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Affording patients the right to access experimental stem cell treatment: A comparative analysis of the legal and ethical consequences

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Jai Shri Ram

ABSTRACT

Despite revolutionary advances in the medical field, with specific reference to stem cell technologies and therapies, South African laws do not adequately address gaps that currently exist when it comes to legally accessing the various forms of experimental therapy. The Constitution of South Africa does make provision for the right to access health care, however most stem cell therapies are not yet approved or registered by the relevant authorities and can therefore not be considered as accessible health care. Patients are increasingly becoming aware of their rights when it comes to health care which may be partially linked to the advances in, and knowledge of medical professionals diagnosing and treating auto immune and other previously incurable diseases. While conventional treatments yield positive results, there are a number of incurable and novel diseases that cannot be managed with approved treatments. Stem cell therapies, currently still in its experimental phase have shown some great promise in treating and managing various diseases. The fact of the matter is that that access to such experimental therapies is limited. The rationale behind this is reasonable and justified. The safety and interests of patients are protected by numerous laws and ethical principles as such, if the safety and efficacy of medical treatments have not been clinically proven, it is not in the patient's best interests to be subjected to such treatment. However, the principle of patient autonomy does support the position that a patient should be able to choose whether or not he or she wishes to be subjected to experimental medicines, such as stem cell therapies or not, on condition that they are fully informed about the risk and consequences of doing so. Against this background, other countries, such as the United States, have enacted laws to address the lack of access to potentially lifesaving treatments. Considering that the benefits of stem cell therapies are becoming more and more evident, access to these therapies whilst not yet fully clinically approved and registered as a medicine or therapy, should, in certain circumstances, be an option for those patients who have exhausted all legally available medicine and treatments without success. Laws that afford access to experimental medicine are seen as both controversial and progressive. A balance must therefore be struck between the individual patient's right to access and his or her safety. Although expanded access programs have been around for a while, the restrictive nature of these programs often does not necessarily result in access to experimental therapies. It is important that there are viable, legal and ethical ways to access experimental stem cell therapies, whether through right to try laws or through expanded access programs.

DECLARATION REGARDING ORIGINALITY

I, Yadhna Gosai (204504870) declare that:

A. The research reported in this dissertation, except where otherwise indicated, is my original research.

B. This dissertation has not been submitted for any degree or examination at any other university.

C. This dissertation does not contain other persons' data, pictures, graphs or other information, unless specifically acknowledged as being sourced from other persons.

D. This dissertation does not contain other persons' writing, unless specifically acknowledged as being sourced from other researchers. Where other written sources have been quoted, then:

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Date: 16 August 2021

ABBREVIATIONS AND ACRONYMS

FDA – Food and Drug Administration

HPCSA – Health Professions Council of South Africa

ISSCR - International Society for Stem Cell Research

MCC – Medicines Control Council

MRSCA – Medicines and Related Substances Control Act 101 of 1965

NHA – National Health Act 61 of 2003

SAHPRA - South African Health Products Regulatory Authority

SCBI – Stem Cell Based Medical Interventions

CHAPTER ONE: PERSPECTIVES ON STEM CELL THERAPY, IMPLEMENTATION AND REGULATION

1.1 INTRODUCTION

In 1981 scientists developed a way to harvest embryonic stem cells from mouse embryos. Through technological advancements and consistent research, the use of stem cells in treating both communicable and non-communicable diseases have yet to be proven as effective. The capabilities of stem cells are growing and its influence on regenerative medicine is vast. Human tissues in general do not regenerate spontaneously, which is why cell therapy is regarded as significant when it comes to organ and tissue repair. Stem cell treatment however is still largely considered as being experimental.[1] The safety of this specific therapy has not yet been firmly established. Pioneering scientific and medical advancements will therefore always have to be carefully regulated in order to ensure that they are both ethical and safe.[2]

South Africa was one of the first African nations to actively investigate stem cell therapies in the mid 1980's. Stem cell transplantation, specifically from bone marrow, started to become established as common practice at hospitals in Johannesburg and in Cape Town.[3] Although most countries around the world have imposed regulations for conducting research using human subjects, as well as medical malpractice and licensing laws, many of these guidelines are not specific to stem cell therapy.[4] Regulation of stem cell therapy must therefore be considered along with the social and ethical implications that flow from the implementation thereof.

The key ethical issues in stem cell research relate to the sourcing of stem cells, informed consent, moral status of the human embryo, reproductive as opposed to therapeutic cloning and the clinical use of stem cells.[5] Other areas of concern involve the possible exploitation of donors or human subjects who are an integral part of the process. Once again, if we choose to

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[1] J F Stoltz et al 'Stem Cells and Regenerative Medicine: Myth or Reality of the 21th Century' available at *https://www.hindawi.com/journals/sci/2015/734731/* , accessed on 05 April 2020.

[2] Zakrzewski W et al '*Stem cells: past, present, and future'* available at *https://doi.org/10.1186/s13287-019-1165-5* , accessed on 05 April 2020.

[3] S Sigamoney 'The History and the Future of Stem Cell Transplantation and Regenerative Therapy' available *at https://nextbio.co.za/history-future-stem-cell-transplantation-regenerative-therapy/* , accessed on 04 April 2020.

[4] S Mahomed, M Nöthling Slabbert 'Stem cell tourism in South Africa' (2012) 5 *SAJBL* at 2.

[5] Botes WM et al *Stem Cell Processing: Clinical Safety and Regulations (2015)* 6.

adequately regulate this form of research and therapy, a robust legal framework is necessary to regulate these issues. In this dissertation, the legal and ethical issues surrounding access to unproven stem cell therapy will be discussed.

Permitting patients the right to access treatments that are still in an experimental phase is ethically frowned upon and in fact, expressly prohibited in many countries.[6] Evaluating the efficacy and safety of a treatment is difficult and time consuming, having regard to the amount of very limited available research evidence. Often there is little or no clinical experience of use which in turn creates uncertainty.[7] However, for terminally ill patients, or patients diagnosed with an incurable disease, this uncertainty may be outweighed by the possibility that experimental treatment may be effective.

It is a scientific fact that embryonic stem cells can develop into all cell types of the body because they are pluripotent. Adult stem cells, on the other hand, are limited to developing into cell types based of their tissue of origin.[8] This means that stem cells harvested from an embryo would warrant greater use in the field of regenerative therapy. However, serious ethical questions are raised due to the destruction of the embryo (post harvesting) relating to when human life actually begins and leads to controversial discussions linked to debates about abortion.[9] In the case of *Christian Lawyers Association v Minister of Health and Others*[10] the court had to determine if the word "everyone" included a foetus. The court held that there are no express provisions affording a foetus legal personality or protection. In terms of section 12(2) of the Constitution[11], everyone has the right to make decisions concerning reproduction, and the court found that nowhere in the Constitution can it be said that this right is qualified in order to protect a foetus. Based on the courts reasoning it can be deduced that the right to life cannot extend to an embryo and that the embryo does not qualify for protection.

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[6] Michelle Ralston 'Stem cell research around the world' available at *https://www.pewforum.org/2008/07/17/stem-cell-research-around-the-world/* accessed on 29 May 2020.

[7] 'Patient access to experimental treatments' available at https://www.nuffieldbioethics.org/publications/experimental-treatments/introduction/ethical-issues-arising-from-the-use-of-experimental-treatments accessed on 29 May 2020.

[8] 'Stem cell basics' available at *https://stemcells.nih.gov/info/basics.htm* , accessed on 10 April 2020.

[9] Lo B, Parham L 'Ethical issues in stem cell research' available at *https://doi.org/10.1210/er.2008-0031* , accessed on 07 April 2020.

[10] *Christian Lawyers Association of SA and Others* v *Minister of Health and Others* 1998 (11) BCLR 1434 (T).

[11] The Constitution of South Africa, 1996.

In South Africa stem cell therapy is regulated by the National Health Act[12] (NHA) as well as the Medicines and Related Substances Control Act (MRSCA).[13] While these laws are progressive, they remain scant in properly regulating experimental treatment being offered. Due to the impact of experimental therapy on moral values, global society and basic human rights, it is imperative that experimental therapies are regulated by laws that supplement current legislation.

In the United States, federal law called the Right to Try Act (Right to Try Act) was enacted. [14] From May 2018 terminally ill patients could now legally access experimental treatments without needing to navigate the obstacles posed by the Food and Drug Association (FDA). These would still be subjected to certain conditions and in certain circumstances more relaxed conditions aim to allow easier access. While legislative restrictions are present to safeguard patients against the use of medications and treatments that could potentially be dangerous, the purpose of the Right to Try Act is to help those who have exhausted their medical remedies in terms of available health care and effective treatments.

The Right to Try Act is very similar to the expanded access program[15] that is also available in the United States, which entails providing a more efficient process for terminally ill patients to access experimental drugs. There have been various movements towards affording terminally ill patients the right to choose, especially after end-of-life decisions which lead to rather intense ethical debates and ultimately led to affording patients the right to access experimental treatment. Just a terminally ill patients, through a lack of options, would want to end suffering by opting for voluntary termination of life, these patients should have alternative - and well regulated - options to end suffering. These options are similarly founded on principles of human dignity and freedom of choice when it comes to one's own body. These human rights are protected and promoted in numerous countries, even if the medical result is substantially unimpressive, but is still respecting a patient's right to life.

[12] 61 of 2003.

[13] 101 of 1965.

[14] Public Law 115-176

[15] FDA 'Expanded Access' available at *https://www.fda.gov/news-events/public-health-focus/expanded-access* accessed on 25 May 2020.

Although the United States has been quite progressive in this regard, they were also heavily criticised by some authors, especially with regards to the regulation of experimental treatments. Defining who constitutes an eligible patient could provide more clarity when considering who is entitled to access any controversial and experimental treatment. However, with most potential stem cell therapies still in their experimental phases, regulation under any right to try legislation is the only regulated option to provide safe access to such unregistered medication. A statutory framework that incorporates some of the provisions of the FDA and the Right to Try Act in this regard is necessary in view of the increase in patients seeking access to unregistered stem cell therapies.

While the South African Constitution[16] provides for the right to access to health care, there is no mention of whether this right is broad enough to include experimental treatment, as opposed to the US Right to Try Act that clearly provides the right to have access to try experimental treatments. Sections 11 and 71 of the NHA make provision for experimental treatment, but only to the extent that it broadly states that experimental treatment may be made available (with written consent) to both adults and minors in a prescribed manner and subject to the regulations generally applicable to health research which means that, in South Africa, patients will only be able to access experimental stem cell therapies as a participant in a clinical trial. These sections further determine that prior authorisation must be obtained from the patient, his or her healthcare provider, the head of the healthcare establishment, the research ethics committee, and any other person to whom this authority has been delegated.[17]

After considering our current legislation, in light of the constant developments surrounding potential stem cell treatment, it still remains evident that we lack relevant laws that are able to adequately govern or provide access to experimental stem cell treatments. In these circumstances, this dissertation will analyse existing laws enacted in other countries, specifically the United States, to ascertain whether these laws can provide some beneficial regulatory insights for the South African context.

[16] The Constitution of South Africa, 1996.

[17] Section 11 of the National Health Act 61 of 2003.

1.2 RATIONALE AND RESEARCH QUESTIONS

With the introduction and spread of novel diseases, medical technology and health research are necessitated to develop and progress at a rapid pace. Medical research involves the analyses and investigation of the use of experimental treatments or therapies to determine how safe and effective they are in combating diseases. Ideally, the benefits should outweigh the side effects, however in a scenario where a terminally ill patient or a patient suffering from chronic illness is unable to benefit from existing approved treatment, the provision of access to experimental treatments seems to be a necessary and logical next step.[18] It may even be argued that there is a legal and ethical duty on the state to ensure that patients have access to experimental therapies that are properly regulated.

Current clinical experiments with stem cells holds great potential for the treatment of various previously untreatable or uncurable diseases and may therefore constitute promising innovative and scientific medical development. Stem cells have been called everything from cure-alls to miracle treatments.[19] There is, however, concerns about the safety, efficacy, and long-term consequences of experimental stem cell treatments. Furthermore, most regulatory authorities, such as the South African Health Products Regulatory Authority (SAHPRA), who is tasked with the investigation and registration of medicine in terms of existing legislation, will only register clinically proven medicine. However, section 21 of the MRSCA does state that the SAHPRA may authorise the sale of unregistered medicine for certain purposes. [20]

Albeit a daunting task, the United States has been quite proactive in constantly being able to somehow govern the evolution of experimental treatment. According to medical historians, the modern version of controlled clinical trials is mainly an American invention as statistically based clinical trials became a critically important part of evidence-based medicine in the United States.[21]

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[18] Emergency access was authorised by SAHPRA, during the COVID pandemic, to the medicine Ivermectin which was only registered for use in animals and not humans.

[19] U.S Food and Drug Administration 'https://www.fda.gov/consumers/consumer-updates/fda-warns-about-stem-cell-therapies' available at *https://www.fda.gov/consumers/consumer-updates/fda-warns-about-stem-cell-therapies,* accessed on 11 July 2021.

[20] Vikki A. Entwistle et al 'Supporting Patient Autonomy: The Importance of Clinician-patient Relationships' available at *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2881979/*, accessed on 11 July 2021.

[21] U.S Food and Drug Administration 'FDA and Clinical Drug Trials: A Short History' available at *https://www.fda.gov/media/110437/download*, accessed on 11 July 2021.

In South Africa, the MRSCA acts as the decisive authority when it comes to accessing experimental treatment. With stem cell therapy being investigated as a possible 'cure' for HIV-1, South African citizens may benefit greatly from a legal framework that adequately regulates stem cell treatments and allow access to some of these experimental therapies.[22] Given the prevalence of this disease in South Africa, it could be argued that affording access to experimental treatment may be more beneficial than not.

In this context, the research questions that will be addressed in this dissertation are: 1) what is the existing regulatory framework within which possible access to unregistered stem cell therapies are readily available in South African? 2) considering the current clinical developments in respect of stem cell research and potential therapies, will the benefits of stem cell therapies greatly outweigh the risks to require any changes to the existing regulatory framework justifiable? 3) what can South Africa learn from the access to experimental medicine regulatory framework of the United States and what recommendations can be made to develop experimental access to stem cell therapies in the South African context?

1.3 RESEARCH OUTLINE

Chapter 1 is an introductory chapter. The need for proper regulation of important medical advancements such as stem cell therapies and access to experimental therapies in this regard is discussed. More specifically, access to unproven stem cell therapies are considered.

The sources of stem cells, the classification, potency, and differentiation are discussed in Chapter 2. To inform regulatory instruments, a good grasp of the medical terms and technologies associated with stem cell research and treatments are necessary. A discussion of how and when stem cells are applied as therapy is important in order to understand why this specific treatment should be regulated.

Chapter 3 will be a discussion of how stem cell therapies are currently regulated in South Africa. Aside from outlining the laws and regulations that govern this treatment, the effect and consequences of a vaguely regulated therapy will be discussed.

Chapter 4 will investigate how access to unregistered or yet unapproved stem cell therapies are regulated in other countries, with specific focus on the Right to Try Act of the United States. The expanded access program will also be discussed as part of my argument that

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[22] EurekAlert 'Formula predicts ideal dose of stem cells to cure HIV' available at *https://www.eurekalert.org/pub_releases/2021-01/e-fpi011221.php*, accessed on 12 July 2021.

South Africa needs a legal framework to allow for compassionate use of experimental medication and treatment within the context of stem cell therapies. Ethical considerations include issues such as the autonomy and dignity of patient, their rights to choose medical treatment and the duty of medical practitioners in life and death situations. Guidelines as drafted by the International Society for Stem Cell Research will also be analysed under this chapter.

In the concluding chapter, a discussion will outline whether South Africa needs regulation that would allow access to experimental stem cell therapies, including recommendations that are informed by the research and analytical results made in this dissertation.

1.4 LITERATURE REVIEW

Below, I briefly review both South African legislation, as well as the Right to Try Act To determine the current extent of the regulatory framework that governs possible access to experimental medicines.

1.4.1 Primary Sources

The South African Constitution,[23] is the supreme law of the Republic of South Africa and to that effect, any legislation that contradicts its provisions may be declared unconstitutional and subsequently invalid. The Constitution also embodies a broad spectrum of basic human rights that are based on the United Nations Declaration of Human Rights.[24] Human rights deserve diligent constitutional protection and with the development of a possible new legal framework that seeks to govern experimental treatment which will directly impact human beings, the impact of such developments on rights contained in the Bill of Rights will be discussed.

Section 27 of the Constitution, the right to access health care services, does not elaborate on the type of health care services that a person may access in terms of this provision. One could then, seemingly, propose that given the broad nature of this provision, a patient should also be entitled to access experimental treatment in certain carefully regulated circumstances. This argument may be supported by a patient's innate right to life, coupled

[23] Constitution of the Republic of South Africa, 1996.

[24] United Nations 'Universal Declaration of Human Rights' available at *https://www.un.org/en/about-us/universal-declaration-of-human-rights*, accessed on 11 July 2021.

with ethical principles allowing a patient to make autonomous decisions pertaining to his or her own body. Section 27 specifically mentions "access" as a prominent term. Accordingly, having access to treatment is a fundamental right. This does not imply that the treatment must be successful. Individuals suffering from debilitating diseases must be safeguarded by the Constitution as detailed in national legislation, and if allowing access to experimental medicine is one way of doing so the law must be expanded to allow for such.

The right to life as provided for in section 11 of the Constitution should therefore also be considered in extreme circumstances where a dying patient has no other options but to access treatment that is still under clinical investigation and not yet been legally registered. As O'Regan J in the case of *S v Makwanyane*[25] acknowledged, the right to life as protected in the Constitution is the right to a human life and not the right to life as 'mere organic matter'. Therefore, the right to dignity primarily informs the content of the right to life.[26] Patient autonomy is similarly an equally important factor when considering whether access should be granted to experimental treatments such as stem cell therapies.[27] This patient autonomy may be offset by the State's legislative or paternal tendency to protect patients from medicines or treatments that may causing more harm than good. Laws, post implementation of the United Declaration of Human Rights, are enacted to protect people against harm. Whether this harm is inflicted by the State or by other people is irrelevant under these circumstances. One could then potentially argue that the State has an obligation to enact laws that allow access to experimental stem cell therapy that, based on the same argument, also prevent harm to those for whom no effective, or approved or registered medicines or treatments are legally available.

Proposing a framework to allow access to experimental stem cell therapy means that consideration must be given to other provisions contained in the Bill of Rights as well.[28] The right to human dignity and bodily integrity highlights the fact that the possible benefits that can be derived from stem cell therapy, in the context of a terminally ill patient, should ultimately outweigh any need by the State to prohibit access via strict regulations. The right to access to healthcare can only be realised within the parameters of the State's available

[25] *S* v *Makwanyane and Another* 1995 (3) SA 391.

[26] Ibid at para 330.

[27] S Mahomed, M Nöthling Slabbert 'Stem cell tourism in South Africa' (2012) 5 SAJBL at 42.

[28] Chapter 2 of Constitution of the Republic of South Africa, 1996.

resources. This situation was confirmed in the *Soobramoney* case[29] where the court denied Soobramoney renal dialysis via State resources due to his various co-morbidities and the fact that the court was slow to interfere with the practical management of scarce State resources by medical practitioners who are faced with these shortages on a daily basis and the burden of making life changing decisions despite thereof.[30]

The majority of stem cell therapies are still stuck in various stages of experimental phases. The safety and efficacy of these ground-breaking therapies are not yet proven to enable it to be registered and regulated as a medicine or medical treatment. By enacting regulations to allow access to these types of therapies after specific minimum safety standards have been established will open medical therapeutic options to many patients who previously had none.

The Clinical Trial Unit of the SAHPRA provides a legal framework for the review of clinical trials.[31] Considering these guidelines, the lengthy process outlined therein does not ideally benefit a patient who is terminally ill and who has exhausted all legally available medicines and treatments. Guidelines such as those provided under the 2006 Department of Health's Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants do provide some insight into the clinical trial process, however there are no guidelines in respect of accessing experimental medicines of treatments like stem cell therapies. The completion of successful clinical trials is lengthy, and the registration process can be equally slow. With the need to access Ivermectin for human use during the COVID-19 pandemic, the SAHPRA allowed such access in terms of section 21 of the MRSCA and authorized the emergency use of Ivermectin based on compassionate use. However, Ivermectin remains only legally approved as registered for use in animals. While this authorized emergency access and use is welcomed, the issued access guidelines still impose a lengthy, rigid process on medical professionals who seek to use the drug to help those infected with the COVID-19 virus.[32]

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[29] *Soobramoney* v *Minister of Health (Kwazulu-Natal)* 1998 (1) SA 765 (CC).

[30] Supra note 29.

[31] SAHPRA 'Clinical Trials' available at *https://www.sahpra.org.za/clinical-trials/* accessed on 06 June 2021.

[32] TrialSiteNews 'SAHPRA's Article 21 Process too Lengthy: Activist Group Makes More Court Moves to Access Ivermectin Faster for COVID-19 Patients in South Africa' available at *https://trialsitenews.com/sahpras-article-21-process-too-lengthy-activist-group-makes-more-court-moves-to-access-ivermectin-faster-for-covid-19-patients-in-south-africa/*, accessed on 12 July 2021.

The SAHPRA, formally known as the Medicines Control Council, functions as the regulatory body that is responsible for the registration of clinically approved medicine and medical devices. This body is bound by the regulations as prescribed under the MRSCA. The Health Professions Council of South Africa (HPCSA) and (previous) Medicines Control Council (MCC) have approved guidelines to regulate the good practice of healthcare professionals and researchers. These guidelines are designed to protect patients and research subjects, and to regulate the registration of medicines, including biological medicines, and more recently medical devices.[33] International guidelines also protect the rights of patients which is why we must take the Guidelines for the Clinical Translation of Stem Cells as provided by the International Society for Stem Cell Research (ISSCR) into account.[34] Recommendation 3.5.4 of the abovementioned guidelines stipulates that pre-approval access to experimental stem cell-based interventions should be limited to well-structured and regulated programs that require prior authorisation from national regulators. It is therefore clear, that these experimental treatments will be permitted if afforded and approved through an expanded access program. In turn, one must consider whether right to try laws in the United States also incorporates some of these international guidelines.

On 30 May 2018 President Trump signed the Right to Try bill into law in the US.[35] This law permits patients to access experimental or investigational drugs outside of clinical trials. These drugs are not FDA approved and could patients previously, with life threatening ailments who have exhausted lawfully available medical treatments, not access experimental medicines in the absence of this law. One of the alternatives, to access experimental medicine in the absence of the Right to Try Act was to participate in a clinical trial on condition that the patient was eligible to participate as such. Ideally the treating physician and the drug company would work together to propose an ethical protocol that would be in the best interests of the eligible patient.[36]

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[33] Health Professions Council of South Africa 'Conduct and Ethics' available at *https://www.hpcsa.co.za/?contentId=79* accessed on 06 June 2020.

[34] International Society for Stem Cell Research 'Guidelines for the Field of Stem Cell Research and Regenerative Medicine' available at *https://www.isscr.org/policy/guidelines-for-stem-cell-research-and-clinical-translation* accessed on 10 June 2020.

[35] 'President Trump signs Right to Try bill into law' available at *https://pharmaceuticalcommerce.com/legal-regulatory/president-trump-signs-right-to-try-bill-into-law/*, accessed on 16 April 2020.

[36] Department of Health 'South African Good Clinical Practice: Clinical Trial Guidelines' available at *https://www.sahpra.org.za/wp-content/uploads/2021/06/SA-GCP-2020_Final.pdf*, accessed on 08 July 2021.

The Right to Try Act adds to the current regulatory framework without undermining or circumventing the authority of the FDA. There is still a reliance on the FDA process for evaluating the safety, efficacy, and dosage as clinically determined and to monitor possible side or adverse effects of the drug. The premise is that an adequately regulated process is necessary if experimental drugs are to reach patients who may not have other options. The Right to Try Act allows patients to work directly with doctors to acquire non-clinically tested drugs.[37] Except for emergency authorisation in terms of the MRSCA or participation in clinical trials allowed by the SAPRHA, South African laws do not offer alternative avenues to access stem cell treatments.

Citizens in the US, prior to the implementation of the Right to Try Act, were also able to exercise their right to access experimental stem cell treatment under an expanded access program.[38] This initiative was progressive in its own right, despite still being facilitated by the FDA. A look into how the expanded access program paved the way for the approval of the Right to Try Act[39] is necessary given the context and aim of this study.[40]

Stem cell therapy, in particular is currently regulated in South Africa[41] by the NHA and MRSCA. Developing a framework, inspired by the Right to Try Actin the US would ultimately assist in developing South African laws in the medical field. An analysis is conducted in Chapter 4 below in the context of existing regulations in South Africa and the recently enacted Right to Try Act in the US.

The United States Right to Try Act was built upon its existing expanded access regulations.[42] Through the expanded access regulations, terminally ill patients who have no

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[37] The Journal of Nuclear Medicine 'Assessment of the Right-to-Try Law: The Pros and the Cons' available at *https://jnm.snmjournals.org/content/59/10/1492*, accessed on 08 July 2021.

[38] Yale Journal of Health Policy, Law and Ethics 'Early Access to Unapproved Medicines in the United States and France' available at *https://digitalcommons.law.yale.edu/cgi/viewcontent.cgi?article=1270&context=yjhple*, accessed on 08 July 2021.

[39] Lexology 'Passage of Federal Right-to-Try law poses risks and opportunities for patients and the biopharmaceutical industry' available at *https://www.lexology.com/library/detail.aspx?g=66c4841b-46e3-4847-be57-6c82fa5162fa*, accessed on 10 July 2021.

[40] US Food and Drug Administration 'Right to Try' available at *https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/right-try* accessed on 19 June 2021.

[41] Botes WM et al Stem Cell Processing: Clinical Safety and Regulations (2015) 5

[42] 'Expanded access' available at *https://www.fda.gov/news-events/public-health-focus/expanded-access*, accessed on 29 April 2020.

other option in terms of accessing investigational drugs through clinical trials may submit applications together with their doctor to the FDA to request access to stem cell therapy.[43] Even though terminally ill patients in South Africa are able to access unregistered medicines through the emergency use procedure as provided for in section 21 of the MRSCA, South African laws do not allow access outside this context. Without these flexible access laws, South Africans not only run the risk of being denied the benefits of cutting-edge research but the potential exists that they could be exposed to unethical practices and financial exploitation.[44]

1.4.2 Secondary Sources

Given the controversial nature of experimental novel advances therapies such as stem cell therapies, it is critical to also consider the advantages, disadvantages and ethical considerations to inform any argument for or against the allowance of any access to experimental stem cell therapies.

Coughlin et al,[45] provide an objective view on the implementation of the Right to Try Act with specific reference to regenerative medicine. Overall it sounds almost heroic to propose that a simple change in legislation could help thousands of terminally ill patients. The promise of effective treatment that is adequately regulated surely does sound too good to be true. To that effect, an analysis of the Right to Try Act with a critical lens is necessary.

According to White,[46] we must be extremely cautious when imposing laws that could spark up various authentic ethical debates. Consideration must be given to the numerous ethical concerns that would follow the proper regulation of stem cell therapies. The ethical debates need not have a conclusive solution, however, stem cell therapy must and should benefit the masses or must serve a greater good.

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[43] S Levy 'Right to try vs Expanded access; Whats the difference?', available at *https://www.pancan.org/news/right-to-try-vs-expanded-access-whats-the-difference/*, accessed on 02 April 2020.

[44] Pepper M S 'The stem cell regulatory environment in South Africa: cause for concern' (2009) 99 *SAMJ* at 7.

[45] Christine Coughlin, Nancy M.P. King & Melissa McKinney 'Regenerative Medicine and the Right to Try' (2018) 18 *Wake Forest Journal of Business & Intellectual Property Law* 590.

[46] Mercatus Centre, George Mason University 'The Ethical Issues Behind Expanding the Right to Try Preapproval Drugs and Medical Devices' available at *https://www.mercatus.org/publications/technology-and-innovation/ethical-issues-behind-expanding-right-try-preapproval-drugs* accessed on 15 June 2020.

Pepper[47] intuitively yet succinctly highlights the concerns surrounding unproven stem cell therapy. Before imposing legal provisions to govern this medical advancement, a thorough understanding of how stem cell therapy works and is applied are important. This must include a consideration of how effective this therapy has been over numerous years of its application.

Informed consent, which is critical to exercise patient autonomy and provided for in the NHA must be viewed critically considering that the nature of experimental therapies makes it almost impossible to provide any patient with sufficient information regarding the risks and consequences of the treatment to enable the patient to provide legal and ethical informed consent. If the research conducted is a long-term study, once-off consent will not necessarily constitute consent for the duration of the entire study. When new information is disclosed to the patient, he or she may change their mind and opt to rather withdraw consent.[48]

The Right to Try Act has been viewed by other jurisdictions as progressive. Although unsuccessful, England and Wales attempted to introduce similar access laws in terms of the Medical Innovation Bill (MIB) inspired by the US Right to Try Act. The Right to Try Act and the MIB seek to address the same problem but from different starting points. The MIB, if implemented, would loosen the shackles that fear of the law placed on medical professionals. With the Right to Try Act, the starting point was based on the view that limited governance was to be encouraged, and that it is the right of individuals rather than government to determine what treatments they should be able to access.[49]

1.5 RESEARCH DESIGN AND METHODS

To compare the existing regulatory framework that provide access to experimental stem cell treatments, a quantitative desktop literature review and analysis has been done. This involved the collection of information from both primary and secondary sources referred to above, including additional literary resources. Considering that this is a fairly novel area of study in South Africa specifically, there is no directly related case law. There is, however, a plethora of secondary sources available, critically analysing the current position. A reasonable portion of this study will consist of legal comparisons of different jurisdictions, with specific focus on

[47] Pepper, M 'Cell-based therapy – navigating troubled waters' (2010) 100 *SAMJ* 5.

[48] Britz Retha, Le Roux Kemp Andra 'Voluntary informed consent and good clinical practice for clinical research in South Africa: Ethical and legal perspectives' (2012) 102 (9) *South African Medical Journal* 747.

[49] Jose Miola & Bernadette J. Richards 'Would We Be Right to Try "Right to Try"?' (2021) 107 (31) *Health Matrix* 114.

the recently enacted Right to Try Act in the United States. Given the current and urgent need for vaccines to treat pandemics, a brief look at the laws governing experimental medication in the US become relevant to this study. A further critical analysis has been done of the ethical concerns that surrounded the implementation of laws that permit the use of unregulated and otherwise inaccessible stem cell therapy.

CHAPTER TWO: STEM CELL TECHNOLOGY

2.1 INTRODUCTION

Stem cell therapy is considered as being both groundbreaking and controversial. There are various factors that may contribute to this form of treatment being viewed in this manner. As we evolve, there is a strong need to prolong human life and even though stem cell therapy is ultimately still an experimental medical treatment, researchers, through various techniques and trials conducted over recent years, are able to prove that the benefits are significant to a terminally ill person who has exhausted numerous regulated treatments. Disease is rampant and manifests in various forms. Given the number of available medical technologies and advancements we are able to diagnose and discover more in terms of the types of diseases and illnesses that currently affect the human race.

Whether derived from human embryos or adult tissues, stems cells have the ability to divide for an indefinite period, making them special cells which can give rise to various other specialised cell types. This unique ability is termed developmental plasticity. Interestingly enough, developmental plasticity is a common feature of embryonic cells which is what makes them so valuable in the field of regenerative medicine.[50] The ethical concerns surrounding the use of embryonic stem cells will be briefly discussed further on in this study.

Stem cells offer so much hope for radical advances in medicine. Before we can delve into the different types of cells and their applications, it's important that a background is provided into exactly how this revolutionary therapy came to be.

2.2 A BRIEF HISTORY

In 1981 scientist's Martin Evans and Matt Kaufmann were the first to identify embryonic stem cells in mice.[51]This discovery paved the way for other scientists like Ian Wilmut and his colleagues to create the first animal clone, Dolly the sheep. In 1998, James Thomson and John Gearhart were able to isolate embryonic stem cells from human beings and cultivate them in a lab.[52] This specific development can be documented as a turning point in the medical field in

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[50] Joseph Panno *Stem Cell Research: Medical Applications and Ethical Controversy* (2005) 1.

[51] Lyle Armstrong, Majlinda Lako, Noel Buckley, Terry R.J. Lappin, Martin J. Murphy, Jan A. Nolta, Mark Pittenger, Miodrag Stojkovic 'Our Top 10 Developments in Stem Cell Biology over the Last 30 Years' available at *https://doi.org/10.1002/stem.1007* accessed on 31 January 2021.

[52] Andy Coghlan 'Stem cell timeline: The history of a medical sensation' available at *https://www.newscientist.com/article/dn24970-stem-cell-timeline-the-history-of-a-medical-sensation/#ixzz6YstzJQWW* accessed, on 12 August 2020.

that these cells could now possibly be used to treat various ailments and diseases in human beings. Concerns, specifically from an ethical standpoint, arose around the fact that embryos were ultimately being destroyed and discarded through the stem cell harvesting process. This then prompted a researcher by the name of Shinya Yamanka to identify conditions that would allow some specialised adult cells to be "reprogrammed" genetically to adopt a stem cell-like state. This new type of stem cell is now known as induced pluripotent stem cells.[53] This scientific breakthrough avoids the need to destroy or discard embryos and in turn will address the ethical concerns highlighted above.

Moving forward to present day we see that through various studies, the use and implementation of stem cell therapy yields promising results especially with specific diseases like diabetes.[54] There have been numerous human trials to prove its effectiveness in treating a wide range of ailments ranging from age related blindness to spinal injuries.[55]

In order to understand the far-reaching benefits of stem cell therapy and its potential in the medical field, we must understand more about what they actually are. Understanding its application in the medical field will in turn make it easier to understand why regulation is necessary and why certain ethical concerns persist.

2.3 CLASSIFICATION OF STEM CELLS

This classification is mainly based on its origin as opposed to its differentiation potential. All stem cells, depending on their differentiation potential, can be classified, into five groups: a) toti- (omni-); b) pluri-; c) multi-; d) oligo-; and e) unipotent.[56] Cell differentiation is the process through which a cell undergoes changes in gene expression to become a specified type

[53] University of Nebraska Medical Centre 'History of Stem Cell Use' available at *https://www.unmc.edu/stemcells/educational-resources/history.html#:~:text=Scientists%20discovered%20ways%20to%20derive,30%20years%20ago%2C%20in%201981.&text=These%20cells%20are%20called%20human,through%20in%20vitro%20fertilization%20procedures,* accessed on 15 August 2020.

[54] Madsen, O.D. 'Stem cells and diabetes treatment' available *at https://doi.org/10.1111/j.1600-0463.2005.apm_418.x* accessed on 02 April 2021.

[55] Alan Trounson, Courtney McDonald 'Stem Cell Therapies in Clinical Trials: Progress and Challenges' available at *https://doi.org/10.1016/j.stem.2015.06.007* accessed on 02 April 2021.

[56] Dusko Ilic, Julia M. Polak 'Stem cells in regenerative medicine: introduction' available at *https://doi.org/10.1093/bmb/ldr012* accessed on 02 April 2021.

of cell.[57] An in depth study of cell biology is not necessary for the purposes of this dissertation as this work mainly focusses on the legal and ethical aspects of accessing these therapies.

2.3.1 Embryonic Stem Cells

A fertilised egg is often regarded as the ultimate stem cell because it can give rise to an entire organism consisting of hundreds of different kinds of cells. Embryonic cells, including and up to the first couple of cell divisions after fertilisation, are the only cells that are totipotent.[58] Totipotent stem cells have the potential to develop into any cell found in the human body and this is why these cells are considered as one of the most important stem cells in regenerative medicine. Totipotent cells are therefore perfect for cell and gene therapy. Further application can be found in tissue engineering for transplants and replacement of diseased cells.[59]

Embryonic stem cells, derived from the inner mass of cells known as the blastocyst, which is created 5 to 6 days post fertilisation, are regarded as pluripotent. They have the capacity to grow for an indefinite period while maintaining pluripotency (the ability to produce any cells the body needs to repair itself).[60]

Pluripotent stem cells are exceptional laboratory models which aid scientists in understanding how specific diseases develop and then in locating and tracking the earliest disease-causing actions in cells. Pluripotent stem cells could be modified to provide a perfect genetic match for any patient. Because these types of cells can potentially be modified to provide a perfect genetic match for any patient, the possibility exists that a patient could get transplants of tissue and cells without matching tissue and subsequently suffer tissue rejection.[61] Immune suppressing drugs to treat various diseases, specifically auto immune

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[57] Ibid.

[58] Joseph Panno op cit note 26 at 5.

[59] Isabella Murray 'Totipotent Stem Cells' available at *http://www.explorestemcells.co.uk/totipotentstemcells.html#:~:text=Totipotent%20stem%20cells%20are%20one,found%20in%20the%20human%20body.&text=The%20zygote%20from%20that%20fusion,forming%20the%20entire%20human%20body* accessed on 15 August 2020.

[60] University of Nebraska Medical Centre 'What are stem cells?' available at *https://www.unmc.edu/stemcells/stemcells/* accessed on 15 August 2020.

[61] Boston Childrens Hospital 'Why are Pluripotent Stem Cells Important?' available at *http://stemcell.childrenshospital.org/about-stem-cells/pluripotent-stem-cells-101/why-are-pluripotent-stem-cells-important/* accessed on 24 August 2020.

diseases, could be a thing of the past if scientists and researchers can move stem cell therapy successfully out of the experimental phase and into clinical treatment facilities.[62]

Stem cells obtained from the embryos of terminated pregnancies are referred to as foetal stem cells and will not be discussed any further than this as they are not as potent as embryonic stem cells, even though they may be considered as less controversial in countries like South Africa where the termination of a pregnancy in certain circumstances is permissible. They are unable to divide indefinitely in cell culture without some coercion. This intervention is dependent on how each country is able to regulate this.[63] It is necessary to note here that the regulation of foetal tissue in South Africa is currently governed by Chapter 8 of the NHA.

2.3.2 Adult Stem Cells

Adult stem cells are undifferentiated cells found throughout the body such as in bone marrow or the brain. Known as somatic stem cells they possess the ability to renew indefinitely and can regenerate an entire organ from a few cells. They can be found in children as well as in adults.[64] This makes them more accessible. Various studies suggest that some of these stem cells are multipotent.[65] Although adult stem cells are considered as difficult to identify, purify as they are to maintain in an undifferentiated state, they hold distinct advantages for all patients due to the fact that the production of an adult stem cell does not require the destruction of an embryo.[66] There are numerous trials which suggest potential cardiovascular benefits from bone marrow-derived adult stem cells.[67] There have also been striking results reported using these cells to treat neurological conditions like chronic stroke, and positive outcomes have been noted for diseases like multiple sclerosis and diabetes.[68] Adult stem cells are considered as the

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[62] Ibid.

[63] Dusko Ilic, Julia M. Polak 'Stem cells in regenerative medicine: introduction' available at https://doi.org/10.1093/bmb/ldr012 accessed on 02 April 2021.

[64] Science Daily 'Adult Stem Cells' available at *https://www.sciencedaily.com/terms/adult_stem_cell.htm* accessed on 24 August 2020.

[65] Committee on the Biological and Biomedical Applications of Stem Cell Research & Commission on Life Sciences National Research Council *Stem cells and the future of regenerative medicine* (2002) 16.

[66] David A. Prentice 'Adult Stem Cells: Successful Standard for Regenerative Medicine' (2019) 124 *AHA Journals* 837.

[67] Jeevanantham V, Afzal MR, Zuba-Surma EK, Dawn B. 'Clinical trials of cardiac repair with adult bone marrow- derived cells' available at *doi:10.1007/978-1-62703-511-8_15* accessed on 24 August 2020.

[68] David A. Prentice 'Adult Stem Cells: Successful Standard for Regenerative Medicine' (2019) 124 AHA Journals 839.

gold standard when it comes to clinical applications and are currently being tested for a growing number of conditions, including the COVID-19 virus.[69] A patient may even, under certain circumstances, opt to use stem cells from their own body. This is called autologous stem cell therapy and is particularly useful in instances where the patient's blood cells are destroyed by high doses of chemotherapy and other treatments.[70]

2.3.2 Perinatal stem cells

Perinatal stem cells can be sourced from 3 specific biological areas: from amniotic fluid; the placenta; and the umbilical cord. Cord blood banking is a popular and flourishing business, and on a global scale attracts parents by promising a cure to various diseases, specifically for their children.[71] Stem cells from cord blood can be used to treat hematopoietic system disorders as they represent a rich source of hematopoietic stem cells which are able to restore the blood system after disease or even chemotherapy.[72] A practical problem that is presented comes from the fact that there are a very limited number of stem cells that may be present in the single sample of umbilical cord blood taken after birth. In a new clinical trial, researchers will use a small molecule called UM171 to multiply cord blood samples.[73] Multiplying a sample will increase treatment opportunities. This in turn will afford families the freedom to make the most from a single sampled of umbilical cord blood. While cord blood banking is currently regulated in terms of the NHA[74], any isolated stem cells and their application in the medical field is still vaguely regulated. Regulation of and access to experimental stem cell therapies, especially those still involved in ongoing clinical trials, is necessary to enable parents to access experimental stem cell therapies for their terminally ill children.

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[69] Ibid.

[70] Leukemia and Lymphoma Society 'Stem cell transplantation' available at *https://www.lls.org/treatment/types-treatment/stem-cell-transplantation* accessed on 10 December 2021.

[71] Chima Sylvester C, Mamdoo Fahmida 'Ethical and regulatory issues surrounding umbilical cord blood banking in South Africa' (2011) 4 *SAJBL* 79.

[72] Parent's Guide to Cord Blood Foundation 'Umbilical Cord Blood Stem Cell Scams: They're pulling your cord' available at *https://parentsguidecordblood.org/en/news/umbilical-cord-blood-stem-cell-scams-theyre-pulling-your-cord* accessed on 30 August 2020.

[73]Cells4life 'Making cord blood go further – stem cell expansion' available at https://cells4life.com/2018/08/making-cord-blood-go-stem-cell-expansion/ accessed on 30 August 2020.

[74] Section 8 of the National Health Act of 2003.

2.3.3 Induced Pluripotent Stem Cells

As mentioned above, researchers are now able to genetically reprogramme adult stem cells to assume an embryonic stem cell like state.[75] Since then researchers have improved the techniques used to generate induced pluripotent stem cells which in turn has created a powerful and innovative way to "de-differentiate" cells.[76] These cells are an extremely valuable resource as they can be harvested from a healthy person and used in regenerative medicine to replace or replenish diseased and damaged tissues.[77] Induced pluripotent stem cells are derived from a wide variety of cell types and differentiates into an equally broad range of cell types involved in cardio-vascular, haematological, metabolic, neurological, pancreatic and hepatic conditions.[78]

2.4 REGENERATIVE MEDICINE

The most recent branch of medical science deals with the functional restoration of tissues or organs. This is classified as regenerative medicine and are there numerous studies which demonstrate benefits for patients who may be suffering from severe injuries and more specifically chronic and incurable diseases.[79] Rapid progress within the field of stem cell research provides the foundation for cell-based therapies for diseases which generally cannot be cured by regulated or conventional medicines and treatments. The stem cell's ability to differentiate into other types of cells and self-renew makes stem cell therapy the fore runner when it comes to regenerative medicine.[80]

Neurological disorders, such as Parkinson's disease, amyotrophic lateral sclerosis, Huntington's disease and strokes, are considered to be chronic diseases and are often life threatening. Human pluripotent stem cell-based therapies have been shown to provide

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[75] University of Nebraska Medical Centre 'History of Stem Cell Use' available at *https://www.unmc.edu/stemcells/educational-resources/history.html* accessed on 25 August 2020.

[76] Ye, L., Swingen, C., & Zhang, J 'Induced pluripotent stem cells and their potential for basic and clinical sciences' (2013) 9 *Current cardiology reviews* 63.

[77] Stem cell research and therapy 'Research and therapy with induced pluripotent stem cells (iPSCs): social, legal, and ethical considerations' available at *https://stemcellres.biomedcentral.com/articles/10.1186/s13287-019-1455-y* accessed on 30 August 2020.

[78] Park IH, Arora N, Huo H, et al 'Disease-specific induced pluripotent stem cells' available at *http://dx.doi.org/10.1016/j.cell.2008.07.041* accessed on 30 August 2020.

[79] Trounson, A., Thakar, R.G., Lomax, G. et al. 'Clinical trials for stem cell therapies' (2011) 9 *BMC Med* 52.

[80] Ranjeet Singh Mahla 'Stem Cells Applications in Regenerative Medicine and Disease Therapeutics' available at *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4969512/* accessed on 30 August 2020.

symptomatic relief.[81] This in itself is considered as being a huge step forward as there are currently no known cures for the abovementioned diseases[82].

Haematological diseases like leukaemia, anaemia, multiple myeloma, lymphomas and melanomas are also considered to be life threatening. Hematopoietic stem cells, which are stem cells that give rise to other blood cells, has been proved to be the most successful application of stem cell therapy. Compared to conventional hemotherapy, stem cell-based therapy presents a more effective and less toxic way of treating these diseases.[83]

Heart failure results from different reasons including chronic cardiac disorders and myocardial infarction. Cardiomyocytes (cells that make up the heart muscle/cardiac muscle) in adult mammals have very limited distinctive ability to renew. This makes it very challenging for the heart to recover after injury.[84] Although conventional treatments like interventions and transplantation are successful, there are various limitations to these treatments. Stem cell therapy for heart disease has received great attention with the hope of rescuing patients after heart failure.[85]

End-stage liver diseases such as hepatic cirrhosis, viral hepatitis and hepatic carcinoma may cause irreversible damage.[86] A liver transplant is currently the only effective treatment. There are however numerous obstacles in achieving this form of treatment. Often there is a lack of organ donors and even if there is a donor available, there could be issues with rejection of the organ which is ultimately related to immune compatibility.[87] Stem cells are a promising alternative treatment method for liver diseases. Recently, studies have demonstrated that

[81] University of Sydney 'First treatment for pain using human stem cells a success' available at *www.sciencedaily.com/releases/2020/01/200123152507.htm* accessed on 02 April 2021.

[82] Harvard Stem Cell Institute 'Parkinsons Disease' available at *https://hsci.harvard.edu/parkinsons-disease-0 accessed* on 05 September 2020.

[83] NCBI 'Progress and prospects in stem cell therapy' available at *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3674518/* accessed on 05 September 2020.

[84] Kikuchi, K., & Poss, K. D. 'Cardiac regenerative capacity and mechanisms' (2012) 28 *Annual review of cell and developmental biology* 720.

[85] Michler R. E. 'Stem cell therapy for heart failure' (2013) 9(4) *Methodist DeBakey cardiovascular journal* 187.

[86] Rai, Rakesh 'Liver transplantation- an overview' (2013) 75.3 *The Indian journal of surgery* 187.

[87] Ibid at 189.

human embryonic stem cells can be efficiently differentiated into functional hepatocytes (which make up a large percentage of the liver's mass) both in vitro and in vivo[88].

With the exception of bone marrow transplants, the majority of applications in regenerative medicine are mostly still in experimental stages. Although there seems to be enough data to show success within this field, especially with the use of stem cells, unknown factors that relate to long terms consequences, treatment potential and biological reaction, still brand stem cell therapies as experimental.[89]

Newer research now suggests that stem cells may be used to treat infertility, may have a positive impact on Multiple Sclerosis[90] and may even be useful in treating COVID-19 patients.[91] While we still await clinical proof that stem cell therapy is sufficiently safe, effective and reliable enough to be registered as a legal medicine or treatment, access to these treatments may either remain unavailable or new legal ways to access them must be created.

2.5 CONCLUSION

In trying to understand the need for stem cell therapy, it is important to understand the various sources and its application in the medical field. The rapid rate of progression in terms of stem cell therapy research prompts a discussion surrounding its regulation. Various countries have found the need to regulate this treatment, and more often than not, terminally ill patients are willing to try experimental treatments.

South Africa currently regulates this type of therapy under various pieces of legislation, however the regulation of access to experimental stem cell therapies are not provided for. By allowing patients access to experimental treatments like stem cell therapies, we will be providing a legal and ethical way to safely access such therapies as opposed to accessing such therapies on the black market in the absence of any regulation of safeguards.

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[88] Wen-Li Zhou, Claire N Medine and David C Hay 'Stem cell differentiation and human liver disease' (2012) 17 *World Journal Gastroenterology* 2018.

[89] J.-F. Stoltz, N. de Isla, Y. P. Li, D. Bensoussan, L. Zhang, C. Huselstein, Y. Chen, V. Decot, J. Magdalou, N. Li, L. Reppel, Y. He, 'Stem Cells and Regenerative Medicine: Myth or Reality of the 21th Century' 2015 *Stem Cells International* 2.

[90] Louis A. Cona 'Louis A. Cona' available at *https://www.dvcstem.com/post/stem-cell-therapy-for-ms* accessed on 30 May 2021.

[91] Choudhery MS, Harris DT 'Stem cell therapy for COVID-19: Possibilities and challenges' (2020) 44(11) *Cell Biol Int* 2182.

CHAPTER THREE: CURRENT REGULATION OF STEM CELL THERAPY IN SOUTH AFRICA

3.1 INTRODUCTION

With an ever-expanding number of diseases being diagnosed and treated on a global scale, it is necessary that cell-based therapy is recognised for its role in the successful treatment of a large portion of these illnesses. When it comes to health care, the priority in developing countries is to ensure that basic medical services are made available to the masses. Stem cell therapy is still largely considered as experimental and would therefore not be categorised as basic. In comparison to other African countries, South Africa is considered as advanced when it comes to stem cell technologies.[92] Aside from the fact that stem cell therapy is an expensive form of treatment, limited accessibility of this therapy means that fewer people are able to benefit from it. In South Africa, many resources are directed towards the testing for, treatment and management of infectious diseases such as HIV/AIDS and tuberculosis (TB), which remains the leading cause of death among HIV infected individuals in South Africa.[93] The availability of resources for the implementation of specialised therapies such as stem cell therapies therefore remain scarce. However, if stem cell therapies prove to be effective against these diseases, huge amounts of medical costs may be saved, and life quality may increase dramatically, which adds the argument for allowing access to experimental stem cell therapies.

3.2 THE CONSTITUTION OF THE REPUBLIC OF SOUTH AFRICA, 1996.

South Africa has been a democratic nation for the past 27 years.[94] Under this regime, the Constitution of the Republic of South Africa, 1996 ('the Constitution') with its progressive laws, reigned supreme. Influenced heavily by the Universal Declaration of Human Rights, other International Human Rights laws[95] and the ethical principles that form the foundation of other renound constitutions, the Constitution imposes laws that seek to uphold basic human rights and protect all those who would otherwise be considered as vulnerable. The Bill of

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[92] Jackson, C.S., Pepper, M.S. 'Opportunities and barriers to establishing a cell therapy programme in South Africa' (2013) 4 *Stem Cell Res Ther* 54.

[93] World Health Organisation 'Tuberculosis' available at *https://www.afro.who.int/health-topics/tuberculosis-tb* accessed on 26 June 2021.

[94] Wilson Centre 'South Africa at 27' available at *https://www.wilsoncenter.org/blog-post/south-africa-27* accessed on 04 June 2021.

[95] Schwelb, Egon. 'The influence of the Universal Declaration of Human Rights on international and national law' (1959) 53 *JSTOR* 217.

Human Rights contained in Chapter 2 of the Constitution grants every South African citizen certain rights and liberties.

The Constitution is the foundation upon which all other legislative provisions are analysed. For purposes of this dissertation, constitutional principles as it pertains to stem cell therapy will be closely examined. Potential stem cell therapies are still shrouded in uncertainty, especially considering that it is still regarded as experimental therapies. Once we are able to scientifically prove that stem cell therapies are safe and effective any unanswered uncertainties can be addressed. But, until then, aside from being illegal[96], the use of such therapies may also violate various Constitutional rights. On the other hand, denying an individual the right to access this treatment may equally be considered as a violation of inherent human rights. This is why a balance must be struck in order to conclusively ascertain whether it is in fact necessary to afford patients the freedom to access experimental therapies.

3.2.1 The Equality Clause

The right to equality[97] is seen as one of the most transformative basic human rights, however, its relevance when it comes to regenerative medicine may not always be obvious. Given the fact that stem cell therapy or any related therapies are still being researched on a global scale, the role of the research participant is critical. Without the participation of human subjects, it would be difficult to obtain accurate data which would indicate the true impact of stem cell therapy on a human body. Being an integral part of the study, the research participant should not be discriminated against on any of the grounds as provided for in section 9 of the Constitution, being the equality clause. The focus of this dissertation however is not on the research participant but rather on the typical health care user who would benefit from a pathway to legally access experimental therapies which is affordable not only to the rich and connected, but to every health care user in need of such therapies.

The application of the equality clause within the context of medicine determines that every person or patient must have access to and receive equal opportunities for medical treatment. This right is equally applicable to stem cell therapies. Access to stem cell therapies should ideally be readily available to a large population irrespective of socio-economic background. In regulating experimental therapy, the embodiment of the equality clause would

[96] Section 14 of the Medicines and Related Substances Control Act 101 of 1965.

[97] Section 9 of the Constitution of the Republic of South Africa, 1996.

also mean that terminally ill patients would not be discriminated against on the basis of their health status. In considering the potential for stem cell therapy to cure life-threatening diseases,[98] one could also argue that the state has a duty to make this therapy available (within its available resources) to the public especially if there are no other means of treatment, to protect and materialize people's right to life. The States obligation to afford access to healthcare within its available resources is discussed further on in this thesis.

3.2.2 The Right to Human Dignity

Currently entrenched as a right in the Constitution[99], the right to human dignity is closely linked to health care. Any decision relating to one's own body or bodily integrity must be carefully considered especially within the context of medical treatment. Any form of experimental therapy or treatment could possibly be seen as infringing actions on human dignity. Conversely, denying a patient treatment in a situation where refusal could lead to further suffering, may similarly result in an infringement of dignity. At the outset, it is important to properly understand the meaning of the term human dignity. In the case of *S v Dodo*,[100] it was stated that:

> 'Human beings are not commodities to which a price can be attached, they are creatures with inherent and intrinsic worth; they ought to be treated as ends themselves, never really as means to an end'.

Section 10 of the Constitution stipulates that, 'everyone has inherent dignity and the right to have their dignity respected and protected'. The landmark case of *S v Makwanyane,*[101] which in turn was the judgment responsible for the abolition of the death penalty in South Africa, was quite clear on the relationship between the life and human dignity. The right to life does ultimately incorporate the right to dignity. The right to life is more than existence, it is a right to be treated as a human being with dignity, because a life without dignity, is a human life that is significantly reduced. In essence, without life, there cannot be dignity.[102]

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[98] Aly RM. 'Current state of stem cell-based therapies: an overview' (2020) 7 *Stem Cell Investig 8.*

[99] Section 10 of the Constitution of the Republic of South Africa, 1996.

[100] *S* v *Dodo* 2001 (3) SA 382 (CC) at para 38.

[101] *S* v *Makwanyane and Another* 1995 (6) BCLR 665 (CC)

[102] *S* v *Makwanyane and Another* 1995 (6) BCLR 665 (CC) at para 326.

This value is also entrenched in the General Ethical Guidelines for the Health Care Professions of the HPCSA which states that health care researchers should always place the life, wellbeing, health, privacy and dignity of their research participants before all other interests. Turning to international conventions, recognition of the right to dignity can be found in the 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, otherwise known as the Oviedo Convention. It is a framework Convention aimed at protecting the dignity and identity of all human beings, with regard to the application of biology and medicine.[103] The UNESCO Universal Declaration on Bioethics and Human Rights dictates that human dignity, human rights and fundamental freedoms must be fully respected. The welfare and interests of the individual should have priority over the sole interest of science, medicine or society.

It is entirely possible to infringe upon human dignity when a patient is receiving any form of medical treatment. This includes treatment that is deemed as being experimental in nature. If informed consent, an ethical concept contained in the NHA,[104] is not obtained by the treating medical practitioner (or researcher), any medical treatment may result not only in an infringement of the patient's human dignity but may even amounts to criminal assault. Informed consent can be defined as, 'an autonomous action by a patient or participant that authorises a professional to either involve him or her in a research protocol or treatment for the patient'.[105]

Informed consent becomes especially important considering the doctor-patient relationship and the trust that patients place in the medical practitioners and their expertise. The preservation regulation of this relationship is key to enabling the patient to exercise a truly informed decision, based on the bioethical principle of patient autonomy.[106]

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[103] Council of Europe 'Oviedo Convention and its Protocols' available at *https://www.coe.int/en/web/bioethics/oviedo-convention* accessed on 01 October 2020.

[104] Section 7 of the National Health Act 61 of 2003.

[105] Epstein M. 'Why effective consent presupposes autonomous authorisation: a counter orthodox argument' (2006) 36(6) *J Med Ethics.*

[106] Samuel Reis-Dennis 'Understanding Autonomy: An Urgent Intervention' (2020) 7 *Journal of Law and the Biosciences*.

Within the context of stem cell technologies, patient autonomy would play a lead role. The idea that the patient has the right to make his or her own decisions when it comes to his or her own health and life, such decisions may have dramatic consequences and should be respected. However, the question of whether consent within the context of experimental therapies can truly be informed has yet to be answered.

Stem cell technology is advancing at a rapid pace and with the availability of reliable medical data, medical practitioners and researchers are in a better position to provide the patient with vital information.[107] Regardless of such information, express disclaimers can be found on most official medical documentation or websites.[108] This is slowly becoming common practice especially because patient awareness in the era of consumer rights and knowledge of medical malpractice litigation is increasing. Accordingly, an infringement of any human rights may even be justified in terms of such limitation clauses.[109] The limitations clause was designed to limit the application of certain human rights as entrenched in the Constitution. While at the outset, this may be deemed as a harsh section to include, it is on the contrary, essential. Human rights cannot and should not be abused as there is an equal right to both enforce and protect human rights.

3.2.3 The Right to Life

Everyone has the right to life.[110] The State is under constitutional obligation to protect human life with a concurrent duty on society not to take another's life. By deduction he State also has a duty to protect patients from unethical or unsafe medicine or medical treatments. In recognising the fact that human rights are interdependent, a further plausible deduction is that in ensuring that everyone enjoys the right to life, the State must ensure that this life is of a certain quality. From a patient's standpoint, the use of beneficial stem cell therapy is necessary if there is even the slightest chance that this therapy could save patients' lives, or at the very least, improve the quality of life.[111] Healthcare providers must avoid doing harm, help the patient, and ensure that any harm inflicted will be outweighed by the expected benefits of the

[107] King, N.M., Perrin, J 'Ethical issues in stem cell research and therapy' (2014) 5 *Stem Cell Res Ther* 85.

[108] Cell Surgical Network 'FDA' available at *https://stemcellrevolution.com/fda/* accessed on 01 October 2020.

[109] Section 36 of the Constitution of the Republic of South Africa, 1996.

[110] Section 11 of the Constitution of the Republic of South Africa, 1996.

[111] Jennifer A Chandler, 'Does a Patient have a Constitutional Right to the Freedom of Medical Research?' (2012) 1 *McGill Journal of Law and Health* 17.

medicine or medical treatment[112] The violation of this human right may also become apparent if stem cell treatment does more harm than good to the extent that death is the resultant effect. This is where informed consent must be considered. If the patient is providing informed consent, then it must be assumed that the effects of the treatment have been considered by the patient. The concept of expanded access, as found in the US, will be discussed in Chapter 4 of this dissertation.

With regards to the origins of stem cells used to develop stem cell therapies, anti-abortion and certain religious groups may regard a blastocyst as human life.[113] With special reference to the legal status of the unborn, the judiciary has on more than one occasion proclaimed its exclusion on matters so complex.[114] Whatever the reasons for judges' reluctance to take into consideration advances in medical science and technology in interpreting and applying the law, it is clear that their approach to the beginning of human personhood is incompatible with the imperative that law be impartial, relevant and dynamic.[115] In this regard, the European Court of Human Rights in the recent case of Vo v. France[116] stated (as per majority judgment): "they (human embryos) are beginning to receive some protection in the light of scientific progress and the potential consequences of research into genetic engineering, medically assisted procreation or embryo experimentation".[117] This makes the harvesting of embryonic stem cells seem quite unethical. There is however the induced pluripotent stem cell, which has been showing great promise,[118] and the use of somatic stem cells in various therapies which eliminates any concerns over the harvesting of embryonic stem cells. However, South

[112] Arthur L Caplan, Alison Bateman-House 'Should patients in need be given access to experimental drugs?' (2015) 16 (9) *Expert Opinion on Pharmacotherapy* 1275.

[113] Vorster JM 'A Christian ethical perspective on the moral status of the human embryo' (2011) 31 *Acta theol* 189.

[114]de Freitas, S 'The South African Constitutional Court and the unborn' (2012) 5 *International Journal of Religious Freedom* 57.

[115] Pillay, Rani 'The beginning of human personhood: Is South African law outdated?' (2010) 2 *Stellenbosch Law Review* 238.

[116] App. No. 53924/00, Eur. Ct. H.R., 8 July 2004.

[117] Joseph, Rita *Human rights and the unborn child* (2009) 211.

[118] Omole, Adekunle Ebenezer, Adegbenro Omotuyi John Fakoya 'Ten years of progress and promise of induced pluripotent stem cells: historical origins, characteristics, mechanisms, limitations, and potential applications' (2018) 6 *PeerJ* 2.

African legislation does not regard the embryo as having human life for purposes of constitutional protection.[119]

3.2.4 The Right to Freedom and Security of the Person

Section 12 (2) (c)[120] is of particular relevance here. According to this section, everyone has the right to bodily and psychological integrity, which includes the right not to be subjected to medical or scientific experiments without their informed consent. The concept of informed consent is yet again an important factor to consider. Obtaining informed consent is necessary. This is especially the case when a patient is entering a clinical trial as a research participant. The glaring issue that is presented within the context of accessing experimental treatment is the fact that informed consent cannot actually fully be obtained if specific aspects of the experimental therapy remain uncertain. The patient however in this instance, would be furnishing informed consent by agreeing that there are potentially even more risks associated with obtaining experimental treatment.

3.2.5 The Right to Access Health Care

Section 27(1) of the Constitution guarantees that, 'everyone has the right of access to health care services.' Section 27(2) furthermore imposes on the state, a duty to take reasonable measures within its available resources to achieve the progressive realisation of this right.

The right to access health care is especially relevant when it comes to understanding the reason as to why stem cell therapy should be regulated. The Constitution only provides for access to and not a direct right to health care. Through interpreting this, one could then deduce that within the context of stem cell therapy, a demand to have access to it, is protected. This right affords the patient the right to have access to medical treatment. The state is only obliged to provide access within its means. The Constitutional Court in the case of *S v Soobramoney*[121] has indicated that the realisation of a right to access healthcare services is a progressive right. Access to healthcare services, as a right, is defined not with reference to the health of the individual but rather the deployment of the resources that are available to ensure that as many people as possible are healthy.[122] The case also highlights the fact that even though the right to

[119] Robinson, Robbie 'The Legal Nature of the Embryo: Legal Subject or Legal Object?' (2018) 21 (1) Potchefstroom Electronic Law Journal 13.

[120] Constitution of the Republic of South Africa, 1996.

[121] *Soobramoney* v *Minister of Health (Kwazulu-Natal)* 1998 (1) SA 765 (CC).

[122] N. Kirby 'Access to Healthcare Services as a Human Right' (2010) 29 *Medicine and Law* 492.

life may come to be defined in South Africa, there is in reality no meaningful way in which it can constitutionally be extended to encompass the right indefinitely to evade death.[123] While death is inevitable, it is important to consider that terminally ill patients are often riddled with pain and other debilitating symptoms. Stem cell therapy has the propensity to relieve symptoms and therefore improve quality of life. Improving one's quality of life might prove to be more meaningful to a terminally ill patient, especially when they have reconciled themselves with the fact that there are simply no cures available for certain diseases. South Africa is extremely limited when it comes to its available healthcare resources however this should not mean that any further development of laws which can regulate new forms of medical treatment must come to a halt. Medical aid schemes and health insurers are always an option for patients when it comes to therapy that is unaffordable.

The section does not go on to further elaborate upon whether the term health care is inclusive of any experimental treatments. In effect a patient may have legal grounds to claim access to experimental stem cell therapy that has not yet been approved by the SAHPRA.[124] This is where the question of proper regulation comes into the picture.

Regulation is essential to allow access to experimental stem cell therapies, subject to certain safeguards as provided for in such regulations to still protect the patient from harm. It may happen in future that stem cell therapy is indicated as the last possible treatment for a disease and its infringement on the patient's human right to dignity, access to health care and his or her autonomy if such a patient is not allowed to access such treatments.

3.3 THE NATIONAL HEALTH ACT 61 OF 2003

The NHA makes provision in Chapter 8 for the control of the use of blood, blood products, tissue, and gametes in humans.[125] Aspects pertaining to human tissues were formerly legislated under the Human Tissue Act 65 of 1983, which has been repealed with the enactment of the final sections, specifically Chapter 8, of the NHA in 2012.

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[123] *Soobramoney* supra note 120 para 57.

[124] Jordaan Donrich W, 'Regulatory crackdown on stem cell therapy: What would the position be in South Africa?' (2012) 102 (4) *SAMJ* 220.

[125] 61 of 2003

The provisions contained in chapter 8 of the NHA regulate the 'removal and use of tissue, blood, blood products or gametes from living persons and the transplantation of tissue from one living person to another'.[126] The removal or withdrawal of stem cells (excluding umbilical cord progenitor cells) from a living person for medical or dental purposes requires ministerial authorisation.[127] It is not entirely clear why there is an exception when it comes to cord cells.

The abovementioned chapter also covers the harvesting, storage, import and export and processing of stem cells. Given the fact that research and technology in this field has progressed quite rapidly, there is very little in the NHA that provides guidance on who can access this form of therapy, when and in which circumstances.[128] Current legislation does not regulate embryonic stem cells produced through a process which does not require conception. Neither is there any regulations pertaining to induced pluripotent stem cells.

Section 71[129] which deals with research or experimentation on a living person, describes the legal norms when undertaking health research. This section mentions that research must be conducted in a prescribed manner and goes on to cover the aspects of consent. It has been criticised for making the legal framework overprotective of human subjects, removing flexibility from research ethics committees and creating conflict as it is inconsistent with popular ethical norms.[130] Ethical norms and guidelines will be discussed further on in this dissertation. While the NHA is quite thorough in its regulation of healthcare in South Africa, there is very little to properly regulate the use of experimental therapy.

3.4 MEDICINES AND RELATED SUBSTANCES ACT 101 OF 1965

The Medicines and Related Substances Act (previously the Drugs Control Act) 101 of 1965 aims to provide for the registration of drugs intended for human use, for the establishment of a

[126] Section 55 and 56 of the National Health Act 61 of 2003.

[127] MS Pepper, C Gouveia, M Nőthling Slabbert 'Legislation governing pluripotent stem cells in South Africa' (2015) 8 (2) *SAJBL* 25.

[128] Michael Sean Pepper, Janine Scholefield, Melodie Slabbert, Robea Ballo 'Why South Africa needs better laws for stem cell research and therapy' available at *https://theconversation.com/why-south-africa-needs-better-laws-for-stem-cell-research-and-therapy-45498,* accessed on 01 October 2020.

[129] National Health Act 61 of 2003.

[130] Strode Ann E 'The parameters of the current legal framework for health research: Forms of health research which are regulated and obligations imposed on researchers' (2013) 6 (2) *SAJBL* 69.

Drugs Control Council (now called the SAHRA) and for any other related matters.[131] In order for medicine (including biological medicine) to be sold legally in South Africa, it has to be registered. However, it is important to note that section 21 of the abovementioned Act, as amended provides that;

> 'Authority may authorise sale of unregistered medicines, medical devices or IVDs for certain purposes. The Authority may in writing authorise any person to sell during a specified period to any specified person or institution a specified quantity of any particular medicine, medical device or IVD which is not registered. Any medicine, medical device or IVD sold in pursuance of any authority granted under subsection (1) may be used for such purposes and in such manner and during such period as the Authority may in writing determine. The Authority may at any time by notice in writing withdraw any authority granted in terms of subsection (1) if effect is not given to any determination made in terms of subsection (2)'.[132]

This section indicates that there is some room for a more flexible approach. An approach which is promoted by right to try laws. As much as there is provision, access is not provided as freely as it is under the Right to Try Act. The recent need to access Ivermectin and vaccines within the context of the Covid-19 pandemic has proven that our laws are not as flexible as we would have needed them to be under current circumstances.

In order for medicines to be registered, the Registrar of Medicines would have to be satisfied that the medicine is of good quality, efficacious, safe, and suitable for the purpose for which it is intended, complies with the prescribed requirements and that registration thereof is in public interest.[133] An application for the registration of a medicine should therefore be submitted for evaluation and approval. The enactment of the recently amended MRSCA prompted the establishment of the SAHPRA. This acts as a separate juristic person outside of the National Department of Health to replace the former medicine regulatory authority the Medicines Control Council (MCC) which was a council mandated to act in terms of the abovementioned legislation. The legislative mandate of SAHPRA is derived from the

[131] Medicines and Related Substances Act 101 of 1965.

[132] Section 21 of the Medicines and Related Substances Act 101 of 1965.

[133] W M Botes, Alessandrini, 'Legal implications of translational promises of unproven stem cell therapy' (2015) (8) 2 *SAJBL* 37.

Constitution.[134] Bearing this in mind, it can be concluded that there is essentially an obligation placed on the state to progressively realise socio-economic rights including access to health care (discussed above).

3.5 CONCLUSION

Given the number of regulations in South Africa governing medical treatment and health care, it would be reasonable to presume that medical treatment, once approved by the SAHPRA in terms of the MRSCA, is adequately regulated. However, save for the emergency approval process as provided for in the MRSCA, there seems to be no other legal route to access experimental stem cell therapies, unless a patient enrolls in a clinical trial in the hope of getting the relevant therapy and not the placebo thereof. The existing regulatory framework emphasises the importance of acting in a patient's best interests, which is further based on ethical principles and obtaining informed consent from the patient.[135] This is in line with the basic human rights as entrenched in the Constitution.

Enacting legislation to properly govern access to experimental therapies such as stem cell therapies would ensure that such therapies are well monitored and controlled once access are allowed and treatments, that entails material that will be re(introduced) into patients is conducted in an accredited institution under strictly controlled conditions.[136] What remains problematic is making such stem cell therapies available to the public in general.

The argument presented is that, at the very least, access should be properly regulated so as to afford the most desperate patients an alternative to non-responsive treatments and medicines based on experimental therapies where existing and legally registered therapies cannot successfully treat or cure the patient. Legislation or regulation would not only provide a way to access therapies that are still being researched, but it would also provide for a framework that would essentially protect the patient and given the current COVID-19 pandemic, serve as a support for further medical advancements.

[134] Constitution of the Republic of South Africa, 1996.

[135] Section 7 of the National Health Act 61 of 2003.

[136] Pepper, Michael, M Nőthling Slabbert 'Human tissue legislation in South Africa: Focus on stem cell research and therapy' (2015) (8) 2 SAJBL 11.

CHAPTER FOUR: ACCESSING STEM CELL THERAPY

4.1 INTRODUCTION

Access to medicine is a fundamental human right. The 1946 Constitution of the World Health Organization and the 1948 Universal Declaration of Human Rights both expressly recognise the right to health, which right can only be exercise once access has been granted and made possible. Over the past several decades, there has been notable advances in scientific and technological innovation which has in turn changed the current depiction of the world's access to medicines. Even though some countries have implemented laws that allow access to experimental medicine, there are different legal and scientific opinions on which types of medicines the general population should have access to.

Medicines and various therapies, which may still be deemed as unsafe, because clinical trials have not yet been concluded, are often not made available to patients suffering from incurable disease. This has become a contentious issue over the years. As a result, there are numerous countries which have implemented expanded access or compassionate use programs. More recently, an expanded access program permitting the use of the unregistered drug, Ivermectin, was necessary to allow patients access to a medicine that is not registered for human use in an effort to treat serious COVID-19 infections. The purpose of these programs is to afford access to unapproved, but promising drugs without having to expose a patient to unnecessary risk, without jeopardising clinical trials, or delaying the development of new medication for marketing approval.[137] Understanding how these programs are implemented may support the argument that access to regenerative therapy, specifically stem cell therapies are necessary.

Aside from implementing expanded access programs, there are other ways to access experimental therapy. In May 2018, the United States federal government created another avenue for gaining access to investigational drugs. Congress enacted the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Mathew Bellina Right to Try Act of 2017 (hereinafter referred to as the Right to Try Act)[138]. This act (named after compelling individuals who all

[137] Jarow, Jonathan P et al 'Overview of FDA's Expanded Access Program for Investigational Drugs' (2017) 51 (2) *Therapeutic innovation & regulatory science* 177.

[138] US Food and Drug Administration 'Right to Try' available at *https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/right-try* accessed on 19 June 2021.

had or have terminal diagnoses),[139] which will be discussed in more detail below, protects the right of terminally ill patients to access medicine that has acquired only the very basic safety approval from the FDA.[140]

The Right to Try Act is a fairly recent development in US law. It is therefore important to consider how expanded access programs and the Right to Try Act may impact access to stem cell trials and eventual therapy, and how this act may pave the way for similar future legal developments in other jurisdictions.

4.2 EXPANDED ACCESS AND COMPASSIONATE USE PROGRAMS

Through the clinical trial process, patients are able to gain access to experimental treatment. These treatments do not have regulatory approval nor are they commercially available. The clinical trial process is designed to determine the medical safety and efficacy of experimental treatment and ethically necessary to benefit and protect patients. There are, however, instances where a patient suffering from a serious or life-threatening disease would require access to experimental treatment outside of a clinical trial setting. There may be no approved treatments available, approved treatments may have failed that particular patient, the patient may be unable to participate in the clinical trial, or it may be that the patient is in such a serious condition that he or she is unable to wait for commercial approval of newly developed medicines or treatment. There is however no need to tamper with the actual clinical trial process. The process has to be stringently followed so that safety and efficacy can be established. There is however a gap that exists when it comes to patients who are in dire circumstances when it comes to their health status. This is where a different pathway could benefit a patient who has already exhausted all existing registered therapies.

This is where the expanded access programs (often referred to a compassionate use programs) become relevant. Unlike a clinical trial, expanded access focuses on providing treatment rather than on gathering safety and efficacy data.[141] Expanded access varies globally and can include treatment of a large group of patients, an individual patient, and in some

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[139] Christine Coughlin, Nancy M.P. King & Melissa McKinney 'Regenerative Medicine and the Right to Try' (2018) 18 *Wake Forest Journal of Business & Intellectual Property Law* 614.

[140] Right to Try 'Why We Need Right to Try' available at *http://righttotry.org/about-right-to-try/* accessed on 09 December 2020.

[141] Klopfenstein, Mitchell et al 'Expanded Access Programs: Ethical and Practical Considerations for Biopharmaceutical Sponsors' (2015) 49 (3) *Therapeutic innovation & regulatory science* 352.

instances provide access to experimental treatment that is at the conclusion phase of clinical trials but has yet to receive commercial approval.[142]

Expanded access programs should be authorised as these programs offer hope to desperate terminally ill patients. It may be their last opportunity for treatment and often, patients in such dire need would be willing to assume the risks associated with experimental treatment, which risks may be more beneficial than the lack of any successful treatment. As briefly mentioned above, the recent COVID-19 pandemic has prompted the SAPHRA to implement an expanded access program to afford seriously ill Covid19 patient access to Ivermectin. Using section 21 of the MRSCA, [143] the SAHPRA enabled a controlled compassionate access programme, which permits registered medical practitioners to apply for approval of access to Ivermectin, that is not registered for use in humans, for the treatment and management of COVID-19 symptoms in seriously ill individually named patients. Expanded access program authorisation can be complicated due to the ethical implications. It is not a certainty that experimental treatments will work and whether the treatments are safe. As it stands, Ivermectin cannot be considered as a miracle drug. There are various side effects reported however conclusions are drawn from small, early trials. Nonetheless, in the face of a global pandemic, health officials and governments of several countries have recommended the use of Ivermectin for COVID-19 treatment and prevention.[144]

The clinical trial process ensures that treatments are tested in a well-controlled environment in order to ascertain whether the benefit of the therapy would far outweigh any risks associated with the treatment. In phase I the treatment is undertaken in small first-in-human studies to ascertain the safety of the treatment, the size of the dose, route of administration and schedule of administration. The treatment is then studied in a smaller group of patients with the disease or condition under study in order to ascertain the efficacy and to gather short term safety information. This is done in phase II. Finally, the treatment is studied in a larger population to gain confirmation on the safety, efficacy and overall benefit-risk

[142] Ibid.

[143] 101 of 1965.

[144] Cochrane 'Ivermectin: Cochrane's most talked about review so far, ever. Why?' available at *https://www.cochrane.org/news/ivermectin-cochranes-most-talked-about-review-so-far-ever-why* accessed on 06 December 2021.

relationship of the treatment.[145] This is all done in phase III which also provides the information for labeling instructions. Only once all three phases have been successfully completed can a regulatory body decide whether a medical treatment can be approved and registered to be made commercially available. Researchers are required to follow strict rules in order to ensure that participants are safe. Although safety and efficacy are important aspects to consider when accessing experimental treatment, this is not always something that is guaranteed within the clinical trial process. Participants are made aware of the fact that the treatment may cause serious side effects or be uncomfortable, the treatment may not work, or it may not be better than the standard treatment. It can also mean that the participant will not actually be part of the treatment group (or experimental group) that gets the new treatment. Instead, the participant may be part of the control group, which means you get the standard treatment or a no-treatment placebo.[146] It can be argued that some the abovementioned challenges reflect the same challenges that a patient wanting to access experimental therapy through right to try laws would face. The benefits of unproven stem cell therapy, however, could seriously tip the scales favouring the position of right to try activists.

As much as it is important that experimental treatments are subjected to the 3-phase clinical trial process, this process can also be lengthy, is very expensive, and it does not necessarily mean that every drug or treatment that enters this process is eventually approved.**[147]** Expanded access programs offer numerous benefits like allowing pharmaceutical companies and physicians to meet the need of terminally ill patients by providing potentially effective treatments in an ethical and compliant manner.**[148]** In order to ensure a basic standard of modern research ethics and research policy, namely participant voluntariness, is met, it is necessary that eligible patients have alternative access routes to experimental therapy that do not depend on their willingness to enrol in a randomised clinical trial.[149] The basis for this argument is the

[145] Klopfenstein, Mitchell et al 'Expanded Access Programs: Ethical and Practical Considerations for Biopharmaceutical Sponsors' (2015) 49 (3) *Therapeutic innovation & regulatory science* 352.

[146] NIH: National Institute on Aging Clinical Trials: Benefits, Risks, and Safety' available at *https://www.nia.nih.gov/health/clinical-trials-benefits-risks-and-safety* accessed on 10 December 2021.

[147] Caplan, A 'Is it sound public policy to let the terminally ill access experimental medical innovations?' (2007) 7(6) *Am J Bioeth.*

[148] Patil, Sanjaykumar 'Early access programs: Benefits, challenges, and key considerations for successful implementation' (2016) 7 (1) *Perspectives in clinical research* 6.

[149] Udo Schuklenk & Ricardo Smalling 'The Moral Case for Granting Catastrophically Ill Patients the Right to Access Unregistered Medical Interventions' (2017) 45 *The Journal of Law, Medicine and Ethics* 383.

legal doctrine of necessity, which permits non-compliance with society's rules, where an individual faces a situation of clear and imminent peril.[150]

In the US, expanded access programs are still governed by the FDA. This may still present some problems for the patient if the FDA imposes additional restrictions. The FDA is currently functioning effectively in terms of the submissions made and approved. In 2017 (a year before the Right to Try bill was enacted) the FDA boasted an approval rate of 99% in respect of all applications requiring access to unregistered medicines, however even with these impressive approval rates, manufacturers are still able to deny expanded access to patients. The FDA cannot force manufacturers to make unapproved products available on the market.[151]

As a result, there is a limited number of pharmaceutical companies who would choose to participate in expanded access programmes.[152] Furthermore, companies may refuse to provide access to their products because the use of experimental drugs outside of a clinical trial setting can be considered high risk, with adverse effects. This could potentially mean that the pharmaceutical company could incur civil liability for harm and damages suffered by the patient.[153] The chance for terminally ill patients to then access potentially lifesaving drugs is greatly reduced.[154]

Ultimately, the most important benefit derived from an expanded access program is that it allows the physicians and the pharmaceutical company to meet the needs of patients, especially those suffering from serious life-threatening or rare diseases, by providing potentially life-saving drugs in an ethical and a compliant manner.[155]

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[150] Ibid

[151] Christina Sandefur 'Safeguarding the Right to Try' (2017) 49 (2) *Arizona State Law Journal* 521.

[152] Jonathan J. Darrow et al 'Practical, Legal, and Ethical Issues in Expanded Access to Investigational Drugs' (2015) 372 *The New England Journal of Medicine* 280.

[153] Wep Clinical 'Why might companies refuse to provide pre-approval drug access?' available at *https://www.wepclinical.com/why-might-companies-refuse-to-provide-pre-approval-drug-access/* accessed on 27 January 2021.

[154] Ellen A. Black 'State Right to Try Acts: A Good Start, but a Federal Act Is Necessary' (2016) 45 *Southwestern Law Review* 719.

[155] Patil, Sanjaykumar 'Early access programs: Benefits, challenges, and key considerations for successful implementation' (2016) 7 (1) Perspectives in clinical research 6.

4.3 THE RIGHT TO TRY

The Abigail Alliance for Better Access to Developmental Drugs v von Eschenbach[156] was the catalyst that inspired the implementation to the Right to Try Act. Abigail, who was diagnosed with terminal head and neck cancer, under the recommendation of her oncologist, wanted to try an experimental drug, Erbitux. This drug was undergoing clinical trials for the treatment of colorectal cancer. She was ineligible to participate in the clinical trials and was furthermore denied the drug by the FDA. In 2003, Frank Burroughs, her father, sued the FDA for access to the experimental drug, Erbitux, on the pretext that an investigational drug by terminally ill patients after phase I approval was a constitutional right.[157] This is why, patient advocates, focused reform efforts on promulgating state laws to circumvent the FDA's regulations.[158] Two years after the court's decision in the *Abigail Alliance*-case, the FDA finally issued revised expanded access regulation clarifying the process by which an individual patient could request expanded access.[159] There are now three possible channels for expanded access;

> '1) The FDA allows expanded access on a case-by-case basis for individual patients if the probable risk of ill effects from the drug is not greater than the probable risk posed by the disease and if the patient cannot gain access to the drug in other ways. A drug sponsor or physician must file the paperwork to open this channel. 2) Small groups of patients can gain access to experimental therapies if they do not qualify for an experimental trial and there is sufficient evidence of experimental therapy's safety and efficacy. 3) Lastly, larger groups may gain access to the drug once it has passed phase III (or rarely, with strong evidence of safety and effectiveness, phase II) and the sponsor is seeking marketing approval'.[160]

Even though these changes were effected, the FDA ultimately still has regulatory control when it comes to expanded access programs. As of August 2018, 41 states have enacted

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[156] *Abigail Alliance for Better Access to Developmental Drugs* v. *von Eschenbach*, 495 F.3d 695 (D.C. Cir. 2007).

[157] Vijay Mahant '"Right-to-Try" experimental drugs: an overview' available at *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7309195/* accessed on 20 April 2021.

[158] Sylvia Zaich *An examination of the Right to Try Act of 2017 and industry's potential path moving forward* (2019) 377.

[159] Ibid at 347.

[160] Valarie Blake, JD 'The Terminally Ill, Access to Investigational Drugs, and FDA Rule' (2013) 15 (8) *American Medical Association Journal of Ethics* 690.

laws allowing terminally ill patients access to experimental therapies that have not yet been approved by the FDA.[161] Based on model legislation, promulgated by a libertarian think-tank, the Goldwater Institute, right to try laws are promoted as helping terminally ill patients access investigational medical products.[162] Patients and their physicians should be able to acquire these drugs or biologics that have completed Phase 1 clinical trials and are actively being tested in Phase 2 or 3 trials directly from manufacturers without having to go through any of the restrictions imposed by the FDA.[163]

The term eligible patient is adequately defined in the Right to Try Act. This was necessary in order to promote the flexible nature of the act and to afford access in a manner that was not as restricted as the FDA's expanded access programmes. To be eligible, a patient must have a 'life-threatening disease or condition'. Senator Johnson chose this disease threshold, rather than the "immediately life-threatening disease" standard previously used in the expanded access program because he believed that the 'immediately life-threating disease' definition would exclude patients with Duchenne muscular dystrophy, an illness that was clearly intended to be covered.[164] The patient must have exhausted approved treatment options and be unable to participate in a clinical trial. This must be certified by a physician. The certifying physician, who may not be the treating physician, must be in good standing and cannot be compensated by a manufacturer as a direct response to the certification. Thirdly, the patient must provide written informed consent.[165] According to the Right to Try Act, an investigational drug must satisfy four requirements;

> 'First, it must have completed a phase I clinical trial. Second, the drug must not be approved for any other use. Third, the manufacturer must either (1) have already filed

[161] Right to Try 'Right to Try in your State' available at *https://righttotry.org/in-your-state/* accessed on 22 January 2021.

[162] Corieri C. 'Everyone Deserves the Right to Try: Empowering the Terminally Ill to Take Control of Their Treatment' available *at https://goldwaterinstitute.org/article/everyone-deserves-right-try-empowering-terminally/* accessed on 22 January 2021.

[163] Ibid.

[164] Oren Oppenheim 'The RNC puts a spotlight on Sen. Ron Johnson's 'right to try' health care law. What you need to know' available at *https://www.jsonline.com/story/news/politics/elections/2020/08/26/rnc-highlights-ron-johnsons-right-try-health-care-law/3444070001/* accessed on 27 January 2021.

[165] Brenda Lin 'Federal Right to Try Act: Heightened Informed Consent and Price Regulation Measures Will Improve Quality, Autonomy, and Exploitation Issues Jacqueline Howard, What You Need to Know About Right-to-Try Legislation' (2021) 17 (2) *Hastings Business Law Journal* 213.

a marketing application for the investigational drug with the FDA, or (2) be investigating the drug in a clinical trial that is "intended to form the primary basis of a claim of effectiveness in support of approval" and is the subject of an active investigational drug. Fourth, the drug must be in active development (that is, not discontinued) and not subject to a clinical hold'.[166]

The Right to Try Act also provided limited liability protection for physicians, prohibiting licensure revocation based on the recommendation of or treatment with an experimental product.[167] The implementation of the Right to Try Act, which in effect is deemed as the right to access, is progressive.

4.3.1 Concerns over implementing right to try laws

The establishment of the safety and efficacy of medicine and medical treatments are most important when considering the impact upon human life and quality of human life. Removing the FDA's review of expanded access requests is dangerous. This is mainly due to the fact that most of the drugs that succeed in phase 1 trials turn out to be too unsafe or ineffective for clinical use in following clinical trial phases.[168] Another point of concern is the fact that if immunity is created for the health professionals who prescribe experimental treatments and the companies that dispense these treatments, room would be created for negligent acts or financial conflicts of interest. This is of course not ideal. The patient in this instance would then be left with no legal remedy. Provisions of this nature may further pose a problem in that they would be seen as contradictory to the faultless liability provisions that are currently applicable under the South African Consumer Protection Act (CPA).[169] The CPA applies to consumers and patients alike. It enforces strict liability for harm caused by goods and services. If the experimental medication supplied causes harm, the patient, as a consumer, would be able to claim for damages as per the CPA.[170] This may then intimidate health care professionals and

[166] Sylvia Zaich An examination of the Right to Try Act of 2017 and industry's potential path moving forward (2019) 378.

[167] Corieri C. 'Everyone Deserves the Right to Try: Empowering the Terminally Ill to Take Control of Their Treatment' available *at https://goldwaterinstitute.org/article/everyone-deserves-right-try-empowering-terminally/* accessed on 22 January 2021.

[168] Alison Bateman-House, Christopher T Robinson 'The Federal Right to Try Act of 2017 - A Wrong Turn for Access to Investigational Drugs and the Path Forward' (2018) 178 (3) *JAMA Internal Medicine* 322.

[169] No 68 of 2008.

[170] Slabbert, M., & Pepper, M 'The Consumer Protection Act: No-fault liability of health care providers' (2011) 101 (11) *SAMJ* 800.

as such, for access to be provided on a flexible basis, new regulations would have to provide as an exception to the above. Patients, instead of doctors, are now the ultimate decision-makers with regards to their own bodies and health. Self-determination trumps the concept of the doctor, as an expert, knowing what's best for the particular patient and making medical decisions on behalf of the patient.[171]

If Congress, however, seeks to provide immunity, it should be premised on FDA review of the protocol and the patient having received independent advice from a physician who has no reputational or stake in the investigational drug.[172] In South Africa, the concept of informed consent is important when it comes to patient rights. If full informed consent cannot be obtained, as provided for in the NHA,[173] then surely it may be regarded as unethical to completely exclude liability when it comes to the treating physician, supplying or manufacturing pharmaceutical or biotechnological company. There is a section in the Right to Try Act that completely exculpates drug sponsors and manufacturers and exculpates physicians against ordinary negligence. A prescriber, dispenser, or other individual entity providing such treatment may only be found liable as a result of reckless or willful misconduct, gross negligence, or an intentional delict. Liability should therefore not be completely excluded, however in the case of accessing experimental therapy after providing informed consent, it would be unethical to hold the treating physician completely liable. It is imperative to note that there is no obligation for a physician, manufacturer, or other entity to provide a drug under this Act.

The FDA also implements policy which limits what a company can charge for in terms of investigational drugs. This in turn provides for an important incentive for companies to complete clinical trials. Expanded access programmes provide that companies can only charge shipping and manufacturing costs for their investigational products.[174] The Right to Try Act

[171] Rowe, K., & Moodley, K 'Patients as consumers of health care in South Africa: the ethical and legal implications' (2013) 14 (15) *BMC medical ethics* 5.

[172] Alison Bateman-House, Christopher T Robinson 'The Federal Right to Try Act of 2017 - A Wrong Turn for Access to Investigational Drugs and the Path Forward' (2018) 178 (3) JAMA Internal Medicine 321.

[173] Section 7 of the National Health Act 61 of 2003.

[174] Alison Bateman-House, Christopher T Robinson 'The Federal Right to Try Act of 2017 - A Wrong Turn for Access to Investigational Drugs and the Path Forward' (2018) 178 (3) *JAMA Internal Medicine* 322.

however has no such restrictions. This has further ethical implications in that companies are able to profit from selling unproven drugs.

Right to try laws require patients' informed consent.[175] There is a requirement that patients provide written informed consent however there are no provisions which state that patients must be told about the experimental treatment that they would be considering. Some state laws are more demanding and establish standards for information disclosure.[176] The requirement of informed consent generally ensures that terminal patients considering the option of experimental treatment are fully aware of the risks involved.**[177]** The question that arises is whether a patient who is willing to undergo experimental treatment could ever be deemed as fully informed. This is especially the case when considering the fact that medical professionals and scientists would not have a full understanding of every serious risk that could be associated with the treatment.

Ever since the enactment of the Right to Try Act, multiple stem cell companies have begun to provide unapproved or experimental products to terminally or seriously ill patients. The Right to Try Act may even be used as a loophole to make these unapproved therapies available in general. Even with the Right to Try Act, most companies will continue to use expanded access programs. The issues presented entails well documented physical and financial harms that ensue through the marketing of these stem cell interventions. Patient safety is of course compromised and can potentially jeopardise further stem cell treatment development.[178] Right to try supporters argue, the patient has the right to try to preserve his own life. However, patients in very serious conditions might judge the potential benefits and risks differently than scientists do and they might not sense the irrationality of their own optimisms.[179] Bioethical considerations are therefore important as there is a balance that must

[175] Rebecca Dresser 'The "Right to Try" Investigational Drugs: Science and Stories in the Access Debate' (2015) 93 *Texas Law Review* 1641.

[176] Ibid at 1654.

[177] Section 7 of the National Health Act 61 of 2003.

[178] Cell Press 'Stem cell businesses and Right to Try laws' available at *https://doi.org/10.1016/j.stem.2019.08.012* accessed on 31 January 2021.

[179] Luciana Riva, Laura Campanozzi, Massimiliano Vitali et al 'Unproven stem cell therapies: is it my right to try?' (2019) 55(2) *Ann Ist Super Sanità* 180.

be struck between the needs of the patient and the rights and interests of the different stakeholders.

4.3.2 A progressive right

While there are clearly ways to access stem cell therapy, the Right to Try laws are viewed as less restrictive than the regulations provided by the FDA. It is however important to note that this legislation does not empower the patient to compel either a physician or a drug company to provide a drug under this Act. According to the provisions of the Right to Try Act, if an eligible patient seeks an eligible drug, the determination of eligibility is made purely between the patient, the treating physician, and the manufacturer. There exists a misunderstanding amoung Right to Try Act cynics that access is a right that can be demanded. If the provisions are carefully considered, the provisions more likely dictate that this Act does not provide a patient with an actual right to try a drug, but rather facilitates the provision of an eligible drug to an eligible patient if both the physician and the sponsor agree to do so.[180] The Right to Try Act should be viewed as laws that empower the terminally ill rather than laws that seek to afford a free pass to access unsafe treatment. Patients who are not battling an immediately life-threatening illness are likely less risk-tolerant and more willing to wait for a proven cure, but terminal patients do not have the luxury of time and may be eager, to try medications whose efficacy has not yet been established.

Of the many cases that have been the background against which the Right to Try Act was approved; the following is a clear indication of why access laws are considered as progressive. In 2002, Kianna Karnes, a 41-year-old mother of four children, was diagnosed with kidney cancer. She was treated with, the only medication approved by the FDA. The treatment failed however after some research conducted by her father it was found that Pfizer and Bayer (two pharmaceutical companies) were conducting clinical trials for new investigational medications to treat kidney cancer. Karnes however was ineligible for the clinical trial because her cancer had previously spread to her brain. Her father sought expanded access however months passed before he was able to secure access for his daughter. He contacted Congressman Dan Burton's office for assistance, and this resulted in media coverage of her struggle in the Wall Street Journal. On March 24, 2005, the FDA notified the family that it had approved a single-patient investigational new drug for Karnes. Unfortunately, it was too

[180] Agarwal, Rajiv, and Leonard B Saltz 'Understanding the Right to Try Act' available at *doi:10.1158/1078-0432.CCR-19-2015* accessed on 21 December 2021.

late as Kianna Karnes died the same day access was approved. Less than a year later, both drugs were given final FDA approval to treat advanced kidney cancer. Speaking after his daughter's death, her father stated that he didn't know if either of those drugs would have saved Kianna's life, but it would have been nice to have afforded her the chance.[181]

4.4 ETHICAL CONSIDERATIONS AND INTERNATIONAL GUIDELINES

4.4.1 Introduction

Ethical codes of conduct are not binding unless incorporated into national laws and legally authorised regulations. Given the fact that stem cell therapy and other forms of experimental treatments are very vaguely regulated, dominant ethical principles and practices will weigh heavily in the consideration of whether or not access to experimental therapy is justified.

To promote the ethical behaviour of medical practitioners, the Health Professions Council of South Africa, in consultation with professional boards, created a code of conduct that is in line with the provisions of the Health Products Association specifying that 'conduct which constitutes unethical behaviour and would be subject to review'.[182] This code however does not specifically address access to stem cell therapies. Using general codes to assess whether access to unproven therapies is ethical may not necessarily yield a fair outcome for the patient. Health care professionals have a mandatory and multifaceted duty placed on them to abide by the core ethical values necessary for good clinical practice.[183] This duty is a duty to patients, society, the environment, colleagues, the profession, and other healthcare professionals.[184] The duty toward a patient is quite important within the context of regenerative medicine. The patient's best interests and well-being are at the forefront and the various ethical principles aid in understanding whether access to experimental therapy would do more harm than good. When it comes to accessing medical care that is still deemed as experimental, consideration must be had for aspects like informed consent, patient confidentiality, patient

[181] Goldwater Institute 'Everyone deserves the Right to Try: Empowering the Terminally ill to take control of their treatment' available at *https://goldwaterinstitute.org/article/everyone-deserves-right-try-empowering-terminally/* accessed on 21 December 2021.

[182] Ethical and Professional Rules of the Health Professions Council of South Africa available at *http://www.hpcsa.co.za/Uploads/editor/* accessed on 22 January 2021.

[183] Moyo M, Goodyear-Smith FA, Weller J et al 'Healthcare practitioners' personal and professional values' (2016) 21 *Advances in Health Sciences Education* 257.

[184] Johannes Bernardus Laurens *A comparative analysis of the regulatory framework of the therapeutic application of stem cell technologies* (unpublished LLM theses, University of Pretoria, 2017) 46.

participation in their own healthcare decisions, impartiality and justice, and avoiding potential conflicts of interest.[185] In understanding the ethical implications, it's important to unpack the four bioethical principles that have the greatest impact on the medical field. Beauchamp and Childress's 'Four Principles' approach to bioethics has become the standard not only in the field of tertiary education, but also within medicine itself.[186] Their textbook was one of the first books to 'present a detailed systematic treatment of ethical decision-making in healthcare and biomedical research, and it laid the groundwork for contemporary research and teaching in this area'.[187] The four principles are respect for autonomy, non-maleficence, beneficence and justice. We can apply these four principles in order to ascertain what the potential ethical viewpoint on providing access to stem cell therapy in South Africa is.

4.4.2 Patient Autonomy

Exercising freedom is crucial to patient autonomy. The right of autonomy, a fundamental principle of every code of biomedical ethics, is closely linked to respect for human dignity but the two cannot and must not be used synonymously or interchangeably.[188] A patient should be able to make rational decisions upon a foundation of knowledge and understanding. Previously, it was commonly accepted that a doctor-patient relationship was mainly based on the principle of paternalism. This was ideal given the expertise held by the medical professional. As we move into an era where medical knowledge is accessible and medical negligence is more prevalent, patient autonomy is a necessary principle that will have to be respected. What is presented as a potential issue is the fact that when it comes to experimental treatment like stem cell therapy, it is difficult for a patient to be fully informed of all potential risks and benefits. Patient autonomy therefore plays a critical role when it comes to affording unrestricted access to experimental therapies. The patient in question would however be exercising this discretion within the context of having no other viable option. It has been argued that palliative care is sometimes the only option, however if a terminally ill patient is not ready to face such a grim conclusion, the use of unproven therapies may not present as being so risky. In fact the problem

[185] Ibid.

[186] Brendan Shea 'The "Four Principles" at 40: What is Their Role in Introductory Bioethics Classes?' available at *DOI:10.13140/RG.2.2.14942.79686* accessed on 27 January 2021.

[187] Ibid.

[188] Salako, S E 'The council of europe convention on human rights and biomedicine: new look at international biomedical law and ethics' (2008) 27 (2) *Medicine and Law* 342.

that may arise is that if a patient decides to pursue a "cure" through accessing unproven therapies, it may negatively impact on his or her ability to receive beneficial palliative care.[189]

Terminally ill patients with little to no hope of recovery are and should be at liberty to make their own decisions when it comes to their bodies. This is especially the case in an instance where the patient has tried all approved treatment avenues. The World Medical Association's Declaration of Helsinki stipulates that participation by individuals capable of giving informed consent as subjects in medical research must be voluntary.[190] This requirement reflects the commitment that even participation in research, should be a matter of choice.

Globally there are numerous clinics offering stem cell "therapies" to patients outside the context of a clinical trial setting. Aside from being, in some instances, ineffective, stem cell therapies have been associated with complications such as infection, rejection, tumorigenesis and death.[191] Physicians, researchers, scientists, regulatory bodies and advocacy groups are encouraged to work together to improve patient and physician education and address current legislative deficiencies.[192] When it comes to introducing new access legislation, it would be imperative to include guidance on how to deal with fraudulent or bogus therapies and clinics. Although we are unable to truly ascertain the exact number of patients who have received these stem cell-based therapies, anecdotal reports suggest that a significant portion of the patient population are willing to try them.[193] This is despite the unresolved questions about their safety and efficacy.[194] Given the current restrictions surrounding travel across international borders, it will be interesting to see if COVID-19 will have an impact on stem cell tourism.

While patient autonomy is an important freedom to protect, some persons are in need of comprehensive protection, even to the point of omitting them from activities that may harm

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[189] Jim Parker 'Right to Try Act could delay palliative care' available at *https://hospicenews.com/2019/03/08/right-to-try-act-could-delay-palliative-care%EF%BB%BF/* accessed on 31 January 2021.

[190] WMA 'Declaration of Helsinki' available at *https://www.wma.net/policies-post/wma-declarationof-helsinki-ethical-principles-for-medical-research-involvinghuman-subjects/* accessed on 10 December 2021.

[191] McMahon DS 'The global industry for unproven stem cell interventions and stem cell tourism' (2014) 11 *Journal of Tissue Engineering and Regenerative Medicine* 5.

[192] Samantha Lyons, Shival Salgaonkar, Gerard T Flaherty 'International stem cell tourism: a critical literature review and evidence-based recommendations' available at *https://doi.org/10.1093/inthealth/ihab050* accessed on 11 December 2021.

[193] Aaron D. Levine & Leslie E. Wolf 'The Roles and Responsibilities of Physicians in Patients' Decisions about Unproven Stem Cell Therapies' (2012) 40 *Journal of Law, Medicine and Ethics* 122.

[194] Ibid.

them; other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequences.[195] Patients, through having a medical condition or through undergoing treatment, may sometimes not be able to exercise discretion and will therefore be unable to make a rational decision. This has an impact on their right to exercise patient autonomy and their right to provide informed consent.

4.4.3 non-Maleficence

The principle of non-maleficence imposes obligations on the health professional to do no harm, minimize risks or to take precautions against possible risks or harms from medical treatment.[196] The application of this specific bioethical principle poses some difficulties if the argument is that patients deserve to at least access experimental therapy. This again is mainly because of the fact that stem cell therapy is experimental and if there are still various risks associated with this form of regenerative medicine, the medical professional will not be able to safely advise that a patient access this form of treatment without breaching this ethical principle. The medical professional will not be able to provide the patient with the information required for the proper exercise of informed consent. In fact, this may be almost impossible for the medical professional as unproven stem cell therapies may carry risks that the practitioner would be unaware of. Perhaps it can be argued that in not affording a terminal patient access to a potentially life-saving therapy is in itself doing harm.

4.5.4 Beneficence

Beneficence dictates that medical professional has an obligation to affirmatively promote good and act in the best interests of the patient.[197] The medical practitioner, based on his expert knowledge is ultimately best positioned to disseminate information to the benefit of the patient and to allow the patient to make a properly informed decision. The expertise of the medical professional in this instance carries a lot of weight. Different to minimising risk, this principle focuses on affording the medical professional the right to actually suggest therapy that would be beneficial (even if not all the risks are evident). This bodes well for stem cell therapy especially because research in this field is fluid and ongoing. Health care workers are able to suggest that stem cell therapy would be beneficial especially if through their own research

[195] J. A. Singh Ethical Decision-making. In: MA Dada and DJ Mcquoid-Mason (eds.) Introduction to Medico-Legal Practice (2001) 36.

[196] Ibo van de Poel 'An Ethical Framework for Evaluating Experimental Technology' available at *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4912576/* accessed on 31 January 2021.

[197] Ibid.

believe it to be something that could at the very least provide symptomatic relief. Acting in a patient's best interests surely should entail supporting a patient's right to try or access stem cell therapy. It has been argued that beneficence captures the true moral essence of the professional responsibilities of health care providers. The Hippocratic Oath requires physicians to benefit their patients "according to their best judgement".[198]

4.4.5 Justice

The principle of justice asks the question of who ought to receive benefits and who would bear the burdens. This principle encompasses the notion of what is deserved or what is fair. An injustice occurs, when some benefit to which a person is entitled is denied without good reason, or when some burden is imposed unduly. If consideration is had for those patients who have access to healthcare but don't have access to experimental therapy like stem cell therapy, then the question of fairness must be addressed. If medical science is advancing daily, rapidly enough to provide further information about stem cell therapy and its benefit to risk ratio, then surely it can only be deemed fair that patients in dire need have access to experimental treatment. In fact, it is also important to address the fact that access to unproven stem cell therapies has financial implications. This would also impact upon who would essentially have access to the therapies versus who would not. In providing informed consent, practitioners are required to inform patients about the cost of services or treatment provided as part of seeking consent from patients.[199] It would be deemed as ethical when in obtaining true informed consent from the patient, the financial affordability of unproven stem cell therapies is addressed with the patient.

4.4.6 International Guidelines based on ethical principles

The International Society for Stem Cell Research (hereinafter referred to as the ISSCR) developed guidelines that addressed the international diversity of cultural, political, legal, and ethical issues associated with stem cell research and its translation to medicine.[200] These

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[198] J. A. Singh Ethical Decision-making. In: MA Dada and DJ Mcquoid-Mason (eds.) Introduction to Medico-Legal Practice (2001) 36.

[199] Health Professions Council of South Africa 'Informed Consent' available at *https://www.hpcsa-blogs.co.za/informed-consent/* accessed on 01 February 2021.

[200] International Society for Stem Cell Research 'Guidelines for the Field of Stem Cell Research and Regenerative Medicine' available at *https://www.isscr.org/policy/guidelines-for-stem-cell-research-and-clinical-translation* accessed on 15 June 2021.

guidelines mainly encourage an 'ethical, practical, appropriate, and sustainable enterprise' for stem cell research and the development of cell therapies.[201]

Apart from the ethical issues, there are also safety and medical concerns. Embryonic stem cells (because of their plasticity) are inclined to form tumors (called teratomas, sometimes containing hair and teeth) when used in human therapy. This has led to the claim that embryonic stem cells are unsuitable, not only on moral and ethical grounds, but also on scientific and medical ones.[202] It has been argued that the advent of induced pluripotent stem cells means that embryonic stem cells need no longer be used. However, it still needs to be determined whether the induced pluripotent stem cells will be effective and safe for use in humans.[203]

The ISSCR has recently updated their guidelines due to rapid developments in the field of regenerative medicine.[204] The guidelines are quite comprehensive in how they govern stem cell therapy and are quite prescriptive in terms how stem cell therapy should be administered. It is important to note that these guidelines do not promote the use of stem cells that have not been subject to some form of testing within a clinical trial process. According to recommendation 3.5.1 and 3.5.2.:

> 'The clinical use of unproven stem cell-based interventions should be limited to well-regulated clinical trials and medical innovations compliant with these guidelines and local laws, policies, and regulations. Government authorities and professional organisations should establish and strictly enforce policies and regulations governing the commercial use of stem cell based medical interventions (SCBIs)'.[205]

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[201] International Society for Stem Cell Research 'ISSCR Guidelines for Stem Cell Research and Clinical translation' available at *https://www.isscr.org/docs/default-source/all-isscr-guidelines/2021-guidelines/isscr-guidelines-for-stem-cell-research-and-clinical-translation-2021.pdf?sfvrsn=979d58b1_4* accessed on 20 June 2021.

[202] Christa van Wyk 'In Search of the Holy Grail of Medicine (and a Coherent Legal Framework for Stem Cell Research)' (2013) 76 *THRHR* 208.

[203] Ibid at 209.

[204] Stem Cell Reports 'ISSCR Guidelines for Stem Cell Research and Clinical Translation: The 2021 update' available at *https://www.sciencedirect.com/science/article/pii/S2213671121002630* accessed on 20 June 2021.

[205] International Society for Stem Cell Research 'ISSCR Guidelines for Stem Cell Research and Clinical translation' available at *https://www.isscr.org/docs/default-source/all-isscr-guidelines/2021-guidelines/isscr-guidelines-for-stem-cell-research-and-clinical-translation-2021.pdf?sfvrsn=979d58b1_4* accessed on 20 June 2021.

To help address their concerns with unproven SCBIs, the ISSCR also created a patient handbook to "help patients and their doctors make informed choices when contemplating a stem cell-based intervention either locally or abroad".[206] The main questions that a patient should be asking is "What should I look for if I am considering a stem cell therapy?" and "What should I be cautious about if I am considering a stem cell therapy?".

ISSCR guidelines encourage physicians to;

> 'Have knowledge of stem cell-based medicine or the likely development of this field to help assess preclinical evidence and potential treatment modalities. At the very least, they suggest that physicians must help patients access and interpret the medical literature, which may be outside the physician's area of expertise'.[207]

It is quite clear that international guidelines are in favour of the use of stem cell therapy. The question of its efficacy is not a primary question however, it is highlighted above that this therapy should not be provided unless its has been subjected to testing under clinical trial processes. These guidelines, while also a bit restrictive, are reasonable. As such, it would be important to incorporate certain aspects outlined into new access laws. It would be contradictory to mirror the entire set of guiding principles into new regulations, especially in South Africa. Providing access to stem cell therapy in South Africa, is especially beneficial for those researchers looking to understand the impact of stem cell therapy on patients diagnosed with HIV and AIDS. A good starting point would be to include the physician as a part of the decision-making process as often, patients do not fully understand medical literature and jargon.

4.5 CONCLUSION

Alternative ways and methods to access yet unregistered or experimental medicines are essential if we want science and medical treatments to advance. Enacting legislation or regulation that would afford this type or form of access already assist various countries by legally and ethically providing medication that is not yet fully approved.

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[206] International Society for Stem Cell Research 'Patient Handbook on Stem Cell Therapies' available at *https://www.isscr.org/docs/default-source/patient-handbook/isscrpatienthandbook.pdf* accessed on 22 March 2021.

[207] Aaron D. Levine & Leslie E. Wolf 'The Roles and Responsibilities of Physicians in Patients' Decisions about Unproven Stem Cell Therapies' (2012) 40 *Journal of Law, Medicine and Ethics* 126.

The US has successfully implemented expanded access programs over the years which have yielded favourable results for both the patient and industry. The Right to Try Act was enacted to remove restrictions that prevented numerous patients from accessing investigational drugs that were still being tested in clinical trials. The demise of terminally ill patients, while awaiting access to these drugs often causes a public outcry. Based on this premise, the Right to Try Act gained momentum and a large following of people who have either lost someone close to them or who are currently suffering from a disease that is deemed incurable according to available therapeutic measures.

The Right to Try Act has the intention of allowing terminally ill patients access to experimental therapies. If we view this as the main objective, the advantage of enacting laws of a similar nature in South Africa is quite evident. South African legislation and regulation, currently, very vaguely and poorly regulates stem cell therapies. Through enacting laws that are similar to the provisions found in the Right to Try Act, we may find that regulation around unproven stem cell therapies will evolve and perhaps the fact that more people would have access to these therapies, would in turn mean that we would have more research data in this field that may lead to better therapies. While there are numerous flaws that are inherent in legislation that try to remove or bypass important restrictions, it is necessary that alternative legal pathways are made available to access stem cell therapies that are being investigated, developed and tested at a rapid pace. Even if we cannot ethically advocate for legislation that afford unrestricted access to unapproved stem cell therapies, we can perhaps, based on an ethical standpoint, advocate for expanded access programs in South Africa which would open the door to accessing experimental therapies.

CHAPTER 5: RECOMMENDATIONS AND CONCLUSION

5.1 INTRODUCTION

Deliberate, efficient, and careful regulation is key to harvesting the true potential of stem cell therapy. We have been able to establish that there are various ways in which stem cell therapy is regulated. Ethical rules should surpass legal rules and on a global scale there are various countries that implement laws which promote and keep up to speed with stem cell research.[208]

In terms of medical ethics in South Africa, guidelines provided by the HPCSA, dictate that it would be unethical to administer treatment that is not proven to be safe, efficacious or of good quality.[209] The balancing of patient interests, however, is most important when considering whether or not it would be wise to permit access to medicines or therapies that are still in an experimental phase (or rather those which are still in the clinical trial process). A discussion of our Constitutional rights was necessary to establish whether further regulation would infringe upon the already entrenched rights contained in the Bill of Rights. These rights are important to uphold due to the fact that they embody ethical principles. However, again, the balancing of rights is a necessary exercise.[210]

For more than 2 decades China has approved access to a number of experimental drugs.[211] The China Food and Drug Administration approved experimental oncolytic viral therapy for head and neck cancer, an angiogenic Endostar inhibitors for treating non-small cell lung cancer and Gendicine for treating head and neck cancer.[212] During December 2019 the Chinese Drug Administration Law came into effect.[213] The Drug Administration Law addresses several issues such as drug innovation, drug accessibility, drug safety and public

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[208] Pew Research Center 'Stem cell research around the world' available at *https://www.pewforum.org/2008/07/17/stem-cell-research-around-the-world/* accessed on 11 July 2021.

[209] Health Professions Council of South Africa 'Ethical Guidelines for Health Researchers' available at *https://www.hpcsa.co.za/Uploads/Professional_Practice/Conduct%20%26%20Ethics/Booklet%2013%20Gen%20Ethical%20Guidelines%20for%20Health%20Researchers.pdf* accessed on 20 April 2021.

[210] S36 of the Constitution of the Republic of South Africa 1996.

[211] Baker McKenzie 'China: Drug Administrative Law Amended to Encourage Innovation and Deter Safety Violations' available at *https://www.bakermckenzie.com/en/insight/publications/2019/10/drug-administrative-law-amended* accessed on 21 May 2021.

[212] Vijay Mahant '"Right-to-Try" experimental drugs: an overview' available at *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7309195/* accessed on 20 April 2021.

[213] Baker McKenzie 'China: Drug Administrative Law Amended to Encourage Innovation and Deter Safety Violations' available at *https://www.bakermckenzie.com/en/insight/publications/2019/10/drug-administrative-law-amended* accessed on 21 May 2021.

health concerns.[214] Considering the outbreak of recent epidemics such as Ebola, MERS and more recently the outbreak of the coronavirus, SARS-CoV2 in 2019, the use of emergency drugs and compassionate use of experiential drugs may warrant further consideration of the options available during a pandemic.[215] In the case of a catastrophic, fast-acting illness, such as infection with the Ebola virus, where any detrimental effects resulting from being randomised in a given trial arm be irreversible, it seems reasonable to suggest that competent patients should be able to choose whether they would prefer to take their chances with experimental treatment or the clinical trial process.[216]

5.2 A GLOBAL PERSPECTIVE ON ACCESSING STEM CELL THERAPIES

The scenario of a terminal patient, on his or her death bed, having tried every form of approved medical treatment or therapy is at the forefront of the argument in favour of access to unregistered medicines to be an available option under certain strict regulatory conditions. From an ethical perspective, providing even the most minute sliver of hope to a desperate patient facing grim consequences is a solution especially when preventing access could be seen as a cruel, inhumane and undignified act. Consideration, however, must be had to the fact that affording patients access to unproven stem cell therapies may mean that proper regulation (setting boundaries) is imperative.

An American case study that illustrates the clear disadvantage of limiting access is that of Jenn McNary and her 2 sons. Both her sons, Austin (three years old) and Max (newborn), were diagnosed with Duchenne's Muscular Dystrophy. This disease is incurable, fatal and is a degenerative muscular disorder. Austin's health had declined so badly that he was restricted to a wheelchair. When Jenn learned of a promising treatment undergoing testing in clinical trials, she immediately tried to enroll both boys in the trial, only to learn that the trial was limited to ambulatory patients. Max was therefore eligible, but Austin's disease had progressed too far to qualify. Jenn had to watch as one son's condition improved drastically under treatment, and her

[214] Ibid.

[215] Vijay Mahant '"Right-to-Try" experimental drugs: an overview' available at *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7309195/* accessed on 20 April 2021.

[216] Udo Schuklenk & Ricardo Smalling 'The Moral Case for Granting Catastrophically Ill Patients the Right to Access Unregistered Medical Interventions' (2017) 45 *The Journal of Law, Medicine and Ethics* 387.

other son's condition worsened until he could no longer dress or use the restroom without help. Thirteen-year-old Max became sixteen-year-old Austin's caregiver.[217]

When it comes to Duchenne's Muscular Dystrophy, Dr Yoshitsugu Aoki of the National Center of Neurology and Psychiatry, Tokyo and colleagues have drawn on research from around the world to illustrate the current state of urine-derived stem cell research. This covers several promising new findings, offering hope for patients with these potentially life-limiting conditions.[218]

In the United Kingdom, the Medical Innovation Bill (hereinafter referred to as MIB) mirrored the Right to Try Act to some extent.[219] As currently drafted, it seeks to solve an equally straightforward problem. Unfortunately, unlike the Right to Try Act, the MIB was not enacted. Another difference between these two pieces of legislation lies in the purpose behind why these bills were drafted. After Lord Saatchi's wife died of cancer, Lord Saatchi, a member in the House of Lords, observed and highlighted that medical practitioners were afraid of litigation and that this in turn created a 'barrier to more innovative treatments being developed and used by specialist doctors'.[220] The fundamental idea of the Bill is therefore that medical professionals should not fail to act, due to a fear of being sued. It is imperative that appropriate safeguards for patients are still maintained. Its purpose is to 'encourage responsible innovation'.[221]

Thus, the MIB provides that a doctor who moves away from applying accepted or approved treatments (which constitutes its definition of 'innovation') in a 'responsible' manner is 'not negligent'.[222] The fact that this bill provides extensive immunity to such doctors, what would be crucial to the Bill, is the definition of what constitutes responsible innovation. Section

[217] Darcey Olsen *The Right to Try: How the Federal Government prevents Americans form getting lifesaving treatments they need* (2015) 34.

[218] Dr Yoshitsugu Aoki 'Stem cells could offer hope for muscular dystrophy' available at *https://researchoutreach.org/articles/stem-cells-offer-hope-muscular-dystrophy/* accessed on 03 May 2021.

[219] Jose Miola & Bernadette J. Richards 'Would We Be Right to Try "Right to Try"?' (2021) 107 (31) *Health Matrix* 114.

[220]Jose Miola 'Bye-Bye Bolitho: The Curious Case of the Medical Innovation Bill' (2015) 15 *Medical Law International* 127.

[221] Medical Innovation Bill section 1(1).

[222] Medical Innovation Bill, section 1(2).

1(3) sets out the criteria that a doctor must comply with, and spells out that the circumstances in which the Bill applies are where, in the doctor's opinion:

> 'It is unclear whether the medical treatment that the doctor proposes to carry out has or would have the support of a responsible body of medical opinion; or the proposed treatment does not, or would not, have such support'.[223]

A small number of examples were provided to identifying both the medical condition and a particular innovation. A medical professional described the case of a relative who had not been offered haematopoietic stem cell transplantation (HSCT), which he described as 'currently the only curative treatment for myeloma', because offering the treatment would expose the consultant concerned to 'disciplinary sanctions from her regulatory body for not following "standard and proper treatment'.[224]

In 2014, Italy was the subject of a highly contentious legal battle, *Durisotto vs Italy*[225], also known as the "*Stamina*-case", about an alleged innovative stem-cell therapy. Administered to numerous patients, the stamina treatment was based on the use of mesenchymal stem cells, intended for the treatment of neurodegenerative diseases. Mr. Durisotto applied to the European Court of Human Rights following the refusal by the Italian courts to authorise compassionate therapy (specifically, the "Stamina" method) to treat his daughter's degenerative cerebral illness. The European Court ruled on the patient's right to decide to resort to unproven treatments, stem cell therapies, in the absence of other therapeutic possibilities. The aforementioned court rejected the patient's claim. In particular, it declared the application inadmissible under Article 8 of the European Convention on Human Rights, more specifically the right to respect for private and family life, stating that 'the interference in the right to respect for the private life, represented by the refusal to grant the request for medical therapy, could be

[223] Jose Miola 'Bye-Bye Bolitho: The Curious Case of the Medical Innovation Bill' (2015) 15 *Medical Law International* 127.

[224] Department of Health 'Report on the consultation on the Medical Innovation Bill' available at *https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/338274/medinnbill_response.pdf*, accessed on 11 July 2021.

[225] Rial-Sebbag E, Blasimme A 'The European Court of Human Rights' ruling on unproven stem cell therapies: a missed opportunity?' available at *doi:10.1089/scd.2014.0361* accessed on 21 May 2021.

considered as necessary in a democratic society'. The prohibition on access to the therapy in question 'pursued the legitimate aim of protecting health and was proportionate to that aim'.[226]

There have been global concerns surrounding stem cell therapies, where patients may be seeking unproven treatments in other countries giving rise to an increase in the figures of medical tourism.[227] While this would sometimes have a negative impact and lead to the administration of therapies that do more harm than good, there are instances where affording access may yield a positive outcome. Prior to the implementation of the Right to Try laws in the US, there was a case involving Michael Phelan, chief executive officer and co-founder of a successful software company recently had to step down due to health issues related to multiple sclerosis. Approved treatments provided by top neurologists in the United States proved to be ineffective. He began to research promising clinical trials and found the results with autologous stem cell treatments impressive. However to access these treatments, he had to enter into an approved trial however after spending thousands of dollars, he was told that he did not meet the requirements for the two separate trials that he had tried to qualify for. After corresponding with physicians and researchers at the Stem Cell Institute in Panama, and after noting that they had published some of their research, he pursued therapy there, receiving an autologous stem cell treatment using cells that were derived from his adipose tissue. These therapies had proven to be successful and a lot of the medical problems that he had encountered, improved and in turn improved his quality of life.[228]

The Right to Try Act in the United States has provided the world with some insight into what it would be like to afforded unhindered access to experimental therapies. There are various issues that arise out of affording access under this type or form of regulation. In this dissertation, an analysis of expanded access was done in order to ascertain whether there was in fact a need to further regulate access to experimental treatment.[229]

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[226] Emmanuelle Rial-Sebbag and Alessandro Blasimme 'The European Court of Human Rights' Ruling on Unproven Stem Cell Therapies: A Missed Opportunity?' available at doi: 10.1089/scd.2014.0361 accessed on 20 May 2021.

[227] Catherine Sturman 'The rise of medical tourism is impacting stem cell treatments' available at *https://healthcareglobal.com/hospitals/rise-medical-tourism-impacting-stem-cell-treatments* accessed on 20 May 2021.

[228] National Academy of Sciences 'Stem Cell Therapies: Opportunities for Ensuring the Quality and Safety of Clinical Offerings: Summary of a Joint Workshop' available at h*ttps://www.ncbi.nlm.nih.gov/books/NBK223194/* accessed on 19 March 2021.

[229] Vijay Mahant '"Right-to-Try" experimental drugs: an overview' available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7309195/ accessed on 20 April 2021.

5.3 CONCERNS ARISING FROM AFFORDING ACCESS TO EXPERIMENTAL MEDICINE OR TREATMENTS

There is great media hype surrounding stem cell research. There is a hope that exists that this form of regenerative medicine will lead to novel cures, and this creates a public perception that stem cell therapies are or will soon be readily available. At first glance, the right to try appears to empower a patient, in all situations, to access identified drugs to treatment. Even though the Right to Try Act presents the patient with the opportunity to access medical treatment without restriction from the FDA, there are still some conditions attached.[230] Aside from the patient being considered as terminally ill, the patient's physician must recommend the drug, the patient must provide informed consent, the manufacturer must agree to provide the drug and the patient is the one who pays if the drug is made available by the manufacturer.[231] The patient may only use the legislation if he or she is terminally ill rather than, for example, if he or she feels subjectively that her condition is unbearable or untreatable. The physician acts as a gatekeeper and the manufacturer may choose whether to provide the drug at all, and also whether to charge for it.

Therefore, a patient who may not be deemed to be terminally ill or lack the support of his or her doctor, will not have a 'right' to try any experimental medicine. Even if the patient is terminally ill and the doctor has provided support, there is no directive imposed on manufacturers to provide access to the drug and if they choose not to provide access, then they may charge as much for that access as they wish.[232] While the Constitution[233] does promote patients' rights when it comes to accessing health care in South Africa and on a global scale, the Right to Try Act serves to restrict a significant patient right. The patient would in effect, automatically relinquish the right to sue for medical or professional negligence if he or she believes, for example, that the wrong dosage caused him or her to suffer harm or an adverse effect. Therefore, not only does the law fails to enshrine a right to access treatment, but it also actively diminishes other well-established rights.[234]

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[230] Jose Miola & Bernadette J. Richards 'Would We Be Right to Try "Right to Try"?' (2011) 31 *Health Matrix* 111.

[231] Ibid.

[232] US Food and Drug Administration 'Right to Try, FDA Fact Sheet' available at *https://www.fda.gov/media/133864/download* accessed on 02 June 2021.

[233] Section 27 of the Constitution of South Africa, 1996.

[234] Jose Miola & Bernadette J. Richards 'Would We Be Right to Try "Right to Try"?' (2011) 31

The unproven stem cell intervention industry has been growing internationally and there are numerous factors that would contribute toward the rising number of clinics. The promise that stem cell therapy holds coupled with the fact that stem cell therapy can be used for an array of diseases or ailments (from knee pain to Parkinson's disease) can result in the mushrooming of clinics globally.[235] Due to the global increase of clinics offering unproven stem cell therapies, it is vital to turn to and consult international health organizations like the World Health Organisation.

Prof. Maneesha S Inamdar, an Indian stem cell and developmental biologist, has been part of the WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing.[236] Two new companion reports providing the first global recommendations to help ensure that human genome editing is used for public health, with an emphasis on safety, effectiveness, and ethics were released.[237] Perhaps one of the most important topics that the World Health Organisation's Expert Advisory Committee on Regenerative Medicine can address is the harmonisation of regulatory definitions and practices for cell-based therapies. Regulations need unambiguous definitions of key concepts that are harmonised and adopted consistently between countries.[238] This would ensure that clinics who market unproven stem cell therapies cannot escape regulatory oversight. There would be little room for regulatory gaps if guidelines proposed by the international organisation were taken into serious account when drafting country or state specific laws.

5.4 RECOMMENDATIONS

In consideration of stem cell therapies and the proven benefits of such therapies, it can be argued that access to these therapies is essential in certain circumstances. The current COVID-19 pandemic has been an eye-opening experience. We have never depended more on the rapid

Health Matrix 112.

[235] WebMD Health News 'Stem Cell Clinics: Effective or Pricey False Hope?' available at *https://www.webmd.com/brain/news/20190813/stem-cell-clinics-effective-or-pricey-false-hope*, accessed on 12 July 2021.

[236] Mint 'Indian stem cell developmental biologist, part of WHO advisory committee' available at *https://www.livemint.com/science/health/indian-stem-cell-developmental-biologist-part-of-who-advisory-committee-11626109636912.html*, accessed on 12 July 2021.

[237] Ibid.

[238] Stem Cell Reports 'Unproven stem cell interventions: A global public health problem requiring global deliberation' available at *https://www.sciencedirect.com/science/article/pii/S2213671121002551* accessed on 03 June 2021.

developments in medical science and technology more than we have during the past 2 years. The use of Ivermectin through emergency or expanded access programmes and the implementation of vaccination programs for novel diseases provides us with some context here. Global health depended on access to unproven therapies and partially proven vaccines.

The COVID-19 virus has caused a global health emergency since late 2019. The clinical study of several new biological interventions, including innovative applications of existing medicines were necessitated by this pandemic to investigate efficient treatments and a possible cure for COVID-19 and its many variants.[239] Mesenchymal stem cells are known for their immunomodulation potential, defenses against viral infections, and tissue regeneration, including its newly emerged use for designing vaccines.[240]

It is quite clear from the above that a need to access unproven therapies is necessary , especially when countries are submersed in a global health emergency. The evolution of diseases and the mutation of viruses, as we have seen with COVID-19, is inevitable. Considering the pace at which biology evolves and science develops, laws do not seem to keep pace with any of these developments. Access to novel experimental medicines should not be hindered by a tardy legislative process which may be detrimental for patients suffering from incurable diseases. Governments must work to keep up with all advancements in medicine to ensure that access is granted where and when it may prove to be life changing. This is a delicate balance as a duty imposed on most governments is to ensure the protection of its citizens, which cannot be achieved if promising medical interventions are inaccessible because it is struck in clinical or approval processes.

If South African legislature is to embrace the Right to Try Act as the foundation for the creation of regulations affording access rights, it would be necessary to impose certain restrictions that would ultimately act in the best interest of the patient. In order to avoid the apparent issues highlighted by the recently enacted US laws, it would be ideal for any new law or regulation in South Africa to be formulated using both the existing expanded access framework and the US Right to Try Act.

[239] Mehrdad Afarid, Fatemeh Sanie-Jahromi 'Mesenchymal Stem Cells and COVID-19: Cure, Prevention, and Vaccination' 2021 *Stem Cells International* 1.

[240] Ibid.

The first step in entrenching the right to access experimental therapy would be to consider the introduction of further regulations. Aside from the emergency access program approved by the SAHPRA in terms of the MRSCA, access as provided for in the US Right to Try Act should be considered. Factors and conditions imposed under the Right to Try Act, as discussed in chapter 4, and the MIB must be considered and implemented in a similar manner. The main aim is to still ensure that these laws are respectful of patients' rights. The following recommendations are made in terms of what the new laws should regulate:

1. the provisions of new laws must never conflict with the fundamental human rights as entrenched in the South African Constitution.[241] Regard must be had for all basic human rights. As per the discussion in chapter 3, it can be justifiably argued that patients have a clear right to gain access to experimental treatment as provided for in the US Right to Try Act;
2. ethical standards and practices, as discussed in chapter 4, must be taken into consideration when drafting these provisions. This will involve the balancing of patient rights like the right to access experimental treatment versus the patient's right to be protected, and the patient's autonomy versus what may be beneficial for the community at large;
3. the laws must impose conditions and safeguards, which may be restrictive to a certain extent. The conditions contained in the Right to Try Act are quite fair in that the patient wishing to access experimental therapies must be terminally ill. It would not be ideal for every person in the country to have the freedom to access experimental treatments. As a further safeguard, the patient must provide evidence of the fact that they have exhausted all available medicines and therapies. Since stem cell therapy is able to address a wide variety of diseases and illnesses, some more serious than others, it is important that access be afforded to patients who suffer from chronic, incurable conditions;
4. informed consent must play a vital role when a patient is seeking experimental stem cell therapy. Whether proven or unproven, all available information must be provided to the patient. The patient must also be given the option of withdrawing informed consent if there is new research or information that has come to light which pertains to the stem cell treatment that the patient initially consented to;

[241] The Constitution of South Africa, 1996.

5. medical professionals, in the instance where a patient is desperate to access experimental treatment, must remain exempt from liability. Some of the only circumstances under which medical professionals treating the patient should be held liable is if they were knowledgeable but proceeded to withhold important information about the specific stem cell therapy, if the professional in question intentionally promoted bogus treatments, especially in the view of benefitting financially;
6. as a further safeguard to patient rights, laws must determine that the physicians must first approach the SAPHRA, being the first approving body, as opposed to going directly to the manufacturer, as is permitted in the Right to Try Act.

The accessibility of unproven treatments should be dealt with explicitly. This will leave little room for South Africans to seek alternative medical treatments cross borders. By affording access within the Republic of South Africa, the presumption is that there would be better control over the implementation and continued regulation thereof. To address the concerns that come along with affording access to experimental stem cell therapies, it is necessary to impose certain restrictions such as in terms of any emergency or expanded access program. This would ensure that right to try laws are not abused. This would mean that access to experimental therapies may be regulated in such a way that access is only given to those who are in dire need, such as terminally ill patients or those who have exhausted all other available therapies.

With the onset of the recent COVID-19 pandemic, the development of an adequate regulatory framework is necessary. Considering the number of diseases that South Africans in particular are suffering from such as HIV/AIDS and Tuberculosis,[242] it is important that the government provides access to health care which includes access to experimental treatments.

Affording such access can be beneficial to the patient, medical professionals, medical researchers and to the State. There is a host of information that can be gathered from the implementation of such therapies which may increase the quality of many people's lives.

[242] Centers for disease control and prevention 'CDC's HIV/AIDS Care and Treatment Programs in South Africa: TB and HIV' available at *cdc.gov/globalhealth/countries/southafrica/what/tb_hiv.htm*, accessed on 12 July 2021.

As Judge Judith W. Rogers, dissenting in Abigail Alliance, said: "While the potential cures may not prove sufficient to save the life of a terminally ill patient, they are surely necessary if there is to be any possibility of preserving her life".[243]

[243] Abigail Alliance for Better Access to Developmental Drugs v. von Eschenbach, 495 F.3d 695 (D.C. Cir. 2007).

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APPENDIX I

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

Mrs Yadhna Gosai (204504870)
School Of Law
Howard College

Dear Mrs Yadhna Gosai,

Protocol reference number: 00006785
Project title: Affording patients the right to access experimental stem cell treatment: A comparative analysis of the legal and ethical consequences.

Exemption from Ethics Review

In response to your application received on 28 July 2021 , your school has indicated that the protocol has been granted **EXEMPTION FROM ETHICS REVIEW.**

Any alteration/s to the exempted research protocol, e.g., Title of the Project, Location of the Study, Research Approach and Methods must be reviewed and approved through an amendment/modification prior to its implementation. The original exemption number must be cited.

For any changes that could result in potential risk, an ethics application including the proposed amendments must be submitted to the relevant UKZN Research Ethics Committee. The original exemption number must be cited.

In case you have further queries, please quote the above reference number.

PLEASE NOTE:
Research data should be securely stored in the discipline/department for a period of 5 years.

I take this opportunity of wishing you everything of the best with your study.

Yours sincerely,

[redacted]

Mr Simphiwe Peaceful Phungula
obo Academic Leader Research
School Of Law