20th August 2000 covered management concerning using human pluripotent stem cell obtained from human fetal tissue (National Institute of Health (NIH), 2000). President Clinton also established the National Bioethics Advisory Commission (NBAC) in 1995 to review and guide the

National Science and Technology Council including other public bodies on bioethical issues due to research involving human subjects.

In 2001 President George W. Bush took office, by then scientists Martin (1981) and Thomson et al. (1998), both had their breakthroughs and stem cell research began to progress, particularly hESC. He announced a ban on the use of federal funds for research on human embryos which involves creating new cell lines, and declared that federal funds will only be accessible for human embryonic stem cell lines created before 9th August 2001 (Kiessling & Anderson, 2003; Matthews & Rowland, 2009). The NIH presented a 200 over page long report as requested by the president detailing the significance of stem cell research, but not about the issue of funding. The report led to President Bush addressing the nation on televised speech about moral, beginning with defining stem cell and explaining how they are derived. He also focused on the matters of 'when a human life begins' while highlighting the potential benefit of stem cell research, claiming that the federal funds would only be available for the existing 64 cell lines remained in fertility clinics (Patel & Rushefsky, 2015; Wertz, 2002). The Stem Cell Research Enhancement Act was introduced in the House of Representative, it was passed twice in 2005 and 2007 but was vetoed by the president, and were not legislated (Mitka, 2006). The act was then re-introduced again in 2009, although read twice but it was referred to the Senate Committee on Health, Education, Labour and Pensions, then finally to the House Committee on Energy and Commerce (Vertes et al., 2015).

In 2009, President Barrack Obama lifted the funding ban placed in by the former president, when he signed the Executive Order 13505: 'Removing Barriers to Responsible Scientific Research Involving Human Stem Cells'. The order stipulates that through the support of the Director of NIH the Secretary of Health and Human Services could encourage and perform valuable human embryonic stem cell research allowed by law. Sworn to produce "strict guidelines" to safeguard stem cell research from triggering

reproductive cloning in creating more embryos, President Obama directed the NIH to develop a revised guideline which will also address the matters of federal funding. On 23rd April 2009, a draft was presented by the NIH receiving over 49,000 comments from a range of concerned people. Considering the comments, the guideline came in force on 7th July 2009 (Murugan, 2009; NIH, 2016).

Research on human embryos and human embryonic stem cell research all over the world is often associated with human cloning, especially concerning the creation of embryos using SCNT and parthenogenesis. Although James Watson exposed the prospects of cloning, however the cloned sheep, Dolly created by Wilmut et al. (1997) and the first hybrid human clone created by Advanced Cell Technology in 1998 (Coghlan, 2003), initiated the whole debate on human cloning (Nabavizadeh et al., 2016). The Human Cloning Prohibition Act bill was introduced several times over the last 20 years (1998, 2001, 2003, 2005, 2007, 2009, 2012) but due to the divisions in Senate or the veto power of president, it has yet to be passed. In 2015, the act was introduced again but it is pending amendments not sure if it will pass. Apart from the Human Cloning Prohibition Act, there were also Human Cloning Ban and Stem Cell Research Protection Act introduced in the House and Senate 2003 and 2005 but was not passed or enacted to into law as the bill expired at the end of that Congress (Cohen, 2007).

Just before President Obama left office, he enacted the 21st Century Cures Act into law on December 2016. The act approved a total of US$6.3 billion as fund for the NIH to assure suitable regulatory assessment of regenerative therapies which includes stem cell therapy research (United States Congress, 2016).

6.3.4 Singapore

The reviews of policies and regulations of pioneering countries like the United Kingdom, Australia, and the United States by scholar have proven valuable and it is equally important to review countries in Asia, since this research intends to study the regulative development of stem cell research in Malaysia, which is an Asian country, not to mention with pluralistic society which is quite common in Asia. Singapore was chosen due to its research position as well as for its comprehensive nature of stem cell regulation, unlike China whose stem cell research regulation still has a lot of work to do. Singapore is considered largely by some as the Asia's stem cell center apart from Japan, Taiwan or China, as it is greatly invested in stem cell research. The research, especially the embryonic stem cell is positioned as a national priority by the Singapore government (Svendsen & Ebert, 2008). The stem cell research investments are responsible as a motivating initiative intended to improve the blooming economy. Biopolis and Fusionopolis (A*STAR) are two biomedical research centers set up which also conduct stem cell research equipped with top scientists around the world (Colman, 2008).

The flexible and relaxed regulation of stem cell research, with significant funding and encouragement by the Singapore government concerns other countries governments greatly. The liberal policy which concentrates on expanding the stem cell research drawing many top-notch scientists from other countries, like the United States to Singapore indirectly intensifying their position (Svendsen & Ebert, 2008). Despite popular citation of James Thomson's discovery of hESC, Singapore's very own Ariff Bongso, a researcher at the National University of Singapore (NUS) and his team of researchers was the first to derive the embryonic cell from 5-day old human blastocysts obtained from IVF program in 1994 (Bongso, Fong, Ng, & Ratnam, 1994). In June 2000, with Bongso's breakthrough, Singapore established the country's first stem cell, academic start-up company called ES Cell International (ESI) Pte Ltd at the Biopolis

center, with more than US$20million approved for stem cell research (Colman, 2008; Odorico et al., 2004).

In December 2000, the Bioethics Advisory Committee (BAC) was established by the Singapore Cabinet, to evaluate the ELSI due to biomedical research and development in Singapore (O'Brien, 2014). They basically made appropriate recommendations depending on their findings. The BAC also formed the Human Stem Cell Research (HSR) Sub-Committee in February 2001, to manage the ELSI resulting especially from human stem cell research as well as reproductive and therapeutic cloning. In June 2002, the committee published a broad report titled, 'Ethical, Legal and Social Issues in Human Stem Cell Research Reproductive and Therapeutic Cloning" which acknowledged the significance of establishing a comprehensive legislation and regulatory framework aimed to manage human embryonic stem cell research, and suggested introducing a regulatory body that will help license, regulate and overlook the entire human stem cell research in Singapore, as its 11 recommendations. The report also recommends that embryonic stem cell research is permitted only with cells derived from 14 days old and younger embryos and prohibiting reproductive cloning (O'Brien, 2014; The Bioethics Advisory Committee (BAC), 2002).

The MOH drafted the Regulation of Biomedical Research Bill on November 2003 which will forbid reproductive cloning and placed it in the web for public consultation. The BAC 2002 report and the drafted bill, both led to the public accepting the creation of embryos by IVF and through SCNT (Lee, 2007; Walters, 2004). Since then the BAC have published six other reports between 2002 and 2010, concerning biomedical research including research using human subjects, genetic research, donation of human eggs and human-animal hybrid creation and research (BAC, 2016). The MOH of Singapore also made it compulsory for all government and restructured hospitals to set up ethics committees or institutional review boards (IRB) and also adhere to the "Ethical

Guidelines on Research Involving Human Subjects" published in 1997, which aims to offer a comprehensive framework of ethical principle that ethics committee can consider during their review. All research involving human subjects, including clinical trials are required to submit their research protocols to the ethics committee and the IRB for review (National Medical Ethics Committee (NMEC), 1997). The Human Cloning and Other Prohibited Practices Bill was drafted in May, by the MOH to prohibit reproductive cloning which was passed on 2nd September 2004. The act is considered as a step-by-step measure in governing biomedical research, which also imposes a penalty of up to SGD $100,000 or imprisonment of 10 years (Pincock, 2004).

In 2012, the "Ethics Guidelines for Human Biomedical Research" was drafted and it was published on 23rd June 2015 after receiving valuable feedbacks during the public consultation sessions by the BAC. The guideline was perfected judging on previous papers and compiled by the committee taking into considerations the viewpoints of the general public, scientific and healthcare experts and religious figures (BAC, 2015; Tan, 2015). Following that, the Human Biomedical Research Act which was placed for public consultation between 6th November 2014 and 18th December 2014 was passed in the Parliament on 18th August 2015 and approved by the president on 21st August 2015. The act aimed to offer transparency concerning duties and positions of individuals and corporate bodies engaging in human biomedical research and manage the use of human tissues in research. With the act in place, the MOH intend to safeguard the human biomedical research and tissue banking, which indirectly includes stem cell research. The act compels researchers and those involved to obey the law and the good clinical practices (GCP) that conform to ethics and integrity in research (Singapore Parliament, 2015).

6.4 The regulation of Malaysian stem cell research and its technologies

Today the question, "*do we have stem cell treatment for __?"* has become a very regular pursuit. Doctors, medical practitioners and even family members of suffering patients are facing this question on a daily basis. The discovery of stem cells with its unique regenerative characteristics even initiated experts to revisit debilitating diseases without successful treatment or cure hoping to find some relieve using stem cell (Nadig, 2009). The R&D of stem cell is an ongoing process with extensive experimentations conducted by many ambitious scientists worldwide. Recognizing its potential Malaysian scientists are also greatly involved in both research and its clinical trials. Unfortunately, the stem cell research in Malaysia is currently unregulated as verified by the local policymakers. This section answers the most significant research questions concerning the current regulation of stem cell research and technologies in Malaysia, which are, (e) 'How are the internationally published and Malaysian publications reflect in terms of the ethical inquiry of stem cell research and therapy?', (f) 'Is the current stem cell guideline adequate in regulating the entire stem cell research and therapy?', and (g) 'How and where can the current regulatory measures be compromised due to continuous development of stem cell technologies'

Stem cell research in Malaysia begun in the 1980s with its first transplantation documented in 1987. The number of stem cell transplantation have increased tremendously over the years since with more types of stem cell transplantations carried out as clinical trials.[69] Given that, all the pioneering stem cell countries like the United States, Australia and the United Kingdom developed their stem cell guidelines and legislations due to specific event such as the birth of the first test tube baby, the Supreme Court case Roe vs Wade that legalized abortion, the pro-life movements against the ruling, the increased number of ART and other reproductive technology such as IVF as

[69] This information is discussed in detail in Chapter 1

well as the various reports either to present the social or legal implication of assisted reproductive technology, cloning or even stem cell which eventually urged the authority to begin re-evaluating the necessity of a legal framework to regulate the stem cell research and its technology directly or otherwise.[70] This is established as a pattern considering the origins of stem cell regulation.

Similarly, in Malaysia a significant clinical trial and the first of its kind in Malaysia in the form of cardiovascular stem cell transplantation became the motivation in the development of its Guideline on Stem Cell Research in 2006. However, the guideline has its own reservations and implications.

6.4.1 Factor that spurred the stem cell guideline

Malaysia's first cardiovascular stem cell transplantation involving patient, Allagara Arumugam was the trigger for the stem cell guideline formulation. According to the article written by O. Lee (2003), the involved experts were confident of their technique and with the successful clinical trial proving that it works they were hoping to subject others for the study with two already in queue. The guideline formulation is timely and a step in the right direction, in order to protect the rights and welfare of doctors and patients.[71] Regrettably it does not hold wrongdoers accountable or address the matters of misconducts or noncompliance, at least not with a legal statute. In his statement for the stem cell guideline, the Director General of Health Malaysia, of the MOH at the time, Tan Sri Dato' Seri Dr. Hj. Mohd Ismail Merican said (in pg. 6-7) that, "Practitioners and scientists involved in stem cell research and therapy must adhere to these guidelines to ensure that no harm is done to the patients. Failure to do so may result in repercussions which mat put the practitioners or scientists in a difficult position especially if they are

[70] This information is discussed in detail in Section 6.3.1
[71] Verified by local ethicist

proven to be unethical in their practice or research with regards to the use of stem cells. We all have the responsibility to uphold the highest standards in medical care and medical ethics".

However, any unethical conduct said to 'put the practitioners or scientists in a difficult position' acts as a warning to prevent the misconducts in the first place, similar to the famous proverb, prevention is better than cure. But without any formal complaint or whistleblowers bringing the issue to light, the MOH is unable to take the necessary actions even if there are such cases.[72]

6.4.2 The public sector

Stem cell research is still ongoing in Malaysia with many unknown elements and the process of offering stem cell therapy as a routine risk-free and safe treatment still has a long way to go (Brazier, 2016; Muraca et al., 2006; Ye et al., 2016). Currently, the research and transplantation of stem cell is still reviewed and assessed individually before it is authorized to carry on. All stem cell researchers are required to gain the necessary approvals beginning with the IRB, the institutional ethics committee (IEC), the National Medical Research Registry (NMRR), the MREC and conform with the National Stem Cell Research and Therapy Sub-Committee (NSCERT) checklist before pursuing their study which is described in detail in Chapter 1. Apart from the National Guideline for Stem Cell Research and Therapy 2009 and these approvals, there are regulative circulars released by the MOH which are legally binding nothing like the guideline. The two such circulars which are (1) dated 14th November 2011 (Ref: KKM87/P1/26/10Jld/13(39)) signed by the former Director General of Health of the Ministry of Health (MOH) and (2) dated 2nd April 2015 (Ref: KKM87/P1/26/10Jld18(41)) signed by the current Director General of Health, of the MOH are high level formal documents required to follow

[72] Verified by local policymakers

although Malaysia do not have any statute or law in particular regarding stem cell research (MOH, 2011, 2015).

Regrettably, the circular may hold legal mandate but without speaking to a MOH personnel, no lay person could ever know about this. Even so, the circular may implicate public servants within public hospitals and medical facilities but not the private sector although they do have other legislation implicated to them directly such as the Private Healthcare Facilities and Services (PHFS) Act (1998). This is a case of different sets of laws regulating the same thing (the ethical conduct, safeguarding the rights and welfare of medical practitioners and patients), although overlooked by the same authority. Separating these duties to separate divisions may be productive in regulating duties kind of way, but having them be based on different laws or regulation is not only counterproductive but plain bias. I believe doctors and medical practitioners should be governed by the same code or law like the Code of Medical Ethics, which is pretty straight-forward. Regardless of its statute, these circulars like the guideline did not address or specify the matter of non-compliance and accountability, instead it simply 'requests for compliance'. According to the policymakers, without whistleblowers and formal complaints regarding any misconducts it is nearly impossible for them to proceed accordingly (MOH, 2015).

The public sector of stem cell research includes the doctors, the medical practitioners, researchers and even students attached to a number of research facilitates, such as the Clinical Research Centers (CRC) established within the hospitals, research laboratories of the institution of higher learnings (universities) and other NIH laboratories including Institute of Medical Research (IMR), National Cancer Institute (NCI) and the National Heart Institute (NHI). Being a public servant, these experts and their research are properly regulated since they have an inclination to adhere strictly to the guideline and the circulars (including the service circulars for the Civil Servants (JPA)), and obey

the Public Service Code of Conduct as they have pledged initially (Public Service Department (JPA), 2017).

However, there is some concern considering the step by step process of gaining the required approvals. Firstly, the possibility of scientists carrying out a stem cell research without registering their study in the NMRR or gain the necessary MREC approval not knowing the proper process. Although some experienced scientists may be aware, but inexperienced research students may fail to follow through not knowing the actual protocol or standard. Secondly, the lengthy processing (timeline) from the point of complete submission that takes 45 to 60 working days for processing often compel scientists to apply for the approvals while concurrently carrying out their study to prevent delay in their experimentations, which is unethical (National Medical Research Register (NMRR), 2017). Finally, it is customary for the gained approvals to have a valid timeline or expiry date, and this entails the research either completed by within the given timeline, or is require to renew them on a timely manner, which they will receive reminders from NMRR and MREC.

The tedious application and the renewal process, although done online may intimidate researchers to not follow protocol that could go undetected. There is no oversight by NMRR or MREC as far as ensuring the research conducted are based on approval or if they pursued within a valid timeline as these applications are often on self-regulation basis with the investigator being ethical following protocol (MREC, 2012). There are no clear mentions of the repercussions of failing to follow except being unethical. MREC does not have jurisdiction to take action against those that violate the code. The unethical investigators are often monitored and regulated by their IRB and the IEC first and foremost as there are no generic of 'blanket ethical approval (renewal)' which goes across organization allowing easy detection.[73] The stem cell research and the

[73] This information is verified by a MREC personnel based on a phone call

investigators involved within the institution of higher learnings (universities) and other laboratories within the NIH are regulated and monitored by the organizational or institution themselves. The discrepancies and the ethical issues are within their jurisdiction, however without whistleblowers it is hard to capture these problems.

6.4.3 The private sector

There are many companies that are associated with stem cell lately in Malaysia. They are either stem cell banks which stores umbilical cord blood or tissues, those that conduct stem cell research as clinical trials, those that offer stem cell therapy as a form of anti-aging treatment in the aesthetic medicine and finally those that simply market foreign stem cell cosmetics products (namely from Taiwan, Korea, Japan and China). Apart from them, there are several privately owned medical healthcare facilities which also conduct research on stem cell and perform clinical trials with the approval of right authorities. In order for these private entities to run their operations, they need to gain authorization from the MOH specifically the Medical Practicing Division, which actually divided into several branches which are, the Private Medical Practice Control, the Medico Legal Branch, and the Branch Drafting Act (MOH, 2009b).

The Medical Practicing Division actually functions as the division within the MOH that enacts new laws related to medical practices, implements and enforces the PHFS Act 1998, [Act 586] and its regulations including the registration and licensing of the many private hospitals, clinics, and even the medical practitioners (MOH, 2009b). The difference between the Medical Development Division and the Medical Practicing Division is that the latter is solely in charge of the private sector.

The regulation of the private sector of stem cell research and technologies, although, they are overlooked by the PHFS Act 1998, which is a strict law managing healthcare, however it does not include the specific stem cell innovations or its unique

characteristics, allowing these entities to exploit. All stem cell entities are required to register, gain the necessary approval and get their establishment licensed in order to operate within the legal boundaries. Once the authority receives the application, they will conduct an audit of the premises to ensure if they comply with the necessary protocols (i.e. the building layout, construction and specification, equipment, material, standard operating procedure etc.).

Once licensed, they are allowed to operate given that they also adhere to the Guideline for Stem Cell Research and Therapy 2009. However, their clinical trials will still be reviewed individually by the NSCERT before authorization. There are other stem cell products (cosmetics and wellness based) that are registered and licensed within the National Pharmaceutical Regulatory Agency (NPRA) such as FDF Anti Wrinkles Stem Cell Crème & Masque, the CELTEC Stem Cell Serum and Bio Stem Cell Ampoule just to name a few. These products may have the term 'stem cell' in their labels however, the source of stem cell (may be plant or animal based), how it was manufactured or even how to use it may not entail the actual potential of stem cell and its technologies. Although, they are stem cell based, they do not come under other jurisdiction of NSCERT as stem cell therapy instead it is recognized just like other cosmetic or wellness-based products. Companies use these terms loosely to avoid scrutiny or criticism or even to stay under radar, while still capture the attention of customers for it stem cell significance, although it may not entirely what it claims to be. The naïve customers are the victims.

Marketing unproven products as stem cell-based products is still a concern, even though they are just face masks, face serums, creams, lotions or even wellness drinks. This led people to believe as long as there is no need for bloodstream introduction then products like these can still be marketed without scrutiny. They are not genuine stem cell products but they are projected as such for profit gain by conning the general public. This

may be one of the many ways stem cell is exploited creating a grey area due to the regulatory loopholes.

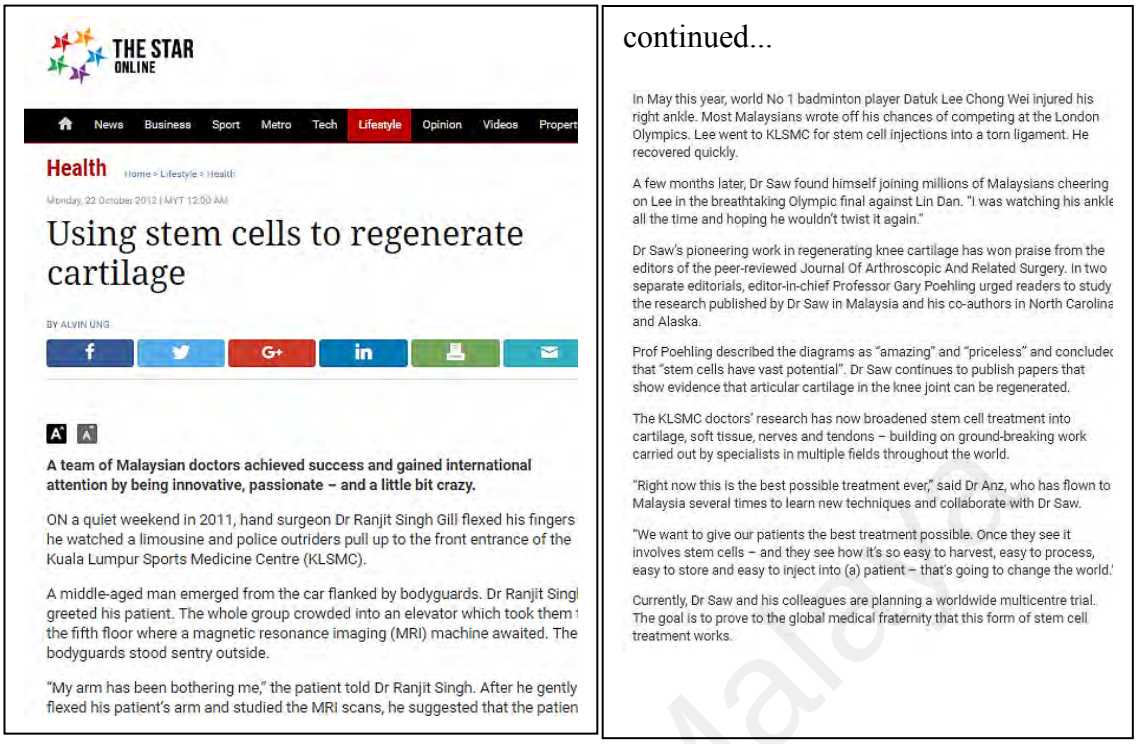
6.4.4 The implication of current regulation: Regulatory loopholes (grey area)

There are many challenges in regulating stem cell research and its technologies. The public sector and the private sector both have very different concerns, however the latter has projected more than the former. The challenges are mainly due to the lack of comprehensive policy or legislation which indirectly created room for exploitation. The current regulation has its drawback as the elements of stem cell is not incorporated in fact, there has been no revision of the PHFS Act 1998 since it was first devised. The insufficiency and deficiency of the stem cell guideline and the PHFS Act 1998 overlooking stem cell innovations introduced several regulatory loopholes also known as grey area as illustrated in the thematic map in Chapter 4. The regulatory loopholes basically identify the implication resulting due to the deficiency, for example the attempt of Bio-Cellular Research Organization (BCRO) as mentioned in Chapter 1.

The PHFS Act 1998 is successful in overlooking the healthcare facilities and services regarding their registration, licensing and even with the premise inspection, ensuring their laboratories and facilities are up to standard of operation (SOP). Unfortunately, it does not evaluate or review the treatments offered. While the policymakers continue to deliberate either to incorporate stem cell in its existing legislation or in the formulation of the new act, these entities are making use of the opportunity taking advantage of the regulatory gap or deficiency by introducing unproven stem cell therapies despite the instructions in the Guideline for Stem Cell Research and Therapy 2009, which states, "Haemopoietic stem cell and umbilical cord stem cell transplantations are the most established form of stem cell therapy. The use of other stem

cells including hES and somatic stem cells is considered experimental" (Guideline for Stem Cell Research and Therapy, 2009, pg. 38)

There are several issues beginning with, the growing number of unlicensed private healthcare facilities advertising, promoting their unproven stem cell therapies, the marketing of unproven stem cell products imported from elsewhere (i.e. Korea, Taiwan, Japan, China) by private entities and the licensed healthcare facilities failing to obtain the necessary approval in conducting clinical trials or offering stem cell therapies are few of the identified implications owing to the current stem cell regulation apart from the BCRO case. Several private healthcare facilities including a few that are unlicensed are advertising these therapies in their official websites and internet promoting their costly but unproven stem cell therapies. Although some of these facilities are licensed establishments but they failed to obtain the necessary approval for their state-of-the-art therapies. While some were not even listed under the 'List of Licensed Facilities and Services Private Healthcare as of 31st December 2016', published by the Medical Practicing Division (MOH) (2016) in their official portal in 2012 but were seen advertising their stem cell therapies and even tried to get the endorsement of national athlete for their therapies as reported by Ung (2012) in TheStar Online in Figure 6.5. Although, it may appear that few of these entities failed to apply for licensing despite advertising their service, but it is hard to verify if it could be a case of doing things concurrently. Several businesses tend to advertise and promote their services to gain public support while applying for licensing. It is meant to make full use of wasted time as it easily takes months before they finally obtain their authorization credentials.



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Monday, 22 October 2012 | MYT 12:00 AM

Using stem cells to regenerate cartilage

BY ALVIN UNG

A team of Malaysian doctors achieved success and gained international attention by being innovative, passionate – and a little bit crazy.

ON a quiet weekend in 2011, hand surgeon Dr Ranjit Singh Gill flexed his fingers he watched a limousine and police outriders pull up to the front entrance of the Kuala Lumpur Sports Medicine Centre (KLSMC).

A middle-aged man emerged from the car flanked by bodyguards. Dr Ranjit Singl greeted his patient. The whole group crowded into an elevator which took them the fifth floor where a magnetic resonance imaging (MRI) machine awaited. The bodyguards stood sentry outside.

"My arm has been bothering me," the patient told Dr Ranjit Singh. After he gently flexed his patient's arm and studied the MRI scans, he suggested that the patien

continued...

In May this year, world No 1 badminton player Datuk Lee Chong Wei injured his right ankle. Most Malaysians wrote off his chances of competing at the London Olympics. Lee went to KLSMC for stem cell injections into a torn ligament. He recovered quickly.

A few months later, Dr Saw found himself joining millions of Malaysians cheering on Lee in the breathtaking Olympic final against Lin Dan. "I was watching his ankle all the time and hoping he wouldn't twist it again."

Dr Saw's pioneering work in regenerating knee cartilage has won praise from the editors of the peer-reviewed Journal Of Arthroscopic And Related Surgery. In two separate editorials, editor-in-chief Professor Gary Poehling urged readers to study the research published by Dr Saw in Malaysia and his co-authors in North Carolina and Alaska.

Prof Poehling described the diagrams as "amazing" and "priceless" and concluded that "stem cells have vast potential". Dr Saw continues to publish papers that show evidence that articular cartilage in the knee joint can be regenerated.

The KLSMC doctors' research has now broadened stem cell treatment into cartilage, soft tissue, nerves and tendons – building on ground-breaking work carried out by specialists in multiple fields throughout the world.

"Right now this is the best possible treatment ever," said Dr Anz, who has flown to Malaysia several times to learn new techniques and collaborate with Dr Saw.

"We want to give our patients the best treatment possible. Once they see it involves stem cells – and they see how it's so easy to harvest, easy to process, easy to store and easy to inject into (a) patient – that's going to change the world."

Currently, Dr Saw and his colleagues are planning a worldwide multicentre trial. The goal is to prove to the global medical fraternity that this form of stem cell treatment works.

Figure 6.5: The write-up on stem cell therapy by unlicensed establishment.

[Source: Ung (2012) in The Star Online]

The aesthetic clinics are also a part of the private healthcare facilities that are offering unproven stem cell therapies within their facilities. Aesthetic medicine is a new field in Malaysia and it is beginning to receive recognition as a new trend of medicine, with the MOH devising the 'Guideline on Aesthetic Medical Practice 2013'. It provides guidelines specifically in setting up aesthetic medical practice and aiding in regulating the medical practitioner practicing aesthetic medicine. Sadly, the guideline does not mention stem cell anywhere in its instructions. The aesthetic medical practitioners are required to register themselves and their practice under the National Registry of Registered Medical Practitioners, practicing aesthetic medical practice in order to license them as authorized establishment. Figure 6.6 displays the step by step registration process of the aesthetic medical practitioner and their facilities.

The registration of the medical practitioners and their establishments are not the only consideration, there is also the basic consideration of the scope of practice which is presented in the Guideline on Aesthetic Medical Practice in 2013 (Table 1 of pg. 21 and Table 2 of pg. 28). However, despite the list of procedures from non-invasive to minimally invasive in two separate tables, stem cell therapy was not mentioned in any of the procedures. Although it does mention that any new evidence-based treatment other than those listed will be subjected to review by the relevant authority. However, the policymakers (member of the NSCERT) verified that they did not receive any such application from these aesthetic clinics, but they are confidently offering these therapies within their facilities (as advertised in their websites).

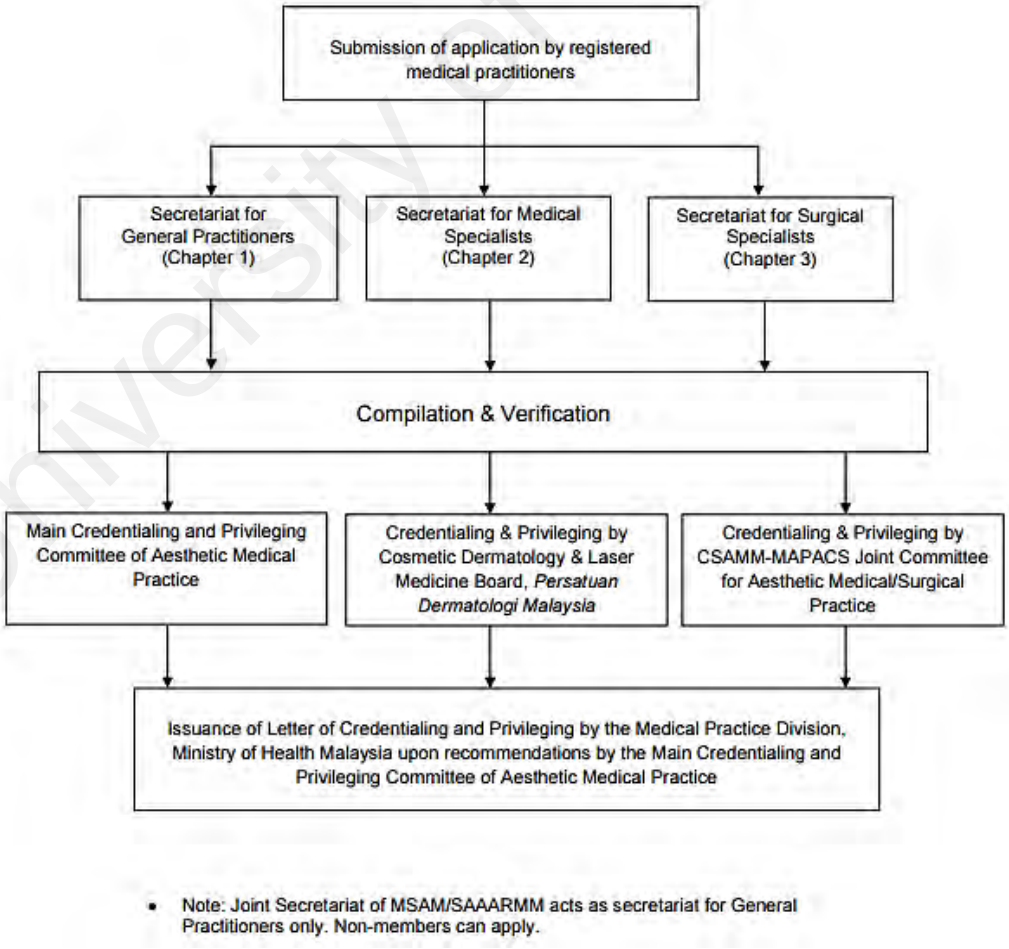

Figure 6.6: The registration process of aesthetic medical practitioners.
[Source: The Guideline on Aesthetic Medical Practice pg. 14 (MOH, 2013)]

Which brings us another overlooked matter that is the private entities that are in the midst of applying for licensing are required to also submit their advertisements for approval. According to the PFHS Act 1998, in Section 108 (pg. 48 Part XVIII – Miscellaneous);

> *Section 108. Advertisement.*
>
> *No private healthcare facility or service or health-related facility or service shall publish any advertisement –*
>
> *(a) in such a manner as to mislead the public on the type or nature of the healthcare facilities or services or health-related facilities or services provided; or*
> *(b) which is contrary to any direction on advertisement issued by the Director General* (PFHS Act, 1998)

Regrettably, the private entities fail to submit their advertisement or information related to promoting their faciltities and services during their application process, assuming there is no misleading facts. Honestly, not informing the public the fact that some procedures are not approved or aware by the MOH is misleading enough and an offence. Unfortunately, even this is identified as a regulatory loopholes and a grey area often manipulated by the private healthcare providers and other entities.

The many issues considering the private healthcare facilities and services comes down to one serious challenge, which is formal complaints which is considered as standard potocol. Honestly, a person who intend to complaint (both public and private sector) can access the Public Complaints Management System (SisPAA) at (http://moh.spab.gov.my/eApps/system/index.do) through the official portal of the MOH (http://www.moh.gov.my/index.php) and and the Medical Practicing Division (http://medicalprac.moh.gov.my/v2/index.php) as displayed in Figure 6.7. The page is meant to retrieve feedback or complaints from public on medical healthcare facilities and services only.

Figure 6.7: The public complaints management system (SisPAA)

[Source: The official portal of MOH (2014)]

If the general public wanted to complaint on the private companies that is involved in selling illegal stem cell products they need to access the NPRA and click the link 'Contact Us' (http://npra.moh.gov.my/index.php/contact-us/enquiry-complaint) as shown in Figure 6.8.

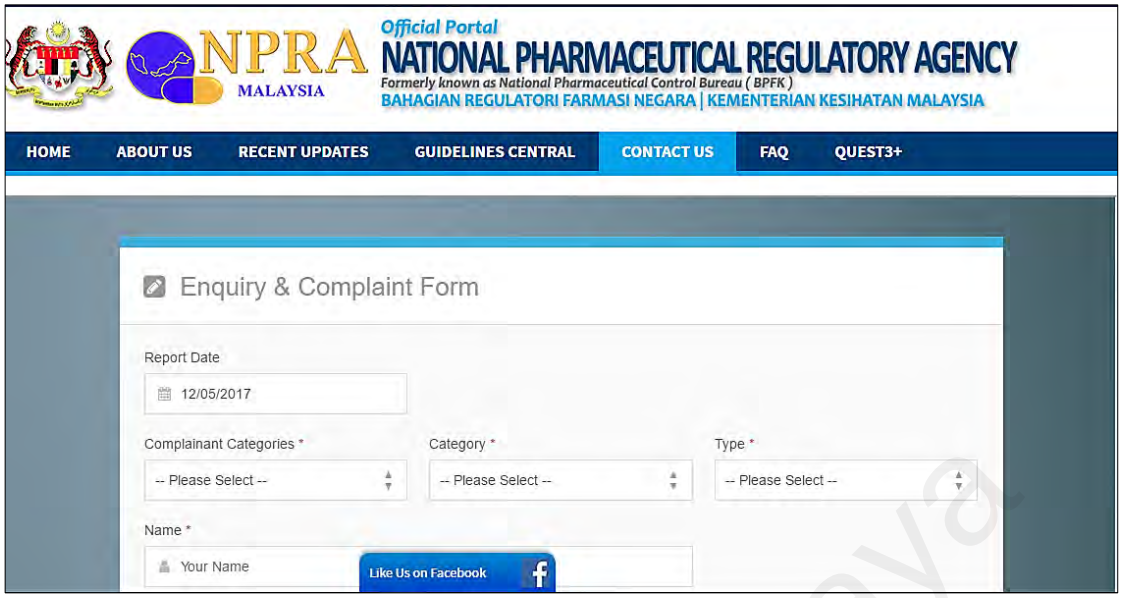

Figure 6.8: The enquiry & complaint form of National Pharmaceutical Regulatory Agency (NPRA)

[Source: NPRA (2017)]

The process may be at your fingertips but the system still requires the complainant to register their name and create a login and password before they can proceed with their complaints. They are even required to include contact information. The red asterisk symbol entails compulsory information. This is clearly too transparent for any person who are about to complaint on a large organization regarding sensitive matter such as illegal trading or medical malpractice involving unethical people. A more user-friendly system allowing complainant to have a choice of either forthcoming or remain anonymous which will encourage them to come forward without fear of being identified or publicized should be practiced.

The list of implications due to the deficiencies in regulation is growing ranging from growing numbers of unlicensed entities, to those offering unapproved stem cell therapies. However, these issues and concerns will continue to spread without the general public bringing the matter to the authority. Once the MOH receives the official complaint only then they are able to take the necessary step towards containing the problem. Otherwise, even though it is an offence the MOH is unable to respond accordingly despite

being standard protocol. Even if some responsible public do submit an official complaint, not reaching the right department it will still remain ignored.

Lastly, the overlapping jurisdiction within the MOH overlooking stem cell research, its therapy and its many products is also identified as a grey area. First there is the Medical Development Division regulating the public sector of stem cell including the many clinical trials, then there is the Medical Practicing Division which regulating the private sector of stem cell, but without putting the necessary pressure in the service offered, and finally there is the NPRA which supposed to regulate stem cell 'products' which includes therapies but have not fully launch its function since stem cell still being largely reviewed by the Medical Developing Division as clinical trials. However, the NPRA do license and manage the other stem cell products.

Judging from the current stem cell research and its technologies regulation there are many negative implications and it is clear mostly are arising from the private sectors due to simple neglect or their non-compliance to the available standard protocols. However, it is a serious concern and one that without resolving them the victims are the innocent public.

6.5 The stem cell research ethics

This section addresses the second part of this study which is the research ethics of stem cell and its technologies based on written publications. The ethics of stem cell research and its technologies are extensively studied and debated by national and international scholars. They are written to either justify if stem cell research using human embryos are ethical or no, which goes into the discussion of 'when life begins' as presented by Table 5.6 and 5.7 in Chapter 5. The stem cell research ethics identified many concerns ranging from the personhood theory and the moral status of the human embryo due to their destruction, the issue of informed consent, the exploitation of women donors for their eggs (oocytes), the right time to translate from preclinical to clinical trials, stem cell tourism, and many others. These issues have been comprehensively discussed from various perspectives and viewpoints, however, for the purpose of this study the assessment of local, Malaysian experts and international experts are valuable to show the distinct approach that is so common but lacks documentation.

6.5.1 Ethics and its inquiry

Ethics is a broad subject, that is also known as moral philosophy (Mackinnon, 2004). It includes organizing, justifying and suggesting the concept of right and wrong. It is a term that was derived from the ancient Greek word *'ethikos',* which came from the word '*ethos'* meaning 'custom' which behaviors are guided by (Lovin, 2011). According to Lovin (2011), when translated to Latin the term '*ethos'* could have been rendered "*mos"* or "*mores"* (pl.) which gives us our English word morals. Although, contemporary philosophers characterize ethics as critical thinking in relation to life, and morals as the basic principles that influences people regarding what is right and wrong even before they begin thinking critically. However, this is a false judgement, as ethics and morals are in fact used interchangeably (Lovin, 2011).

The subject of ethics has stirred many civilizations, many centuries ago, beginning with the ancient Greek all the way to the Medieval times to the modern, contemporary ethics. Sappho (637-577 B.C.E) was made famous for her 'pre-philosophical' poetry that appear to explore ethics (Blevins, 2008), Socrates (469-399 B.C.E) who never wrote his own thoughts, inspired his students such as Plato (427-347 B.C.E) and Aristotle (384-322 B.C.E) to write his dialogues, as well as their own significant writing of ethics like Apology, Euthyphro, Nicomachean Ethics and Eudemian Ethics (Richard Kraut, 2017; Woodruff, 2016). Other civilization such as Hindu and Islamic have also written different angle of ethics in their scriptures (Hindery, 1978; Quigley, 2007). These days, philosophers are inclined to divide ethics into four main branches which are meta-ethics, normative ethics, applied ethics and descriptive ethics (Fieser, 2009; Icheku, 2011). Within these four branches of ethics, there are many sub-fields of study (Reviews, 2016), and often time it is interrelated depending on the objective of a study, the ethical theory in discussion or the justification of an action. According to Reviews (2016) the four branches of ethics are significantly different whereby each one answers only specific question such as,

Descriptive ethics: What do people think is right?
Meta-ethics: What does 'right' even mean?
Normative ethics: How should people act?
Applied ethics: How do we take moral knowledge and put it into practice?

Aristotle is said to have been the first to use term ethics, a field which his predecessors Socrates and Plato established. Since the ancient Greek, the philosophical ethics struggled to present rational responses as to how people should live best. Aristotle is known to regard ethics and politics as two connected but distinct fields of study, whereby ethics evaluates the virtue of the person, while politics evaluates the virtue of a nation (Kraut, 2008). It is very similar to the approach of this study which although intend

to address the regulative matters of stem cell research, but it also encourages to highlight the ethics of the research which defines our approach being Malaysian.

It is important to understand the beginning of Aristotle's intention of ethical inquiry for a range of purposes. It could be to learn theoretical knowledge on its own or to consider the aim of ethical inquiry which is different compared to the aims of other type of analysis. The ethical inquiry actually means to inquire into ethical issues, to explore, examine, reflect and question about important matters (Tessitore, 1996). This led to the foundation of applied ethics or in this case bioethics, which scholars live by, reflecting and questioning the ethical rightness or wrongness of controversial scientific innovations.

Somewhat similar to Aristotle's Nicomacheon Ethics which discussed the distinct relationship between ethical inquiry and politics, this study aims to look into the ethical inquiry of stem cell research (as a comparison between international and local, Malaysian publications) as well as of its regulatory concerns. The fundamental idea of how Aristotle often begin his inquiry is to review the differences of opinion regarding what is acceptable for people, therefore determining the motivation or reason that causes the difference, we benefit from such ethical inquiry (Kraut, 2017). According to Kraut (2017), Aristotle claim that ethics is not just a theoretical field, in fact to study a good human behavior is not to simply gain the knowledge but to be able to build a deeper understanding how to prosper and thrive.

With that idea in mind, it is greatly valuable for this study of stem cell research ethics and its policy implication to first begin by looking into what scholars have extensively researched and discussed regarding the ethical implication or issues pertaining to stem cells, especially with the destruction of human embryos to understand the deeper significance of those study, and eventually evaluate how these publications impact stem research, its regulations as well as our lives especially in Malaysia.

6.5.2 The basis of publication: International vs Malaysian

The stem cell research ethics publication led to two very distinct perspective as presented in Chapter 5 which are the universalist ethics and relativist ethics. It is very clear that currently most of the ethical inquiry of stem cell research and its technologies written by Malaysian authors are largely founded on the religious beliefs and practices, especially the Islamic law since it is the religion that represents the majority population of Malaysia (Weintraub, 2011). Based on the Article 3 of the Malaysian Constitution, 'Islam is the religion of the Federation; but other religions may be practised in peace and harmony in any part of the Federation' which clearly accepts religion other than Islam (Malaysian Parliament, 2010; Shanmuga, 2004). Therefore, when the policymakers first revised the Guideline on Stem Cell Research (2006) they also approached in on the basis of considering all the other religious practices in Malaysia apart from the Islamic *Fatwa* as a duty to respect other religions (MOH, 2006). The is quite common in Malaysia whereby their multicultural and multireligious identity often compel them to first deliberate any concerning matter from the religious viewpoint first to ensure mostly that there are no breech on religious boundaries (Bakar, 2009).

Although, the guideline revision included religious consideration by consulting the many religious experts, but it is clear that there is no uniformity due to the many denomination that exists among religion and the intricacies of their religious norms and beliefs. Similar to the many nations before them, Malaysia decided to adopt the 14th day rule to form a universal basis. They also prohibited the act of therapeutic cloning ensuring the human embryos used for stem cell extraction are from IVF surplus embryos. The religious consideration is indeed a very common practice in Malaysia, and so the relativist ethics is approprite to distinguish Malaysian authors from others.

In the beginning, soon after James Thomson published his paper on the derivation of hESC from embryos, several articles were written from a religious

perspective mostly around the year 2004 then the United States' President Bush made public his conflict against hESC founded on the basis of his faith (Frazzetto, 2004; Mannoia, 2004; Pittman, 2006; Sandel, 2004; Wertz, 2002). The international authors may have begun their ethical inquiry on stem cell from a religious perspective but the majority of discussion are still from a universalist ethics perspective. This can be seen as a shift towards a more universal approach with research being an international actvity involving collaborative works globally promote the need for a more universal take on all subject matter considering stem cell. Or it could be a view of what is more relevant based on the current approach of addresing the issue as a global concern. Etiher way, what is clear is that most international authors are evaluating the issue of stem cell and its technologies from a universalist ethics perspective, while Malaysians are still more tuned to their personal roots.

6.6 The stem cell guideline: A case of what it is and is not

The Guideline for Stem Cell Research and Therapy 2009 as verified by the policymakers is only a general statement with no obligatory control lacking the legal stature. According to Howard (2003) a guideline only establishes the parameters within a policy, standard or procedure. It is a reinforce document which is discretionary and flexible (Howard, 2003). A few, defined guideline as a methodically acquired statements that assist experts in deciding about care in particular clinical situations (Manchikanti et al., 2009; Woolf et al., 1999). Therefore, a guideline would be more definitive and persuasive consolidated with a formal decree embarked to accomplish main objectives. It is clear that a policy would be more appropriate and influential compared to a guideline as the Figure 6.9 presents the hierarchy of policy and guideline.

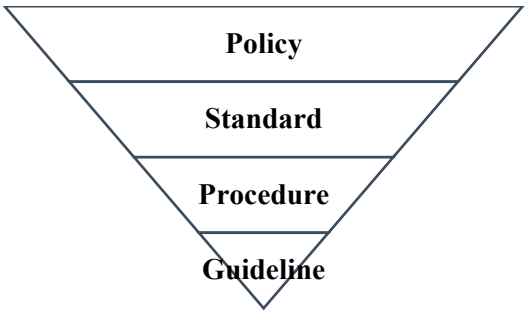

Figure 6.9: Policies, standard, procedure & guideline.

[Source: Tipton and Krause (2006). Reprinted with permission.]

According to the Oxford (2012) dictionary, policy is defined as, 'a course or principle of action adopted or proposed by an organization or individual'. Hare (2009) defined policy as a comprehensive document that states how the institution is to perform. It is a high-level formal document which is compulsory. It basically describes the preferred outcome, solution and objectives of an administration that is further reinforced by standards and guidelines. Lowi (1985) defined policy as a rule, formulated by govermental body meant to guide the public either individually or collectively using negative or positive restrictions which is similar to the definition of rule in jurisprudence. No doubt, there are a variety in the definition of policy on the grounds that it is hard to characterize or depict, however, putting it simply for the context of this study, a policy is decribed as the principle and system applied by government ministries to achieve their target goals (Hare, 2009; Tipton & Krause, 2006). Figure 6.10 illustrates the policy hierarchy within any administration, starting with the primary guidelines all the way up to the policy and legislation, such as acts and laws.

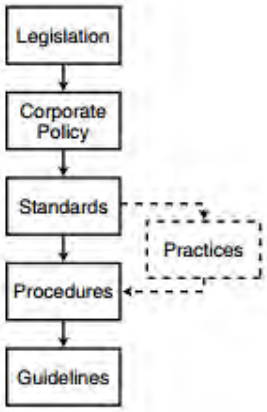

Figure 6.10: The policy management hierarchy.

[Source: Image reproduced with permission from Tipton and Krause (2006).]

With that in mind, the revision of the guideline was timely and despite its shortfalls it managed to capture several emerging concerns like the use of animal stem cell for human administration known as xenotransplantation, the inclusion of stem cell therapy oversight instead of research alone and the other standard regulation of private sector of stem cell including the procurement of the cells complying with the National Standards of Procurement and Processing of Stem Cells (MOH, 2009a). The stipulations are considered as standard rules and regrettably any non-compliance could go undetected as these stipulations remain passive without the legal mandate a legislation brings. Therefore, it would be a valuable to link the guideline to an act or regulatory policy giving the guideline stipulations stature. A whistleblower whose claims are based on these standards can be rest assured that their complaints will be dealt with seriously since lawfully required to follow protocol.

There are four major categories of policies known as regulatory, distributive, redistributive and constituent as shown by Figure 6.11 (Lowi, 1985). In a big administration like a ministry, policies are designed to (1) fit the entire organization or within their many divisions and departments, or (2) especially certain subject area or even technology. In regards to that, a regulatory policy would definitely prove valuable in

regulating the stem cell research and its technologies in Malaysia (Tipton & Krause, 2006). Beside bestowing legal mandate, why should the government formulate a regulatory policy managing stem cell research and its technologies? Regulatory policy is broadly defined as the pursuit of regulative excellence with definite, dynamic and reliable 'whole-of-government' policy. In a larger scale, it is formulated to keep the nation from falling prey to corruption (Noll, 1985), but it is also proved beneficial in healthcare as shown by Figure 6.11 as adopted by many nations. Generally, the formulation of regulatory policies by governments are to encourage better regulation of a particular department, subject area or field within public interest, similar to stem cell research. It highlights the justification of how regulations and regulatory frameworks should be of

FORM OF EXPRESSED INTENTION	FORM OF INTENDED IMPACT	
	Works through Individual Conduct	*Works through Environment of Conduct*
Primary Rule (imposes obligations or positions)	*Regulatory policies:* *Rules* impose obligations; rules of individual conduct, criminal in form *Synonyms:* police power, government intervention *Examples:* public health laws, industrial safety, traffic laws, antitrust	*Redistributive policies:* *Rules* impose classification or status; rules categorizing activity *Synonyms:* fiscal and monetary policy, overall budget policies *Examples:* income tax, Federal Reserve discount rates, Social Security
Secondary Rule (confers powers or privileges)	*Distributive policies:* *Rules* confer facilities or privileges unconditionally *Synonyms:* patronage, subsidy, pork barrel *Examples:* public works, agricultural extension, land grants	*Constituent policies:* *Rules* confer powers; rules about rules and about authority *Synonyms:* overhead, auxiliary, government organization *Examples:* agencies for budgetary and personnel policy, laws establishing judicial jurisdiction

Figure 6.11: Categorization of Public Policies

[Source: Image reproduced with permission from Lowi (1985).]

good quality and 'fit for purpose'. In Malaysia, the 'National Policy on The Development and Implementation of Regulations' developed by the Malaysia Productive Corporation

(MPC) and launched in 2013, focused on the gaps in management system intended for regulations while meeting the top global system or Good Regulatory Practice (GRP). Figure 6.12 illustrates the mapping of the National Policy on The Development and Implementation of Regulations Principle to the regulatory governance cycle as published in the 'Implementing Good Regulatory Practice in Malaysia report published by the Organisation for Economic Co-Operation and Development (OECD) (Malaysia Productivity Corporation (MPC), 2013; Organisation for Economic Co-Operation and Development (OECD), 2015).

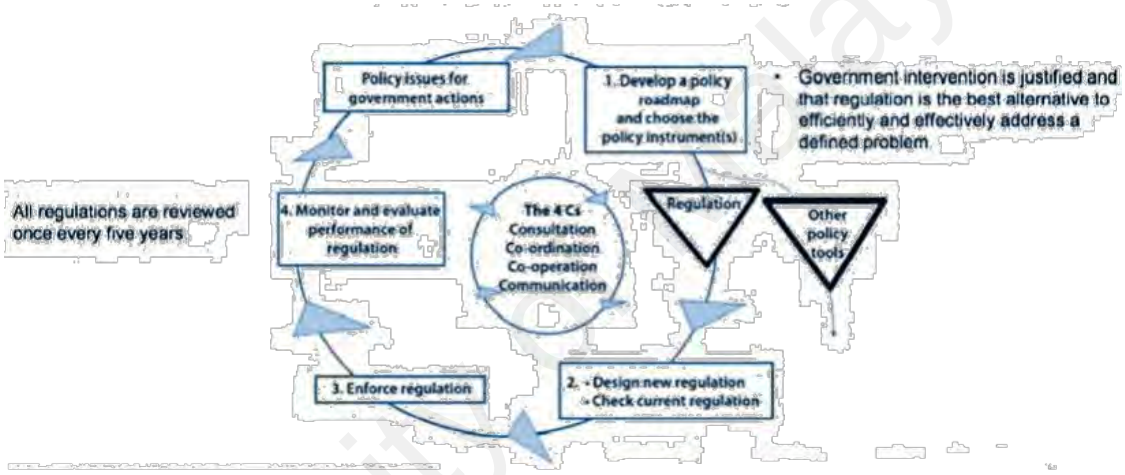

Figure 6.12: The mapping of the national policy on the development and implementation of regulations' principle to the regulatory governance cycle.
[Source: The National Policy on The Development and Implementation of Regulations' (2013)]

According to the Malaysian National Policy on The Development and Implementation of Regulations, published by the Regulatory Review Department MPC, first a policy is developed and with that, a new regulation is designed and enforced. In the meantime, the performance of the newly designed regulation is regularly monitored and evaluated and any concerning issues are brought forward to the government's attention. The policies and regulations formulated are to effectively and efficiently address distinguished problems and these regulations are required for timely review of once every five years. A periodic regulatory impact analysis (RIA) is customary to ensure that the objectives are still relevant serving the country and its people in a balanced and equitable

fashion with transparent implementation. The ongoing assessment of the regulation or regulatory framework notifies the policymakers regarding the achievements, the setbacks and the demand for modification to the existing form of regulation to present efficient provision of public policy targets.

However, as far as Malaysian stem cell research is concerned, there has yet to be a policy or legislation. Judging by the Guideline for Stem Cell Research and Therapy (2009) although first published in 2006 and revised in 2009, it has remained the same for the past eight years now without any review (MPC, 2013; OECD, 2015). Perhaps, the national regulatory policy is still very new since the process commenced in June 2011 and published in 2013. However, the formulation is mainly as sustenance to the modernization of the regulatory system and basically as a part of Vision 2020 which Malaysia's former prime minister envisioned. Acknowledging Malaysia's stem cell research regulation has its shortcoming, brings us a step closer towards improving or bridging the deficiencies but the implementation aspects still indecisive. A good regulatory policy is one with clear objectives, consistent but transparent, targets the right crowd and addresses the issue of accountability as presented by the causative order of Figure 6.13 (Parker & Kirkpatrick, 2012).

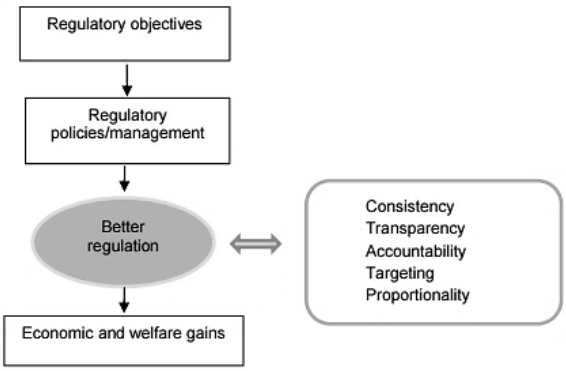

Figure 6.13: Causative order.
[Source: Image reproduced with permission from Parker and Kirkpatrick (2012).]

The fact that a policy holds the legal mandate while a guideline does not, is not the only significant point. In fact, a regulatory policy outlines the relationship between

different stakeholders as an integral part of effective public governance while helping the policymakers reach informed consent regarding the what, who, and how of the involved regulation (Parker & Kirkpatrick, 2012). In the context of this study, it is the regulation of stem cell research and its technologies (the what) and involving the general public, the donors, the human subjects, the medical practitioners and the service providers (the who). Unfortunately, in Malaysia the 'how' of the regulation, is currently unfulfilling and despite being an ongoing procedure the outcome is still uncertain and undecided.

According to Lowi (1985) any rule that establishes restrictions or enforce duty and responsibility while posing penalties for noncompliance, regulatory policies are most appropriate as presented by Figure 6.14. Therefore, a stem cell regulatory policy in place would definitely be appropriate in addressing all the major issues discussed previously.

Question	*Response, Comment*
1. Does the rule of the statute (or decree) apply to persons or conducts in the private or in the public sphere?	If in the public sphere, the police is almost certainly constituent. If private, it could be any of the other three types.
2. Does the rule set conditions or impose obligations and provide penalties for nonperformance?	If yes, the policy is regulatory. This applies even to public officials because in matters of crime and tort all persons are private citizens.
3. Does the rule set conditions without sanctions?	If yes, the policy could still be regulatory if there is an implicit sanction such as exposure or publicity. The policy could be distributive, if the policy sets a process in train or provides for a facility without setting conditions of performance for participation.
4. Does the rule pertain to individuals and deal with them by name or provide specific facilities without providing general standards from which the privileges or facilities derive?	If yes, the policy is almost certainly distributive; a clear example is a "pork barrel" act authorizing projects by name
5. Does the rule create an agency?	If yes, the policy is constituent.
6. Does the rule provide an agency with jurisdiction over other agencies?	If yes, the policy is constituent; a clear example is a budget bureau.
7. Does there appear to be a rule without contemplation of action by public or private persons?	If the rule sets a public process in train or defines the jurisdiction of an agency, it is a constituent policy. If the rule provides for a process for all or a large, defined aggregate of persons, it is probably redistributive. (See also q. 9.)
8. Does the rule ignore individual conduct and concentrate on characteristics or properties of individuals, i.e., does the rule attempt to discriminate among defined aggregates of persons without regard to their conduct?	If yes, as in identifying all persons below a certain income or age, and if the category is invidious and involuntary, the policy is almost certainly redistributive (e.g., tax categories, welfare classification).
9. Does the rule provide for or alter a process or structure that is economy-wide?	If yes, the policy is almost certainly redistributive (e.g., Federal Reserve System; low-interest loan programs). In such cases, the entire citizenry is the category defined in the rule.

Figure 6.14: The guideline for classifying policy statute.

[Source: Image reproduced with permission from Noll (1985).]

In retrospect, it will capture the regulatory deficiencies (the illegal entities, unproven stem cell therapies, the uncovered aesthetic medicine, minimizing the overlapping jurisdictions and many others) while safeguarding the rights and welfare of the stakeholders (the general public, the donors, the research subjects, the medical practitioners, the private entities providing services). It will put public safety in central importance while the stem cell research continues to bring innovations the issue of noncompliance through unethical acts and misconducts gets penalized to prevent future implication.

Hence, it is the duty of the MOH Malaysia which operates within the interest of public to develop an effective and efficient regulatory policy that will regulate the entire stem cell research and its technologies including the private and public sector within one big oversight. The policy will also bring in the guideline into its decree and ultimately gives the guideline the statute it deserves. Lately, many countries have recognized the significance and have undertaken several initiatives in addressing the issue of policy for better regulation. I strongly believe it is time for Malaysia to join in the pursuit reaching regulatory excellence with its experienced and qualified officers in the MOH.

6.7 The ideal regulatory policy

Although government resources are at the policymakers' disposal, however utilizing it efficiently would mean to ensure the resulting product, that is the policy, is one that help provide oversight of the many subject areas with similar objectives, like stem cell research, biomedical innovations and even ART. As established based on Chapter 2 of Global Stem Cell Laws and Policies of the World, there is a trend in regulating stem cell research and its technologies. Nations with extensive ART often adopt policies along the line of that, while those that have reservation concerning cloning

issue opt for something that combines the use of human embryos for research and cloning in their policy development.

In Malaysia, we have the concern of multi-religious perspective regarding the use of human embryos for research as previously discussed. Some of the nations like Iran, and the Vatican City have chosen to rely on their constitution that is religiously inclined. Despite Malaysia's religious identity, its constitution does not specifically reflect a single religion, instead it states that people of Malaysia have the freedom to choose their religion (Malaysian Parliament, 2010). Therefore, regulating stem cell using constitutional law will not be practical for Malaysian people in any case, not only stem cell research or its technologies. In the process of learning from the pioneering countries, the MOH Malaysia should urge its NSCERT to work out a report similar to the Warnock's Committee as well as the Singapore's BAC concerning the social and legal implication of stem cell research and its technologies and make the necessary recommendation concerning its effective regulation. This study can equally serve as a catalyst the policymakers need to generate the right action or move them towards the right directions.

Regardless of the report, judging by the various laws and policies that are available, it is important to review if any of them fit the position of the Malaysian people. The cloning law may be the most appropriate as it lays out the specific restrictions concerning the use of human embryos, since both reproductive and therapeutic cloning are prohibited in Malaysia just as it is in Canada and Australia. The ART law and policies may not be quite suitable for Malaysia, just as it is adopted by nations including China, Japan and Hong Kong that have very liberal position concerning reproductive and therapeutic cloning. Although, adopting Singapore's biomedical law would have its merits being a nation within similar population as Malaysia, but their liberal position is not reflective to the Malaysian position that values religious norms.

Although, a cloning law would prove valuable and quite straightforward, but it will not include the other biomedical innovations involving animals or those that have not been discovered but equally controversial like the iPSC. Therefore, instead of a cloning law, Malaysia should devise an extensive formal R&D policy, one that incorporates all the research and clinical trials involving human subjects, the up-and-coming scientific technologies including stem cell technology and those that have yet to reached the mainframe is formulated instead one that addresses a single area. It should be comprehensive, sustainable and focused, while still include the various unpredictable elements but within expectations and eventually assist the regulators to clearly see the vision and direction of any issue regarding medical and healthcare. Ultimately, the regulators are able to discuss freely and deliberate on designing legislation addressing specific concerns within the borders of the policy without fear of manipulation and exploitation while the policy is authorized and in place.

While the legislation design committee continues to deliberate, the policy will be reviewed by the RIA team in accordance to the national regulatory policy every five year once, to ensure that they are still relevant and effective in addressing the concerns within the subject area. This eventually aids in the administrative management and simplification, reducing burden while creating the transparency in terms of regulatory decision-making. The RIA should ideally include the consultations of the stakeholders which actually leans towards adopting a more risk-based or evidence-based approach in regulating and dealing with issue of compliance and enforcement (Parker & Kirkpatrick, 2012).

This ideal policy would not only resolve the issue of unconducive regulation by the local authorities which created too much perplexities, in fact it will create a form of harmonization considering all biomedical innovations including the ones that have yet to emerge. Some argue strict regulations in stem cell research or any biomedical science

hinder research progress that inhibit economic market dynamics which may not impact economic growth positively (Parker & Kirkpatrick, 2012), however it is necessary to maintain order and quite frankly Malaysia has a long way to go before stem cell research and its technologies reaches the economic mainframe. By the time they reach to that level, based on the national regulatory policy 2013, the existing policy could easily be reviewed to incorporate current concerns including how it can improve economic growth professionally instead of side tracking from the current challenges. It is necessary to deal with current pressing matters before we deal with the future ones, as they may not convene objectively.

A part from the policy development, the MOH Malaysia should also adopt the initiative towards public awareness. Their medical experts involved in the regulative decision-making should conduct campaigns regularly in hospitals (both private and public), location with high public turn out like malls and even release community service messages in radios, television and the social medias to educate the general public regarding the existence of stem cell, how they can treat people but most importantly the impact of unproven therapies offered by the authorities. They should relay all the necessary domains where information is easily accessed by public to allow them to capture the transparency of regulation. This would create inquisitive thinking among the general public, (1) regarding their civic duty of whistleblowing, (2) when faced in a situation to either pursue or not a clinical trial they will be prepared instead of being victimized and (3) to keep the policymakers to their toes with critical feedbacks during the periodic RIA.

The formulation of the R&D policy will address all the issue of unlicensed entities, unproven stem cell therapies reaching the public within the private sector by first, compelling all private stem cell entities to proceed for registration of their entities, which second, brings in the strict review phase. This review phase, includes evaluation of the

services hoped to offer by the applicant and the legitimacy of their products and to ensure they conform with the policy and the stem cell guideline. Thirdly, if the product and services (including their facilities) conforms with the requirements, then they will be licensed and allowed to operate within the jurisdiction and borders of the policy and the guideline. However, if there are any discrepancies, these applications will be denied but allowed for re-application once matter is dealt with within six months or sooner. Failing to re-submit creates doubt (if they are operating without license) hence, reminders will be sent to proceed with the paperwork. Ignoring the reminder will result in penalties which expresses the authority's seriousness in carrying out their duties. Finally, the licensed entities will be audited once every year (their product, services and facilities) as the matter of healthcare is quite delicate and serious if overlooked.

The transparent policy and the awareness initiatives by the MOH Malaysia will urge the private stem cell entities to be cautious when offering their services to the public. Since, all private entities are given the opportunity to license their establishment reviewed, which help reduce the issue of illegal entities operating unlawfully. If there are such entities, they could be the ones that were originally denied for licensing (did not conform with the policy and guideline) and were penalized for not re-submitting their re-application. These entities will be easily identified as they will not be in the list of the licensed entities released in hospitals, medical service providers and even in the public domains for easy access, thus the public could easily avoid them or report them to the MOH Malaysia for further action which are much stricter and severe involving jail term.

This policy will ultimately keep order and create apprehension among private service providers and other private entities from any unethical action or misconducts that can result in them losing their license and authority to provide service in the field of stem cell. The general public will be more tuned to their responsibility and with the available transparent regulation which makes it is easy to identify the wrongdoers to penalize them.

CHAPTER 7: CONCLUSION

This chapter draws on the research findings of this study while providing the motivation on the grounds of better regulation involving stem cell research and its technologies in Malaysia. It is evident that stem cell research and its technologies in Malaysia has tremendously improved over the course of 30 years with many advances in both public and private sectors.

7.1 The accomplishment of research objectives

The three research objectives were successfully achieved. First, it is discovered that stem cell research in Malaysia was unregulated and have major shortcomings with mere guideline in place to overlook the entire subject area. Many deficiencies were identified and were well addressed in the discussion chapter. These challenges faced by the regulators are quite substantial however they still remain without a final decision regarding the policy or law making.

Second, the ethical inquiry of stem cell research written by international and Malaysian authors were explained. The search led to the discovery of many perspectives in the ethical inquiry of stem cell research, but most significantly universalist ethics and relativist ethics. Between the foreign and Malaysian scholars, Malaysians were more tuned to religious ethics or relativist ethics, while the foreign scholars were more into universalizability. Malaysia's cultural differences may seem like a drawback, with many religious denominations to consider making it impossible to reach consensus. However, this practice is not new and apart from ethical inquiry we incorporate cultural difference even in the regulatory decision-making or law making. Considering the many religious norms and principles is actually a part of being a Malaysian which only a multi-religious country would understand, as Einstein once said, 'Science without religion is lame,

religion without science is blind'. Therefore, trying to adopt a foreign policy may not be as feasible to our ways, although reflecting the issue from a universal point of view could be favorable nonetheless.

Finally, the implication due to the current regulatory standard and protocol was discussed as quite serious and noteworthy. It is important to highlight the inadequacies of the current regulative shortcomings to prevent further implication which resulted in many critical issues identified as grey area or regulatory loopholes ranging from sprouting unlicensed entities, unproven stem cell therapies reaching the public, the exploitation of established aesthetic clinics offering unrecognized stem cell-based treatments and the overlapping jurisdiction that causes some issues to fall through the cracks. By highlighting these implications, we are able to see the seriousness of the matter. It takes us a step closer to remedy the flaw and make the necessary improvements in fulfilling the original objectives of serving the general public with quality healthcare. By ignoring and neglecting these threats we could be facing even severe repercussions which could prove damaging to the welfare of the people as a whole.

7.2 Incorporating findings into research framework

This study was based on the research framework presented in Chapter 2. The key findings were incorporated into the research framework to give a complete vision of the entire research. Figure 7.1 displayed the findings of this study integrated into the original research framework proposed at the start of this study. It only highlights the key findings concerning stem cell research regulations. Other secondary concerns and the external factors influencing the many implications were not incorporated as they were more extensive in nature.

Beginning with identifying the current status of stem cell research to the existing regulatory standard, the framework brought focus into the multitude of policies devised

by many countries whose regulatory protocols were more adjusted to their countries' own agenda and concerns, which was distinctive compared to Malaysia. Using the chosen methodologies deemed suitable responding to the research objectives and the research questions, the study resulted in its major findings from a range of experts pertaining to stem cell research.

The fact that the research is unregulated, and that it resulted in many implications such as research hindrance due to following the current regulation, to the various grey area and regulatory loopholes was acknowledged. The focus then was shifted to the future policy ideal in bridging the gap of the regulatory discrepancies and deficiencies. The designed research framework therefore proved quite practical and substantial for the context of this study as it gaged all angles well and systematically.

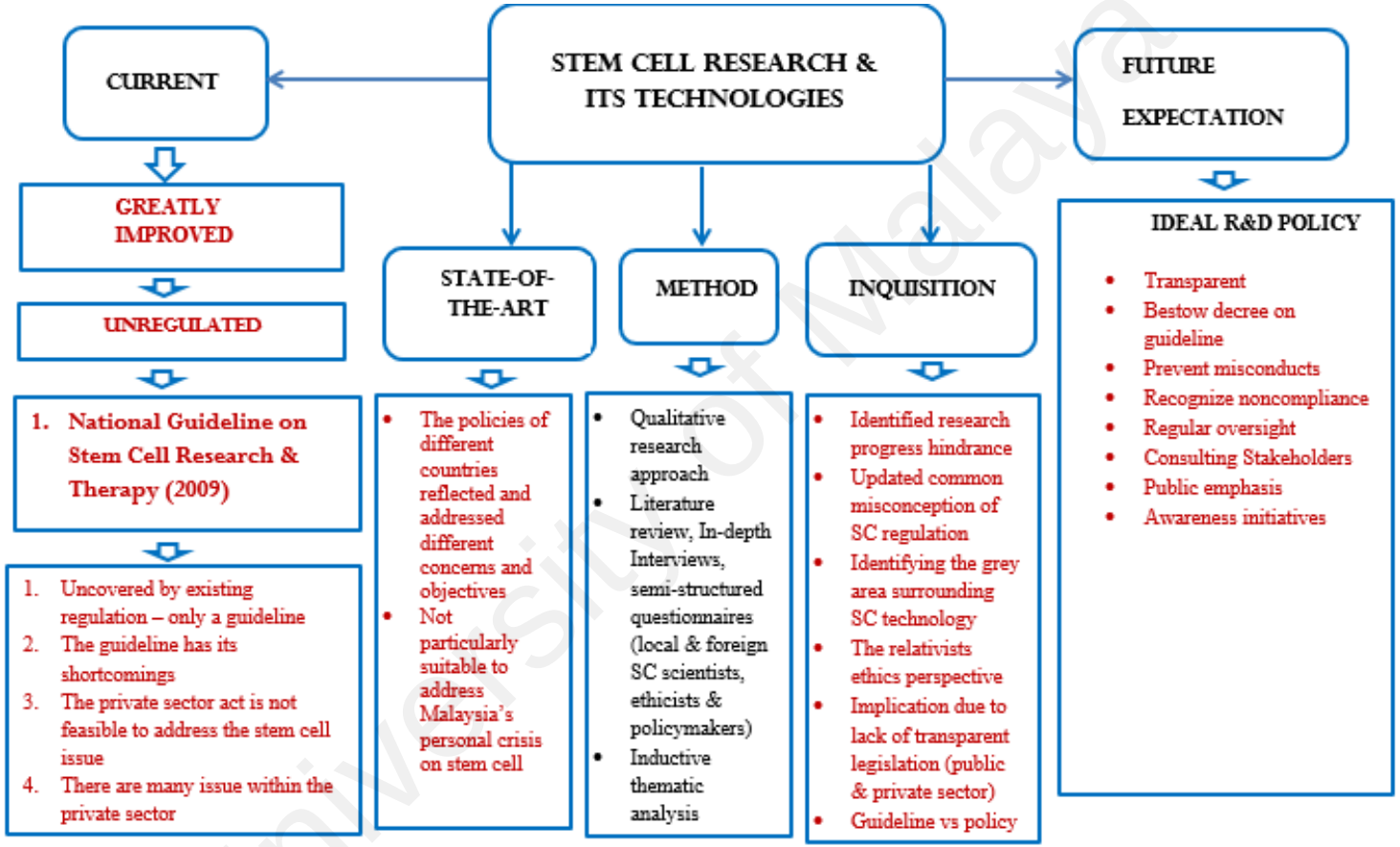

Figure 7.1: Research finding consolidated with research framework.

7.3 The research contribution

Stem cell research and its technologies are undeniably beneficial to everyone. It is the future of medicine and how doctors treat patient. Since healthcare comes within the jurisdiction of the Malaysian MOH with their vision to create a country that function collectively for the betterment of health, including innovative biomedical technologies. Hence, they are duty-bound to address the concerns of unregulated stem cell research and its technologies to ensure they are conducted ethically especially since it is extracted from human subjects such as bone marrow, umbilical cord and even embryos.

They made it their mission to safeguard high-quality healthcare system which is not only customer focused but one that emphasizes community participation. Therefore, it is necessary to bring the matter of implication to the attention of the Malaysian MOH. The policymakers may be continuously deliberating on how to regulate stem cell research effectively and efficiently, but the regulatory gap that exists gradually pose a bigger threat if not addressed. This study not only identified, examined and evaluated the implications of the current regulatory protocol in Malaysia for further assessment by the policymakers, but it also highlighted the benefit of formulating a regulatory policy compared to the existing guideline. Consulting the different stakeholders during policy and law making is also essential in guaranteeing that the authority considers all angle and their perspectives which is easily neglected.

The MOH's acknowledgement of the shortcomings of the current regulatory system in overlooking stem cell research during data collection is already a positive note that there is a crisis that need careful examination and evaluation. Thus, this study will present them with all the necessary data they need to take the next step in improving the situation, as it is the liability of the MOH considering the many stakeholders involved. Hopefully, the authorities involved will one day effectively regulate the stem cell research and its technologies in Malaysia keeping the issues of ethics and legal close, proving the

quote by the famous Lebanese-American scholar Nassim Nicholas Taleb that, 'My biggest problem with modernity may lie in the growing separation of the ethical and the legal' wrong (Taleb, 2010). That by tying all the lose-ends Malaysia becomes a nation to be reckoned with as far as regulatory excellence is concerned. The astounding success will only inspire other developing countries like Indonesia, Thailand and Vietnam within the Southeast Asian region whose research is progressing but their regulatory aspects are inactive or undeveloped.

7.4 Suggestion for future research

This study mainly explored the status and implications of the current regulation of stem cell research and its technologies. While it highlights the regulatory aspects and the effects of the unregulated stem cell research, it also drew attention to the nature of the ethical inquiry accustomed to Malaysian scholars. The majority of the previous studies are mostly focused on the ethical issues concerning stem cell research from a religious perspective either looking into the different religious perspective or specifically into one particular religion.

Future study could expand by looking further and deeper into the main context of this study, which is the regulation of stem cell research and its technologies. This study was more preliminary in nature as it begun to assess the regulation crisis concerning stem cell research in Malaysia. There are other focus areas and perspectives worth exploring as further study which will provide a more comprehensive information regarding stem cell research and its regulation in Malaysia, such as;

1) Conducting a detailed analysis and review of different regulatory policies and legislation formulated by countries such as Singapore, United Kingdom, Canada and Australia from a legal perspective, to gage its provisional feasibility in respect to our stem cell regulatory objectives. The findings of

this study will provide our authority with data necessary for decision-making during their many regulatory deliberations.

2) The phenomenon of stem cell tourism in Malaysia and the many issues concerning the lack of stem cell regulation and enforcement especially involving the private sector.
3) Conducting a largescale survey of the general public to assess their exposure, view, understanding and awareness considering stem cell research in Malaysia, including the element of regulation. This study will provoke the inquisitive thinking of the public regarding the topic of stem cell while educate them of their civic duty as whistleblowers.
4) A study that looks into the different stakeholders considering stem cell research and its technologies such as the patients, the medical doctors, the medical healthcare providers and others.
5) A study that explores the IRB and IEC of the different institution of higher learning particularly on the matters of review and evaluation of stem cell research by scientists in academia
6) A study that particularly addresses the concerns and perspectives of the private stem cell entities and service providers regarding the issues of compliance, regulation and misconducts.

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