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The CRISPR patent landscape: A South African perspective

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This mini-dissertation is submitted in partial fulfilment of the requirements for
the degree of Master of Laws in Business Law.

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2020

ABSTRACT

The patent rights to CRISPR technology in different jurisdictions have been fought over tirelessly by both public and private actors. This battle has raised questions regarding the privatisation of publicly-funded research. Further complicating this landscape – these actors have implemented exclusive licensing regimes that many have argued serve as a hindrance to the access and development of CRISPR technology.

Within this complex patent regime and the great potential that this technology has in the prevention and treatment of disease, it is important to consider: (1) whether this patent and licensing regime is serving the public interest; and (2) what impact these regimes will have on developing countries such as South Africa.

In answering both of the above questions, I find that the current patent and licensing regimes are not conducive to the public interest, and further, may hold even more dire consequences for applications of CRISPR technology in developing countries.

ACKNOWLEDGEMENTS

To my mentors – Dr Thaldar and Dr Kinderlerer – I thank you for your support, guidance and compassion. For showing me doors that I never knew existed.

To my partner and best friend, Amy, I thank you for sharing this difficult journey with me. This is as much my achievement as it is yours.

To my father. Much of the research and work on this document was done whilst crying inside a hospital. I am trying to reconcile the guilt that I feel for spending valuable time on this, with the immense joy that it will bring to us both. I hope I've done you proud, father. Thank you for making it, when I didn't think that you would. I love you very much.

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DECLARATION REGARDING ORIGINALITY

I, Meshandren Naidoo (214549331) declare that:

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



Date: 05 March 2020

LIST OF ACRONYMS

CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
Cas9	CRISPR Associated Protein 9
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
ARV	Antiretroviral
IP	Intellectual Property
HIV	Human Immunodeficiency Virus
AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Treatment
WIPO	World Intellectual Property Organization
FTO	Freedom to Operate
NHA	National Health Act 61 of 2003
UC	University of California, Berkeley
SSE	Substantive Search and Examination
SALC	South African Law Commission
USPTO	United States Patent and Trademark Office
PTAB	Patent Trial and Appeal Board
sgRNA	Single Guide Ribonucleic Acid
USC	United States Code
DNA	Deoxyribonucleic Acid
EPO	European Patent Office
OD	Opposition Division
PCT	Patent Cooperation Treaty
PAM	Protospacer Adjacent Motif
NIH	National Institutes of Health
NSF	National Science Foundation
IPRPFRA	Intellectual Property Rights from Publicly Financed Research and Development Act 51 of 2008

NIPMO	National Intellectual Property Management Office
BBBEE	Broad-Based Black Economic Empowerment
LCA10	Leber Congenital Amaurosis Type 10
USH2A	Usher Syndrome Type 2A
HSV-1	Herpes Simplex Virus Type 1
CIPC	Companies Intellectual Properties Commission
SAPO	South African Patent Office
TB	Tuberculosis
IPAP	Industrial Policy Action Plan
OECD	Organisation for Economic Co-operation and Development
NPI	Non-Patent Incentives
FRAND	Fair, Reasonable, and Non-Discriminatory
SEP	Standard Essential Patents
MPP	Medicines Patent Pool
IDT	Integrated DNA Technologies
ONT	Oxford Nanopore Technologies
DHHS	US Department of Health and Human Services
KEI	Knowledge Ecology International
FDA	Food and Drug Administration
NRF	National Research Foundation

CHAPTER 1

INTRODUCTION

I INTRODUCTION

Genome editing has grown enormously, predominantly since the development of the CRISPR-Cas9 system, which thrust the field of biotechnology into the public view.¹ This revolutionary technology provides a reasonably quick, easy, precise, and inexpensive method of targeting and editing specific genetic sequences, in comparison to current research tools.² CRISPR-Cas9 holds the potential to promote scientific research, enhance biotechnology, and aid in the diagnosis and treatment of human disease.³

Despite its capabilities, CRISPR-Cas9 has emphasised the contentious and expanding field of patents covering the technology and its application.⁴ The patenting of CRISPR-Cas9 has led to an array of litigation internationally as two institutions have battled for sole rights over the technology.⁵ Notwithstanding the foundational patents, CRISPR has been the subject of numerous additional patent applications by various institutions. This has created a complex landscape,⁶ resulting in uncertainty as to how this technology can be utilised or researched further.⁷

¹ Genome editing refers to ‘the deliberate alteration of a selected DNA sequence in a living cell’ in order to change a gene’s function. Nuffield Council on Bioethics ‘Genome editing and human reproduction: Social and ethical issues short guide’ (2018) *Nuffield Council on Bioethics* 3; Neil Kirby ‘Gene editing and South African law’ (2016) 16(3) *Without Prejudice* 17.

² Catherine Jewell & Vijay Shankar Balakrishnan ‘The battle to own the CRISPR-Cas9 gene-editing tool’ *WIPO Magazine* April 2017, available at https://www.wipo.int/wipo_magazine/en/2017/02/article_0005.html, accessed on 10 September 2019.

³ It is worth noting some of the potential therapeutic benefits of CRISPR technology. There are numerous industries in which CRISPR can be, and has been, applied. The most significant of these are the medical and healthcare fields where CRISPR can be utilised in the treatment and prevention of a variety of genetic and infectious diseases including cystic fibrosis, Huntington's disease, muscular dystrophy, sickle cell anemia, beta-thalassemia, blindness, certain cancers, and HIV/AIDS. Further, CRISPR can be used in diagnostics for disease detection. Ibid; CB Insights ‘Healthcare is only the beginning: 15 big industries CRISPR technology could disrupt’ 1 August 2018 available at <https://www.cbinsights.com/research/crispr-industries-disruption/>, accessed on 13 December 2019; Clara Rodríguez Fernández ‘7 diseases CRISPR technology could cure’ *Labiotech* 23 July 2019, available at <https://www.labiotech.eu/crispr/crispr-technology-cure-disease/>, accessed on 23 January 2020.

⁴ Jacob S Sherkow ‘The CRISPR patent landscape: Past, present, and future’ (2018) 1(1) *The CRISPR Journal* 2.

⁵ Washington AFP ‘Broad Institute wins gene-editing patent case’ 25 July 2014 available at <http://bedfordviewedenvalenews.co.za/afp/248543/broad-institute-wins-gene-editing-patent-case>, accessed on 26 September 2019.

⁶ As the number of patents that are granted increases, the patent claims outlining the scope of protection will narrow, decrease in value, and become more challenging to enforce. Timothé Cynober ‘CRISPR: One patent to rule them all’ *Labiotech* 11 February 2019, available at <https://labiotech.eu/features/crispr-patent-dispute-licensing/>, accessed on 10 September 2019.

⁷ This may impact what the technology covers as well as the countries in which the patent applies. This is because patents are territorial and are required in each country where the invention is intended to be utilised. Joanne van

While patenting CRISPR-Cas9 techniques and products may establish ownership over certain processes and generate revenue for specific institutions, it may also hinder the field of science and medicine by limiting the use of such technology without licenses. Further, in cases where there is extensive scientific involvement, patents can be more of a hindrance, forcing scientists to apply for licenses in order to continue their work.⁸

II RATIONALE AND RESEARCH QUESTIONS

Patents serve to grant the proprietor the exclusive right to prevent others from making, utilising, selling, and importing their invention. Also, the context of CRISPR, the patent holder has the right to prescribe the manner in which licensed parties use the invention in order to limit what the proprietor perceives as an unethical use of the technology.⁹

The primary research question is whether the current CRISPR-Cas9 patent regime (with regards to human therapeutics) is optimal for the public interest. There are additional research questions, relevant to the chapters of this dissertation, which assist in answering the main research question. These are –

- (a) What issues does the CRISPR patent and licensing regime pose to the research and commercialisation of CRISPR human therapeutic applications?
- (b) Are the current CRISPR licensing regimes optimal for the public interest?
- (c) Due to the patent regime, what are the challenges that South Africa faces in bringing CRISPR human therapeutic applications to the public?
- (d) How can the discussed challenges be addressed to optimise CRISPR technology for the public interest?

Harmelen 'Intellectual property rights and genome editing: Navigating the patent thicket' *ENS Africa* available at http://biosafety.org.za/cms/modules/media/scripts/documents/document.handler.php?media_files_id=1201, accessed on 15 September 2019; Sherkow op cit note 4 at 2.

⁸ Shobita Parthasarathy 'CRISPR dispute raises bigger patent issues that we're not talking about' *The Conversation* 4 April 2016, available at <http://theconversation.com/crispr-dispute-raises-bigger-patent-issues-that-were-not-talking-about-56715>, accessed on 16 September 2019.

⁹ Daniel Mak 'South Africa: Can patents help regulate future experimentation with designer babies?' *KISCH IP* 12 December 2018, available at <http://www.mondaq.com/southafrica/x/763558/Patent/Can+Patents+Help+Regulate+Future+Experimentation+With+Designer+Babies>, accessed on 10 September 2019.

III CHAPTER BREAKDOWN AND RESEARCH OUTLINE

The main body of this dissertation will comprise of three chapters, as well as an introduction and conclusion. Chapter 1 introduces the topic and provides a rationale and the research questions to be addressed, followed by a literature review of the central sources of work utilised in this dissertation.

Chapter 2 aims to show that the global patent landscape, as a result of the immense number of CRISPR patents, is suboptimal for research and commercialisation and thus does not serve the public interest. It provides a detailed background of the ongoing CRISPR patent dispute in the US and its relevance to South Africa. It contains a South African CRISPR patent landscaping search to highlight issues. Policy suggestions are made that aim to solve some of these concerns.

Chapter 3 examines licensing regimes and surrogate companies (surrogates) and shows that exclusive patent rights as well as the breadth of these rights, can hinder research and development of potential applications of CRISPR technology that may aid in priority disease treatment. This Chapter includes a critical take on arguments for and against the need for exclusivity and surrogates to determine whether they are absolutely necessary.

Chapter 4 deals with Freedom to Operate (FTO) in light of the points raised in Chapters 2 and 3 and other conditions, such as ethical license restrictions imposed by the foundational CRISPR patent holders. Additionally, FTO is explored through the lens of the National Health Act 61 of 2003 (NHA). Recommendations regarding its interpretation, giving effect to the public interest, are provided. This Chapter concludes with an evaluation of patent pools as a potential solution to the issues raised in the previous chapters.

Chapter 5 forms the conclusion of this dissertation and contains a summation of the issues and topics discussed. It offers recommendations that attempt to balance private rights and public interest in order to address concerns relating to the current CRISPR patent landscape.

IV LITERATURE REVIEW

This dissertation approaches the topic in a pragmatic manner and explores a variety of patents, licensing agreements, business models, statutes, and policies. This literature review contains a discussion of the main sources regarding (a) the relevance of the US CRISPR patent dispute; (b) licensing agreements; and (c) the patent system and legislation in South Africa and the US.

(a) *The relevance of the US CRISPR patent dispute*

Scientific literature has emphasised the potential of CRISPR-Cas9 in transforming biotechnology and public health concerns.¹⁰ In light of the CRISPR patent dispute, it is necessary to examine the current patent landscape in the US as well as Europe and South Africa. This will provide an insight into the key patent holders, the technologies available, and the challenges associated with patenting technologies that fall within the public interest. It will entail studying the pending patent applications as well as granted patents relating to CRISPR in these jurisdictions, including the initial patent applications filed by the University of California, Berkeley (UC) (No. 13/842,859) and the Broad Institute (Broad) (No. 14/054,414), as well as their subsequent applications.¹¹ Furthermore, the relevant interference proceedings and appeal decisions in the US CRISPR patent dispute will be examined.¹²

The literature surrounding the CRISPR patent dispute in the US is comprehensive. As well as US legislation, case law, patents, and other documents, there have been numerous commentaries on the dispute and various opinions from experts in the field. These sources will be examined in order to establish the challenges that the CRISPR patent landscape poses to the research and commercialisation of CRISPR human therapeutic applications, as well as the difficulties facing South Africa in bringing such applications to the public.

(b) *Licensing agreements*

Patents are supposed to assist in the commercial development of a technology. However, technological advances, as well as the future of CRISPR-Cas9 and its patents, are contingent on the conduct of researchers and their institutions.¹³ While universities commonly collaborate to distribute innovation and knowledge, patent exclusivity conflicts with, and discourages, these traditional values and limits the potential widespread usage of CRISPR technology. The

¹⁰ Itziar de Lecuona ‘Gene editing in humans: Towards a global and inclusive debate for responsible research’ (2017) 90(4) *Yale J Biol Med* 674.

¹¹ These include Broad’s patents 8,697,359; 8,771,945; 8,865,406; 8,871,445; 8,889,356; 8,895,308; 8,906,616; 8,932,814; 8,945,839; 8,993,233; 8,99,641; 9,840,713 and application 14/704,551 as well as UC’s applications 15/947,680; 15/947,700; 15/947,718; 15/981,807; 15/981,808; 15/981,809; 16/136,159; 16/136,165; 16/136,168; and 16/136,175.

¹² These include *Broad Institute, Inc. v. Regents of the Univ. of Cal.*, Decision on Motions, Patent Interference No. 106,048 (PTAB Feb. 15, 2017); *Regents of the University of California v Broad Institute* No. 2017-1907 (Fed. Cir. Sep. 10. 2018); and *The Regents of the University of California, University of Vienna, and Emmanuelle Charpentier v The Broad Institute, Inc., Massachusetts Institute of Technology, and President and Fellows of Harvard College* Patent Interference No. 106,115 (DK).

¹³ Sherkow op cit note 4 at 4.

result of the US CRISPR patent dispute will determine who invented the technology, which will have vast benefits.¹⁴

Notwithstanding the continuing patent litigation, Broad and UC have formed spin-out companies (spin-outs) and have granted them exclusive licenses for the use of their CRISPR portfolios. This licensing regime may inhibit innovation and development by excluding others from the industry, unless they pay large amounts for sub-licenses.¹⁵

(c) *The patent system and legislation in South Africa and the US*

The US Patent and Trademark Law Amendment Act,¹⁶ commonly referred to as the Bayh-Dole Act (Bayh-Dole), allows grant recipients to patent government-funded inventions.¹⁷ This deserves attention, especially in light of the US CRISPR patent dispute, as the technologies developed by Broad and UC are both federally-funded.¹⁸ It has been questioned whether the privatisation of publicly-funded inventions, through patents and licensing, serves the public interest. The US CRISPR patent dispute seems to have diminished established scientific values by focusing on exclusivity. However, if these two institutions worked together, science could progress.¹⁹ Due to the numerous CRISPR patents that exist internationally, it is important to determine what mechanisms South Africa has at its disposal to prevent the excessive granting of patents, which may cause the landscape to become saturated. One such mechanism is the shift from a depository system to a search and examination system as per the Intellectual Property Policy of the Republic of South Africa (IP Policy).²⁰

The government suggests that a sturdier framework, including the introduction of substantive search and examination (SSE) procedures and patent opposition proceedings, will

¹⁴ This is because the owner of the rights to CRISPR-Cas9 may gain financially and determine who uses the technology. Broad and UC have an interest in numerous spin-out companies, which have invested in CRISPR-Cas9 technologies for new treatments in a variety of genetic diseases. Jewell & Balakrishnan op cit note 2; Parthasarathy op cit note 8.

¹⁵ Sherkow op cit note 4 at 4.

¹⁶ 1980, Pub. L. No. 96-517 (codified at 35 U.S.C §§ 200-212 (2000)).

¹⁷ Lisa Larrimore Ouellette & Rebecca Weires 'University patenting: Is private law serving public values?' (2019) *Michigan State Law Review*, *Forthcoming*; *Stanford Law and Economics Olin Working Paper No. 537 2*.

¹⁸ Sarah Zhang 'How the CRISPR patent dispute became so heated' *The Atlantic* 6 December 2016, available at <https://www.theatlantic.com/science/archive/2016/12/crispr-patent-in-court/509579/>, accessed on 5 January 2020.

¹⁹ Jacob S Sherkow 'Patent protection for CRISPR: An ELSI review' 2017 *Journal of Law and the Bioscience* 574.

²⁰ Department of Trade and Industry 'Intellectual property policy of the Republic of South Africa Phase I' (2018). The IP Policy is viewed as an essential component of the National Development Plan which seeks to grow innovation and efficiency. Emma Smith 'Draft IP Policy released' *Michalsons* 10 August 2017, available at <https://www.michalsons.com/blog/draft-ip-policy-released/30555>, accessed on 3 September 2019; Janice Galvad & Ramon Pereira 'Phase I of South Africa's IP Policy: What you need to know' *Go Legal* 26 July 2018, available at <https://www.golegal.co.za/ip-policy-south-africa/>, accessed on 24 August 2019.

ensure that certain goals are met, including access to public health.²¹ Although the Patents Act 57 of 1978 (Patents Act) makes provision for such proceedings, these have not been implemented due to a lack of infrastructure and no clear guidance as to its operation.²²

In this dissertation, the Patents Act and its various regulations, as well as the IP Policy, will be examined, and recommendations made that consider the public interest.

V RESEARCH DESIGN AND METHODS

This dissertation centres on desktop research of primary and secondary sources. Primary sources include, but are not limited to, international treaties and agreements; various national, foreign, and international statutes; case law (including national and foreign judgments); national policies, strategies, and guidelines; patent literature in the public domain, including examiner's comments; and patent databases.

Secondary sources predominantly include scientific and legal academic textbooks and journal articles; internet sources and articles; online magazine articles; interviews, presentations, and panel discussions; news reports; expert opinions on various topics; articles and columns; reports; and commentary on legislation and cases.

²¹ The IP Policy highlights the case of *Pharmaceutical Manufacturers Association of South Africa: In re Ex Parte President of the Republic of South Africa* 2000 (2) SA 674, which recognised the convergence of IP and public health. The Constitution of the Republic of South Africa, 1996 recognises the right of access to healthcare. The IP Policy accepts that there is no connection between greater IP protection and innovation. However, government maintains that a secure framework will aid in the realisation of other goals, such as access to public health. CRISPR in the context of human therapeutics shows great potential in the treatment and prevention of disease, including HIV, which is a prime target for eradication in various South African and international policies. South Africa should capitalise on this technology in order to fulfil public health imperatives. *Ibid.*

²² However, it should be noted that the Patents Act does not make provision for either pre- or post-grant opposition proceedings.

CHAPTER 2

THE CONTEMPORARY CRISPR PATENT LANDSCAPE

I INTRODUCTION

The CRISPR patent dispute in the US has influenced the patent landscape, specifically in terms of international health-related research and innovation. Additionally, it brought to light various issues relating to the patenting of nascent biotechnologies. Understanding the history of this dispute and its resolution is important in the South African context as the country is in the process of reforming its patent laws, policy, and infrastructure.

II OVERVIEW

This Chapter aims to inform policy development that furthers the public interest, and highlights concerns regarding patents in health-related research globally, as well as in the South African context. I begin with an overview of the ongoing CRISPR patent dispute in the US as it concerns the two largest controllers of the technology, from which all other CRISPR developers will need to obtain licenses – including South African ones. The current CRISPR patent landscape in the US and Europe is reviewed, and shows that this landscape is both increasingly complex and uncertain. To understand why this is the case in the US, I analyse the legislative framework governing patents, which reveals broader issues of patenting publicly-funded inventions. I question whether this commercial system serves the public interest. Thereafter, I conduct a CRISPR patent landscaping search to ascertain whether the situation is as complex in South Africa and find that there already exists a CRISPR patent thicket. In order to combat this issue, I discuss how to adapt the imminent SSE procedures and opposition proceedings in South Africa.

This Chapter puts forth the idea that the global patent landscape, due to the vast number of CRISPR patents, both applications and grants, is not optimal for research and commercialisation.¹ Further, an analysis of some of the potential reasons for these CRISPR patents is presented, along with working solutions to resolve the issues.

¹ This includes researchers as well as those who wish to commercialise CRISPR technologies.

III POINT OF DEPARTURE

(a) *Public interest*

This dissertation aims to elucidate how CRISPR-related patents and licensing agreements do not serve the public interest in South Africa, and globally. Therefore, as it is an ongoing theme in this dissertation, it is necessary to define what is meant by public interest. Public interest ‘is not one homogenous undivided concept’,² making it a complex term that is context-specific and challenging to define.³ Globally, public interest includes access to, and development of, CRISPR technology; the dissemination and protection of knowledge and data surrounding CRISPR; the interests of scientific values such as collaboration and accessibility; and the interests of investors and investees. Science should act in the public interest by focusing on the promotion of, and access to, public health benefits. The privatisation of CRISPR is contentious due to the public interest, the utilisation of public resources in this technology, and its potential health benefits.⁴

(i) *A private versus public goods perspective*

Before raising arguments as to why medical technologies, such as CRISPR, can be considered ‘public goods’, it is important to distinguish between two different usages of CRISPR technology: (1) somatic uses; and (2) germline uses.

Somatic uses entail a private interest dimension, as well as a public interest dimension.⁵ The private interest dimension is that the individual is either, independently or in combination, cured, treated to reduce symptoms or lifespan of an ailment, or prevented (ex post or pre-emptively) from developing a certain ailment. This alteration is not passed down through generations as somatic uses only affect that specific individual.

² In *McKinnon v Secretary, Department of Treasury* [2005] FCAFC 142 para 12, it was stated that public interest ‘will often be multi-faceted and the decision-maker will have to consider and evaluate the relative weight of these facets before reaching a final conclusion as to where the public interest resides’. Jane Johnston ‘Whose interests? Why defining the “public interest” is such a challenge’ *The Conversation* 23 January 2019, available at <https://theconversation.com/whose-interests-why-defining-the-public-interest-is-such-a-challenge-84278>, accessed on 19 January 2020.

³ *Ibid.*

⁴ Benjamin Capps et al ‘Falling giants and the rise of gene editing: ethics, private interests and the public good’ (2017) 11(20) *Human Genomics* 5.

⁵ Somatic cells refer to any cell in the body that do not constitute gametes, germ cells, or stem cells. Somatic gene editing therapy endeavours to alter the DNA within multiple target cells, typically through a virus or vector. Biology Dictionary ‘Somatic cells’ available at <https://biologydictionary.net/somatic-cells/>, accessed on 10 November 2019; Francis Fukuyama *Our Posthuman Future: Consequences of the Biotechnology Revolution* (2002) 76.

Germline uses refer to gamete or embryonic edits,⁶ which result in a genetic alteration being passed on to descendants.⁷ This has a ‘contagion’ effect, in that the genetic alteration could be expressed vertically in many generations down the line from the initial edit.

Whilst germline applications of CRISPR technologies currently remain purely academic and, as demonstrated throughout this dissertation, may remain so, somatic applications have successfully been applied in the clinical context. As CRISPR technology advances and shows even greater potential in alleviating certain conditions,⁸ it is clear that this technology will likely become a therapeutic technology unlike any other – possibly eclipsing the efficacy, impact, and necessity of essential drugs,⁹ or scarce treatments.¹⁰ Due to the site-specific nature of gene editing technologies like CRISPR – through both somatic and germline edits – it is possible that essential drugs may become redundant – or at the very least, may not be needed to such a degree in South Africa. If this does eventuate, states like South Africa will have more funds available for other purposes.

According to Vawda and Baker,¹¹ health technologies are social in nature, meaning that they benefit not only the individual using it, but also others who are in contact with that individual.¹² The following is an adapted version of Vawda and Baker’s¹³ arguments explaining why CRISPR technologies fall into the category of public goods: (1) health technologies, specifically CRISPR, have a significant impact on public health; (2) its impact, development, and use is universal and subject globally to regulation; and (3) there are public consequences resulting from decisions on the research, development, and use of these health technologies.¹⁴

⁶ A germ cell is a reproductive cell, either an egg or sperm cell. Medicine Net ‘Medical definition of germ cell’ 2018 available at <https://www.medicinenet.com/script/main/art.asp?articlekey=8591>, accessed on 10 November 2019.

⁷ Germline alterations are duplicated in each cell of the embryo, meaning that edits would be transferred to all progeny cells and passed on to descendants. Joanne van Harmelen ‘Human genome editing with CRISPR-Cas9: South African legal perspective’ *International Law Office* 17 May 2017, available at <https://www.internationallawoffice.com/Newsletters/Healthcare-Life-Sciences/South-Africa/ENSAfrica/Human-genome-editing-with-CRISPR-Cas9-South-African-legal-perspective?redir=1>, accessed on 30 August 2019.

⁸ This is in terms of more effective screening, testing, and therapeutically. A current example is the SARS-CoV-2 pandemic.

⁹ For example, antiretroviral (ARV) drugs used to control HIV.

¹⁰ Such as dialysis machines and the requisite staff needed for patients with kidney failure.

¹¹ Yousuf A Vawda & Brook K Baker ‘Achieving social justice in the human rights/intellectual property debate: Realising the goal of access to medicines’ (2013) 13(1) *AHRLJ* 76.

¹² For example, vaccines.

¹³ Vawda & Baker op cit note 11 at 76.

¹⁴ This includes risk and loss in terms of public expenditure that was used to fund research and development that was privatised through patents, and public expenditure being drawn away from other important diseases.

(ii) *Somatic technologies as public goods*

The repercussions of health technologies, like CRISPR, on an individual translate into wider ranging, albeit linear, effects.¹⁵ The corresponding public benefit is that reliance on the state for medical and social support may be reduced. This alteration has a positive impact, in the form of reduced strain on an individual's family sphere in the same way that regular medicines, such as ARV drugs, would. Another positive effect is that, depending on the therapy, it may render an individual able to work, provide, and contribute to the state and the public.¹⁶

(iii) *Germline technologies as public goods*

Germline alterations could lead to permanent multigenerational consequences. In this way, the global community can both benefit, but also be harmed by such methods. An example is a germline edit that makes one resistant to HIV. This benefits not only the person themselves, but that person's family,¹⁷ spouse,¹⁸ the state,¹⁹ and global populations.²⁰ The same can be said of any potential harm – it can be expressed in future generations. In this way, certain ailments can be eliminated entirely from families, communities, ethnicities, and countries. The results of germline editing are not linear, but rather asymmetric and, as a result, have the potential to exponentially impact on the genetic makeup of the global population over many generations.²¹

There have been groups, organisations, and political leaders calling for a ban on germline editing due to its uncertainty and impact, not only on the individual, but the public at large. Apprehensions include the type of negative intergenerational effects that may result. Such concerns are shared by the patent holding institutions themselves, namely Broad and UC, who have incorporated restrictions in their license agreements that prohibit germline editing – as will be discussed in Chapter 3.

¹⁵ This reduces the impact that an individual has on immediate family, partners, and the state

¹⁶ An example of this would be a somatic edit designed to cure a form of blindness.

¹⁷ This is due to a reduced social and economic burden. Offspring may also be positively affected, and their offspring – and so on.

¹⁸ By reducing the risk of transmission to the partner and offspring.

¹⁹ By reducing the burden on the state in terms of any social welfare in the form of medical and pharmaceutical claims.

²⁰ By reducing the number of infections which, on a larger scale of implementation, can also reduce the risk of contracting HIV, hence possibly removing the virus from communities all over the world.

²¹ This is due to widespread travel between states, reproduction, and the heritability factor associated with germline editing.

(iv) A South African Constitutional perspective

The importance of therapeutic applications of CRISPR technology are multidimensional, as demonstrated above, and should thus be central in policies and legislation dealing with the right to health and disease management. The promotion of the right to health is central in realising the spirit and purport of the Constitution of the Republic of South Africa, 1996 (the Constitution) and the Bill of Rights, as enumerated in the Preamble,²² section (1)(a),²³ section (7)(1),²⁴ and section 7(2).²⁵ In the following, I suggest that there is a duty on the state, at all levels, to create an enabling environment for the dissemination and implementation of CRISPR technology in South Africa.²⁶ This duty accordingly requires that patent law be developed to facilitate the use of such technology.

The Bill of Rights encapsulates various public interest considerations – such as the right to healthcare in section 27(1)(a),²⁷ and the right to scientific and academic freedom in section 16(1)(d).²⁸ The rights in section 27(1) of the Constitution are welfare rights aimed at supporting

²² The Preamble to the Constitution holds that '[w]e, the people of South Africa, Recognise the injustices of our past; Honour those who suffered for justice and freedom in our land; Respect those who have worked to build and develop our country; and Believe that South Africa belongs to all who live in it, united in our diversity. We therefore, through our freely elected representatives, adopt this Constitution as the supreme law of the Republic so as to –

Heal the divisions of the past and establish a society based on democratic values, social justice and fundamental human rights;
Lay the foundations for a democratic and open society in which government is based on the will of the people and every citizen is equally protected by law;
Improve the quality of life of all citizens and free the potential of each person; and
Build a united and democratic South Africa able to take its rightful place as a sovereign state in the family of nations.

May God protect our people. Nkosi Sikelel' iAfrika. Morena boloka setjhaba sa heso. God seën Suid-Afrika. God bless South Africa. Mudzimu fhatutshedza Afurika. Hosi katekisa Afrika'.

²³ Section 1(a) of the Constitution states that '[t]he Republic of South Africa is one, sovereign, democratic state founded on the following values... (a) Human dignity, the achievement of equality and the advancement of human rights and freedoms'.

²⁴ Section 7(1) of the Constitution holds that '[t]his Bill of Rights is a cornerstone of democracy in South Africa. It enshrines the rights of all people in our country and affirms the democratic values of human dignity, equality and freedom'.

²⁵ Section 7(2) of the Constitution states that '[t]he state must respect, protect, promote and fulfil the rights in the Bill of Rights'.

²⁶ The Competition Act 89 of 1998 also references the public interest both directly and indirectly in its Preamble. It states that its purpose is inter alia to 'regulate the transfer of economic ownership in keeping with the public interest'. The transfer of economic ownership in line with the public interest is significant as it exemplifies the states commitment to considering public interests.

²⁷ This section states that 'everyone has the right to have access to...health care services, including reproductive health care'.

²⁸ This section holds that 'everyone has the right to freedom of expression, which include...academic freedom and freedom of scientific research'.

citizens.²⁹ This section must be read with section 27(2) of the Constitution,³⁰ which imposes a positive duty on the state to take ‘reasonable legislative measures’³¹ to enable the ‘progressive realisation’ of the right.³² However, the scope of this duty, and the rights by extension, is limited to the available resources.³³ In *Government of the Republic of South Africa v Grootboom* (*Grootboom*),³⁴ the Court noted that although section 26 of the Constitution does not expressly state that there is a negative obligation on the state, there is in fact a negative duty that precludes the state and other entities from interfering with the right of access to adequate housing.³⁵

The ‘reasonableness’ criterion, as developed in *Grootboom*, was interpreted to be multi-dimensional. However, a key aspect in determining reasonableness is evaluating both the historical and current context of measures that have been introduced, and the reasons for doing so. HIV/AIDS provides a snapshot of a single challenge facing South Africa.³⁶ In 2018, there were almost 250,000 new HIV infections, suggesting substantial growth of the virus, despite the implementation of state-wide measures. South Africa has spent a monumental sum of money, comprising mostly of its own funds, for the antiretroviral treatment (ART) programme.³⁷ While these are great measures, the costs of life and expenditure are too high,

²⁹ Section 27(1) of the Constitution states that ‘[e]veryone has the right to have access to –

(a) health care services, including reproductive health care;

(b) sufficient food and water; and

(c) social security, including, if they are unable to support themselves and their dependants, appropriate social assistance’.

³⁰ Section 27(2) of the Constitution holds that ‘[t]he state must take reasonable legislative and other measures, within its available resources, to achieve the progressive realisation of each of these rights’.

³¹ Section 27(2) of the Constitution.

³² *Ibid.*

³³ *Soobramoney v Minister of Health (Kwazulu-Natal)* 1998 (1) SA 765 (CC) para 11.

³⁴ 2001 (1) SA 46. This case focused on the right of access to adequate housing in section 26 of the Constitution, and the state’s duty associated therewith. *Grootboom*, amongst others, resided in an informal settlement in terrible conditions. Despite the state offering to assist in ameliorating their situation, it failed to do so. In a unanimous decision by the Constitutional Court, it held that the Constitution imposes a positive duty on the state help those living in appalling conditions by providing access to housing, healthcare, food and water, and social security. As the rights contained in the Bill of Rights are interlinked, the right of access to adequate housing cannot be viewed in isolation. However, the state is only required to use the resources it has available and is not expected to realise these rights straight away. The question is whether the state’s measures, in realising the rights in section 26 of the Constitution, are reasonable. Those with the most serious needs must not be overlooked. Measures that appear to succeed, but do not acknowledge the needs of those most critical, may not be reasonable. Although section 26 and section 28(1)(c) of the Constitution did not entitle the *Grootboom* community to immediate shelter, the programme in place at the time did not satisfy section 26 of the Constitution and failed to provide interim assistance to those who were desperate. Although *Grootboom* dealt with section 26 of the Constitution, the interpretation lends itself to section 27 too.

³⁵ *Grootboom* para 35. The Court also held that the state must create conditions for access to adequate housing. This must be achieved through policy etc.

³⁶ Currently, the country has the largest HIV epidemic in the world, with close to eight million positive cases. In 2018, there were over 70,000 HIV-related deaths. Avert ‘HIV and AIDS in South Africa’ 15 April 2020 available at <https://www.avert.org/professionals/hiv-around-world/sub-saharan-africa/south-africa>, accessed on 9 January 2020.

³⁷ South Africa has the world’s biggest ART programme. The money spent on the ART programme is equivalent to over 1.5 billion dollars per year. *Ibid.*

and a suitable alternative should be explored. CRISPR technology poses a cheaper and more effective multigenerational, global scale solution.³⁸ The biggest challenges are currently patent laws, access, investment, and development.

I suggest that these rights are encapsulated, and can be furthered, by the research, development, and utilisation of CRISPR technologies in order to bring human therapeutic applications into fruition. This is imperative from a public health perspective as CRISPR shows great potential in the prevention and treatment of priority diseases such as HIV/AIDS.

(v) *The private industry*

The public also has an interest in maintaining a thriving bio-economy with a prosperous private sector. In order to create an enabling environment from one that is currently destitute, the private sector should not be subject to a stranglehold, and hence dissuaded from investment, but should in fact be supported. I suggest that a balancing act, which takes into account the necessity of private rights, should be implemented. It should focus on when these rights must be tempered in terms of policy reform for a more equitable social outcome that does not stifle the private industry, and hence aids in South Africa's difficulty in creating a thriving biotechnology industry.

In short, public interest, for the purpose of this dissertation, means the interests of the public broadly. This encompasses the interests of citizens in obtaining improved healthcare treatments for priority and genetic diseases; and the interests of innovators in researching, developing, obtaining licenses, patenting, sharing knowledge, and commercialising CRISPR applications.

³⁸ HIV attacks the immune system by targeting CD4 immune cells. HIV-1 enters host cells by fusing with the CD4 receptor and CCR5 co-receptors. A homozygous 32-bp deletion in the CCR5 gene (CCR5 Δ 32) can cause resistance to HIV-1 infection. CCR5 Δ 32 is a genetic mutation which disables the CCR5 receptor on white blood cells, thus preventing HIV from penetrating the cells of the immune system. CRISPR-Cas9 has the ability to produce deletion variations of CCR5 that mirrors the CCR5 Δ 32 mutation and prevents the virus from entering the cell. Qiaoqiao Xiao et al 'Application of CRISPR/Cas9-based gene editing in HIV-1/AIDS therapy' (2019) 9(69) *Front. Cell. Infect. Microbiol* 6; Sheena Saayman et al 'The therapeutic application of CRISPR/Cas9 technologies for HIV' (2015) 15(6) *Expert Opin Biol Ther.* 6-8; Martha Kempner 'The genetic mutation behind the only apparent cure for HIV' *The Body Pro* 14 March 2019, available at <https://www.thebodypro.com/article/staying-on-prep-commercial-insurance-vs-medicaid>, accessed on 23 November 2019.

IV THE CRISPR PATENT DISPUTE IN THE US

(a) Background leading up to the dispute

The patenting of CRISPR-Cas9 has resulted in international litigation as two institutions battle over sole rights to the technology.³⁹ This dispute has brought the perils associated with patents in health-based research and innovation to the fore. The key foundational patent holders for the CRISPR-Cas9 technology are Emmanuelle Charpentier from the University of Vienna, Jennifer Doudna from UC, and Feng Zhang of Broad.⁴⁰

CRISPR gained publicity in 2012 with the publication of a paper by Doudna and Charpentier.⁴¹ The paper outlined how CRISPR, aided by an enzyme known as Cas9, could be converted into a tool for gene editing.⁴² Doudna and Charpentier, who filed their original patent application (No. 13/842,859) on 15 March 2013, but had a priority date of 25 May 2012 (see below for an explanation), were the first to invent methods for using CRISPR-Cas9 beyond its natural environment. Their patent covered broad claims to the CRISPR-Cas9 technology in ‘transgenic non-human multicellular organisms’.⁴³

This is where the distinction between prokaryotes and eukaryotes is important. Prokaryotes include bacteria and archaea, and refer to organisms lacking a membrane-bound nucleus, mitochondria, and organelles.⁴⁴ On the other hand, eukaryotes refer to living

³⁹ Although CRISPR itself cannot be patented, Cas9 is an enzyme found in a natural bacterial process. What was sought to be patented were the methods, engineered elements, and structures modified from their natural state to be used for editing the genomes of living mammalian cells. Broad Communications ‘For journalists: Statement and background on the CRISPR patent process’ *Broad Institute* 16 January 2020, available at <https://www.broadinstitute.org/crispr/journalists-statement-and-background-crispr-patent-process>, accessed on 18 January 2020; Washington AFP ‘Broad Institute wins gene-editing patent case’ 25 July 2014 available at <http://bedfordviewedenvalenews.co.za/afp/248543/broad-institute-wins-gene-editing-patent-case>, accessed on 26 September 2019.

⁴⁰ Catherine Jewell & Vijay Shankar Balakrishnan ‘The battle to own the CRISPR-Cas9 gene-editing tool’ *WIPO Magazine* April 2017, available at https://www.wipo.int/wipo_magazine/en/2017/02/article_0005.html, accessed on 10 September 2019.

⁴¹ Martin Jinek et al ‘A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity’ (2012) 337(6096) *Science* 816-821.

⁴² Although Doudna and Charpentier’s paper attracted a great deal of interest in CRISPR, it had been discovered prior to 2012. CRISPR was initially recognised as a ‘general purpose gene-editing tool’ in a paper published by Erik Sontheimer and Luciano Marrafini in 2008. A patent application was filed, but rejected due to the scientists’ inability to ‘reduce it to any practical application’. Jewell & Balakrishnan op cit note 40.

⁴³ Jacob S Sherkow ‘The CRISPR patent interference showdown is on: How did we get here and what comes next?’ *SLS Blogs* 29 December 2015, available at <https://law.stanford.edu/2015/12/29/the-crispr-patent-interference-showdown-is-on-how-did-we-get-here-and-what-comes-next/>, accessed on 24 October 2019; Washington AFP op cit note 39.

⁴⁴ The components within a cell such as proteins, DNA, and metabolites, exist together within the cell membrane and not in separate cellular compartments. UC’s patent applications are based on work in test tubes rather than cells, and therefore do not focus on eukaryotes. Nature ‘Prokaryotes’ available at <https://www.nature.com/subjects/prokaryote>, accessed on 2 January 2020; Broad Communications op cit note 39.

organisms with a nucleus and internal membranes, and may be multicellular. These include animals, plants, and fungi.⁴⁵

In 2012, Zhang, through the publication of a paper in *Science*,⁴⁶ reported the discovery of a method to use CRISPR-Cas9 to edit eukaryotic cells. This promoted interest in the technology's potential to produce new and more effective medical treatments, thus increasing its commercial value. Simply put, Doudna and Charpentier demonstrated a broad utilisation of the CRISPR-Cas9 system for gene editing in bacteria and cell-free systems (prokaryotes),⁴⁷ whereas Zhang showed the usage of this system in more complex organisms (eukaryotes).

Zhang filed his CRISPR patent application (No. 14/054,414) for the use of the technology in eukaryotes on 15 October 2013, but received a priority date of 12 December 2012.⁴⁸ He simultaneously filed for an Accelerated Examination Request; a fast-track review process,⁴⁹ which allows for a patent application to be expedited in exchange for a fee.⁵⁰ Zhang's expedited review was accepted,⁵¹ resulting in the United States Patent and Trademark Office (USPTO) granting Zhang's patent in April 2014, with numerous other patents being awarded to Broad thereafter.⁵² Therefore, although it appeared that Doudna and Charpentier were the initial inventors of a workable CRISPR system, as well as the first to file a patent application encompassing it,⁵³ Zhang was triumphant regarding particular claims covering eukaryotic applications of CRISPR.⁵⁴ This ignited the current patent dispute between the two parties.⁵⁵

An influential factor in the proceedings was the patent system utilised in the US at the time. Prior to 2013, the USPTO held that a patent would be awarded to the first inventor,⁵⁶ in

⁴⁵ Nature 'Eukaryotes' available at <https://www.nature.com/subjects/eukaryote>, accessed on 2 January 2020; Ulrich Storz 'CRISPR Cas9 – licensing the unlicensable' (2018) 265 *Journal of Biotechnology* 86; Broad Communications op cit note 39.

⁴⁶ Le Cong et al 'Multiplex genome engineering using CRISPR/Cas systems' (2013) 339(6121) *Science* 819-823.

⁴⁷ UC's patent application covered essential elements of the CRISPR-Cas9 system to alter the DNA of bacteria, plant, animal, and human cells. Storz op cit note 45 at 86.

⁴⁸ Jacob S Sherkow 'The CRISPR patent landscape: Past, present, and future' (2018) 1(1) *The CRISPR Journal* 2; Sherkow op cit note 43.

⁴⁹ Jacob S Sherkow 'Patents in the time of CRISPR' 2016 *Genome Editing* 26.

⁵⁰ This procedure requests the United States Patent and Trademark Office to decide an application provided that it is concise (a maximum of three independent claims), related to one invention, and on condition that the patentability of individual claims will not be contended during prosecution. The inventor must agree to an 'all-or-nothing' decision on the application. Ibid at 26; Sherkow op cit note 43.

⁵¹ Sherkow op cit note 43.

⁵² Washington AFP op cit note 39.

⁵³ Sherkow op cit note 49 at 26; Jacob S Sherkow 'What the CRISPR patent dispute is all about' *Scientific American* 12 December 2016, available at <https://blogs.scientificamerican.com/guest-blog/what-the-crispr-patent-dispute-is-all-about/>, accessed on 15 September 2019.

⁵⁴ Sherkow op cit note 43.

⁵⁵ Sherkow op cit note 48 at 2.

⁵⁶ Sherkow op cit note 49 at 27.

line with the first-to-invent patent system.⁵⁷ When multiple inventors filed similar patent applications, it was held that the patent should be granted to the inventor who first formulated and reduced the concept to practice, even if they were not the initial filers of an application.⁵⁸ However, this changed with the enactment of the Leahy-Smith America Invents Act,⁵⁹ which introduced the current first-to-file patent system.⁶⁰

(b) *Battle one: The first interference proceedings*

(i) *Issues leading up to the proceedings in the Patent Trial and Appeal Board*

Due to the expedition of Zhang's patent application, UC requested the USPTO to launch a patent interference proceeding against the patents awarded to Broad because they interfered with UC's patent application.⁶¹ This request also sought to determine if the inventions were identical, and who the original inventor of CRISPR-Cas9 was.⁶² As the filing of the patents in the CRISPR dispute occurred prior to March 2013, the first-to-invent system was still in place.⁶³ In terms of this system, an interference procedure was applicable, resulting in UC's request being granted by the USPTO's Patent Trial and Appeal Board (PTAB).⁶⁴

⁵⁷ Jewell & Balakrishnan op cit note 40.

⁵⁸ Ibid; Leonid Kravets 'First-to-file patent law is imminent, but what will it mean?' *Tech Crunch* 17 February 2013, available at <https://techcrunch.com/2013/02/16/first-to-file-a-primer/>, accessed on 2 August 2019.

⁵⁹ 125 STAT. 284. The 'first to invent' system was utilised in the US until March 2013, when it was replaced by the Leahy-Smith America Invents Act. Jewell & Balakrishnan op cit note 40.

⁶⁰ US patent law focuses on the first applicant for a patent, but this does not guarantee a patent to the inventor who files first. However, where similar inventions are filed, the initial filer will be entitled to pursue their patent. This system allows more certainty and objectivity. Additionally, it brings the USPTO in line with other jurisdictions. USPTO 'First inventor to file is here: Learn how it works' *Inventors Eye* April 2013, available at <https://www.uspto.gov/learning-and-resources/newsletter/inventors-eye/first-inventor-file-here-learn-how-it-works>, accessed on 26 August 2019.

⁶¹ Sherkow op cit note 43.

⁶² This is a proceeding within the structures of the USPTO to determine the first inventor of a certain technology. Sherkow op cit note 49 at 26; Jewell & Balakrishnan op cit note 40; Joanne van Harmelen 'Intellectual property rights and genome editing: Navigating the patent thicket' *ENS Africa* available at http://biosafety.org.za/cms/modules/media/scripts/documents/document.handler.php?media_files_id=1201, accessed on 15 September 2019.

⁶³ Doudna's original patent application was filed on 15 March 2013, one day before the first-to-file system was implemented. However, Doudna's invention was given a priority date of 25 May 2012. Zhang filed his patent application on 15 October 2013, after the first-to-file system was implemented. However, Zhang claimed a priority date of 12 December 2012 which meant that his patent application fell under the preceding first-to-invent system. Sherkow op cit note 43; Jewell & Balakrishnan op cit note 40.

⁶⁴ The interference proceeding operates as a trial within the USPTO to determine the initial inventor of the subject in dispute and to decide the scope and importance of the conflicting patent applications. This proceeding is utilised in order to determine who invented what by comparing the claims of both parties. A two-way test, taken from the case of *Eli Lilly and Company v Human Genome Sciences Inc* [2011] UKSC 51, was used to compare the involved claims. The test revolves around the finding of obviousness and asks whether the claims of one party, if taken to be prior art, would render the claims of the opposing party obvious (and vice versa). A three judge panel hears evidence on the work undertaken by each party, what was disclosed in their original patent applications, and how 'an average molecular biologist would have viewed this information as the technology progressed through 2012'. The panel then determines which aspects of the disputed patents, if any, overlap. To assist in this process, the

The dispute centred on whether UC's initial patent application contained sufficient information to allow an ordinary molecular biologist to utilise the technology in eukaryotes. If this was the case, UC would be entitled to CRISPR patents in any cell system. However, if the application failed to reveal adequate information regarding use in eukaryotes, Zhang would be granted multiple CRISPR patents.⁶⁵ What the issue comes down to is: whether there was interference between the patents issued to Broad and UC's foundational patent application, and if so, who was the first to invent a single guide RNA (sgRNA) mediated CRISPR-Cas9 gene editing system in a eukaryotic cell?

(ii) *The decision in the Patent Trial and Appeal Board*

The issue in the PTAB, which was decided under 35 U.S.C § 102(g),⁶⁶ required an examination into whether both parties had patently indistinct subject matter.⁶⁷ Broad argued that there was no interference-in-fact as their patents were inventive over UC's application,⁶⁸ and were thus separately patentable.⁶⁹

panel drafts a 'count', which is a hypothetical patent that covers both sets of technologies. The scientists' attorneys file several sets of motions arguing that the count does or does not cover the technology in dispute, or that the count needs to be rewritten or divided in order to cover the contested inventions. In addition, the attorneys file motions arguing that their clients were the first to invent the CRISPR technology. Sherkow op cit note 48 at 2; Sherkow op cit note 49 at 27-28; Sherkow op cit note 43; Jewell & Balakrishnan op cit note 40; see, *Regents of University of California v Broad Institute Inc.* United States Court of Appeals of the Federal Circuit, 2018 903 F 3d 1286 at 8.

⁶⁵ Sherkow op cit note 53.

⁶⁶ This section reads 'A person shall be entitled to patent unless...(g)(1) during the course of an interference...another inventor involved therein establishes...that before such person's invention thereof the invention was made by such other inventor and not abandoned, suppressed, or concealed'.

⁶⁷ *Regents of University of California v Broad Institute Inc.* supra note 64 at 8. UC argued that there was interference because, without their work on CRISPR, Broad's research would not have occurred. If that was found to be the case, an interference would be established, resulting in the patent being awarded to the first inventor. During the initial interlocutory stage of the interference proceedings, the parties have the opportunity to present initial briefs which consist of substantive statements regarding the patentability of the disputed invention, whether there is interference-in-fact, or whether the PTAB should specify the interference's ambit. Moreover, the PTAB may examine motions regarding why the parties qualify for particular priority dates; the decisive factor in the granting of patents if an interference-in-fact exists. Following the interlocutory phase, the three judge panel determines unresolved motions. Ultimately, the panel will determine interference and award the relevant patents to one, or none, of the parties. Sherkow op cit note 43; Alessandra Potenza 'Who owns CRISPR – one of the most important genetic inventions of our time?' *The Verge* 6 December 2016, available at <https://www.theverge.com/2016/12/6/13857674/crispr-gene-editing-patent-dispute-berkeley-broad-mit-jennifer-doudna-feng-zhang>, accessed on 3 September 2019.

⁶⁸ Broad argued that there should not be an interference as Zhang had done something different and was therefore entitled to his own patents. NYU School of Law 'The CRISPR patent battle: Implications for downstream innovation in gene editing' Engelberg Center on Innovation Law & Policy 21 March 2017.

⁶⁹ This would mean that Broad would hold various patents involving CRISPR in eukaryotes, including human gene editing, while UC would only be allowed to use CRISPR in bacteria, which is less profitable. Sherkow op cit note 53.

The PTAB focused on whether Broad's work was original or whether it was 'the next obvious step to take, and/or fundamentally based on prior art'.⁷⁰ UC argued that Broad's process, for editing eukaryotic cell genes, was a clear extension of their work on cutting purified DNA in test tubes, and hence unpatentable. Further, UC contended that the decision should not turn on distinguishing between prokaryotes and eukaryotes, but rather the sgRNA utilised in any cell system. This was because transferring UC's invention from bacteria to eukaryotes was straightforward and could be accomplished by an ordinary molecular biologist.⁷¹ However, the judges were not convinced on the simplicity of translating CRISPR to eukaryotes.⁷²

In examining the claims of Broad's patent and UC's application,⁷³ the PTAB found that none of UC's claims were limited to a particular environment, whereas Broad's claims were eukaryote-specific.⁷⁴ The PTAB examined whether one of ordinary skill, in light of the prior art, would see the claim as having 'a reasonable likelihood of success'.⁷⁵ In 2017, the PTAB decided that the patents awarded to Broad for the use of CRISPR-Cas9 in eukaryotic cells involved dissimilar inventions and did not overlap or inhibit those of UC,⁷⁶ for the use of CRISPR-Cas9 in any environment.⁷⁷ Therefore, the inventions were separately patentable.⁷⁸ While the PTAB did not determine who the first inventor of the CRISPR-Cas9 system in

⁷⁰ Jewell & Balakrishnan op cit note 40.

⁷¹ If this argument was successful, UC would be granted a broad patent covering the majority of uses of CRISPR, while Broad would lose their patents. Sherkow op cit note 53.

⁷² This was due to the fact that other systems, not just CRISPR, experienced difficulties in moving the process to eukaryotic cells. Moreover, simultaneous experiments did not mean that scientists were certain that CRISPR could be successfully or easily applied in eukaryotes. Ibid.

⁷³ *Regents of University of California v Broad Institute Inc.* supra note 64 at 8.

⁷⁴ Ibid at 11.

⁷⁵ Ibid at 12. The rationale for this decision was the limitation present in Broad's patents, being the eukaryotic system. The PTAB then found that should UC's claims be treated as prior art, it would not render Broad's claims obvious as the skilled artisan would not have had a reasonable expectation of success. What led the PTAB to this conclusion was evidence based on statements made by persons skilled in the art, information in the Jinek 2012 paper (which did not list that the results of the experiment would work in eukaryotes), and statements made by Doudna in the media regarding her uncertainty about the success of her system in eukaryotes. Jinek et al op cit note 41.

⁷⁶ Jewell & Balakrishnan op cit note 40.

⁷⁷ Ibid.

⁷⁸ Sherkow op cit note 48 at 2.

eukaryotes was,⁷⁹ it did leave both Broad and UC in control of key areas such as gene therapy, drug discovery and development, and other human therapeutic applications.⁸⁰

This outcome means that should a prospective licensee wish to commercialise a human therapeutic application of CRISPR, entailing eukaryotic usage, a license would be required from both Broad and UC.⁸¹ However, those wishing to utilise the CRISPR-Cas9 technology in other cell systems would only need a license from UC. As Doudna explained, ‘[Broad] will have a patent on green tennis balls. [UC] will get a patent on all tennis balls’.⁸²

(c) *Battle two: The appeal*

Following the decision of the PTAB, UC appealed to the US Court of Appeals for the Federal Circuit.⁸³ The Court was required to consider whether there was substantial evidence to support the PTAB’s finding. The purpose of the appeal was not to hear the matter afresh, but rather to evaluate whether the decision of the PTAB was reasonable. UC attempted to convince the judges of its view that a skilled person would have had a reasonable expectation of success in utilising CRISPR-Cas9 in eukaryotes. However, the Court held that although there is evidence ‘that could support this position...[w]e do not reweigh the evidence. It is not our role to ask whether substantial evidence supports fact-findings not made by the [PTAB], but instead whether such evidence supports the findings that were in fact made’.⁸⁴

In 2018, the Court confirmed and upheld the PTAB’s ruling of no interference-in-fact. It held that the PTAB analysed the evidence and ‘considered a variety of statements by experts for both parties and the inventors, past failures and successes in the field, evidence of simultaneous invention, and the extent to which the art provided instructions for applying the

⁷⁹ There was no reason for the PTAB to determine who the first inventor of the CRISPR system in eukaryotes was because the inventions were separately patentable. Due to the fact that there was no interference, the patents were separate and there was no argument over the initial inventor as each party was deemed to be the initial inventor of the claims in their respective patents. Allie Nawrat ‘USPTO reverses decision regarding interfering CRISPR patents’ *Pharmaceutical Technology* 26 June 2019, available at <https://www.pharmaceutical-technology.com/news/uspto-reverses-decision-interfering-crispr-patents/>, accessed on 5 January 2020.

⁸⁰ Genome Web ‘Federal Court hands Broad Institute victory in CRISPR patent fight against UC Berkeley’ 10 September 2018 available at <https://www.genomeweb.com/business-news/federal-court-hands-broad-institute-victory-crispr-patent-fight-against-uc-berkeley#.XkLadVUzbIU>, accessed on 3 January 2020.

⁸¹ This is due to the fact that, while Broad holds patents for the use of CRISPR-Cas9 in eukaryotes, UC’s patents relate to CRISPR-Cas9 in any cell.

⁸² An invention in a certain category may be patented (tennis balls), and this does not prevent a new aspect of that category being eligible for patent protection (green tennis balls). However, if the initial patent was for green tennis balls, one cannot then patent all tennis balls as it forms part of the prior art. Aaron Dy ‘Reactions to CRISPR patent decision’ *PLOS Blogs* 17 February 2017, available at <https://blogs.plos.org/synbio/2017/02/17/reactions-to-crispr-patent-decision/>, accessed on 15 November 2019.

⁸³ *Regents of the University of California v Broad Institute* No. 2017-1907 (Fed. Cir. Sep. 10. 2018).

⁸⁴ *Ibid* at 12.

CRISPR-Cas9 technology in a new environment'.⁸⁵ As a result, the Court held that Broad's patents were sufficiently inventive over UC's.⁸⁶

(d) *Battle three: The new interference proceedings*

On 24 June 2019, the PTAB, of its own accord, declared a new interference proceeding challenging the validity of UC's eukaryotic claims.⁸⁷ The declaration of an interference means that the USPTO has found that more than one patent application defines an invention that is considerably similar to existing patented inventions.⁸⁸ Broad's patents from the previous interference,⁸⁹ and UC's later patent applications are being evaluated⁹⁰ – all of which relate to the usage of CRISPR-Cas9 in eukaryotic systems. Through this second interference proceeding, the PTAB will determine who the first inventor of CRISPR-Cas9 in eukaryotes was.⁹¹ In the new interference proceedings, the USPTO named Broad as the senior party and UC as the junior party. The senior party is listed as the party who filed at the earlier date and is assumed to be the initial inventor, while the junior party carries the burden of proof to show

⁸⁵ Ibid at 16.

⁸⁶ The Court found that Broad's patent utilising CRISPR-Cas9 in plant and animal cells was separately patentable from UC's use in any environment. Therefore, the patent claims involved diverse subject matter that did not interfere with one another. Broad Institute 'Information about licensing CRISPR genome editing systems' 2019 available at <https://www.broadinstitute.org/partnerships/office-strategic-alliances-and-partnering/information-about-licensing-crispr-genome-edition>, accessed on 10 September 2019; Genome Web op cit note 80.

⁸⁷ Patent Interference No. 106,115 (DK) Declaration – 37 C.F.R § 41.203(b). This was decided under 35 U.S.C § 135(a), which deals with derivation proceedings. The decision by the PTAB is expected within the next two years, with parties currently submitting their respective motions. All documents including motions, oppositions, notices, and orders can be accessed through the USPTO at <https://acts.uspto.gov/ifiling/PublicView.jsp?identifier=106115&identifier2=null&tabSel=4&action=filecontent&replyTo=PublicView.jsp>, accessed on 2 January 2020. USPTO '2310 Derivation Proceedings [R-08.2017]' available at <https://www.uspto.gov/web/offices/pac/mpep/s2301.html#d0e238030>, accessed on 22 September 2019.

⁸⁸ According to Eldora L. Ellison, a lead patent strategist on CRISPR matters for UC, 'the initiation of this interference proceeding highlights that previous decisions involving Broad did not determine who was the first to invent this technology, and it lays out a pathway for resolving this important issue'. UC Berkeley 'Patent office renews dispute over patent rights to CRISPR-Cas9' *Berkeley News* 25 June 2019, available at <https://news.berkeley.edu/2019/06/25/patent-office-renews-dispute-over-patent-rights-to-crispr-cas9/>, accessed on 22 January 2020; Sharon Begley 'Patent office reopens major CRISPR battle between Broad Institute and Univ. of California' *STAT* 2019, available at <https://www.statnews.com/2019/06/25/crispr-patents-interference/>, accessed on 11 September 2019.

⁸⁹ Broad patents 8,697,359; 8,771,945; 8,865,406; 8,871,445; 8,889,356; 8,895,308; 8,906,616; 8,932,814; 8,945,839; 8,993,233; 8,99,641; 9,840,713 and application 14/704,551. UC Berkeley op cit note 88.

⁹⁰ UC Applications 15/947,680; 15/947,700; 15/947,718; 15/981,807; 15/981,808; 15/981,809; 16/136,159; 16/136,165; 16/136,168; and 16/136,175.

⁹¹ This new interference proceeding relates only to a sgRNA CRISPR-Cas9 system. Eric Rhodes 'Interference declared over CRISPR-Cas9 for eukaryotic cells, reigniting patent war' *GEN* 28 June 2019, available at <https://www.genengnews.com/news/interference-declared-over-crispr-cas9-for-eukaryotic-cells-reigniting-patent-war/>, accessed on 27 August 2019; Drug Target Review 'Dispute over patent rights to CRISPR-Cas9 renewed by patent office' 2019 available at <https://www.drugtargetreview.com/news/45670/patent-rights-crispr-cas9-patent-office/>, accessed on 11 September 2019.

otherwise. UC is required to prove that Broad did not invent the CRISPR-Cas9 system in eukaryotes, thus making their case challenging.⁹²

V A SNAPSHOT OF THE CURRENT CRISPR PATENT LANDSCAPE

(a) *The US*

The USPTO granted UC its patent No. 10519467. This marks the institution's twentieth CRISPR-Cas9 patent,⁹³ making UC the holder of the largest CRISPR-Cas9 patent portfolio in the US.⁹⁴

(b) *Europe*

In Europe, the legitimacy of Broad's patents was disputed at the European Patent Office (EPO).⁹⁵ The EPO Boards of Appeal, upholding a first instance decision by the Opposition Division (OD), withdrew Broad's patent EP 2771468,⁹⁶ which is a foundational patent for eukaryotic applications of CRISPR.⁹⁷ In addition to this defeat, the OD rejected Broad's divisional patent application EP 2784162 in 2019.⁹⁸

⁹² However, UC has requested, in its Motions List, that the USPTO reverse its designation and assign UC as the senior party instead of Broad. GEN 'Broad Institute, UC file motions lists in latest CRISPR interference proceeding' 1 August 2019 available at <https://www.genengnews.com/news/broad-institute-uc-file-motions-lists-in-latest-crispr-interference-proceeding/>, accessed on 28 December 2019; Donna Young 'US patent office triggers new CRISPR gene-editing fight' *S&P Global* 25 June 2019, available at <https://www.spglobal.com/marketintelligence/en/news-insights/latest-news-headlines/52561540>, accessed on 4 January 2020; Rhodes op cit note 91.

⁹³ This encompasses claims relating to procedures for the production of genetically modified cells through the use of CRISPR-Cas9. University of California Office of the President 'University of California's foundational CRISPR-Cas9 patent portfolio reaches 20 total U.S. patents' *Cision* 31 December 2019, available at <https://www.prnewswire.com/news-releases/university-of-californias-foundational-crispr-cas9-patent-portfolio-reaches-20-total-us-patents-300980003.html>, accessed on 12 January 2020.

⁹⁴ Additionally, UC has received notices of allowance from the USPTO for five additional patent applications. Olivia Buccieri 'UC receives 20th CRISPR patent before end of 2019' *The Daily Californian* 3 January 2020, available at <https://www.dailycal.org/2020/01/03/uc-receives-20th-crispr-patent-before-end-of-2019/>, accessed on 13 January 2020.

⁹⁵ Christopher Wilkins 'European Union: CRISPR patent portfolio edited: The Broad Institute has lost its appeal on a key CRISPR patent in Europe' *Mondaq* 20 January 2020, available at <https://www.mondaq.com/uk/Intellectual-Property/885192/CRISPR-Patent-Portfolio-Edited-The-Broad-Institute-Has-Lost-Its-Appeal-On-A-Key-CRISPR-Patent-In-Europe>, accessed on 23 January 2020.

⁹⁶ *Ibid.*

⁹⁷ Revocation of the parent patent will not necessarily hamper Broad as it has numerous pending European patent applications, as well as a variety of granted European patents based on CRISPR technology. The patent family comprises four other patents; a second divisional application for patent EP 2896697 was upheld to a limited extent. Appeals for both patents are pending. Patents EP 2940140 and EP 2921557 were opposed, and EP 3144390 has not yet been granted. Amy Sandys 'EPO revokes Broad Institute patent – but it's just the beginning for CRISPR-Cas' *JUVE Patent* 17 January 2020, available at <https://www.juve-patent.com/news-and-stories/cases/epo-revokes-broad-institute-patent-but-its-just-the-beginning-for-crispr-cas/>, accessed on 20 January 2020.

⁹⁸ Wilkins op cit note 95.

The reasons for the removal of the EP 2771468 patent are currently withheld,⁹⁹ but the EPO noted that the patent was revoked for a ‘lack of novelty in view of intermediate prior art’.¹⁰⁰ Further, the EPO observed that the Patent Cooperation Treaty (PCT) application,¹⁰¹ on which the EPO patent is based, did not disclose all the relevant inventors as per the US patent application, thus rendering the priority claim invalid.¹⁰²

There are many other patent claims involving CRISPR-Cas9 that are due to be heard in Europe in the upcoming year.¹⁰³ Oral argument in the opposition proceedings against UC’s primary European patent EP 2800811 is planned to commence in February 2020. In August

⁹⁹ EPO ‘Decision in case T 844/18 on the CRISPR gene editing technology’ 17 January 2020 available at <https://www.epo.org/law-practice/case-law-appeals/communications/2020/20200117.html>, accessed on 22 January 2020.

¹⁰⁰ Ibid.

¹⁰¹ 1970, 28 U.F.T. 7647. The PCT is an international treaty that is managed by the World Intellectual Property Organisation (WIPO), and allows patent protection to be sought contemporaneously in numerous countries through the filing of a single, international patent application which replaces the separate foreign applications usually necessary for protection abroad. Gene Quinn ‘PCT basics: Obtaining patent rights around the world’ IP Watchdog 26 December 2015, available at <https://www.ipwatchdog.com/2015/12/26/pct-basics-patent-rights-around-the-world/id=64141/>, accessed on 13 December 2019.

¹⁰² It was held that the priority of patent EP 2771468 B1 was void due to a lack of entitlement and that the patent claim lacked novelty over prior art published in the priority year. A PCT application finds a sole filing date in all member states. A priority claim is a reference in a later filed patent application to a previous application. A priority claim grants the later patent application a priority date of the filing date of the earlier application instead of the later one. In the case of Broad, the prior art was relevant as the OD failed to acknowledge Broad’s ‘claim to priority from a US provisional application naming more applicants than the subsequent PCT application from which EP 2771468 is derived. Since the omitted applicant had not transferred his rights’ to the PCT application, the priority claim was deemed invalid. Broad noted that the inventors naming issue would affect up to nine of the twenty one European patents, including vital patents. EPO op cit note 99; James Yang ‘Claim of priority to an earlier filed patent application’ *OC Patent Lawyer* 25 April 2018, available at <https://ocpatentlawyer.com/priority-claim-patent-application/>, accessed on 5 January 2020; European Patent Academy ‘Priority’ *Patent Litigation Block 1* 4; GenomeWeb ‘Revocation of Broad Institute CRISPR patent upheld in Europe’ 17 January 2020 available at <https://www.genomeweb.com/business-news/revocation-broad-institute-crispr-patent-upheld-europe#.XIBLJZUzbIV>, accessed on 22 January 2020.

¹⁰³ Two other cases are pending before the Boards of Appeal, both involving the same issues of priority. Sandys op cit note 97.

2019, the OD found in favour of UC. Therefore, it is possible that UC may control eukaryotic applications of CRISPR in Europe,¹⁰⁴ contrasting the current situation in the US.¹⁰⁵

VI LEGISLATIVE FRAMEWORK

(a) *Bayh-Dole*

Bayh-Dole grants universities and small businesses patent rights and control of the commercialisation of government-funded inventions.¹⁰⁶ Such patenting and licensing efforts have succeeded in transferring technologies from universities to the public.¹⁰⁷

¹⁰⁴ The central issue in this matter is whether the priority from UC's first provisional US application for the protospacer adjacent motif (PAM) is valid. The PAM is a short DNA sequence that follows the DNA region targeted for cleavage by the CRISPR system. The PAM is an essential targeting component and is required for a Cas nuclease to cut. If not, the patent's effective date would fall after the publication of UC's CRISPR-Cas9 paper in *Science*, thus affecting the patentability of certain claims. However, during examination before the EPO and in other litigation, UC was successful in arguing that PAM formed part of common general knowledge. According to European practice, claiming priority of 'the same invention' in terms of Article 87(1) of the European Patent Convention means that priority can only be acknowledged if a skilled person can derive the subject matter directly and unambiguously, using common general knowledge, from the previous application as a whole. The OD's acceptance that PAM was part of the common general knowledge when P1 was filed, it has tentatively determined that the disclosure of P1 is enabling over the entire claim scope, including eukaryotic applications. The OD also opined that the claims meet the requirements of novelty and inventiveness. The invention's capabilities offer greater versatility in gene editing. Furthermore, the examples provided in UC's patent show that the invention achieves, or is likely to achieve, this result. *Ibid*; Synthego 'Importance of the PAM sequence in CRISPR experiments' available at <https://www.synthego.com/guide/how-to-use-crispr/pam-sequence>, accessed on 19 December 2019; Joanna Applequist 'The Crispr-Cas9 patent tussle continues: The case of UC Berkeley at the EPO' *Lexology* 15 November 2019, available at <https://www.lexology.com/library/detail.aspx?g=01e7cd32-be9e-41ba-99f6-a6cff718c0f6>, accessed on 6 December 2019.

¹⁰⁵ The differences between US and European law have led to contrasting outcomes concerning patents on CRISPR. While the basic principles of patent law are similar in the US and Europe, certain differences do exist, specifically in the fields of pharmaceuticals and biotechnology. The primary distinction between the patent laws of Europe and the US, and the reason why certain CRISPR decisions have had differing outcomes, is due to the fact that the first interference proceedings in the US CRISPR patent dispute were decided based on the old first-to-invent system. Although this practice has now changed and is in line with the European approach, this system had an impact on the patent laws and CRISPR decisions. BusinessWire 'Take a look at the key differences between US and European patent law and examine the patent issues relating to the biopharmaceutical industry' 31 March 2006 available at <https://www.businesswire.com/news/home/20060331005205/en/Key-Differences-European-Patent-Law-Examine-Patent>, accessed on 6 January 2020.

¹⁰⁶ Previously, government-funded research was not being transformed into products that could be commercialised. Bayh-Dole placed the obligation of bringing inventions to market on universities, giving them presumptive patent rights and absolute rights to enter licensing agreements with other entities. Inventions are commonly licensed to private companies with the potential to generate the most royalties. Such companies are those with the resources and capital to develop inventions into commercial products and sell them on the market. Further, the revenue produced by these licenses goes to the universities. By providing incentives for the commercialisation of government-funded inventions, universities can benefit from resulting royalties. Kevin Dietz 'International report - the federal government's march-in right: What does it mean for your intellectual property?' *I Am* 7 December 2016, available at <https://www.i-am-media.com/patents/federal-governments-march-right-what-does-it-mean-your-intellectual-property>, accessed on 29 December 2019; Dovid A Kanarfogel 'Rectifying the missing costs of university patent practices: Addressing Bayh-Dole criticisms through faculty involvement' (2009) 27(2) *Cardozo Arts & Entertainment* 535-536.

¹⁰⁷ Kanarfogel *op cit* note 106 at 533-534. Council on Governmental Relations 'The Bayh-Dole Act: A guide to the law and implementing regulations' 1999 *Council on Governmental Relations* 8.

Bayh-Dole standardised federal policy and allowed for grant recipients to patent inventions developed using government funds.¹⁰⁸ Under Bayh-Dole, university research funded through federal agencies can be patented, and inventors can ‘elect to retain title to’ inventions that resulted from such research.¹⁰⁹ The National Institutes of Health (NIH), which is the world’s largest public funder of biomedical research,¹¹⁰ noted that the right to retain title in Bayh-Dole, entailed ‘corresponding obligations to promote utilization, commercialization, and public availability’ of inventions.¹¹¹ The CRISPR technologies developed by Broad and UC are both federally-funded.¹¹² Finance from federal agencies represent UC’s primary funding source for basic research.¹¹³ Additionally, Broad utilises NIH funding to subsidise its research.¹¹⁴

Many have questioned whether the privatisation of inventions, through patenting and licensing regimes, resulting from research using public funds is ethical from a social welfare perspective, because it essentially forces the public to ‘pay twice’ for an invention.¹¹⁵ Many feel that the public are entitled to the benefits of such research, since it was the public’s taxes that made it possible. Furthermore, these institutions are exempt from paying tax.¹¹⁶ Broad claims to be non-profit,¹¹⁷ however it holds hundreds of millions of dollars in investments and

¹⁰⁸ Lisa Larrimore Ouellette & Rebecca Weires ‘University patenting: Is private law serving public values?’ (2019) *Michigan State Law Review*, Forthcoming; *Stanford Law and Economics Olin Working Paper No. 537 2*.

¹⁰⁹ 37 C.F.R § 401.10(a)(2); *Ibid* at 3.

¹¹⁰ The NIH forms part of the US Department of Health and Human Services. Jim Kozubek ‘The Broad Institute is testing the limits of what “non-profit” means’ *STAT* 25 April 2017, available at <https://www.statnews.com/2017/04/25/broad-institute-nonprofit-crispr/>, accessed on 5 January 2020.

¹¹¹ National Institutes of Health, Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources, 64 Fed. Reg. (Dec. 23, 1999) 72092.

¹¹² However, these universities are fighting over potential profits to be made from licensing CRISPR technology to private companies. Broad’s CRISPR patents, that were deemed not to interfere with those of UC by the USPTO in 2017, declare US funding as does UC’s patent application. Sarah Zhang ‘How the CRISPR patent dispute became so heated’ *The Atlantic* 6 December 2016, available at <https://www.theatlantic.com/science/archive/2016/12/crispr-patent-in-court/509579/>, accessed on 5 January 2020; James Love ‘All 12 Zhang/Broad Institute CRISPR patents declare US funding and rights in inventions’ *Knowledge Ecology International* 16 February 2017, available at <https://www.keionline.org/23269>, accessed on 10 January 2020.

¹¹³ This basic research aims to advance essential knowledge such as the principles and processes governing the functioning of the universe, and how humans perceive and interact with it. Basic research often leads to new concepts and ideas which result in novel applications. The initial work on CRISPR by Doudna was funded by a nominal grant from the National Science Foundation (NSF). Subsequently, her work has been supported by federal and private funding avenues. University of California ‘Federal agency funding’ (2018) *Institutional Research and Academic Planning* 1.

¹¹⁴ Kozubek op cit note 110.

¹¹⁵ In terms of making the public pay twice for an invention, see Rebecca S Eisenberg ‘Patents and data-sharing in public science’ (2006) 15(6) *Industrial and Corporate Change*.

¹¹⁶ Kozubek op cit note 110.

¹¹⁷ On Broad’s website, it states that they are a ‘nonprofit biomedical research enterprise’. Broad Institute ‘Frequently asked questions about BSRP’ available at <https://www.broadinstitute.org/bsrp/frequently-asked-questions-about-bsrp>, accessed on 3 January 2020.

revenue.¹¹⁸ The rewards gained from the commercialisation of CRISPR technologies are not translating directly to the public at large, as many are excluded from utilising the technology due to the extremely high costs of therapies.¹¹⁹ As a result, it has been argued that publicly-funded research, such as CRISPR-Cas9 technologies, should not be patented.¹²⁰

The issue with Bayh-Dole is that it allows for the general patenting of scientific research. This means that even if research is not commercially viable or there is no intention to commercialise it, such research can still be patented. This may lead to the existence of many patents lacking commercial value, which can have negative repercussions in the form of patent thickets.¹²¹ Whilst patents on research existed previously, Ouellette and Weires note that the patenting of academic research has accelerated since the enactment of Bayh-Dole. This raises questions about the effect that privatisation has had on the culture of science. Is this the right route for science? Are these values to which science should ascribe? To me, science has always had an open culture based on wonder, knowledge sharing, and collaboration – testing boundaries of what is and is not possible. As evidenced by the CRISPR patent dispute, on which millions of dollars have been spent, these values seem to be withering away. The lack of collaboration between Broad and UC has dealt a large blow to traditional scientific principles. If these two institutions worked together, the scientific community could make vast leaps forward. Furthermore, disclosure, which I argue is core to good scientific practice, is also being eroded.¹²² Doudna's own statements regarding her uncertainty of the workability of CRISPR-Cas9 in eukaryotes was used against her in court. Whilst this may have been a cunning move on the part of Broad, due to its persuasive value, it could further deter scientists from sharing their failures in the public domain, adding to the issue of publication bias.¹²³

¹¹⁸ Kozubek op cit note 110.

¹¹⁹ Jim Kozubek 'Who will pay for CRISPR?' *STAT* 26 June 2017, available at <https://www.statnews.com/2017/06/26/crispr-insurance-companies-pay/>, accessed on 5 January 2020.

¹²⁰ Kozubek op cit note 110.

¹²¹ Patent thickets are an overlapping set of patents which requires someone who wishes to commercialise a technology to obtain licenses from multiple licensors at great cost usually. Carl Shapiro 'Navigating the patent thicket: Cross licenses, patent pools, and standard-setting' in AB Jaffe et al (eds) *Innovation Policy and the Economy 1* (2001). 119-150.

¹²² Jacob S Sherkow 'Patent protection for CRISPR: An ELSI review' 2017 *Journal of Law and the Bioscience* 574.

¹²³ Publication bias is a phenomenon whereby scientific results are published depending on what the results are. For example, failed experiments are not published. Ridha Joobar et al 'Publication bias: What are the challenges and can they be overcome?' (2012) 37(3) *J Psychiatry Neurosci* 149. This, I argue, is not in the best interests of science as all results should be published for developmental and accessibility reasons, to enable the field of science to advance. This is especially so in the case of publicly-funded research.

(b) *The restrictions in Bayh-Dole*

Under Bayh-Dole, the US government has certain rights in a patented invention, and patent rights are restricted in terms of 35 U.S.C § 203. In an attempt to ‘protect the public against non-use or unreasonable use of inventions’,¹²⁴ Bayh-Dole contains march-in rights, which allow the granting of licenses for patents resulting from public funds.¹²⁵ March-in rights provide federal agencies with the authority, in certain circumstances, to compel a patent holder to grant a ‘nonexclusive, partially exclusive, or exclusive license’ to a third party, failing which the agency may grant the license itself.¹²⁶ The authority to exert march-in rights aims to enforce the licensing of university patents in order to make the invention publicly available on reasonable terms, to mitigate health and safety demands and, in limited circumstances, the constraint or removal of the patent right may be in line with the purposes of Bayh-Dole.¹²⁷

Due to concerns regarding steep pharmaceutical prices and the pivotal role of universities in drug discovery, march-in rights have come to the fore.¹²⁸ However, these rights are yet to be utilised. In the US, the NIH is the only federal agency to have received march-in petitions, although none of them were successful and the NIH refused to march-in and compel the granting of additional licenses.¹²⁹

¹²⁴ 35 U.S.C § 200 (2012).

¹²⁵ March-in rights are used if it is recognised that something more crucial than commercialisation is at risk. Kanarfogel op cit note 106 at 538-539; David S Bloch ‘Alternatives to march-in rights’ (2016) 18(2) *Vand J Ent & Tech L* 253.

¹²⁶ 35 U.S.C § 203(a). Additionally, there are four circumstances under which the march-in right may be exercised: (1) steps have not been taken within a reasonable time to apply an invention in the relevant field; (2) it is required in order to improve unmet health or safety needs; (3) action is essential in meeting the requirements for public use; and (4) the agreement required by 35 U.S.C § 204 is not in effect. 35 U.S.C § 204 holds that small businesses or non-profit organisations that receive title to an invention shall not grant exclusive rights to use or sell an invention in the US unless it is agreed that any products utilising the invention will be largely manufactured in the US. Further, the entity which receives a license as a result of the exercise of march-in rights may utilise the invention without fear of patent infringement. John R Thomas ‘March-in rights under the Bayh-Dole Act’ 2016 *Congressional Research Service* 7-8; Dietz op cit note 106.

¹²⁷ Ian Ayres & Lisa Larrimore Ouellette ‘A market test for Bayh-Dole patents’ (2017) 102 *Cornell Law Review* 277.

¹²⁸ *Ibid* at 277.

¹²⁹ The government may exercise march-in rights of their own accord or in response to a third party petition (37 C.F.R § 401.6(b)). These petitions, which related to pharmaceuticals, were *In re Petition of CellPro, Inc.* (Nat’l Inst. of Health, 1997) (determination), <http://www.ott.nih.gov/sites/default/files/documents/policy/cellpromarchin.pdf> (*In re CellPro*); *In the case of Norvir manufactured by Abbott Laboratories, Inc.* (Nat’l Inst. of Health, 2004) (determination), <http://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Norvir.pdf> (*In re Norvir I*); *In the case of Xalatan manufactured by Pfizer, Inc.* (Nat’l Inst. of Health, 2004) (determination), <http://www.ott.nih.gov/sites/default/files/documents/policy/March-in-xalatan.pdf> (*In re Xalatan*); *In the case of Fabrazyme manufactured by Genzyme Corporation* (Nat’l Inst. Of Health, 2010) (determination), <http://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Fabrazyme.pdf> (*In re Fabrazyme*); and *In the case of Norvir manufactured by AbbVie* (Nat’l Inst. of Health, 2013) (determination), <http://www.ott.nih.gov/sites/default/files/documents/policy/March-InNorvir2013.pdf> (*In re Norvir II*). What these petitions had in common was the view that drug pricing concerns alone were insufficient to give rise to march-in rights. Thomas op cit note 126 at 8-9; Bloch op cit note 125 at 253.

March-in rights have created apprehension among exclusive licensees of government-funded inventions as they give the government the power to control the market for drugs and other medical technologies, which may stifle innovation.¹³⁰ However, march-in rights are burdened by a variety of regulations preventing their unrestricted utilisation.¹³¹ It is unlikely that agencies will suddenly exercise march-in rights when they have not done so previously.¹³² If a federal agency, such as the NIH, were to exercise these rights it would deter researchers as government funds would mean weakened patent rights, and this may influence the NIH's capability to attract prominent collaborators.¹³³ However, if universities exercise their patent rights in a manner inconsistent with public interest, agencies may be compelled to intervene.¹³⁴

March-in rights allow the government to grant non-exclusive, partially exclusive, or exclusive licenses. In terms of CRISPR-Cas9, Broad offers non-exclusive licenses on the technology for non-profit research and academic purposes. However, for human therapeutic purposes, both Broad and UC have granted exclusive licenses. Therefore, I suggest that march-in rights are an option that should be considered in the future, to allow for the granting of non-exclusive licenses for the use of CRISPR in human therapeutics, should the public interest necessitate a more open use of the technology.

¹³⁰ Dietz op cit note 106.

¹³¹ The government and funding agencies have limited authority to interfere with exclusive licensing under Bayh-Dole. March-in rights may only be utilised following an investigation and satisfying certain criteria such as 'alleviating health or safety needs or when effective steps are not being taken to achieve practical application of the inventions'. 37 C.F.R § 401.6 entails the procedures for the exercise of march-in rights. March-in proceedings may not be initiated without informing the university and requesting comment. An agency must notify the university in writing and request comments and relevant information. The initiation of a march-in proceeding involves the issuance of a written notice by an agency to the university (37 C.F.R § 401.6(c)). The university may, within 30 days of receiving the march-in notice, submit information or argument opposing such march-in proceedings. While march-in proceedings are described as informal, they involve comprehensive fact-finding consisting of the right to counsel, chance to call and examine witnesses, and present documentary evidence. In the event of an adverse decision, a university may appeal to the US Court of Federal Claims. Although march-in proceedings partly seek to improve public health and safety, they are onerous and laborious, thus delaying expeditious action. Where a university fails to apply an invention or meet the requirement of public use march-in rights cannot be exercised until all appeals or petitions have been pursued (35 U.S.C § 203(a) (1) and (2)). Letter from Sylvia M Burwell, Secretary of Health and Human Services, to The Honorable Lloyd Doggett, US House of Representatives 2 March 2016 available at <http://freepdfhosting.com/be7532cfc0.pdf>, accessed on 12 January 2020; Thomas op cit note 126 at 11; Kanarfogel op cit note 106 at 547; Barbara M McGarey & Annette C Levey 'Patents, products, and public health: An analysis of the CellPro march-in petition' (1999) 14(3) 1109-1110.

¹³² Pharmaceutical companies will be unwilling to conduct clinical trials without sufficient patent rights over key compounds, and protracted exclusivity periods distort medical research towards diseases which entail brief clinical trials. Patents were not as imperative in university-industry collaborations, but this has increased due to a need for exclusive licenses. Ayres & Ouellette op cit note 127 at 278.

¹³³ Megan Molteni 'The long-shot bid to put Crispr in the hands of the people' *Wired* 22 February 2017, available at <https://www.wired.com/2017/02/long-shot-bid-put-crispr-hands-people/>, accessed on 6 January 2020.

¹³⁴ Ayres & Ouellette op cit note 127 at 322.

(c) *Intellectual Property Rights from Publicly Financed Research and Development Act 51 of 2008*

In South Africa, the Intellectual Property Rights from Publicly Financed Research and Development Act 51 of 2008 (IPRPFRA) serves as the ‘equivalent’ to Bayh-Dole.¹³⁵ Prior to the IPRPFRA, many South African universities lacked policies regulating research and inventions from public funds.¹³⁶ The IPRPFRA allows recipients of public funding for research to maintain IP ownership and entitles researchers to a share of the profit.¹³⁷ Due to the fact that

¹³⁵ The IPRPFRA’s objective, as stated in section 2(1), is ‘to make provision that intellectual property emanating from publicly financed research and development is identified, protected, utilised and commercialised for the benefit of the people of the Republic, whether it be for a social, economic, military or any other benefit’. Moreover, it aims to reward ingenuity and creativity. Section 3(1) of the IPRPFRA makes it clear that the Act ‘applies to intellectual property emanating from publicly financed research and development’. To assist in the promotion of its objectives, the IPRPFRA founded the National Intellectual Property Management Office (NIPMO). McLean Sibanda ‘Intellectual Property Rights from Publicly Financed Research and Development Act, 2008: Towards improved IPR management and value extraction from public funding of research and development in South Africa’ *Innovus* available at <https://www.innovus.co.za/archived-news/intellectual-property-rights-from-publicly-financed-research-and-development-act-2008-towards-improved-ipr-management-and-value-extraction-from-public-funding-of-research-and-development-in-south-africa.html>, accessed on 21 April 2020; Hanibal Goitom ‘South Africa: Law on Intellectual Property Resulting from Publicly Funded Research’ *The Law Library of Congress* 13 February 2009, available at <https://www.loc.gov/law/foreign-news/article/south-africa-law-on-intellectual-property-resulting-from-publicly-funded-research/>, accessed on 21 April 2020.

¹³⁶ An absence of benefit-sharing agreements to compensate inventors meant that there was no impetus to disclose inventions. The lack of benefits emanating from the commercialisation of inventions as a result of publicly-funded research has been associated with waning university motivation to develop research into marketable products. In the US, the passing of Bayh-Dole resulted in increased economic activity, employment, and the emergence of new companies. Bayh-Dole allowed universities to control their inventions and other IP originating from publicly-funded research, thus increasing university patent activity. In South Africa, NIPMO addressed the Portfolio Committee in 2016 on its implementation of the IPRPFRA. One of the matters discussed was that many small universities lacked resources, such as skills capacity and training. A serious challenge was insufficient skills and a lack of delivery within the institutions. Universities are vital as sources of innovation due to their research. However, little was being offered by such institutions, which could be why science and technology are falling behind in South Africa. In addition, the possibilities of science and technology remained unknown as many were unaware of its significance. The 2007 Innovation Fund Special Report on the State of Patenting in South Africa, which involved studies over a period of fifteen years, found that South African institutions only represented 4% of the total number of patent applications emanating from the country. This patenting rate is small considering the fact that it constitutes South Africa’s largest aggregation of knowledge workers. If the IPRPFRA is implemented effectively, it will increase knowledge regarding the importance of IP, causing enhanced IP management and commercialisation in South Africa. The IPRPFRA has the potential to encourage several economic activities, such as new technology start-ups, increased out-licensing income, employment, and greater research and development. This will ensure that publicly-funded inventions contribute to South Africa’s economic activity. Ramika Bansi & Karunanidhi Reddy ‘Intellectual property from publicly financed research and intellectual property registration by universities: A case study of a university in South Africa’ (2015) 181 *Procedia - Social and Behavioral Sciences* 186-187; Sibanda op cit note 135; M Goqwana ‘Intellectual Property Rights from Publicly Financed Research & Development Act: NIPMO progress report’ *Parliamentary Monitoring Group* 20 April 2016, available at <https://pmg.org.za/committee-meeting/22408/>, accessed on 21 April 2020.

¹³⁷ Section 4 of the IPRPFRA holds that IP stemming from publicly-funded research will, with particular exceptions, be owned by the funding recipient. This implies that IP resulting from research and development undertaken by a university or research council belongs to that institution. If an institution declines to register an IP right, it must inform NIPMO who may then obtain ownership of the IP. If a recipient does not want to retain a right to ownership, the Government may obtain the IP if it serves the national interest. If NIPMO decides not to register the IP, any private entity that assisted in funding the research may register the IP (section 4(4)(b)). Goitom op cit note 135; Bansi & Reddy op cit note 136 at 187.

their work is publicly-funded, researchers are obliged to commercialise their IP and inventions to enable it to benefit society at large.¹³⁸

(i) *Restrictions in the Intellectual Property Rights from Publicly Financed Research and Development Act*

Section 11(1)(a) of the IPRPFRA contains a peremptory provision which states that preference must be given to non-exclusive licenses.¹³⁹ Whilst this is a seemingly effective safeguard against exclusivity, unless absolutely necessary, it does not provide much guidance on what conditions would permit exclusivity. Does it simply mean that a non-exclusive license must always be chosen over an exclusive one, if there is a non-exclusive license? Does it mean that exclusivity is only an option if there are no potential non-exclusive licensees? Furthermore, this provision does not guard against the dangers that far-reaching exclusivity may have – as described in Chapter 3. The provision in the IPRPFRA’s corresponding Regulations made in terms of Section 17 of the Intellectual Property Rights from Publicly Financed Research and Development Act 51 of 2008 (IPRPFRA Regulations)¹⁴⁰ relevant to this section is regulation 11(7).¹⁴¹ Additionally, it is unclear what would occur in the case of conflicting preferences.¹⁴²

Section 11(1)(e) of the IPRPFRA seems to protect the option of irrevocable (and royalty-free) use by the state in necessary (public interest) conditions.¹⁴³ Section 11(2) of the IPRPFRA also stipulates that there be a mandatory inclusion of a public interest clause allowing state

¹³⁸ Previously, the outcomes of research and development would be published in scientific journals. Due to the enactment of the IPRPFRA, researchers and institutions are obliged to commercialise and utilise their inventions to benefit society. Sibanda op cit note 135; Goqwana op cit note 136.

¹³⁹ Section 11(1)(a) of the IPRPFRA states that ‘[t]he recipient determines the nature and conditions of intellectual property transactions relating to any intellectual property held by it, but must take into account the following: (a) Preference must be given to non-exclusive licensing’.

¹⁴⁰ GN R675 GG No. 33433 of 2 August 2010.

¹⁴¹ Regulation 11(7) of the IPRPFRA Regulations states that ‘[t]he recipient must develop and implement policy provisions to give effect to the following preferences in respect of the commercialisation of the intellectual property –

- (a) BBBEE compliant entities and small enterprises;
- (b) parties that seek to use the intellectual property in ways that provide optimal benefits to the Republic; and
- (c) parties that made material contribution to the research and development giving rise to the intellectual property’.

¹⁴² For example, if a potential exclusive licensee is a Broad-Based Black Economic Empowerment (BBBEE) entity or a small enterprise as in section 11(1)(b) of the IPRPFRA, as well as a potential non-exclusive licensee in line with section 11(1)(a) of the IPRPFRA. Section 11(1)(b) of the IPRPFRA holds that ‘[t]he recipient determines the nature and conditions of intellectual property transactions relating to any intellectual property held by it, but must take into account the following:...(b) preference must be given to BBBEE entities and small enterprises’.

¹⁴³ Section 11(1)(e) of the IPRPFRA states that ‘[t]he recipient determines the nature and conditions of intellectual property transactions relating to any intellectual property held by it, but must take into account the following:...(e) each intellectual property transaction must provide the State with an irrevocable and royalty-free licence authorising the State to use or have the intellectual property used throughout the world for the health, security and emergency needs of the Republic’.

intervention.¹⁴⁴ However, upon examining both provisions,¹⁴⁵ as well as the correlating regulations of the IPRPFRA Regulations,¹⁴⁶ the wording ‘each intellectual property transaction...’ notes that these sections only apply to license agreements that the patent holder has subsequently entered into. This limitation in the scope of the application of these state rights makes them ‘weaker’ than those in Bayh-Dole. For example, should the state wish to exercise these rights in terms of publicly-funded inventions, there would need to be a follow-on license agreement stemming from the patent, failing which the state would have to utilise other procedures, such as the compulsory license provisions in sections 55 and 56 of the Patents Act.¹⁴⁷

There is no express provision in the IPRPFRA that deals with state intervention in the absence of license agreements. The only possible applicable provision is section 14 of the

¹⁴⁴ Section 11(2) of the IPRPFRA holds that ‘[e]ach intellectual property transaction must contain a condition to the effect that, should a party fail to commercialise the intellectual property to the benefit of the people of the Republic, the State is entitled to exercise the rights contemplated in section 14’.

¹⁴⁵ Sections 11(1)(e) and 11(2) of the IPRPFRA.

¹⁴⁶ These are regulations 11(4), 11(6)(b), and 11(6)(c) of the IPRPFRA Regulations. Regulation 11(4) of the IPRPFRA Regulations states that ‘[e]ach intellectual property transaction must include the following statement – “The intellectual property under this transaction was created with support from the South African Government ((under the contract number where applicable) awarded by (identify the Funding Agency or relevant government department) where applicable)) and is subject to the requirements of the South African Intellectual Property Rights from Publicly Financed Research and Development Act, 2008 and its regulations (“Act 51 of 2008”). The South African Government has certain rights to the intellectual property in terms of sections 11(1)(e), 11(2) and 14 of Act 51 of 2008”’. Regulation 11(6)(b) of the IPRPFRA Regulations holds that ‘[t]he exclusive licence agreement must in addition to the statement in sub-regulation (4) include appropriate terms and conditions and in particular... (b) the irrevocable and royalty-free right of the State to use or have the intellectual property used on behalf of the Republic, for the health, security and emergency needs of the Republic in terms of the Act’. Regulation 11(6)(c) of the IPRPFRA Regulations states that ‘[t]he exclusive licence agreement must in addition to the statement in sub-regulation (4) include appropriate terms and conditions and in particular... (a) NIPMO's rights in terms of section 14(4) of the Act, if the intellectual property is not commercialised within the reasonable period set out in the exclusive licence agreement’.

¹⁴⁷ Section 55 of the Patents Act deals with compulsory licences in respect of dependent patents, and section 56 of the Patents Act encompasses compulsory licence in case of abuse of patent rights.

IPRPFRA,¹⁴⁸ more specifically, sections 14(4)¹⁴⁹ and 14(5)¹⁵⁰ seem to be the only provisions affording options to the state. The corresponding regulation 14 of the IPRPFRA Regulations, allows state intervention when commercialisation is not taking place, that is either not for the benefit of South Africa, or not in accordance with the terms of the license agreement. However, regulation 14(3)(a) and (b) of the IPRPFRA Regulations adds layers of bureaucracy to the use of these powers by means of procedures, such as consultation processes. Furthermore, the commercialisation for the benefit of South Africa is vague, which can result in parties having more power, as long as they commercialise aspects of that IP. Regulation 14(7) of the IPRPFRA Regulations, which lists the conditions necessary for the operation of state rights under section 11(1)(e) of the IPRPFRA, sets a high bar for the activation of this provision. Prima facie, one would argue that state intervention rights take into account the interests of both parties – and whilst this is true – I suggest that perhaps greater weight should be attributed to public interests as this concerns innovation from public funds. The layers of bureaucracy only open this section up to potential abuses by licensees or patent holders. Additionally, a mere partial usage of the benefit of protected invention may still qualify as commercialisation, hence limiting the state’s ability to interfere.

¹⁴⁸ Section 14 of the IPRPFRA deals with the acquisition of IP rights by the state. This section is comparable to march-in rights in the US. The IPRPFRA grants the Government rights to publicly-funded inventions where necessary for health, security, and emergency needs of the country. Section 14 of the IPRPFRA states inter alia –

- (1) ‘The rights acquired by the State in terms of this section are additional to the rights granted to the State in terms of any other legislation in the Republic.
- (2) NIPMO must conduct reviews of non-commercialised intellectual property in consultation with the recipients.
- (3) If a review contemplated in subsection (2) shows that the intellectual property in question can be commercialised, NIPMO must engage in further consultations with the recipient in an endeavour to ensure that the intellectual property is commercialised’.

Previously, when the state required access to an invention, it had to submit a request to the High Court. However, the IPRPFRA grants the state wider access to IP rights through Presidential Proclamation in an emergency. However, this must be done so as not to prejudice the licensees or recipients of the IP. The IPRPFRA restricts particular types of commercialisation and requires the approval of NIPMO prior to undertaking certain IP transactions. A recipient is prohibited from granting an exclusive license to a third party because, in certain instances, the state may require a license to utilise the IP. Where IP is licensed to a third party, the state must nevertheless retain a fixed royalty-free license in case it needs to utilise the IP, or have it used, anywhere in the world for the emergency needs of the Republic. Sibanda op cit note 135; Goqwana op cit note 136; Dina Biagio ‘The IPR-PFRD Act has come into force’ *Spoor & Fisher* 18 August 2010, available at <https://www.spoor.com/en/News/the-ipr-pfrd-act-has-come-into-force/>, accessed on 21 April 2020.

¹⁴⁹ Section 14(4) of the IPRPFRA states that ‘NIPMO may require a recipient to grant a licence in any field of use to any person on reasonable terms if, after the consultations contemplated in subsection (3) –

- (a) the intellectual property is still not being commercialised; or
- (b) no agreement can be reached with the recipient’.

¹⁵⁰ Section 14(5) of the IPRPFRA holds that ‘NIPMO may, on behalf of the State, demand the assignment of rights to any intellectual property if a recipient fails to make a disclosure to NIPMO as provided for in this Act’.

There are other potential weaknesses in the IPRPFRA, as well as the Patents Act, such as the lack of an express research exception. Further, the only reference to incentives in the IPRPFRA is section 9(4)(b).¹⁵¹

VII IS THE CURRENT PATENT LANDSCAPE IN THE PUBLIC INTEREST?

CRISPR and its derivatives are being used in almost all genetics laboratories worldwide. It must be noted that non-commercial uses of these technologies are allowed, license-free, by both Broad and UC, which complicates this process. However, due to the current patent landscape and the ongoing US patent dispute, licenses for the commercialisation of CRISPR will need to be acquired from Broad or UC, depending on the type of research or development being undertaken.

Should the final decision in the US CRISPR patent dispute favour UC, it would mean that UC's US patents are valid, while Broad's would be invalidated.¹⁵² If Broad were unsuccessful in the patent dispute, it is unclear what would happen to its spin-outs,¹⁵³ such as Editas Medicine (Editas), as well as the licensing agreements relating to the invalidated patents. Companies such as Editas have granted licenses to large pharmaceutical companies in multimillion dollar deals. Large portions of this money have already been used in clinical trials and other costs associated with commercialisation.¹⁵⁴ If Broad's patents were to be revoked, it

¹⁵¹ Section 9(4)(b) of the IPRPFRA states that 'NIPMO must...(b) provide incentives to recipients and their intellectual property creators, to reward them for proactively securing protection for intellectual property and commercialising it and, generally, for promoting innovation'.

¹⁵² This would leave Broad in a difficult position as many of its patents relate to eukaryotic applications. Furthermore, the vast amounts of public money that Broad and UC spent funding the litigation could have been used elsewhere, in furthering scientific innovation.

¹⁵³ A spin-out company is formed through separation from the main entity in order to form a new and independent corporation. Caribou Biosciences and Intellia Therapeutics (Intellia) are associated with UC, while Editas is linked to Broad. Allen & Overy 'Key players in CRISPR' available at <https://www.allenoverly.com/en-gb/global/news-and-insights/crispr/key-players-in-crispr>, accessed on 18 October 2019.

¹⁵⁴ Editas' leading drug candidate is a therapy, EDIT-101, which uses CRISPR in order to treat an uncommon genetic infant blindness known as Leber congenital amaurosis type 10 (LCA10). There is a significant need for successful therapies as the sole treatment that presently exists cannot cure all types of LCA. Editas is developing EDIT-101 in partnership with Allergan, who may in-license up to five eye therapies, including EDIT-101. However, Editas is entitled to receive potential profits and royalties therefrom. Additionally, Editas is developing potential CRISPR treatments for other eye diseases including Usher Syndrome type 2A (USH2A) and ocular Herpes Simplex Virus type 1 (HSV-1). Editas' second major drug candidate is EDIT-301, a gene therapy that aims to treat sickle cell disease and beta-thalassemia. However, CRISPR Therapeutics is also developing its own sickle cell treatment, CTX001. CRISPR Therapeutics has partnered with Vertex Pharmaceuticals (Vertex) in order to jointly develop, and profit from, CTX001. Vertex holds exclusive rights to license up to five other CRISPR-based therapies that arise from the partnership. Editas has collaborations with large pharmaceutical companies regarding its technology, which provide research support and funds to assist in the development of human therapeutic applications of CRISPR. As Editas currently lacks a product portfolio, it is reliant on its partners for revenue. Editas has a collaboration and licensing agreement with Juno Therapeutics (Juno). Editas granted Juno an exclusive license to utilise gene editing methods, including CRISPR-Cas9, for cancer treatments. Editas also has a research and cross-licensing agreement with BlueRock Therapeutics to amalgamate gene editing

would have dire consequences for licensees as commercialising CRISPR applications through Broad's rescinded licenses would then infringe on the patents of UC. Alternatively, Broad could attempt to obtain licenses for UC's patents, but it may be unsuccessful for two reasons: (1) Broad is not entitled to a license, and as such, UC could reject the license request for market-based reasons;¹⁵⁵ and (2) UC exclusively licensed their patents to spin-outs, thus preventing licensing to Broad, as exclusive licenses lack a grant-back clause.¹⁵⁶ The spin-outs to whom UC has granted licenses, have already licensed exclusively to other private companies,¹⁵⁷ which would preclude them from licensing to Broad. This will be dealt with in more detail in Chapter 3.

If Broad were to win the US patent dispute, the status quo would remain, and entities interested in pursuing CRISPR technologies would have to obtain licenses from both Broad and UC for human therapeutic applications.¹⁵⁸ Broad would have to acquire a license from UC as UC holds the foundational patent on CRISPR, and UC would require a license from Broad, whose patents are eukaryote-specific. The costs of cross-licensing will likely be reflected in the prices of the resulting CRISPR-related products which, in turn, would mean that the public would have to pay increased costs.

There is also an inherent risk that the entire US CRISPR patent dispute may be redundant, as it revolves around the Cas9 enzyme. Since 2012, there have been numerous other enzymes

technologies which would assist in the development of novel engineered cell medicines. In 2019, Editas entered into collaboration with AskBio to develop in vivo CRISPR medicines to treat neurological diseases. Mark Prvulovic 'Is Editas Medicine a buy?' *The Motley Fool* 18 December 2019, available at <https://www.fool.com/investing/2019/12/18/is-editas-medicine-a-buy.aspx>, accessed on 12 January 2020; Nasdaq 'Editas (EDIT) focuses on developing eye candidate EDIT-101' 6 January 2020 available at <https://www.nasdaq.com/articles/editas-edit-focuses-on-developing-eye-candidate-edit-101-2020-01-06>, accessed on 15 January 2020; Keith Speights 'Better buy: Editas Medicine vs CRISPR Therapeutics' *Motley Fool* 27 April 2019, available at <https://finance.yahoo.com/news/better-buy-editas-medicine-vs-170000299.html>, accessed on 9 January 2020; Timothé Cynober 'CRISPR: One patent to rule them all' *Labiatech* 11 February 2019, available at <https://labiatech.eu/features/crispr-patent-dispute-licensing/>, accessed on 10 September 2019.¹⁵⁵ UC could be motivated to reject the applications as they would want to control markets and retain a monopoly over human therapeutics. This would result in higher profits for the university and all involved.

¹⁵⁶ A patentee is granted monopoly rights over an invention. However, this exclusive right may be undermined by improvements to, or substitutes for, the patented invention. Grant-backs are often utilised in order to control new developments (improvement patents). Therefore, the patentee (licensor) requires the potential licensee to agree to grant back rights to improvement patents to the patentee. These are improvements developed by the licensee which relate to the initial patent. Richard Schmalbeck 'The validity of grant-back clauses in patent licensing agreements' (1975) 42(4) *University of Chicago Law Review* 733.

¹⁵⁷ Such as Intellia licensing human therapeutic applications of CRISPR to Novartis, and Regeneron. Cynober op cit note 154.

¹⁵⁸ This means that Broad and UC, through their surrogates, would have to cross-license for human therapeutic applications of CRISPR. Cross-licensing involves an agreement between parties to grant mutual rights to one another's intellectual property, meaning that parties license from each another. Shai Jalfin 'The good, bad and ugly of cross-licensing your technology patents' *IP Watchdog* 15 December 2017, available at <https://www.ipwatchdog.com/2017/12/15/good-bad-ugly-cross-licensing-technology-patents/id=90954/>, accessed on 29 December 2019.

that have been found to be more effective than Cas9, such as Cas12a or CasX.¹⁵⁹ It is likely that the patent dispute has centred on, and tirelessly fought over, an aspect of the technology that is slowly becoming irrelevant.¹⁶⁰ This is true, unless it can be shown that the new systems depend on the previous, patented CRISPR-Cas9 systems.

VIII A SOUTH AFRICAN PERSPECTIVE

(a) *Relevance of the US CRISPR patent dispute to South Africa*

The changing CRISPR patent landscape has caused confusion for potential inventors and licensees alike. As patents are territorial in nature, the various decisions regarding CRISPR patents apply only in the countries in which they occurred. If a patent is invalidated in the US or Europe it does not mean that the patent, via the PCT,¹⁶¹ would be invalidated in South Africa.

¹⁵⁹ In 2015, Zhang discovered Cpf1, which was simpler and less error prone than Cas9. UC recently discovered CasX and CasY, which are smaller and may prove more useful than Cas9. Researchers have also discovered a new CRISPR system, C2c2, which has the potential to allow the editing of RNA as opposed to DNA. CRISPR-Cas9 enables the editing of DNA, thus permanently altering a cell's genome. However, C2c2 will allow researchers to target RNA and make provisional alterations to the genome of a cell. Deborah Ku 'The patentability of the CRISPR-Cas9 genome editing tool' (2017) 16(2) *Chicago-Kent Journal of Intellectual Property* 414 & 439.

¹⁶⁰ However, the ultimate decision in the CRISPR patent dispute may influence the scope of patent protection applicable to alternate genome editing tools and enzymes, and could serve to guide researchers and their institutions in approaching similar matters in the future, so as to avoid a repeat of the dispute involving CRISPR-Cas9. *Ibid* at 439.

¹⁶¹ The PCT provides a simpler way of obtaining patents in other jurisdictions. A PCT application has the same effect as if a national patent application had been filed with the patent office in PCT member states. As patents are granted within a country in terms of individual patent laws, an international patent application must evolve into a national patent application. The PCT procedure involves two phases: the International Phase and the National Phase. The International Phase is a convenient way for applicants to acquire patent protection in multiple jurisdictions without having to file patent applications separately for each country. A PCT application is prosecuted during the International Phase, after which it is translated into various national patent applications in chosen countries. The ensuing National Phase results in the PCT application being adapted into various independent patent applications in specific countries. This is the stage at which the costs can increase as national fees are required to be paid to each country where patent protection is sought, as well as the translation of patent applications where necessary. The authority to grant patents rests with national patent offices in countries in which patent protection is requested. These requirements differ between countries, and when the PCT application enters into this phase, it is assessed in terms of national patent laws. This is in line with Article 27(5) of the PCT, which states that '[n]othing in this Treaty and the Regulations is intended to be construed as prescribing anything that would limit the freedom of each Contracting State to prescribe such substantive conditions of patentability as it desires...any Contracting State is free to apply, when determining the patentability of an invention claimed in an international application, the criteria of its national law in respect of prior art and other conditions of patentability not constituting requirements as to the form and contents of applications.' The case of *Eli Lilly Canada Inc. v. Apotex Inc* 2009 FCA 97 para 19 reiterated the provisions of Article 25(7) of the PCT as the Court held that substantive matters relating to patentability of an invention were regulated solely by national law. The PCT provides for the 'supremacy of national law' regarding the essential criteria for patentability. Quinn op cit note 101; Gene Quinn 'PCT 101: International patent application filing basics' IP Watchdog 11 November 2018, available at <https://www.ipwatchdog.com/2018/11/11/pct-international-patent-application-filing-basics/id=103231/>, accessed on 13 December 2019; Mewburn Ellis 'International (PCT) patent applications – the basics' available at <https://www.mewburn.com/law-practice-library/international-pct-patent-applications-the-basics>, accessed on 10 December 2019; WIPO 'PCT FAQs' available at <https://www.wipo.int/pct/en/faqs/faqs.html>, accessed on 9 January 2020; Adrian Hocking 'Knocking-out a patent'

A patent involves a right to exclude others from using an invention without the permission of the patent holder.¹⁶² However, if a patent is invalidated, this restriction would no longer apply.¹⁶³ As the validity of a patent is dependent on the particular laws of a country, a patent on a CRISPR process may be deemed invalid in the US, but may still be granted in South Africa.

However, if a patent such as Broad's is invalidated in the new US interference proceedings, in addition to the revocation of its European patent, one would question whether that patent, if granted in South Africa, would be maintained or withdrawn by Broad. Withdrawal would depend on whether maintaining the patent in South Africa is viewed as commercially viable, as it requires the payment of fees. Commercial importance would be contingent on whether Broad intended to use, license, manufacture, sell, or import any products using the CRISPR patent in South Africa. If a US or European patent is declared invalid, the equivalent South African patent is likely to be withdrawn due to the cost. However, maintaining a patent in such a situation could open the path for challenge by means of a patent opposition proceeding in South Africa.

(b) South Africa: Patent landscaping search

Ascertaining the current CRISPR patent landscape in South Africa is important in order to identify the challenges that South African inventors and researchers may face regarding CRISPR. These potential difficulties must be brought out if South Africa is to create a patent system that maximises public interest.

Albright IP 16 May 2013, available at <https://www.albright-ip.co.uk/2013/05/knocking-out-a-patent/>, accessed on 30 December 2019; WIPO 'Summary of the Patent Cooperation Treaty (PCT) (1970)' available at https://www.wipo.int/treaties/en/registration/pct/summary_pct.html, accessed on 28 August 2019; Dietmar Harhoff et al 'The strategic use of patents and its implications for enterprise and competition policies, Report ENTR/05/82 for DG Enterprise, European Commission' 2014 *Innovation and Entrepreneurship Research* 17; WIPO 'PCT – the international patent system' available at <https://www.wipo.int/pct/en/>, accessed on 27 August 2019; United Nations 'WIPO Patent Cooperation Treaty (PCT)' available at <https://www.un.org/ldcportal/wipo-patent-cooperation-treaty-pct/>, accessed on 30 August 2019.

¹⁶² Sherkow op cit note 53.

¹⁶³ Due to the fact that a PCT application will never become a patent, it is important to consider the implications of this. A patent may be withdrawn or deemed invalid after the International Phase, in which case the patent may be abandoned. The decision to grant a patent is controlled by national offices during the National Phase. WIPO op cit note 161; CIPC 'Patents' available at <http://www.cipc.co.za/index.php/trade-marks-patents-designs-copyright/patents/>, accessed on 28 December 2019.

(i) *Purpose*

I undertook a patent landscaping search in order to provide a brief overview of the current CRISPR patent landscape in South Africa and internationally.¹⁶⁴ Such patent landscaping is essential in FTO analyses (dealt with in Chapter 4), as well as for potential South African inventors (researchers and developers) as it would denote what CRISPR-related technologies have been patented in South Africa (the foundational patents that have been applied for and those which have been granted), by whom (who is the controlling party in South Africa), what potential opportunities there are for exploitation, and the parties from which licenses would be required. This is vital in understanding how CRISPR technology may be used, developed, and shaped within the country. Importantly, by accessing the available information in a patent landscaping search and completing this process myself, I was able to place myself in the shoes of a potential developer and expose myself to any potential hurdles, both in patent searches and the current CRISPR patent landscape, which inventors and researchers alike may face in practice.

(ii) *Aim*

The idea behind the patent landscaping search was to gain an insight into issues regarding CRISPR technologies, such as who has filed patents in South Africa, to whom patents have been awarded, the holder of the greatest number of patents, and the number of core patents that have been granted. However, due to search restrictions and the national patent database being in a constant state of flux,¹⁶⁵ this was not achievable. As the national search was unavailable, an email containing questions relevant to the aim was sent to the Companies Intellectual Properties Commission (CIPC).¹⁶⁶ No response was received and, as a result, the patent landscaping search had to be restricted.

¹⁶⁴ A patent landscaping search is a research process that provides an overview of the patent situation relating to a particular technology, either within a specific country or internationally. This search ascertains pending and granted patents in a certain field. It involves an electronic search of the applicable technology in patent databases, followed by an analysis of the information available. WIPO ‘Patent landscape reports’ available at https://www.wipo.int/patentscope/en/programs/patent_landscapes/, accessed on 10 January 2020; Joanne van Harmelen ‘South Africa: Patent landscaping: The road to success’ *ENSafrica* 11 October 2018, available at <https://www.mondaq.com/southafrica/Intellectual-Property/744754/Patent-Landscaping-The-Road-To-Success>, accessed on 10 January 2020.

¹⁶⁵ CIPC ‘Log in – CIPC Intellectual Property Online’ available at <https://iponline.cipc.co.za/Account/Login.aspx?pb=aVMvEDrYJoBv4STTqmvCTpb7MWDx2eY0ESHMO1dLY8+DkrV5ADDUPw==>, accessed on 24 November 2019.

¹⁶⁶ The functions of the CIPC are inter alia to register and maintain intellectual property and ensure compliance with relevant legislation. National Government of South Africa ‘Companies and Intellectual Property Commission (CIPC)’ available at <https://nationalgovernment.co.za/units/view/84/companies-and-intellectual-property-commission-cipc>, accessed on 5 January 2020.

The objective of the patent landscaping search was to establish which CRISPR patent applications have been filed via the PCT,¹⁶⁷ and granted in South Africa. This provides a surface level understanding of the patent landscape in South Africa regarding CRISPR and can serve as a starting point for a more substantive examination in the future.

(iii) Justification

Patentscope was chosen as the website for this patent landscaping search, over Google Patents, the South African CIPC, and other free search databases,¹⁶⁸ due to practical reasons. Patentscope is the most comprehensive free patent search site and contains more parameters for refining searches.¹⁶⁹ Google Patents and other free patent search databases are not as accurate and lack search variability.

The keyword ‘CRISPR’ was chosen for the patent landscaping search in order to obtain a conclusive result on all CRISPR-centred patents or applications. ‘CRISPR-Cas9’ was also considered as a search term, but there have been many more Cas systems developed since the Cas9 system, and it would be incorrect to exclude these.

(iv) Methodology

1. An advanced search was conducted on the Patentscope website on 12 December 2019.
2. In order to render only results wherein South Africa is a designated state, South Africa (ZA) as a patent office was chosen, and the PCT box was selected.
3. A general CRISPR search was conducted in order to obtain a comprehensive view of the patent landscape regarding the technology in the South African Patent Offices (SAPO). In order to perform this examination, an advanced search was utilised with the code EN_ALLTXT: CRISPR.¹⁷⁰ This code searches every word of every PCT application for the term ‘CRISPR’, hence maximising the results of the data.
4. Thereafter, a more specific front page search was done for ‘CRISPR’ using the code FP: (CRISPR). This brings up results that have the word ‘CRISPR’ on the front page, which

¹⁶⁷ The PCT allows for the filing of patent applications in multiple contracting states simultaneously via a single application. This allows one to possibly gain protection in more than one country, without needing to visit each national patent office. One must file in a desired country within one year of filing the initial patent application. More information regarding the PCT and the process can be obtained from WIPO op cit note 161.

¹⁶⁸ Such as Lens. Lens available at <https://www.lens.org/>, accessed on 13 November 2019.

¹⁶⁹ Patentscope ‘WIPO – Search International and National Patent Collections’ available at https://patentscope.wipo.int/search/en/result.jsf?_vid=P10-K5SAFW-49155, accessed on 24 November 2019.

¹⁷⁰ Ibid.

would include the term being present in the title or the abstract of a patent. This can maximise relevancy, as these patent results would likely utilise CRISPR as a core technology central to the application.

5. For comparative purposes, a search repeating steps 1 to 4 was done, with a change in step 2. Instead of selecting (ZA) to refine the search, ALL was chosen. This reflects all CRISPR patent applications worldwide.

(v) Limitations

Due to limitations in the search functionality of free patent databases and the large volume of results, a duplication of findings and irrelevant data is possible. Multiple database searches would be ideal for companies considering investing in CRISPR. The other free search sites have limited databases or field searches and are not accurate or up to date. Additionally, several sites do not contain South Africa as an option when filtering results.

Searches are generally not completely accurate and may not reflect the true number of existing patent applications because publications take time to reflect. This delay can cause imprecise results.

(vi) Results

The general CRISPR search in South Africa on all texts reflected 6,579 results, whilst the front page search reflected 823 results. Comparatively, a general search on CRISPR in all patent offices worldwide reflected 24,951 results. A front page search reflected 4,172 results.

(vii) Discussion

The first result is voluminous which shows that, despite the US patent dispute, the CRISPR market continues to increase. However, the outcome cannot be relied upon until a manual clean-up is conducted in order to remove any irrelevant results. After a scroll through and a brief examination of the various pages of results, it was clear that in many patents, CRISPR was not the core technology. Rather, it was utilised or mentioned therein, perhaps to extend the

scope of the patent.¹⁷¹ However, this could also occur if the patent revolves around an accessory technology, such as viral vectors.¹⁷²

The front page search yielded a more accurate view of the number of patents containing CRISPR as a core technology – far less than the full text results. However, a simple front page search is also inaccurate, and a manual clean-up will be required to further evaluate which patents are foundational and which are just technology improvement patents. Since Thaldar and Pillay published their article in 2018,¹⁷³ the CRISPR patent landscape has grown. CRISPR research has not slowed down despite the uncertainty of patent ownership.

Examining the CRISPR patent landscape in South Africa alone is a difficult task due to the limitations of online search systems. The CIPC is the only free database that contains updates on South African patents, but the site is inoperative and therefore unhelpful. Another issue with the CIPC is the search functionality. The search fields are limited to simple searches such as the title, inventors, and applicants and does not pick up information unless the search phrase is exact.¹⁷⁴ Furthermore, the CIPC site contains no proximity functions.¹⁷⁵ These are simple infrastructure issues requiring rectification. This will need upgrading if the changes, such as SSE procedures, that the IP Policy intends to implement are to be effective.¹⁷⁶ The South African IP policy mechanisms, to be discussed below, will be rendered ineffective if weaknesses are present in the system and inventors are unable to establish what has been patented in South Africa, as well as it being a tremendous waste of resources.

In order to gain a full understanding of the current patent landscape, one would need to conduct refined searches and patent family searches for accuracy. If, from a researcher's perspective, such patent search difficulties arise, biotechnology entrepreneurs and the like will struggle to conduct these searches on their own and a patent attorney with access to a formidable, up-to-date database, will be required.¹⁷⁷ However, employing the services of a

¹⁷¹ Jacqueline Martin-Laffon et al 'Worldwide CRISPR patent landscape shows strong geographical biases' (2019) 37 *Nature Biotechnology* 614.

¹⁷² Vectors act as a vessel providing a means for enzymes to enter a cell, with viral vectors being most commonly used. Jacob S Sherkow & Christopher Thomas Scott 'The pick-and-shovel play: Bioethics for gene-editing vector patents' (2019) 97 *NC L Rev* 1503.

¹⁷³ S Pillay & DW Thaldar 'CRISPR: Challenges to South African biotechnology law' (2018) 11 *S Afr J BL* 92.

¹⁷⁴ For example, if one searched 'Broad Institute', no results would be found as the exact name is required.

¹⁷⁵ This can make things difficult as sometimes searching by inventor is the only option. Even simply not adding in a space, or adding in a space where there should be one when searching using patent application numbers returns no results.

¹⁷⁶ T Schonwette & YA Vawda 'Comments at the Draft National Policy on Intellectual Property (IP) of South Africa' (2013) 6.

¹⁷⁷ Once such example is Orbit Intelligence. 'Orbit Intelligence' available at <https://www.orbit.com/>, accessed on 15 December 2019.

patent attorney is costly, which may preclude smaller inventors from ascertaining the information that they need. Furthermore, it is good practice for inventors and researchers to undertake a basic patent landscaping search themselves in the early stages of their work, to enable them to determine what is out there, and what gaps exist. The current patent search system fails to assist inventors, researchers, and the general science and innovation society in South Africa.

The last documented patent landscaping search in South Africa reflected that four CRISPR patents had been granted to UC and four to Broad,¹⁷⁸ clearly showing that South Africa is a target area for CRISPR-related inventions. With South Africa currently employing a depository patent system,¹⁷⁹ all applications which pass a formal examination will be granted patents. Therefore, it is likely that a large percentage of those 6,579 patent applications will be granted. Importantly, Broad's PCT application (WO2014093661), which is the foundational patent for eukaryotic applications of CRISPR-Cas9, has South Africa as a designated state.¹⁸⁰

IX SOUTH AFRICAN LEGAL AND POLICY SUBMISSIONS

In an attempt to improve South Africa's IP system, the IP policy aims to 'strike a fair balance between competing private and public interests in the field – taking into consideration South Africa's specific needs and circumstances'.¹⁸¹ It strives to develop a 'pro-health' IP policy that is in line with 'the socio-economic realities of South Africa and its constitutional and international obligations'.¹⁸² In the following section, certain policy submissions are made regarding the IP Policy and the Patents Act, with the intention of developing an enabling environment wherein CRISPR can thrive, hence furthering the public interest.

¹⁷⁸ Note that these numbers have probably since increased. van Harmelen op cit note 62.

¹⁷⁹ This means that patents are only examined for compliance with formal requirements. Catherine Tomlinson et al 'Reforming South Africa's procedures for granting patents to improve medicine access' (2015) 105(9) *SAMJ* 741.

¹⁸⁰ However, according to Patentscope this application has not yet been granted or published in the National Phase in South Africa. Furthermore, the requisite PCT application for UC's foundational patent could not be found.

¹⁸¹ Schonwette & Vawda op cit note 176 at 4; Angelica Di Battista *Finding a Necessary Balance Between Intellectual Property Rights and Access to Medicines: A New Challenge for South Africa and its Upcoming National Policy on Intellectual Property* (unpublished LLM thesis, University of KwaZulu-Natal, 2015) 111-112.

¹⁸² Brook K Baker & Yousuf Vawda 'Submission by University of KwaZulu-Natal-affiliated academics on the Draft Intellectual Property Policy of the Republic of South Africa Phase 1 2017' (2017) *University of KwaZulu-Natal* 1.

(a) *Substantive search and examination procedures*

Unlike the US, South Africa is currently a depository patent system,¹⁸³ which means for patent applications, only a formality examination takes place, and no SSE is required.¹⁸⁴ As Vawda argues, the drawback of this system is that the requirements for patent eligibility are not actually tested in the application process. The IP Policy regards this as contributing to the granting of low quality patents, which affects patent holders and the public.¹⁸⁵ Vawda agrees that without an examination system, many weak patents are granted and it ‘closes the opportunity for pre- and post-grant opposition proceedings’.¹⁸⁶ The IP Policy aims to change this by introducing SSE procedures at the SAPO.¹⁸⁷

As SSE procedures are closer to being a practical reality in South Africa, it is important to consider the issues in this process, with regards to the sui generis nature of biotechnology in particular. CRISPR raises a few nuanced issues such as, what Sherkow terms, the ‘classic disconnect between the legal standards of patent law and the realities of scientific research’,¹⁸⁸ as evidenced by the US CRISPR patent dispute.

In South Africa, patents are valid after passing a formal examination, and obviousness serves as a ground to revoke a patent. However, this will no longer be the case with the

¹⁸³ Ramon Pereira & Gizela Lombard ‘Phase 1 of South Africa’s IP policy: What you need to know’ *Adams & Adams* available at <https://www.adams.africa/insights/phase-1-south-africas-ip-policy-need-know/>, accessed on 4 November 2019.

¹⁸⁴ Section 25 of the Patents Act. This only occurs through revocation or infringement proceedings which dispute a patent’s validity. Typically, this involves a costly and lengthy application before the Commissioner of Patents, a judge of the High Court with jurisdiction. Sections 61 to 64, and sections 65 to 71 of the Patents Act; Yousuf A Vawda ‘Compulsory licensing jurisprudence in South Africa: Do we have our priorities right?’ (2018) Research Paper 90 *South Centre* 3.

¹⁸⁵ Patent quality is determined by a patent’s ability to meet the legal requirements for patentability – novelty, inventiveness, and industrial application. Therefore, a low quality patent is one that is granted for an invention which does not meet these criteria. Low quality patents affect the ability of those working in the field and restrict their operations unless they obtain costly licenses, often for inventions that are undeserving of patent protection. A further concern with low quality patents is that they undermine the patent system, thus impacting researchers, patent holders, and the public. R Polk Wagner ‘Understanding patent-quality mechanisms’ (2009) 157 *University of Pennsylvania Law Review* 2138; Christi J Guerrini ‘Defining patent quality’ (2014) 82(6) *Fordham Law Review* 3092-3093.

¹⁸⁶ Yousuf A Vawda ‘Pharmaceutical innovation, incremental patenting and compulsory licensing country case study: South Africa’ (2011) 27; Coral Jade Joseph *Access to Affordable Life-Saving Medicines: The South African Response* (unpublished LLM thesis, University of KwaZulu-Natal, 2012) 79.

¹⁸⁷ However, according to Baker and Vawda in their 2017 submissions on the IP Policy, regulations 40 and 41 of Patent Regulations 1978 do not currently provide for SSE and would require amendment. Baker & Vawda op cit note 182 at 5; Pereira & Lombard op cit note 183.

¹⁸⁸ Jacob S Sherkow ‘CRISPR patent decision didn’t get the science right, but the ruling was fair’ *STAT* 11 September 2018, available at <https://www.statnews.com/2018/09/11/crispr-patent-decision-science/>, accessed on 25 August 2019; Bheki Zulu et al ‘CIPC to introduce substantive search and examination’ *De Rebus* 31 January 2018, available at <http://www.derebus.org.za/cipc-introduce-substantive-search-examination/>, accessed on 14 October 2019.

introduction of SSE,¹⁸⁹ whereby a patent will only be granted if it meets the legal criteria for patentability, including non-obviousness. Patent examiners will be introduced and their opinions will play a large role in determining obviousness.¹⁹⁰ However, the IP Policy extends beyond SSE and includes the adoption of stricter standards for patentability, which may impact what CRISPR technologies can and cannot be patented. Among other international patent offices,¹⁹¹ the EPO has been tasked with the training of South African patent examiners and has been working with the SAPO to confirm their proficiency.¹⁹² Qualified patent examiners, with the requisite skills, are needed to give effect to the IP Policy.¹⁹³ When determining obviousness utilising the test,¹⁹⁴ the background and training of patent examiners becomes relevant. From a scientist's viewpoint, the issues that the PTAB noted in the US CRISPR patent dispute, which would make the invention non-obvious for one skilled in the art, were not difficult to address.¹⁹⁵ They could be solved with a variety of theoretical solutions – standard in the practice of molecular biology. However, in terms of patent law, this 'experimental road map' was insufficient to meet the threshold of obviousness.¹⁹⁶ It remains to be seen how the requirement of non-obviousness will unfold, but South Africa is likely to follow the European

¹⁸⁹ IP Policy at 17-18.

¹⁹⁰ This is influenced by their training and expertise. The SAPO has completed the task of selecting examiners. The CIPC has already recruited 20 examiners, possessing a variety of technical backgrounds. The South African trainee patent examiners are required to undergo an extensive training programme for two years before they are able to formally examine new patent applications. Von Seidels 'South Africa prepares for a thorough examination' available at <https://www.vonseidels.com/south-africa-prepares-for-a-thorough-examination/>, accessed on 3 November 2019.

¹⁹¹ This includes the Japanese Patent Office and WIPO. Ibid.

¹⁹² Another issue to consider is the attrition rate of those being trained as examiners by the EPO. Persons have been leaving the training due to employment conditions. It is important to be able to retain these people once they have been trained in order for the system to work – if there is attrition at the training stage, it does not bode well for the future of this process. It is possible that SSE procedures may be a hindrance to innovation should the resource be outweighed by the sheer volume of applications received. If this is the case, much like India and Brazil, the granting of a patent could take years, which would hurt innovation. There are other solutions which could be used to solve this conundrum, such as outsourcing the examination domestically. Another solution that was not considered is that of 'petty patents' like in Australia. These are patents which can be granted without examination, but should the grantee wish to enforce their patent, they must seek examination first. Ibid; Pereira & Lombard op cit note 183.

¹⁹³ Schonwette & Vawda op cit note 176 at 16-17; Di Battista op cit note 181 at 94.

¹⁹⁴ This test for obviousness examines whether a person of ordinary skill would view a claim as having a reasonable likelihood of success when an opposing claim is viewed as prior art. Daniel J Pereira & Stephen G Kunin 'What is your reasonable expectation of success in obtaining pharmaceutical or biotechnology patents having nonobvious claimed inventions that the courts will uphold? An overview of obviousness court decisions' (2015) 5(4) *Cold Spring Harb Perspect Med* 5.

¹⁹⁵ Sherkow op cit note 188.

¹⁹⁶ Ibid.

approach in terms of SSE,¹⁹⁷ due to similarities between patent laws, and the EPO being responsible for training examiners.¹⁹⁸

As noted in the IP Policy,¹⁹⁹ the SAPO has limited resources. Therefore, strategic sectors will be chosen for full SSE initially, until capacity constraints lessen and other fields can be incorporated.²⁰⁰ The sectors to be chosen will be based on public interest considerations,²⁰¹ and it is likely that initial examination will include the health sector.²⁰² Schonwette and Vawda have supported the idea that SSE be implemented for health technologies.²⁰³ As human therapeutic applications of CRISPR form part of the health category,²⁰⁴ the question is whether it falls within an examination group in the IP Policy. Is it necessary to examine CRISPR patent applications in South Africa? The IP Policy states that its objective is to discern a variety of areas for full SSE, not limited to the health sector.²⁰⁵ However, pharmaceuticals are the immediate focus due to the high costs of life-saving drugs.²⁰⁶

As the above patent landscaping search shows, there are presently numerous pending CRISPR patent applications in South Africa.²⁰⁷ CRISPR has shown great potential in the treatment of various disorders over previous gene editing methods, and the technology is ever-developing.²⁰⁸ However, due to the fact that CRISPR is not yet advanced enough to fall within the class of life-saving technologies, perhaps it is not in immediate need of examination.

¹⁹⁷ The European perspective is based off the problem-solution approach. This approach involves examining the problem, looking at the steps taken by the inventor to solve the problem, what others have done to solve the problem, comparing the different approaches, and then determining if it was an obvious step to take. European Patent Office 'Case law of the Boards of Appeal' available at https://www.epo.org/law-practice/legal-texts/html/caselaw/2016/e/clar_i_d_2.htm, accessed on 3 September 2019.

¹⁹⁸ Von Seidels op cit note 190.

¹⁹⁹ IP Policy at 17-18.

²⁰⁰ This may not be a full examination as per WIPO's guidelines. WIPO 'Alternatives in patent search and examination' policy guide (2014); Pereira & Lombard op cit note 183.

²⁰¹ Although the qualifications of patent examiners are diverse, they predominantly fall in life sciences, with a focus on chemistry, biochemistry, and medicinal chemistry. Secondary fields of qualification include electrical and electronic engineering and pure physics. Therefore, it is likely that patent applications relating to pharmaceuticals and other chemistry-based fields will be examined initially. Von Seidels op cit note 190.

²⁰² The IP Policy states that 'SSE will not *only* apply in the health sphere' and that the 'intention is to identify a range of strategic sectors for full SSE, including and beyond the health sphere' (own emphasis). This means that the health sector is an area of focus, but not the only area. IP Policy at 5 & 18; Pereira & Lombard op cit note 183.

²⁰³ Schonwette & Vawda op cit note 176 at 18.

²⁰⁴ The technology has great potential to treat cancer, viruses, and various genetic disorders.

²⁰⁵ IP Policy at 18.

²⁰⁶ The Industrial Policy Action Plan (IPAP) recognised the pharmaceutical industry as a significant sector. Although the local pharmaceutical market is the largest in Sub-Saharan Africa, this sector does not have a large global impact. The pharmaceutical industry has the potential to develop and contribute to the economy as well as ensure the availability and accessibility of vital drugs. While the importing of medicine is essential, an increase in domestic capacity will ensure security in supply, especially due to South Africa's disease rate. Additionally, a dynamic pharmaceutical sector is essential in the development of science and technology. IP Policy at 16.

²⁰⁷ These will be granted, subject to meeting the formal patent requirements of the SAPO.

²⁰⁸ Ku op cit note 159 at 439.

Nevertheless, given CRISPR's mentioned potential, it would be optimal in the interests of public health to consider CRISPR as critical in achieving goals relating to the treatment and eradication of priority diseases. Therefore, it is vital that patent applications utilising CRISPR technology are examined to ensure that they are valid, beneficial, and of a certain standard as low quality CRISPR patents can impede the progress of this technology. The issue of patent quality is not new, but the increasing numbers of patent applications, the prevalence of litigation, and media attention have caused the matter to resurface. The granting of low quality patents links to apprehension that patents are being awarded for inventions undeserving of patent protection.²⁰⁹

Should an application of CRISPR become as effective as a key drug, but the patent landscape is riddled with low quality patents, the field may be too saturated for a company wishing to pursue research and commercialisation of the technology. Companies may be required to obtain numerous licenses, for which the combined costs are too high. In terms of universities, patents have no direct impact on ensuing academic research due to the fact that patents are largely overlooked by researchers and they often avoid being sued for infringement.²¹⁰ However, patents may affect access to materials,²¹¹ and scientific standards and procedures.²¹² Perhaps innovative research may not be hampered due to researchers 'ignoring' patents, but it may impact commercialisation by companies. Commercialisation and productisation are necessary in bringing products to market in the public interest.²¹³ If patent offices are lenient in their granting of low quality patents, this may hinder research and development, investment, and commercialisation processes, either due to uncertainty regarding FTO or because of possible litigation.²¹⁴

²⁰⁹ There are two ways in which the granting of low quality patents may be occurring. The first is that patent offices may apply too lenient a standard. The second relates to mistakes – granting patents that fail to meet a certain standard. There is concern that patent offices award too many patents for questionable inventions that would not pass a thorough review. Although criteria for patentability exist, subjective factors impact on the uniformity of decisions. The decision to grant a patent depends on a person's (or team's) comparison of the inventive merit of the application, the level of disclosure, and the standards for patentability. Therefore, cohesion of decisions among examiners seems improbable. Gaétan de Rassenfosse et al 'Low-quality patents in the eye of the beholder: Evidence from multiple examiners' 2019 *NBER Working Paper Series Working Paper 2244 2*.

²¹⁰ Ayres & Ouellette op cit note 127 at 282.

²¹¹ Such as cell lines.

²¹² Ayres & Ouellette op cit note 127 at 282.

²¹³ Productisation refers to the process of transforming a development into a product for market. It encompasses a variety of elements, from the early stages of designing a product to the commercial aspects of sale and distribution. Peter Artz et al 'Productization: The process of transforming from customer-specific software development to product software development' (2010) *Department of Information and Computing Sciences Technical Report 7*.

²¹⁴ de Rassenfosse et al op cit note 209 at 2.

Therefore, I suggest that *general* CRISPR human therapeutic applications should be assessed, but not subjected to a full examination initially.²¹⁵ In order to preserve resources and operate despite inadequate infrastructure, human therapeutic applications of CRISPR should be streamlined in accordance with priority health concerns in South Africa such as HIV/AIDS, tuberculosis (TB), and various cancers. I suggest that a formal examination and a full SSE be performed for CRISPR human therapeutic applications *related to priority health concerns*, which is directly in the public interest and conforms to government mandate.

(b) *Patent opposition proceedings*

The IP Policy makes provision for the realisation of patent opposition proceedings.²¹⁶ With the introduction of this procedure, in addition to SSE, companies wishing to patent CRISPR-related inventions in South Africa need to ensure that their patents meet both the formal and substantive requirements.²¹⁷ The competitive CRISPR market, as evidenced by the ongoing US patent dispute, means that patents will likely come under greater scrutiny, not just by examiners, but competitors too.²¹⁸ This procedure allows competitors and other actors to provide expertise in respect of any patent claims.²¹⁹ The upshot of this is that companies interested in CRISPR may now challenge applications and patents outside of court. Extra-curial

²¹⁵ An example of a general human therapeutic application of CRISPR would be in the treatment of blindness. Although beneficial, it is not a priority in South Africa compared to disease such as HIV/AIDS and TB.

²¹⁶ IP Policy at 19-20. The policy aims to introduce pre-grant, post-grant, and third party opposition procedures. These kinds of procedures will have the effect of acting as further preventative and remedial safeguards for the quality of the patents that are granted in South Africa. They allow for public intervention in the application proceedings or after the granting of a patent. This allows third parties to either submit relevant information for consideration by the examiners or actively oppose the application or granting of a patent.

²¹⁷ The introduction of SSE procedures is not a solution in itself. From a logistics point of view, what is important is resources and infrastructure management. This kind of procedure requires large amounts of resources that need to be managed. Infrastructure, such as the systems that ensure applications coming in, need to be maintained and upgraded. Currently, the CIPC is upgrading their systems and should soon allow for electronic filing of patent applications. Despite being able to file electronically, the ensuing processes are still done manually via hard copy, for example, amendments and assignments of patents. Even the current formal examination proceedings are problematic due to delays in things like certificates of granting to be sent to the grantee. It must be noted that SSE procedures add an extra layer of administration. SSE procedures cannot be successful if the formal examination is not optimised. Sadulla Karjiker & Madelein Kleyn 'Commentary: Draft Intellectual Property Policy Phase 1 2017' *CIP* 8 November 2019, available at <https://blogs.sun.ac.za/iplaw/2017/11/08/commentary-draft-intellectual-property-policy-phase-1-2017/>, accessed on 4 October 2019.

²¹⁸ Opposition procedures being open to competitors and other parties could result in information and arguments regarding the prior art and standards of patentability, that could result in higher quality patents. Brook K Baker 'International collaboration on IP/access to medicines: Birth of South Africa's fix the patent laws campaign' (2015/16) 60 *NYL Sch L Rev* 319.

²¹⁹ Schonwette & Vawda op cit note 176 at 16-17.

procedures have an advantage over court proceedings – which have typically proven to be time-consuming and too costly²²⁰ for smaller inventors.²²¹

The introduction of SSE procedures as well as patent opposition proceedings will strengthen South Africa's IP regime, and patent quality, to the advantage of South African inventors and the public. Currently, South Africa is flooded with patent applications from foreign entities, and thus needs to avoid following in the footsteps of the confusion gripping the US and Europe. I suggest that SSE procedures and patent opposition proceedings working in tandem can assist in achieving this by preventing the granting of low quality patents. This aids in avoiding patent thickets – which means that prices for therapeutic applications of CRISPR should reflect lower costs, as FTO costs for developers should be reduced.²²²

X CONCLUSION

The issues raised by the US CRISPR patent dispute and its ensuing repercussions are not optimal for access to, or development of, the technology. Furthermore, the CRISPR patent dispute highlighted a broader societal problem – the privatisation of publicly-funded research. As discussed, the motives and effects of the current licensing and commercialisation models employed by research institutes are not there to serve the public. One questions the effect that this has on the values of science as well.

From a South African perspective, the US CRISPR patent dispute emphasises inadequacies in our law that are in the process of being addressed. However, I suggest that such procedures need proper infrastructure. South African policy should take note of the issues mentioned above in developing solutions that fit our context. Perhaps even reconsidering the patentability of such inventions should not be too unimaginable. To conclude, South African inventors and licensees who wish to utilise CRISPR technology for research or commercial purposes must take heed of the patent landscape in the jurisdiction in which they wish to operate.

²²⁰ Baker op cit note 218 at 319.

²²¹ Challenging a patent requires one to go to the High Court as the court of the Commissioner of Patents is the High Court.

²²² Schonwette and Vawda argue that patent examination also aids in avoiding monopoly prices. They further note that if weak patents are granted, health departments would be required to pay excessive prices for 'improvidently granted pharmaceutical and medical device patents'. Schonwette & Vawda op cit note 176 at 18.

CHAPTER 3

CRISPR LICENSING LANDSCAPE: PUBLIC INTEREST AND IMPLICATIONS FOR SOUTH AFRICA

I INTRODUCTION

Herder and Gold question whether IP rights are absolutely necessary for innovation due to the fact that there is only modest evidence to support such a finding.¹ Exclusive licensing prevents other companies from commercialising potentially beneficial inventions that could aid society in terms of health.² Despite this, exclusivity is still pushed as being essential to innovation. This issue is addressed from the perspective of publicly-funded research and inventions.

II OVERVIEW

In this Chapter, arguments regarding surrogates³ and exclusive licensing, in terms of human therapeutic applications of CRISPR, is evaluated to determine whether they are in the public interest. This Chapter outlines the licensing landscape between patent holders and their spin-outs that were formed for commercialisation reasons. A critical take on the exclusive licensing model, in relation to the depth of the licenses granted and the effects and necessity thereof, reveals that the public interest and social welfare are compromised. Further, it is shown that exclusive licenses are not necessary for every human therapeutic application of CRISPR, and there are other, non-exclusive incentives that may ensure innovation in CRISPR continues, whilst protecting and enhancing social welfare. I ultimately conclude that the current licensing model is not optimised for the public interest.

¹ Matthew Herder & E Richard Gold 'Intellectual property issues in biotechnology: Health and industry' (2007) *OECD* 7. Report from 'OECD international futures project on the bioeconomy to 2030: Designing a policy agenda' third meeting of the steering group Paris, 7-8 February 2008; E Richard Gold et al 'Needed: Models of biotechnology intellectual property' (2002) 20(8) *TRENDS in Biotechnology* 327.

² Ian Ayres & Lisa Larrimore Ouellette 'A market test for Bayh-Dole patents' (2017) 102 *Cornell Law Review* 271.

³ Surrogates are spin-out companies with exclusive rights.

III BACKGROUND

(a) *Setting the scene*

Patent license agreements may be exclusive,⁴ or non-exclusive,⁵ and allow a licensee to develop and commercialise CRISPR technologies.⁶ In contemporary commercial arrangements in universities, there are at least three relevant levels of licensing agreements in terms of CRISPR.

The first level of licensing agreement involves the assignment between the inventor and the research institution. The inventor is sometimes obligated to assign ownership of the patent over to a research institution.⁷ The second level relates to the licensing agreement between the patent holding institution and spin-outs. If such license agreements are exclusive, the licensee companies⁸ effectively act as surrogates on behalf of the patent holding institutions, maintaining full control of the patent in most instances. Within these agreements there are other restrictions that dictate the terms under which these licenses operate, such as ethical licensing considerations (to be dealt with in Chapter 4).⁹ The third level entails the licensing agreement is between the spin-out or surrogate and other private companies who wish to research or commercialise the technology.

Being mindful of these three levels of licensing agreements is important as it denotes the various patent holders for CRISPR technologies and forms the landscape in which licensing takes place. Prospective companies or researchers will need to identify the core CRISPR technology patent holders, and ascertain whether they have patented within the relevant jurisdictions.¹⁰ They would then need to determine the relevant entity from which licenses need to be sought. Following this enquiry, decisions can be made regarding research, commercialisation, licensing, and market considerations. An overarching question is whether

⁴ Exclusive licenses grant the licensee the sole rights to use of the licensed invention for the term of the license. This also excludes the licensor from utilising the invention or from granting licenses to other parties.

⁵ Non-exclusive licenses grant the licensee the right to use the invention for the term of the license, but not to the exclusion of all others. The licensor may use the invention or may license it to third parties.

⁶ A patent license agreement grants a licensee exclusive rights to manufacture, sell, and use a patented invention, subjected to certain terms. Non-exclusive licenses are often valueless to biotechnology companies when ownership or exclusive rights to a molecule, process, or treatment are imperative. Priori 'Patent license agreement' <https://www.priorilegal.com/legal-forms-and-documents/patent-license-agreement>, accessed on 3 January 2020; Rodney L Sparks 'Patent, ownership, and licensing issues of CRISPR-based genome editing: Impact on universities and their licenses' in Krishnarao Appasani (ed) *Genome Editing and Engineering: From TALENs, ZFNs and CRISPRs to Molecular Surgery* (2018) 432.

⁷ For example, Zhang assigned ownership to Broad and Doudna to UC.

⁸ Jorge L Contreras & Jacob S Sherkow 'CRISPR, surrogate licensing, and scientific discovery' (2017) 355(6326) *Science* 698.

⁹ For example, Broad's exclusive license with Editas for human therapeutics.

¹⁰ It is suggested that they also explore other areas in which it has not been patented for potential markets or places to manufacture.

this business model of university patenting and surrogate licensing is optimal for CRISPR technology, and hence optimal for the public interest.

(i) *Spin-outs, surrogates, and exclusivity*

Broad and UC have granted exclusive rights, on their CRISPR patents for human therapeutic purposes, to various spin-outs. However, exclusivity may not be ideal for developing gene editing therapies, and the public interest may be better served without exclusivity limiting the integral technology.¹¹

Universities employ a range of methods for commercialising patented technologies. One such practice is surrogate licensing,¹² which is a particular form of spin-out licensing.¹³ The spin-out is a newly formed company, designed to commercialise a specific patent portfolio belonging to a university.¹⁴

There have been many successful spin-outs in the past,¹⁵ and this business model can work well for commercialisation.¹⁶ However, issues arise with a particular type of spin-out, being surrogates.¹⁷ Patent holding institutions have entered into exclusive agreements to delegate licensing rights to surrogates in an attempt to capitalise on the commercial value of the content of foundational CRISPR patents.¹⁸ Surrogate licensing of patents entails outsourcing the licensing and/or commercialisation of a patent portfolio to a third party

¹¹ Ayres & Ouellette op cit note 2 at 279.

¹² The surrogate licensing of patents entails outsourcing the licensing and commercialisation of a patent portfolio to a third party company. Nuffield Council on Bioethics 'Genome editing and human reproduction' (2018) *Nuffield Council on Bioethics* 146.

¹³ Whilst a regular spin-out arrangement allows the patent holding academic institution to retain the rights to license their IP whenever they wish, surrogates hold exclusive licenses. As mentioned in Chapter 2, a spin-out is formed through separation from the main entity in order to form a new and independent corporation. Allen & Overy 'Key players in CRISPR' available at <https://www.allenoverly.com/en-gb/global/news-and-insights/crispr/key-players-in-crispr>, accessed on 18 October 2019.

¹⁴ Jacob S Sherkow & Jorge L Contreras 'Intellectual property, surrogate licensing, and precision medicine' (2017) *7 IP Theory* 5.

¹⁵ Such as Google being a spin-out of Stanford University and Myriad Genetics being a spin-out of the University of Utah. *Ibid* at 5.

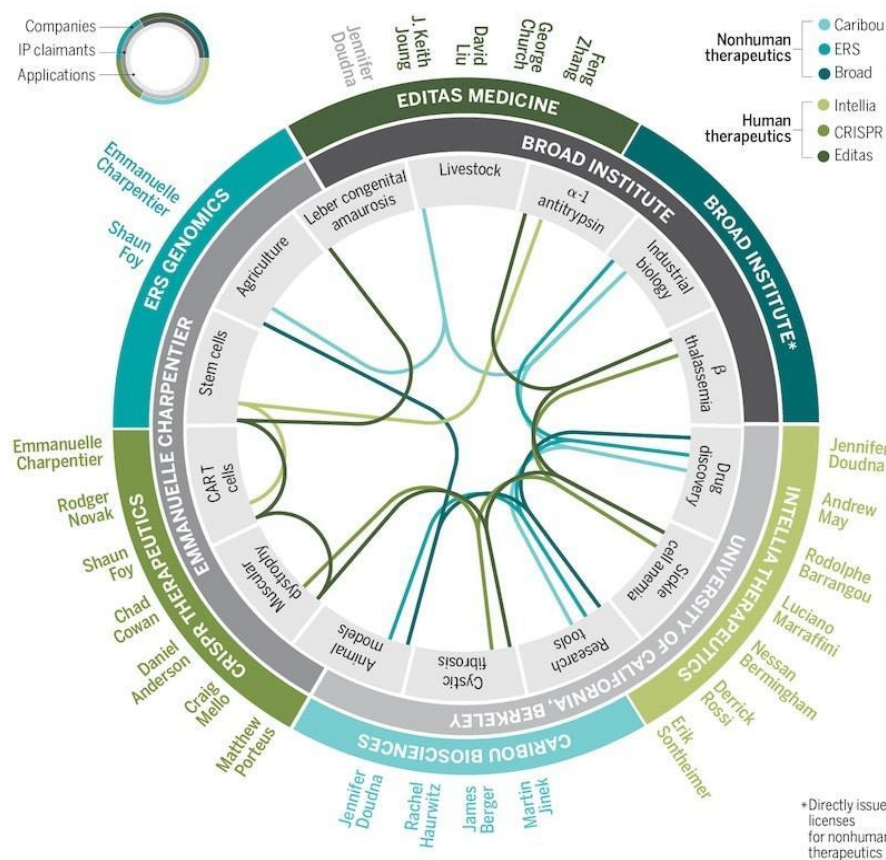
¹⁶ This allows researchers at the university, who may not possess business acumen or ability to extract value from the patents, to purely focus on research. The spin-out will have a singular focus on commercialisation in the form of sub-licensing or product development. They will have the time and expertise to fully extract value from these technologies in the relevant markets.

¹⁷ They are termed this as they effectively stand as surrogates for patent holding institutions. Sherkow notes that universities tend to prefer this model as it allows for a substantial share of profits to be received with minimal risk through their equity interests and royalties generated. This model also allows universities to focus their efforts on more commercialisation projects whilst delegating the responsibility of determining the licensees to those more focussed on that particular technology and the markets. See, Contreras & Sherkow op cit note 8 at 698-699.

¹⁸ *Ibid* at 698.

company.¹⁹ These surrogates have sole authority over further licensing of the patents – they control the development and usage of that specific technology. Surrogates have the freedom to dictate who the sub-licensees are, under what conditions these licenses are granted, and whether they are going to exploit the technology themselves.²⁰ Much of the foundational CRISPR IP is held by these profit-driven surrogates.²¹

Figure 1 below represents the current CRISPR licensing landscape, illustrating the various surrogates and spin-outs belonging to Broad and UC,²² as the foundational patent holders in terms of CRISPR technologies²³ –



¹⁹ Whilst a regular spin-out arrangement allows the patent holding institution to retain the rights to license their IP whenever they wish, surrogates hold exclusive licenses. Nuffield Council on Bioethics op cit note 12 at 146.

²⁰ Contreras & Sherkow op cit note 8 at 698.

²¹ Sherkow & Contreras op cit note 14 at 1.

²² UC passed its licensing operations to Caribou, while Broad passed operations to Editas. One group includes Intellia, Caribou, Doudna, and UC. This group is affiliated to CRISPR Tx, ERS Genomics, and its founder Charpentier. The Doudna and Charpentier camps declared their association in 2016, by signing a global cross-licensing and patent prosecution co-operation agreement. The opposing group is Editas, Zhang, and Broad, who possess a rival collection of foundational CRISPR-Cas9 patents. These spin-outs have partnered with big pharma, venture capitalists, and other disruptive biotech start-up companies in a range of exclusive and non-exclusive licensing deals, joint ventures, and strategic collaborations. Nuffield Council on Bioethics op cit note 12 at 146.

²³ Figure 1. Diagram showing the current CRISPR licensing landscape. Taken from Jon Cohen 'How the battle lines over CRISPR were drawn' *Science* 15 February 2017, available at <https://www.sciencemag.org/news/2017/02/how-battle-lines-over-crispr-were-drawn>, accessed on 20 September 2020. G. Grullón/Science.

Surrogate licensing has the effect of placing ‘a large and lucrative field for the exploitation of the licensed technology’ in the hands of entities driven by duties to shareholders rather than to the public.²⁴ CRISPR’s significance to human healthcare treatment and the public interest raises numerous concerns about these agreements.

IV ARGUMENTS AGAINST SURROGATES AND EXCLUSIVE LICENSING

(a) *Access: Bottlenecking and the exclusivity problem*

(i) *Introduction*

The commercialisation of CRISPR technologies may cause an exclusivity problem, through the granting of exclusive licenses, which serves to limit access to human therapeutic applications of CRISPR.²⁵

As many authors have argued, this model of university patenting and surrogate licensing raises ethical questions, such as: (1) whether the privatisation of research obtained from public funding is contrary to the values of universities as public institutions; and (2) whether this model allows for the full utilisation of nascent technologies or hinders their development.²⁶

(ii) *Bottlenecking*

The uncertainty surrounding the US CRISPR patent dispute obscures the already confusing surrogate arrangements. Many companies have invested in the CRISPR industry and, without an answer as to who the owner of the foundational CRISPR patents is, it remains unclear from whom licenses should be acquired, hampering others from entering the market. The issue with surrogate licensing, as Sherkow and Contreras have noted, is exclusivity which can lead to ‘bottlenecking’.²⁷ A surrogate can grant an exclusive license that is broader than what the licensee requires, without a right to sub-license, preventing a field from being developed by others until the expiry of the ‘head’ license.²⁸

²⁴ Contreras & Sherkow op cit note 8 at 698.

²⁵ Sirpa Soini et al ‘Patenting and licensing in genetic testing: Ethical, legal and social issues’ (2008) 16 *European Journal of Human Genetics* 11.

²⁶ Ibid at 11.

²⁷ Contreras & Sherkow op cit note 8 at 698.

²⁸ Nuffield Council on Bioethics op cit note 12 at 146.

(iii) *Commercial bottlenecking*

The limiting of CRISPR technologies through the granting of exclusive control to a profit-driven entity precludes other interested parties from pursuing the technology commercially. The unrestricted ability to undertake non-commercial research on CRISPR, for non-profit and academic purposes, would not preclude anyone from researching the technology.²⁹ However, any potential commercial CRISPR applications could be impeded by the inability or refusal of the surrogate to grant a license. This could have dire consequences in terms of access to CRISPR technology and variation, as discussed below. Sherkow and Contreras refer to this outcome as ‘commercial bottlenecking’ as commercial applications of CRISPR technology are essentially restricted.³⁰ Thus, other developers in the field may not even have a chance to enter the market.

(b) *Exclusivity and breadth of the licenses*

Currently, the scope of exclusive licenses is an issue.³¹ In many of the principle surrogate licenses, the patent holding institution has granted the surrogate the exclusive right to utilise CRISPR processes in order to develop human therapeutic applications.³² Broad has granted Editas, and UC has granted Caribou Biosciences (Caribou),³³ exclusive licenses to utilise CRISPR-Cas9 for every human therapeutic application of CRISPR, targeting any of the genes in the human genome.³⁴ This is problematic for two reasons: (1) it is impossible for a sole surrogate to explore the full potential of CRISPR technology in relation to every human gene;³⁵

²⁹ A key principle of the NIH is to ‘ensure dissemination of resources that are developed with NIH funds’. In 1999, the NIH published Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources 64 Fed. Reg. (Dec. 23, 1999), and recommended the granting of non-exclusive licenses for research tools developed with federal funds in order to assist in commercialisation. Where an invention is a valuable research tool, exclusive licenses serve to impede commercialisation and access to the invention. However, in instances where exclusive licensing is necessary to attract private companies, such licenses should be designed to ensure ‘expeditious development of as many aspects of the technology as possible and to ensure development of the technology in all research fields and product areas’. Broad and UC are following this NIH recommendation in part, as both institutions have granted non-exclusive licenses for research and non-profit use. However, in order to commercialise a product a sub-license is required from the relevant surrogate who holds it. This extra licensing step may impede innovative applications of CRISPR. Letter from Carrie Wolinetz, Acting Chief of Staff and Associate Director for Science Policy at the NIH to James Love, Director at Knowledge Ecology International 21 June 2017 available at <https://www.keionline.org/23413>, accessed on 12 January 2020; Megan Molteni ‘The long-shot bid to put Crispr in the hands of the people’ *Wired* 22 February 2017, available at <https://www.wired.com/2017/02/long-shot-bid-put-crispr-hands-people/>, accessed on 6 January 2020.

³⁰ Contreras & Sherkow op cit note 8 at 700.

³¹ Sherkow & Contreras op cit note 14 at 6.

³² Contreras & Sherkow op cit note 8 at 699.

³³ Caribou has exclusively licensed human therapeutic applications to Intellia. Allen & Overy op cit note 13.

³⁴ Sherkow & Contreras op cit note 14 at 6.

³⁵ Contreras & Sherkow op cit note 8 at 698.

and (2) the use of this technology in any human therapeutic application is exclusively within the control of a single, commercially-focused entity. This means that the patent holding institution cannot license the technology for usage in any gene to other companies. Broad has developed a solution to this, being the inclusive innovation model, which will be discussed later in this Chapter. Essentially, the exclusive license on all genes immediately excludes other commercial developers from the CRISPR market, unless they obtain a license.

In some instances, exclusivity may be necessary for obtaining investment from the private sector in order to bring a product through the innovation chain, or to recoup costly expenditure involved in development. However, Sherkow and Contreras note that this deep breadth of exclusivity is unnecessary and can lead to adverse consequences for the public as ‘exclusive rights beyond those necessary to develop a particular product are a deadweight loss: society will pay a higher price for the end therapeutic product beyond that necessary to bring it to market’.³⁶

Additionally, exclusivity requires the payment of licensing fees on all uses and functions of CRISPR technology, both known and unknown.³⁷ The idea of implementing licensing fees on the function of a gene that is unidentified or un contemplated by the patent holder cannot be in the public interest, or in the interests of biotechnology and precision medicine as a whole. How would it be in the public interest to exclude others from things that are unknown to the excluding party, and the world at large? That would be laying claim to the unknown, as a sort of foresight. That cannot be in the public interest as it could have the effect of dissuading investment by others to explore the unknown. Furthermore, from the perspective of fairness, it seems contrary to good market practice.

From a business viewpoint, the breadth of exclusive licenses is ideal because it has the effect of capitalising on future inventions relating to genes for which there are currently no plans – by creating the need for licenses and fees where inventions do not exist. In this way, universities have monopolised the human genome, but only with regards to their technology. Although new and more efficient Cas enzymes exist, there are no practical alternatives to CRISPR yet. However, through exclusive licensing practices, Broad and UC have effectively duopolised gene editing in humans.

³⁶ Sherkow & Contreras op cit note 14 at 8.

³⁷ Ibid at 9.

(c) *Competition, costs, and variety control*

(i) *Competition*

It is problematic when potential licensees are also rivals to the licensor, especially in the case of similar technologies. Surrogates act as rivals to some small biotechnology companies.³⁸ This brings into question whether surrogates will grant licenses to competitors or grant them on favourable terms.³⁹ Furthermore, smaller enterprises may be disadvantaged compared to those with larger portfolios, which may result in IP being consolidated amongst larger institutions.⁴⁰

(ii) *Costs*

As Sherkow and Contreras argue,⁴¹ the need for profit in licensing agreements could lead to a situation of multiple sub-licenses which, in turn, may result in royalty stacking, a circumstance whereby the utilisation of an invention calls for numerous licenses from a variety of patent holders, thus raising the cost of end products.⁴² Such royalty stacking would likely translate into higher prices on CRISPR-related therapies for the public.

These considerations, along with bottlenecking and restricted competition, as described above, grant surrogates sole control over the prices of CRISPR therapies. This control could also have a great impact on the variety of applications of CRISPR technology.⁴³ For example, a once-off therapy could cost hundreds of thousands of dollars, thus excluding a large percentage of the public from accessing a therapy at that price.⁴⁴

(iii) *Variety and development*

Variety can also be negatively impacted by exclusive licensing. Different companies will employ diverse methods or processes for the same outcome. However, by reducing competition the licensing regime can limit this variety. Greater diversity is preferred for the following reasons: (1) welfare is enhanced by consumer choice and decreased by a lack of choice; (2)

³⁸ NYU School of Law ‘The CRISPR patent battle: Implications for downstream innovation in gene editing’ Engelberg Center on Innovation Law & Policy 21 March 2017.

³⁹ If a small biotechnology requests a license from a research institution, it is usually not a problem as it is unlikely that the research institution intends to develop a technology commercially. However, issues arise when the entity from whom a license must be requested is a competitor. *Ibid.*

⁴⁰ This opposes the idea of patents existing to benefit the public. Nuffield Council on Bioethics *op cit* note 12 at 146.

⁴¹ Sherkow & Contreras *op cit* note 14 at 15-16.

⁴² Soini et al *op cit* note 25 at 24.

⁴³ Sherkow & Contreras *op cit* note 14 at 9.

⁴⁴ Jim Kozubek ‘Who will pay for CRISPR?’ *STAT* 26 June 2017, available at <https://www.statnews.com/2017/06/26/crispr-insurance-companies-pay/>, accessed on 5 January 2020.

certain processes may need tinkering in order to be adapted to different populations, and variety offers this;⁴⁵ (3) increased variety means increased competition, which can lead to lower prices for the public; and (4) product quality and innovation can be enhanced by increased competition. However, a pressing issue is that some important CRISPR therapies may not be pursued for development. Herder and Gold argue that exclusivity on initial inventions may deter discoveries that build on those inventions.⁴⁶

Being for-profit, surrogates are drawn to development plans for products which maximise revenue streams,⁴⁷ thus focusing on lucrative therapies. One may think that the most profitable therapies would involve priority diseases. While this may be true for some diseases, it is not always the case.⁴⁸ In the hands of a surrogate, the development of therapies is not driven by necessity or public interest and health, but by market considerations. It is for these reasons that exclusive surrogate licensing agreements can result in decreased access to, and development of, CRISPR therapies for the public interest.

(d) Disclosure and secrecy

Genomic or operational data acquired from CRISPR research and usage in humans would be as valuable as the disclosure of the invention in a patent application. The actual data generated would speak to tangible results, issues, solutions, responses, and many other important details for those who wish to develop CRISPR-related products. The sharing of this data would inarguably be vital to developers and inventors globally, as it would save time and numerous other resources, including large financial expenditure that would often act as a barrier towards product development.

However, as evidenced by Myriad Genetics (Myriad), surrogates are not always concerned with the dissemination of knowledge for greater development. Myriad, who held an exclusive license over patents on BRCA1 and BRCA2 genes,⁴⁹ developed an extensive

⁴⁵ This includes third world applications of CRISPR technology.

⁴⁶ Herder & Gold op cit note 1 at 6.

⁴⁷ Sherkow & Contreras op cit note 14 at 15.

⁴⁸ Essentially, the determining factor is the profit potential. This can be established through numerous factors such as people affected on a global or national scale and the number of patients who can afford to pay for the therapy. An example of this is Editas' focus on treating Leber Congenital Amaurosis, a form of blindness that affects between 3000 and 6000 Americans. The cost of a single course of treatment is \$100,000, which means that it is a possible \$3-6 billion industry. Despite the low number of affected persons, the large potential for profit is a prerogative for surrogates. The low number of individuals however, can also largely influence surrogates to shy away from investment – it really depends on market potentials. Ibid at 15.

⁴⁹ Myriad developed DNA tests to determine if women were at risk of developing inherited breast and ovarian cancers. They patented their invention on the BRCA cancer genes, but these were invalidated by the US Supreme Court in 2013 causing Myriad to lose its monopoly on BRCA testing. Sharon Begley 'As revenue falls, a pioneer

database of information (including rare variants),⁵⁰ whilst in control of those patents. This resulted in Myriad protecting the data as a trade secret due to its commercial value. It is not difficult to understand why surrogates would be inclined to keep the resultant data from product development and testing to themselves, and protect it in this way. Although concerns, such as maintaining secrecy on a certain technique or site-specific results in order to maintain monopolies and profit are not unfounded, they do go against the principles of benefit-sharing.⁵¹

(e) Effect on third world countries including South Africa

The effect of exclusivity on third world countries lends itself to the patent debate, but also to exclusive licensing. Both aspects will be discussed as they are interlinked and the arguments run in parallel. The correlation between IP and its management in the context of the developing world has been touched on by many authors, with some arguing that IP results in a biotechnology divide that reduces or retains the social welfare status quo in many countries.⁵²

Herder and Gold argue that IP rights are insufficient incentives for companies to steer their innovative efforts towards products aimed at addressing issues in the developing world, but also to optimise existing products for the successful delivery and functionality in third world populations and conditions.⁵³

Broad and UC have been granted patents in South Africa. This opens South African companies up to litigation should they proceed to productisation that is adopted to the conditions of the country. There is no evidence of plans for clinical trials by Western companies, focusing on the development of human therapeutics, suited to the African context. Furthermore, there are ethical restrictions in the licensing of CRISPR technology that may preclude solutions to African issues. This will be further addressed in Chapter 4. However, it must be noted that any developers, globally or in South Africa, that optimise CRISPR technology for an African context can be precluded from doing so because of the exclusive

of cancer gene testing slams rivals with overblown claims' *STAT* 29 November 2016, available at <https://www.statnews.com/2016/11/29/brca-cancer-myrriad-genetic-tests/>, accessed on 15 October 2019.

⁵⁰ Sherkow & Contreras op cit note 14 at 7.

⁵¹ Benefit-sharing entails the sharing of benefits from genetic and biological data. Article 15 of the Declaration of UNESCO on Bioethics and Human Rights SHS/EST/BIO/06/1 holds that 'benefits resulting from any scientific research and its applications should be shared with society as a whole and within the international community, in particular with developing countries'. It further mentions new diagnostic and therapeutic products or processes emanating from research. Article 12 of the Universal Declaration on the Human Genome and Human Rights states that breakthroughs in biology, medicine, and genetics should be freely available. Soini et al op cit note 25 at 18.

⁵² Herder & Gold op cit note 1 at 4.

⁵³ Herder and Gold draw on the period between 1975-1976 whereby only 1% of new drugs were designed to treat 'tropical diseases'. Ibid at 6.

licensing regime. Moreover, none of the exclusive licensees currently have any African-centric clinical applications in the pipeline – so where does this leave Africa?

V ARGUMENTS FOR SURROGATES AND EXCLUSIVE LICENSING

(a) *Innovation and dissemination are not at risk due to sub-licensing*

Simply put, this argument states that innovation and dissemination in the public interest are not threatened, nor are other developers excluded from utilising CRISPR technologies, as surrogates can sub-license to another company or pursue development themselves. However, in practice, would this be the case? I suggest not. The surrogate is in direct competition with other prospective licensees,⁵⁴ which may affect whether licenses are granted, if they are granted on favourable terms, and other possible restrictions.⁵⁵

(i) *Broad's inclusive innovation model*

It is argued by some that surrogates are not the issue in patent licensing agreements. Perhaps a variation in the surrogacy license could solve these issues? Broad attempted to do just that with its inclusive innovation model.

The goal of the inclusive innovation model is to ‘enable the primary licensee to devote sufficient investment to develop CRISPR-based genome editing technology to treat human diseases’.⁵⁶ Essentially, this model grants ‘exclusivity’ to Editas, being Broad’s primary licensee. However, ‘after an initial period, other companies may apply to license certain CRISPR IP for use against genes that are not being pursued by the primary licensee’.⁵⁷ This allows Broad to grant licenses to other companies for unexplored or un contemplated genetic applications, which is a good idea in part as it tempers exclusivity. However, the issues lie in Broad’s proposed process.

In order for a prospective company to gain a license, they would need to approach Broad with ‘a bona fide development plan’.⁵⁸ Following this, Editas as the primary licensee, has ‘a predefined period’ in which to announce whether they intend to pursue the designated gene as

⁵⁴ For surrogacy and competition concerns, see *Juno Therapeutics Inc v Kite Pharma Inc* No. 2:17-cv-6496 (C.D. Cal. Sept. 1, 2017).

⁵⁵ Sherkow & Contreras op cit note 14 at 10.

⁵⁶ Broad Institute ‘Information about licensing CRISPR systems, including for clinical use’ 2 May 2014 available at <https://www.broadinstitute.org/partnerships/office-strategic-alliances-and-partnering/information-about-licensing-crispr-genome-edited>, accessed on 9 August 2019.

⁵⁷ Ibid.

⁵⁸ Ibid.

per the development plan in the future. If Editas is not currently working on, nor does it plan to work on, a certain gene in the stipulated time period, Broad *may* grant a license to the prospective company.⁵⁹

The first point to note is the vagueness of the inclusive innovation model. There is no indication as to what a ‘predefined period’ is. As it is undefined, it can be extensive, depending on what Broad and Editas agree to.⁶⁰ This in itself may act as a delaying tactic, allowing Editas the necessary time to create a plan of action for utilising the relevant gene. Moreover, it is difficult to believe that any third party inventor would approach Broad with a business plan and hand it over in the hopes that Broad will grant them a license. If the business plan involves a highly profitable invention, what is preventing Broad from simply presenting the plan to Editas and giving them time to create their own plan to commercialise the invention themselves? Editas has the right of first refusal,⁶¹ including the ability to block third parties. Due to the fact that Broad and Editas have contemporaneous financial interests in one another, it would be difficult to counter the possibility of Broad handing the plan to Editas and announcing that Editas is working on the same idea, thereby denying the license.

How does one protect that business plan and prove that they had the initial idea, or were the only ones to possess that idea? This is a near impossible task. However, a viable solution would be to patent the idea because, whilst a third party may not possess FTO (dealt with in Chapter 4), they still hold exclusive rights to the idea. If Broad were then to say that Editas had this idea in the pipeline, they would not be able to operate unless they obtained a license from the patentor. However, as Sherkow notes, patenting CRISPR-based inventions may be difficult as it is questionable whether there are any non-obvious applications of CRISPR.⁶² Therefore, if patenting is not an option, a third party may have no recourse, leading to a situation wherein

⁵⁹ Ibid.

⁶⁰ Without providing a stipulated time, this period could be anywhere between two weeks and twenty years.

⁶¹ A right of first refusal is a contractual mechanism granting the right holder a preference to buy a product if the owner sells it. Snymans ‘The right of first refusal’ available at <https://www.snymans.com/advice/right-first-refusal/>, accessed on 5 January 2020.

⁶² This is because, in the US, patents are required to be new, useful, and non-obvious. As the capabilities of CRISPR have been revealed, it has been questioned whether the application of CRISPR-Cas9 can be non-obvious, which would affect patents. The CRISPR process is already patented, and it is likely that prospective patents will use CRISPR technology in claims for genome edited end products. This makes patenting CRISPR-based inventions difficult. Jacob S Sherkow ‘The CRISPR patent landscape: Past, present, and future’ (2018) 1(1) *The CRISPR Journal* 3.

a third party simply withholds their ideas.⁶³ If a solution that maintains the secrecy of this proposal is developed, the inclusive innovation model may be saved.

However, as it stands, Broad's inclusive innovation model simply excludes other companies from commercialising human therapeutic applications of CRISPR.

(b) Knowledge transfer

It is argued that for the successful productisation and commercialisation of a technology to occur, there needs to be sufficient knowledge transfer. Whilst patents disclose technical information to enable the invention to be practiced, not all relevant information is contained in the patent. Things such as rule of thumb,⁶⁴ background knowledge, tricks of the trade, trial and error skills, and intuition regarding how the invention must behave in certain environments are of great importance. This makes the involvement of an inventor essential in knowledge transfer for commercialisation. As inventors often tend to form part of surrogates, they can assist in this process.

However, I contend that this is a contractual issue between the inventor and the licensee. It is in the best interests of both parties to reach an agreement in terms of the license.⁶⁵ It is not essential for a surrogate to be involved merely because the inventor may hold an interest therein. Collaborative efforts could be fixed by the license terms, which involve the inventor being rewarded in royalty rates proportionate to their efforts. It is true that biotechnological inventions are unpredictable. Therefore, inventor involvement may be necessary as one cannot guarantee the success of the invention simply from the information contained in a patent. However, inventor involvement may be ineffective for that very same reason. Furthermore, patents are not the only means of effective knowledge transfer – a simple conversation or consultation can be beneficial.⁶⁶ I suggest that knowledge transfer, as a *conditio sine qua non* for an invention's success, is also relative to the nature of the invention.

The existence of the internet, and other forms of instant communication, make information sharing much easier.⁶⁷ In addition, with access to information through sites like

⁶³ This is problematic as CRISPR-related inventions, with the potential to assist in the treatment or prevention of certain health conditions in the public interest, may be neglected and overlooked.

⁶⁴ Lisa Larrimore Ouellette & Rebecca Weires 'University patenting: is private law serving public values?' (2019) *Mich St L Rev* 23.

⁶⁵ The inventor and the patent holding institution hold interests in the commercial success of the invention due to the royalties payable to them both, and so it would be in their direct interest to assist without needing extra incentives.

⁶⁶ Ouellette & Weires op cit note 64 at 25-26.

⁶⁷ Ibid at 26.

AddGene,⁶⁸ less direct involvement from the inventor is necessary as much of the information required for research is freely available.

(c) *Exclusivity is necessary for innovation and to bring products to market*

(i) *Assumption 1: Exclusivity is necessary for investment in human therapeutics due to high costs*

The most compelling argument in favour of exclusivity⁶⁹ is the high costs of clinical trials and meeting regulatory burdens. In broad terms, the argument is represented as follows: the substantial costs and risks associated with developing human therapeutic applications of CRISPR lie with the company funding the development.⁷⁰ Hence, exclusivity is needed for: (1) ex ante incentive to encourage investment in these developments as there are potential profits to be made;⁷¹ (2) ensuring that profits are not divided amongst competitors; and (3) warranting that monopoly profits are used to recoup research and development expenditure.

Firstly, it is argued that the risk is not solely with exclusive licensees as this would necessitate a transfer of risk from the public.⁷² I contend that the risk stays with the public as the initial public investment in the invention may not be met with a corresponding benefit, and the risk of non-development remains. However, I assert that due to investment by the licensee, the risk is shared between the public and the private licensee. As a result, the premise that relies on risk as validating exclusivity does not stand. Hence, exclusivity cannot be justified on this ground.

Secondly, risks depend on the nature of the technology as well as other factors.⁷³ In terms of some technologies, public investment that was utilised in the development of an invention may outweigh the costs associated with productisation and commercialisation. Therefore,

⁶⁸ This would also include if data sharing is encouraged and data protection is prohibited to some degree.

⁶⁹ In the form of patents and exclusive licenses.

⁷⁰ Such risks include outright failures or numerous failures until success is achieved in terms of development.

⁷¹ The concept of ex ante denotes that the aim of intellectual property is to 'influence behaviour that occurs before the right comes into being'. There is currently a lack of evidence regarding whether Bayh-Dole misrepresents ex ante incentives towards inventions with a higher or lower social value. Due to the costs involved in a perceived benefit, ex ante incentives fail to justify university patents. Mark A Lemley 'Ex ante versus ex post justifications for intellectual property' (2004) 71(129) *The University of Chicago Law Review* 130; Ayres & Ouellette op cit note 2 at 282.

⁷² This is due to the fact that the public has a risk of an invention not being productised or commercialised, which would be a waste of tax money that was spent on funding the invention as well as losing out on a potential benefit from the failed product.

⁷³ For example, a therapeutic application that targets skin cells will likely be less intricate than a therapeutic application that targets embryos. There will be more risks involved in the former, and more expenses due to the complexity of the application. Furthermore, it will also likely be costlier as there will be more regulatory hurdles to address in clinical trials.

blanket exclusivity, as per Broad's exclusive licensing statement, is invalid.⁷⁴ If Broad believes that exclusivity is necessary for the commercialisation of CRISPR-based inventions, they should be required to support this with statistics and figures in light of the negative effects that these exclusive rights have on the public interest.

Exclusivity was not required for the commercialisation of numerous renowned university inventions, such as Stanford's Cohen-Boyer patents on fundamental recombinant DNA technology, which were licensed non-exclusively.⁷⁵ Eisenberg notes the difficulty in arguing that if these techniques had not been patented, they would not have been pursued or used by industry, even if the technology was placed in the public domain.⁷⁶

Ouellette and Ayres propose a 'market test' as a solution to the exclusivity problem in terms of federally-funded inventions.⁷⁷ This would be used to determine whether inventions funded by government, like CRISPR, require exclusive licensing or if such rights would be unnecessary.⁷⁸ Before licensing exclusively and charging significant licensing fees for inventions,⁷⁹ federally-funded grant recipients should establish whether companies would be willing to commercialise an invention under a non-exclusive license. If a company commits to do so, then an exclusive license would be contrary to the public interest.⁸⁰ Where companies are unwilling to commercialise an invention under a non-exclusive license, there are alternatives other than exclusive licensing. Ouellette and Ayres propose offering inventions under an auction, where the measure is the amount of exclusivity rather than price, and the least restrictive licensing options can be ascertained.⁸¹

⁷⁴ Broad Institute op cit note 56.

⁷⁵ The Cohen-Boyer patents were not only licensed non-exclusively, but also widely to a range of biotechnology and pharmaceutical companies and brought in 255 million dollars for the university. Rebecca S Eisenberg 'Public research and private development: Patents and technology transfer in government-sponsored research' (1996) 82(8) *Virginia Law Review* 1710.

⁷⁶ Ibid at 1710-1711.

⁷⁷ This market test requires that non-exclusive licenses should be offered for an invention, prior to licensing it exclusively. If a company is willing to develop an invention under a non-exclusive license, then free non-exclusive licenses should be offered by the university to others wishing to pursue the invention. Ayres & Ouellette op cit note 2 at 279-280.

⁷⁸ The idea underlying the market test is that universities should figure out ways in which funded inventions can be commercialised while costing society the lowest possible amount. Organisations willing to commercialise an invention non-exclusively means that exclusive licensing is unnecessary. Ibid at 279.

⁷⁹ Ibid at 276.

⁸⁰ Ibid at 279-280.

⁸¹ In a formal commercialisation auction, the winner commits to commercialising an invention in exchange for limited exclusivity rights. Such an auction can determine whether it is mandatory to grant exclusive patent rights, and the required level of exclusivity needed to simulate commercialisation. In this situation, bidders sell commercialisation services in return for limited exclusivity rights. The aim of such an auction is not to determine the lowest bid with the least commercialisation cost. Rather, it seeks to utilise the knowledge of the party with the smallest commercialisation cost (which may or may not rest with that party) in an attempt to curtail the debts

Another solution is government investing in clinical trials. Clinical trials are vastly expensive and unaffordable for smaller companies and academic institutions.⁸² However, if an invention cannot be patented, its development is unlikely.⁸³ Therefore, government should assist in funding clinical trials related to human therapeutic applications of CRISPR in order to encourage commercialisation that serves the public interest.

I am not arguing that exclusivity is unjustifiable, rather I assert that exclusivity is only justifiable in certain contexts with specific technologies, for which the costs of commercialisation sufficiently warrant exclusivity. Moreover, a non-exclusive approach, unless exclusivity is necessary based on the nature of the invention and its market, is in line with the NIH's Best Practices for the Licensing of Genomic Inventions: Final Notice.⁸⁴ Whilst these are just recommendations, it should be noted that through contractual agreements, the NIH can regulate the use of exclusive licenses. Furthermore, the Organisation for Economic Co-operation and Development (OECD) Guidelines for the Licensing of Genetic Inventions stress that licensing for foundational genetic inventions should be non-exclusive for use and access purposes.⁸⁵

In this argument, a more direct meaning of public interest is applied, being the interest of the public to receive benefits from its investment. Should an invention be commercialised, royalties are paid to the licensees and licensors⁸⁶ – the only benefit to the public is that of the end product. However, if the product is only marketed to certain population groups, the benefit lessens. Additionally, if the product is beyond affordability for that group,⁸⁷ the benefit shrinks further. Considering this, I contend that the costs of the product should account for, or be

generated by extraneous exclusive licensing. The motivation of firms winning commercialisation auctions is the ability to generate income as a result of limited exclusivity. *Ibid* at 302-304.

⁸² Clinical trials are costly enough that for-profit firms invest in drugs that are expected to have lengthy remaining patent protection once brought to market. Ouellette & Weires *op cit* note 64 at 17.

⁸³ *Ibid* at 18.

⁸⁴ National Institutes of Health 'Best Practices for the Licensing of Genomic Inventions: Final Notice' 4 November 2005 70 FR 18413 available at <https://www.ott.nih.gov/sites/default/files/documents/pdfs/70fr18413.pdf>, accessed on 4 January 2020 18413-18414.

⁸⁵ These Guidelines, under Best Practise, were issued to address concerns regarding how inventions relating to human health care were licensed or exploited. Article 5.3 under Part I of the Guidelines for the Licensing of Genetic Inventions states that '[l]icense agreements relating to foundational genetic inventions should generally be non-exclusive to encourage broad access for researchers and patients and broad use of the genetic invention'. OECD 'Guidelines for the Licensing of Genetic Inventions' (2006) available at <http://www.oecd.org/sti/emerging-tech/36198812.pdf>, accessed on 3 January 2020 12.

⁸⁶ As well as whomever else as per the license agreements.

⁸⁷ This also includes their health insurance companies, which are now starting to include causes excluding genetic alterations. Kozubek *op cit* note 44.

subsidised by, the commercialising institution. The market test, as proposed by Ouellette and Ayres, is also a good idea to counter profit-driven licensing agreements.

(ii) *Assumption 2: Patenting is essential to appropriate value from innovation*

The focus on patent-based exclusivity tends to focus all the attention on patenting as a means to appropriate value from innovation. Although patenting is clearly an *important* way to achieve this, lawyers should not think of patenting as the *only* way to appropriate value from innovation. This assumption ignores other market-based or non-patent incentives (NPI) such as the first-mover or first-to-market,⁸⁸ access to skills and capital, tax-based incentives, prizes,⁸⁹ contracts, grants, and regulatory exclusivity.⁹⁰ This argument is also based on the premise that science is purely profit-driven, when there are other incentives for inventing, such as curiosity and fame.⁹¹

There are other mechanisms that would provide enough, and sometimes better, incentives than patenting. As Jordaan notes in his analysis of the findings of Graham et al,⁹² that analysed the 2008 Berkley patent survey in the US, first-mover advantage is ranked as moderately important to biotechnology entrepreneurs in terms of their appropriation strategies. Patenting, however, was ranked as just slightly more important than first-to-market. This is indicative of there being other attractive innovation incentives. Tax incentives,⁹³ as another example, allows pharmaceutical firms to claim federal tax credit for 50% of the cost of clinical trials.⁹⁴ Determining which incentive is best depends on the nature of the innovation.⁹⁵ Patents, for example, are granted ex post successful invention. Where there is high risk of failure, a reward

⁸⁸ Donrich W Jordaan 'Patenting decisions by South African biotechnology entrepreneurs' (2016) 35(4) *Biotechnology Law Report* 152.

⁸⁹ Prizes are granted ex post and can be in the form of cash given to a recipient for an innovation.

⁹⁰ Lisa Larrimore Ouellette 'Patentable subject matter and nonpatent innovation incentives' (2015) 5 *UC Irvine Law Review* 1118.

⁹¹ The US Department of Health and Human Services Advisory Committee on Genetics, Health, and Society acknowledged that patents, exclusive licenses, and profits are not the sole motivating factors for researchers. They have an additional 'desire to advance understanding, help their patients by developing treatments for disease, advance their careers, and enhance their reputations'. Secretary's Advisory Committee on Genetics, Health, and Society, Department of Health and Human Services, *Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests* (2010) 20.

⁹² Stuart JH Graham et al 'High technology entrepreneurs and the patent system: Results of the 2008 Berkeley patent survey' (2009) 24(4) *Berkeley Technol Law J*.

⁹³ I.R.C §§ 41, 174 (2012). Research and development tax incentives form a vital source of support for biomedical research. The biggest research and development incentives in the federal Tax Code are section 174, allowing companies to deduct research expenses immediately rather than over a period of future years, and section 41, which provides a tax credit for companies that increase their research and development spending. Ouellette op cit note 90 at 1132-1133.

⁹⁴ *Ibid* at 1133.

⁹⁵ For example, something that has a high failure risk, would be better suited to an ex ante incentive such as a grant rather than an ex post patent. *Ibid* at 1133-1134.

that is guaranteed, regardless of failure, will be more attractive.⁹⁶ In that situation, a grant may be more attractive than a patent. Incentives, such as grants, can also be used to fund research and development costs (ex ante) or recover them (ex post). Jordaan goes on to note that innovation requires strategy in order for value to be appropriated.⁹⁷ Simply put, patenting innovation does not necessarily result in value being drawn out of that innovation – necessary strategies and IP management are just as important for financial returns.

Essentially, I attack this assumption by suggesting that there are other viable NPI available that can drive innovation forward, as they may be more attractive to inventors. I also suggest that patents, on their own, do not automatically result in sufficient financial returns. There are other considerations to be accounted for when patenting in order to appropriate value from that innovation.

(iii) *Advantages of non-patent incentives in CRISPR*

As mentioned above, Sherkow questions whether any non-obvious applications of CRISPR exist.⁹⁸ This may be advantageous as unpatentable inventions could nevertheless result in reward, ensuring that there is still innovation and development. Furthermore, there tends to be ‘moral’ lobbying regarding the patenting of biotechnology⁹⁹ – NPI offer a solution to this. Moreover, reproducibility issues with biotechnological inventions, such as CRISPR, may pose issues for the granting of patents in the future.¹⁰⁰ However, reproducibility is not a pre-requisite for NPI.

Exclusivity may be meaningless if CRISPR-based inventions fail to reach the clinical trial stage prior to the expiration of the patent. Exclusivity is also questionable when looking at new Cas enzymes. Both process and product patents can be invented around (see Chapter 4) or improved, resulting in patents with exclusive rights which have reduced commercial value. NPI can ensure that there is innovation regardless of commercial feasibility.

Something like granted regulatory exclusivity also has the added advantage of enhanced state control.¹⁰¹ For example, in *Association for Molecular Pathology v Myriad Genetics Inc*,¹⁰²

⁹⁶ Ibid at 1133-1134.

⁹⁷ Jordaan op cit note 88 at 152.

⁹⁸ Sherkow op cit note 62 at 3.

⁹⁹ Ouellette op cit note 90 at 1118-1119.

¹⁰⁰ Jacob S Sherkow ‘Inventive steps: The CRISPR patent dispute and scientific progress’ (2017) 18(7) *EMBO Reports* 1048.

¹⁰¹ For more information regarding this incentive, see Ouellette op cit note 90 at 1130.

¹⁰² 69 US 576 (2013).

even though the patents were invalidated, the data that Myriad had generated was protected under a trade secret. With regulatory exclusion, the state can set terms that make it necessary for data to be disclosed and shared.

VI CONCLUSION

The surrogacy agreements, into which universities have entered, have numerous detrimental effects on innovation, translating into decreased public benefits. This is in addition to the confusion that potential licensees and inventors face when trying to ascertain from whom licenses on CRISPR technologies should be obtained. Costs, access, and innovation are bottlenecked by licensing agreements. Further, the depth of the exclusivity granted results in a genetic monopoly which restricts innovation in the technology and prevents new inventors from entering the market.¹⁰³ This clearly has many anti-competitive effects, which translates into higher costs for the public. The inclusive innovation model, proposed by Broad to prevent this, does little more than act as a funnel for third party inventions to be siphoned and claimed. Thus, it seems as if profit is the driving force for innovation in these supposed non-profit institutions.

It is possible that exclusive licenses are necessary for the commercialisation of human therapeutic applications of CRISPR, but this is dependent on multiple factors such as the nature of the invention, the risks, and the costs involved. Different therapies may carry a higher burden, thus justifying exclusivity. However, exclusivity is not always needed to generate a profit. It must be questioned whether the privatisation of publicly-funded inventions fulfils its part of the social contract. In terms of transferring technology or knowledge to the public it is successful, but there are alternative, less costly ways of doing this.

In some instances, NPI (individually and in combination) may be more attractive than patents themselves. Such incentives should not be overlooked, especially since they come at a lower social cost. This is not to say that there is no place for patents or exclusivity, but in terms of CRISPR technologies, blanket exclusivity cannot be justified. Therefore, I conclude that the current CRISPR licensing landscape is not aligned with, nor achieving, public interest considerations.

¹⁰³ The depth of the exclusivity relates to every use of CRISPR technology in every gene in the human genome.

CHAPTER 4

FREEDOM TO OPERATE

I INTRODUCTION

Part of the planning process for the commercialisation of new inventions involves an exercise of risk management.¹ The ability to use, manufacture, and commercialise an invention in specific jurisdictions is determined by an extensive search, known as an FTO analysis.² FTO denotes the ability to experiment with, advertise, or sell a service, product, or use a process in a certain industry.³ This should be undertaken at the beginning of product development to raise awareness of third party IP that is enforceable in a particular country in which an invention will be commercialised.⁴ The search, therefore, must be undertaken in each jurisdiction in which the product is to be researched, developed, marketed, exported, used, and commercialised.

FTO is not just an IP analysis – it includes checking whether there are other restrictions on using an invention, such as laws and regulations. If the invention involves a micro-organism, such as a virus that is used as a vector, especially if that vector is modified as it will be when using CRISPR, safety legislation is immediately implicated. In terms of the patent analysis aspect, it is important to consider the following: (1) patents are territorial;⁵ (2) patents are limited to the claims contained therein;⁶ and (3) the validity of the relevant patent.⁷

¹ It is good practice to conduct this search before entering into research. WIPO ‘New product launch: Evaluating your freedom to operate’ available at https://www.wipo.int/sme/en/documents/freedom_to_operate_fulltext.html, accessed on 2 November 2019.

² UpCounsel ‘Freedom to operate: Everything you need to know’ (2019) available at <https://www.upcounsel.com/freedom-to-operate>, accessed on 25 October 2019.

³ Ibid.

⁴ FTO is commonly used when ‘determining if a specific action can take place without infringing on the intellectual property rights of another’. Ibid; PATEV Associates ‘Freedom to operate in the context of Horizon 2020’ (2018) *Adding value to IP PATEV*.

⁵ This means that in some countries a license for a certain technology may need to be obtained, whereas in others, where a patent has not been applied for, no license is necessary for the use (or creation of a generic) of the technology. It is important for a prospective company to ascertain in which markets and jurisdictions they wish to export, commercialise, and manufacture for this reason.

⁶ Protection of the patent extends in so far as the claims contained in the patent. This is the scope of the patent. WIPO op cit note 1.

⁷ Generally, patent protection lasts for twenty years. Once that time lapses, the patent no longer applies and the invention contained therein forms part of the state of the art, free for all to use without considerations of a license. Another important aspect is validity. Whilst protection may be afforded by a patent, should that patent not be maintained in each jurisdiction, by the payment of fees, the protection pauses for that period until the fees are paid – and the technology may be used by anyone without the requirement of a license. This FTO is only for the time of the pause. Should patent fees be paid within the twenty year period, the pause ends, and the protection activates once more. This would then require the any potential users (in that pause period) to now obtain a license to continue. The life of the patent is not extended due to this pause, hence the lifespan remains twenty years. Ibid.

II OVERVIEW

What are the challenges in obtaining FTO for CRISPR technology? This Chapter is divided into four main aspects of FTO that expand on these challenges, both globally and nationally. Firstly, it deals with general issues in obtaining FTO CRISPR for the research and commercialisation of CRISPR. Secondly, this Chapter argues that an analysis of patent pools seems to lead to the conclusion that they are unsuitable for CRISPR currently, unless a sui generis version of the patent pool is created that lends itself to the needs of biotechnology. Thirdly, a critical take on the ethical restrictions in the licenses of the main patent holders is discussed. These restrictions, along with the imposition of patents, limit a country's ability to meet the needs of its citizens. Lastly, legal restrictions in South Africa that impact FTO are examined – being the NHA. I argue that the NHA should be interpreted in a manner that least restricts CRISPR technology as it arguably furthers rights enshrined in the Bill of Rights.⁸ I conclude that the current CRISPR patent regime is not conducive to the South African public interest.

III CRISPR LICENSING AND FREEDOM TO OPERATE

(a) *Basic non-commercial use*

Research for non-commercial use refers to research that is undertaken with no intention to commercialise, including internal research by non-profit organisations. The outcome of the US CRISPR patent dispute will affect which companies are in control of the technology, to whom licenses to commercially develop the technology are granted, and the conditions for granting such licenses. Institutions which fail to enter into license agreements with the eventual owners of CRISPR patents may be unable to further their research, hence losing invested funds.⁹

As mentioned in Chapter 3, Broad does not require a written license for academic and non-commercial research.¹⁰ This also means that licensing fees are not required. However, an issue in non-commercial research materialises when a researcher, who has been operating without a license (as one was not required), wishes to commercialise the research. In this

⁸ Such as reproductive freedom in section 12(2)(a) of the Constitution and human dignity in section 10 of the Constitution.

⁹ Jacob S Sherkow 'Patents in the time of CRISPR' 2016 *Genome Editing* 29.

¹⁰ Further, non-profit institutions and government agencies can transfer materials that they have generated from their internal research to other non-profit or governmental agencies under the terms of the Material Transfer Agreement without needing the license from Broad. Broad Institute 'Information about licensing CRISPR systems, including for clinical use' 2 May 2014 available at <https://www.broadinstitute.org/partnerships/office-strategic-alliances-and-partnering/information-about-licensing-crispr-genome-ed>, accessed on 9 August 2019.

instance, there are two outcomes: (1) a retrospective license will be granted;¹¹ or (2) a commercialisation license is refused. It is possible that a patent holder may believe that the prospective licensee was intending to bypass licensing whilst utilising CRISPR technology and may be inclined to reject licensing negotiations. A licensor is under no obligation to provide a license, regardless of the time or resources invested in research.

Under the South African Patents Act, there is no research exception. A research exception allows for the usage of a patented invention without the need to acquire a license for the purposes of research.¹² The distinct lack of statutory provision made for a research exception in South African law means that should licensors wish to enforce their patents strictly, even on a non-commercial basis, they may do so. Therefore, researchers need to be wary of potential infringement, as not all institutions allow research without a license. South African researchers and institutions tend to be under the misapprehension that non-commercial work never requires a license, or that there is an exception in law for research. Furthermore, researchers may be aware of patents, but simply ignore them.¹³ This could lead to an institution being challenged for patent infringement by a much larger entity, with many more resources.

¹¹ This is a license that reaches back in time to when the research was originally undertaken, and applies from that moment. It is possible that the licensor would require a greater fee for this reach back. Matthew Todd 'Retrospective patents as an incentive to open research' *Intermolecular* 13 January 2015, available at <https://intermolecular.wordpress.com/2015/01/13/retrospective-patents-as-an-incentive-to-open-research/>, accessed on 5 November 2019.

¹² This is principally used in therapeutics and for non-commercial research. In Europe, a research exception denotes the potential unlicensed use of a patented invention in research, where no commercial ramifications are involved. It is incorrectly believed that the research exception condones additional research using the invention, but it only allows research on the invention. However, this is contingent on the claims of the invention. Strictly speaking, the research exception only permits an analysis of an invention and not additional uses, whether commercial or not. For example, conducting a diagnostic test is not deemed to be research on the invention. The OECD, in a working paper involving the research exception, found that there is proof of patents having harmful outcomes on scientific research. In certain instances, a research exception may be valuable and should be implemented in countries without such a provision, but this must be done in a manner that supports non-commercial research, while preserving a patent holder's return on investment. Nagaoka and Aoki hold that the research exception is advantageous in situations where the nature of an end product is obscure, whether commercial or not. A patent owner is able to determine licensing it and when the end product is commercially feasible. The research exception permits downstream researchers to work without a license. This may be beneficial when inventing around is challenging. Further, it has been proposed that government should be obliged to augment the research exception through the free granting of licenses to other public research institutions, especially those receiving public funding, akin to the approach of the NIH in the US. In addition, industry could self-regulate through the awarding of licenses to public research institutions for a nominal fee. Spoor & Fisher 'South Africa IP Policy' 9 October 2018 available at <https://www.spoor.com/en/News/south-africa-ip-policy/>, accessed on 29 September 2019; Sirpa Soini et al 'Patenting and licensing in genetic testing: Ethical, legal and social issues' (2008) 16 *European Journal of Human Genetics* 27.

¹³ Matthew Herder & E Richard Gold 'Intellectual Property Issues in Biotechnology: Health and Industry' (2007) *OECD* 7. Report from 'OECD international futures project on the bioeconomy to 2030: Designing a policy agenda' third meeting of the steering group Paris, 7-8 February 2008.

A dense patent landscape, as is the case with CRISPR, results in difficulty for prospective researchers or commercial developers in ascertaining which patents are necessary for licensing purposes, how the patent holders will deploy licenses, and on what terms. Moreover, if universities charge exorbitant licensing fees for the use of their patented technology, this could deter companies from investing, and thus hamper the commercialisation of certain key technologies. If CRISPR technology, relevant for usage in research, is not patented in South Africa, researchers are free to utilise the technology as they wish, with no license requirement or communication necessary.¹⁴ Researchers may also create a generic of that technology, should they wish to commercialise it. However, they cannot patent in their jurisdiction, or any other jurisdiction, due to that invention already forming part of the state of the art.¹⁵

As with pharmaceuticals, a patent is not required in order to establish a market and make substantial profit, as the first generic to market generates the most revenue in comparison to any others that follow. It is also important for researchers to know that when a written license is required and it is royalty free, this does not mean that the license itself is free; there is often a license fee involved. Unless it is explicitly stated that no fee is required, it must be assumed that a license fee applies.

(b) Human therapeutics and diagnostics

Human therapeutics and diagnostics is an important area for the application of CRISPR-based technology in the South African context due to its potential for disease prevention and treatment. This field is controlled by spin-outs and subject to exclusive licenses.¹⁶ Due to the state of flux in the CRISPR patent landscape, it is difficult to ascertain from whom licenses should be sought.¹⁷ This will also change, depending on who the victor in the US CRISPR patent dispute is.

¹⁴ The researcher, or commercial developer does not need to inform or request permission of the patent holder for the usage of the patented invention.

¹⁵ The state of the art is defined in section 25(6) of the Patents Act as comprising ‘All matter (whether a product, a process, information about either, or anything else) which has been made available to the public (whether in the Republic or elsewhere) by written or oral description, by use or in any other way’.

¹⁶ Intellia, CRISPR Tx, ERS Genomics, and Editas deal exclusively with human therapeutics; the commercialisation and rights to other fields of use are available to other spin-outs retained by the proprietor institutions. Marc Döring & Daniel Lim ‘Questions about CRISPR’ 2017 *Intellectual Property Magazine* 47-48.

¹⁷ A license must be sought from the controlling entity of the jurisdiction in which an invention wants to be used, manufactured, or sold. Perhaps a license from Entity A would have to be obtained for technology X in the US. Then in Europe that license for technology X would have to be obtained from Entity B. This means that if one were to utilise the technology in both jurisdictions, one would need to obtain two different licenses from two different entities for the same technology. This could impact licensing fees negatively, as if a license was required from just one entity, a single licensing fee would be required. It is also a reality that Entity A would grant a license for technology X, but Entity B could deny granting it due to competition reasons. In South Africa, one would have

IV ACQUISITION OF FREEDOM TO OPERATE

If FTO is limited by patent restrictions, FTO can be acquired by buying or licensing the patent, inventing around,¹⁸ or conducting operational activities in a jurisdiction where the patent does not apply. As noted in the patent landscaping search in Chapter 2, many patents exist and accessing those which are necessary is challenging. A proposed solution to this is patent pools.

(a) Patent pools

In 2016, MPEG LA announced their intention to create a CRISPR-Cas9 patent pool to make the technology accessible.¹⁹ The main question is whether patent pools are appropriate for CRISPR. Although patent pools are beyond the scope of this dissertation, a general evaluation will follow in ascertaining its appropriability.

Patent pools involve agreements between multiple patent owners to combine patents and license them to each other or to third parties.²⁰ They grant numerous companies, in exchange for payment, access to, and use of, several patents. Patent pools are often utilised to create bundle licenses for complex technologies,²¹ and where patent thickets are present, and form the basis of an industry standard. They hold the potential to advance reciprocal technology and lessen transaction costs by alleviating patent thickets. Companies with similar technologies combine their standard, essential patents into a pool in order to establish a clearinghouse for patent rights.

to obtain a license from the controlling entity for that technology in this jurisdiction. Currently, companies who wish to use CRISPR-Cas9 in eukaryotes will likely need a license from both Broad and UC. Ibid at 48.

¹⁸ Inventing around involves adjusting the product or process enough to enable a different patent to be granted. This method denotes directing research or altering the product or process in order to avoid the infringement of patents owned by others. For example, if FTO is limited by a process patent, a company may be able to develop an alternative process for arriving at a similar result and thus be able to commercialise the invention without having to pay a licensing fee to someone else.

¹⁹ MPEGLA 'CRISPR' available at <https://www.mpegla.com/crispr/initiative/>, accessed on 25 January 2020.

²⁰ The pooled patents are available to the members of the pool and to non-members via a license. All the pooled patents will be available to prospective licensees under one single license agreement at a single fee, with a set royalty rate. The patent pool will usually divide the licensing fees collected to each member according to the value of the patents supplied.

²¹ Patent pools hold the potential to advance reciprocal technology and lessen transaction costs by alleviating patent thickets. Patent thickets are upstream, overlapping patents controlled by differing entities which, in turn, would require a prospective innovator to obtain licenses from various different sources. This will be a very costly exercise for said innovator and, as a result, can deter innovation and investment. Currently, with the numerous CRISPR patents, it is very difficult for potential innovators to determine which patents are necessary for them to obtain for this very reason. Soini et al op cit note 12 at 29.

(i) *CRISPR and patent pools*

As it stands, Broad is the only notable patent holder to have joined the CRISPR patent pool. Therefore, the patent pool remains an abstract idea. MPEG LA is an independent²² and neutral²³ administrator with the necessary infrastructure and experience to make the patent pool a reality.

A patent pool comprised of complementary CRISPR patents can create an enabling environment for innovation, therefore increasing efficiency.²⁴ The ‘one stop license’ is cheaper and more convenient for potential licensees to acquire, rather than trying to ascertain which patents are necessary, negotiating with numerous patent holders, and paying multiplicities of fees and royalty stacking.²⁵ It can also eliminate the need for litigation, thus saving money for licensees. If the patent pool consists of complementary patents,²⁶ it will also have the effect of clearing blocking patents.²⁷

However, the patent pool can be used for anti-competitive practices,²⁸ whereby there is collusion amongst competitors, resulting in antitrust behaviour.²⁹ It is important that the patent

²² They are not aligned with any particular shareholder which eliminates that possibility of bias towards a certain group. Tom O’Reilly ‘MPEG LA issues statement regarding CRISPR patent licensing’ *Business Wire* 25 July 2019, available at <https://www.businesswire.com/news/home/20190725005951/en/MPEG-LA-Issues-Statement-CRISPR-Patent-Licensing>, accessed on 25 January 2020.

²³ This contrasts concerns that some surrogates may refuse licenses based on competition considerations. *Ibid.*

²⁴ WIPO ‘Patent pools and antitrust – a comparative analysis’ prepared by the Secretariat (March 2014).

²⁵ Royalty stacking is a circumstance whereby the utilisation of an invention calls for numerous licenses from a variety of patent holders, thus raising the cost of end products. *Ibid*; Soini et al op cit note 12 at 24.

²⁶ Complimentary patents are patents on technologies which are not substitutes for one another, but also rely on one another to bring the invention to life. WIPO op cit note 24 at 4.

²⁷ A blocking patent is one which prohibits a third party from utilising or commercialising of a modified version of patented invention. When a patent prevents another invention from being developed as it would result in infringement, this is referred to as a blocking patent. Amir Adibi ‘Blocking patents explained’ 26 March 2017 available at <https://www.patentlawyer.io/what-is-a-blocking-patent/>, accessed on 6 January 2020.

²⁸ These conditions are: (i) excluded firms cannot effectively compete in the relevant market for the good incorporating the licensed technologies; (ii) the pool participants collectively possess market power in the relevant market; and (iii) the limitations on participation are not reasonably related to the efficient development and exploitation of the pooled technologies. The IP guidelines stipulate that exclusion from pooling arrangements among parties that collectively possess market power may, harm competition. This would allow them to charge more than the competitive rate. The question that WIPO utilises is ‘whether the licensing agreement eliminates competition that would have occurred in the absence of the license?’ This essentially means that the licensing provisions must not add more competitive restrictions than patents themselves already do. WIPO op cit note 24 at 10; US Department of Justice and the Federal Trade Commission ‘Antitrust Guidelines for the Licensing of Intellectual Property’ (2017) 31.

²⁹ The patent pool can serve as a platform in which competitors can share sensitive market information such as pricing and strategies. They can also agree to raise prices of certain technologies, hence ensuring that in order for a customer to access the technology, they would have to pay the elevated price as all substitute technologies are the same price.

pool be monitored to ensure compliance.³⁰ In the US,³¹ one would look to the Antitrust Guidelines for the Licensing of Intellectual Property (IP Guidelines).³² The IP Guidelines acknowledge that patent pools can be pro-competitive.³³ In the South African context, recourse may be had to the Competition Act 89 of 1998 (Competition Act).³⁴

There are seven primary issues in terms of CRISPR and patent pools, independent of anti-competitive concerns: (1) the patent pool has yet to be specified and, as such, there is no direction as to which patents are necessary; (2) no standards exist, nor is there a standard setting body to determine which patents are essential for specific applications relevant to the patent pool;³⁵ (3) membership is voluntary, which may mean that foundational patent holders opt not to join; (4) exclusive licenses granted by patent holding institutions to surrogates preclude them from allowing those patents to be licensed to other third parties, which is inconsistent with the purpose of the patent pool; (5) exclusivity is necessary for leadership in order to secure investment;³⁶ (6) according to Contreras and Sherkow,³⁷ for human therapeutic applications of CRISPR, the costs involved in clinical trials, obtaining regulatory approval, research and development, product development, and marketing do not lend themselves to the patent pool model; and (7) licensing must take place in accordance with FRAND conditions.³⁸ There is guidance on FRAND, but this does not apply in the context of non-standardised technologies, such as CRISPR.

³⁰ Monitoring can be the task of the clearinghouse – MPEG LA in this case, and the relevant competition authorities that monitor the jurisdiction of the clearinghouse.

³¹ The US position will be examined briefly as the patent pool has currently centred on the US. The European position can be ascertained from ‘Guidelines on the application of Article 81 of the EC Treaty to technology transfer agreements’ Official Journal of the European Union (2004/C 101/02).

³² US Department of Justice and the Federal Trade Commission *op cit* note 28.

³³ For further information, the Department of Justice, in response to MPEG LA, noted specific conditions for the patents in pools. This included that the patents must be valid, technically essential, not substitutes, and the patent pool itself must have a limited duration. This can be accessed at Department of Justice available at <https://www.justice.gov/archive/atr/public/busreview/215742.htm>, accessed on 25 January 2020.

³⁴ Specific reference may be had to Part A of the Competition Act, dealing with restrictive practices, in terms of which restrictive horizontal and vertical practices are prohibited.

³⁵ Determining what is an essential patent for a pool is vital to ensuring its functionality. Patents determined by a standard to be essential are called standard essential patents (SEPs). An SEP is a patent deemed essential for the operation of a technology, which is then standardised as required. In context of CRISPR, non-essential patents must not be included in a patent pool, such as accessory technologies, if they are not needed or do not improve the working of the process.

³⁶ However, the existence of exclusive licenses need not bar parties to the agreement as they can, by consensus, revoke same and waive their rights. Donrich W Jordaan ‘Patenting decisions by South African biotechnology entrepreneurs’ 2016 35(4) *Biotechnology Law Report*.

³⁷ Jorge L Contreras and Jacob S Sherkow ‘Patent pools for CRISPR technology – response’ 2017 355(6331) *Science* 1274 at 1274-1275.

³⁸ FRAND is an acronym for fair, reasonable, and non-discriminatory. It relates to licensing in a situation where a patent holder refuses to grant a license or refuses to grant a license on FRAND terms. John Cassels ‘What is FRAND?’ *Field Fisher* 23 August 2013, available at <https://www.fieldfisher.com/en/insights/what-is-frand>, accessed on 8 January 2020.

A counter-argument to Contreras and Sherkow is that of the Medicines Patent Pool (MPP), which aimed to increase access to, and assist in developing, life-saving drugs for low- and medium-income countries.³⁹ However, with the MPP there was a direct interest in life-saving drugs as these had an immediate impact and were fully developed at the time. It was thought that a mechanism like the MPP may be adopted for controlling CRISPR-Cas9 IP, in order to streamline access to the technology.⁴⁰ However, human therapeutic applications of CRISPR are still experimental. As these areas require research and development, involving large finances, such a patent pool may be jumping the gun, and in doing so, may hamper innovation. Perhaps a patent pool for non-human applications of CRISPR is more appropriate in the interim.

If additional key patent holders were to join, the next step would involve focusing the patent pool. A blanket patent pool would be unsuccessful for many reasons, including the number of different patents necessary for various uses of CRISPR technology. Royalties would thus need to be divided amongst a greater number of members, resulting in smaller individual returns and deterring potential members.⁴¹ I recommend that there should be multiple patent pools, or different branches of a single patent pool, focused on different applications of CRISPR technology, which should be developed to operate like a tree. The foundational patents for eukaryotic alterations using CRISPR-Cas9 form the trunk, with the specific branches sprouting outwards, signifying specific applications of the technology.⁴² Each branch would effectively contain leaves, which function as the basket for all relevant patents. Royalties can then be specific to each branch. There can be a set royalty rate for utilising the foundational CRISPR patents, and an additional fee for each specific branch that the licensee wishes to license. Such a model may mitigate the negative consequences that patent pools can have on innovation.⁴³

³⁹ The MPP has been widely utilised in South Africa in order to license patented drugs and manufacturing for access to HIV, viral hepatitis C, and TB. Joanne van Harmelen 'Walking the tightrope: IP rights versus access to medicines in South Africa' 2018 1(5) *IP Briefs*.

⁴⁰ *Ibid*.

⁴¹ Small amounts that are required to be paid for numerous patents accrue and become costly. When large and small companies exist in the same patent pool, the distribution of benefits becomes complex. Thus, diversity in membership causes volatility. However, it has been found that the presence of non-profit research institutions in patent pools assisted in balancing the commercial interests of companies Soini et al op cit note 12 at 29.

⁴² Such as CRISPR application in vitro for CCR5 alteration for use against HIV/AIDS.

⁴³ It is important to be mindful of the fact that IP can be everything to a company, and how it is used and managed dictates whether that company survives, and what the future is for a particular technology. Furthermore, a patent pool should never preclude a company from doing their due diligence FTO searches.

V IMPOSING FOREIGN ETHICS – THE ‘ETHICAL LICENSE’

Patent licenses can control the usage of CRISPR technology,⁴⁴ hence serving as a tool for private governance.⁴⁵ Patent holders can prohibit uses of the technology which it deems unethical. An example of this is Broad⁴⁶ and Caribou’s so-called ‘ethical license’.⁴⁷ Broad and Caribou prohibit the licensing of patents for the use of germline gene editing in clinical applications.⁴⁸

Broad and UC currently have a duopoly over CRISPR applications in eukaryotes. This means that those wishing to use CRISPR, in any country in which the technology has been patented, will need to acquire licenses from both institutions.⁴⁹ By establishing a monopoly over the germline gene editing market for CRISPR, Broad and UC also have control over the

⁴⁴ In the case of CRISPR there are two groups, being Broad and UC, who have the same ethical license conditions.

⁴⁵ Jacob S Sherkow ‘Jake Sherkow: University patent licenses in the CRISPR era’ McGill University Faculty of Law 24 March 2017.

⁴⁶ Broad’s ethical license states that ‘biomedical applications of CRISPR genome-editing technologies do not permit their use for human germline editing’. Broad Institute ‘Principles for disseminating scientific innovations’ available at <https://www.broadinstitute.org/principles-disseminating-scientific-innovations>, accessed on 18 October 2019. If a South African company wishes to acquire a license from Broad with the intention of utilising the technology for germline gene editing, it would be unsuccessful in obtaining that license. If the company were to do so regardless, after obtaining the license, this would fall under a contractual breach, with serious consequences.

⁴⁷ Caribou is the company to which UC has licensed its CRISPR patents and it holds a wide IP portfolio. This includes license agreements with a range of biotechnology companies such as Intellia, Corteva Agriscience, Integrated DNA Technologies (IDT), Novartis, and Oxford Nanopore Technologies (ONT). Caribou co-founded Intellia in 2014 in order to develop therapeutic medicine. Intellia holds exclusive access to Caribou’s CRISPR-Cas9 technology for the development of new human gene and cell therapies as well as anti-viral therapies. However, Caribou reserves rights to pursue possibilities for its technology in other therapeutic markets. In 2015, Caribou and Corteva, who both manage patent portfolios encompassing many foundational CRISPR technologies, undertook a license agreement and collaboration. This included the cross-licensing of vital intellectual property, allowing Caribou to develop and use CRISPR-Cas technology for product development in areas such as therapeutics, industrial biotechnology, research tools, and agriculture. In 2016, Caribou and IDT entered into a non-exclusive license agreement, granting IDT worldwide rights to commercialise CRISPR-Cas9 reagents. Customers utilise IDT’s CRISPR-Cas9 reagents for biological research in a variety of fields including drug discovery and genomics, and enables researchers to edit genomic DNA with exactness and efficiency. Caribou granted Novartis a global, non-exclusive license for internal research which Novartis accepted in 2016. This formed part of a research program to develop the Caribou CRISPR-Cas9 platform for drug target screening and validation technologies. In August 2019, Caribou and ONT entered into a non-exclusive license agreement, which granted ONT global rights to utilise CRISPR-Cas9 technology for nanopore detection and sequencing for research and diagnostics, as well as the right to commercialise CRISPR-Cas9 nanopore sequencing and detection products and services. Caribou Biosciences ‘Licenses’ available at <https://cariboubio.com/licenses>, accessed on 25 October 2019.

⁴⁸ Their licensing restrictions commonly appear in label licenses. Caribou states that their operations are ‘conducted in accordance with the highest ethical standards’. Caribou’s licenses are subject to a research use limited label, meaning that no commercial use on its CRISPR technology is allowed. In terms of such limited use label license, Caribou holds that ‘The End User cannot sell or otherwise transfer Material to a third party or otherwise use the Material for any Excluded Use. “Excluded Use” means any and all: . . . (g) modification of human germline, including editing of human embryo genomes or reproductive cells. . .’ Caribou Biosciences ‘About us’ available at <https://cariboubio.com/about-us>, accessed on 25 September 2019; The Jackson Laboratory ‘Caribou Biosciences limited use label license: Research use only’ available at <https://www.jax.org/about-us/legal-information/licenses/caribou-biosciences-license-human-cells>, accessed on 17 November 2019.

⁴⁹ If they fail to acquire licenses, they are at risk of patent infringement and potential litigation.

development of this technology and the ways in which it can be utilised.⁵⁰ Perhaps this ethical position may (or may not) be acceptable in the US. But should the inventors of CRISPR technologies be the ethical gatekeepers of a gene editing system, which can alter not just individual lives, but also the status of a country by potentially eliminating certain diseases? If CRISPR can be utilised to aid countries with large populations and high mortality rates due to disease, why should university inventors in the US be able to exert control over the technology and the country through patent laws? Is this ethical imposition on a country, which may have a completely different public imperative, not an infringement on state sovereignty?

As there are presently millions of South Africans living with HIV/AIDS,⁵¹ I contend that it is in South Africa's public interest for CRISPR to be developed to address this due to the technology's great potential in the prevention and treatment of HIV/AIDS.⁵²

VI LEGALITY AND PATENTABILITY

In order for an invention to be patentable in South Africa, it must meet the requirements under section 25 of the Patents Act,⁵³ and must not fall into a category of invention that is excluded from patentability.⁵⁴ Patentability is generally viewed as an incentive for investment in research and development, as well as commercialisation. As such, it is necessary to consider both the patentability and legality of CRISPR-based inventions in a South African context. This dissertation does not aim to establish whether CRISPR meets the patentability criteria in section 25 of the Patents Act, but will instead establish: (1) whether certain applications of CRISPR technology are illegal for use in South Africa; and (2) whether this illegality affects patentability.

⁵⁰ Knut J Egelie et al 'The ethics of access to patented biotech research tools from universities and other research institutions' 2018 36(6) *Nature biotechnology* 1.

⁵¹ Avert 'HIV and AIDS in South Africa' available at <https://www.avert.org/professionals/hiv-around-world/sub-saharan-africa/south-africa>, accessed on 9 January 2020.

⁵² Qiaoqiao Xiao 'Application of CRISPR/Cas9-based gene editing in HIV-1/AIDS therapy' (2019) 9 *Front Cell Infect Microbiol.* 69.

⁵³ Section 25(1) of the Patents Act states that '[a] patent may, subject to the provisions of this section, be granted for any new invention which involves an inventive step and which is capable of being used or applied in trade or industry or agriculture'.

⁵⁴ Section 25(2) of the Patents Act. This section holds that '[a]nything which consists of –

- (a) a discovery;
 - (b) a scientific theory;
 - (c) a mathematical method;
 - (d) a literary, dramatic, musical or artistic work or any other aesthetic creation;
 - (e) a scheme, rule or method for performing a mental act, playing a game or doing business;
 - (f) a program for a computer; or
 - (g) the presentation of information,
- shall not be an invention for the purposes of this Act'.

Legality is an important FTO consideration. If the use of an invention is illegal, there is no FTO. However, the invention may still be patentable. Section 36(2) of the Patents Act stipulates that the registrar *may* refuse a patent application on the grounds of illegality.⁵⁵ Illegality is not specifically listed as an exclusion under section 25 of the Patents Act. Furthermore, section 36(2) of the Patents Act is not a complete bar to patent eligibility – as the word *may* denotes that the registrar is vested with discretion regarding whether to grant or deny a patent for the invention. This means that even if an invention can be used for illegal purposes, it may still be patentable. I now question whether there are certain uses of CRISPR technology that are illegal in South African law.

(a) *The National Health Act 61 of 2003*

The NHA does not explicitly refer to genetic editing technologies, besides perhaps section 57, which prohibits the reproductive cloning of humans.⁵⁶ Therefore, the illegality of CRISPR technologies depends on the interpretation of section 57 of the NHA. As Thaldar and Pillay note, there is a compromise to legal certainty due to the NHA being drafted in an ambiguous manner.⁵⁷

(b) *Germline (gametes and embryonic) genetic editing technology*

Upon a plain reading of section 57 of the NHA, it seems that gamete, zygote, or embryonic edits are illegal, but only if they are used for the *purpose* of reproductive cloning of a human being. Reproductive cloning is defined in section 57(6)(a) of the NHA as ‘...the manipulation of genetic material in order to achieve the *reproduction* of a human being and includes nuclear transfer or embryo splitting for such purpose’ (own emphasis).

The word ‘reproduction’ is not defined in the NHA, which creates this ambiguity, as reproduction could have two different constructions: (1) in the ordinary sense of creating a human being (either genetically different or a genetic copy) or; (2) the creation of an exact genetic copy (clone) of an individual.

⁵⁵ Section 36(2) of the Patents Act states that ‘[i]f it appears to the registrar that any invention in respect of which an application for a patent is made might be used in any manner contrary to law, he may refuse the application unless the specification is amended by the addition of such disclaimer in respect of that invention, or such other reference to the illegality thereof, as the registrar may think fit’.

⁵⁶ Section 57 of the National Health Act holds that –

‘(1) A person may not –

(a) manipulate any genetic material, including genetic material of human gametes, zygotes or embryos; or
(b) engage in any activity, including nuclear transfer or embryo splitting, for the purpose of the reproductive cloning of a human being’.

⁵⁷ S Pillay & DW Thaldar ‘CRISPR: Challenges to South African biotechnology law’ (2018) 11(2) *S Afr J BL* 91.

(i) *Construction (I)*

There is a qualification in the scope of the definition of reproductive cloning, being the phrase ‘in order to’.⁵⁸ This would mean that it is only illegal to alter the genetic material of germline cells if the purpose of the alteration is to induce reproduction – there must be a direct link between the genetic alteration and the production of a human being. In other words, the genetic alteration of the gamete takes place as a step in the reproduction process to induce reproduction. The removal of the genetic alteration results in reproduction not occurring. It is not auxiliary to the process or end result of reproduction – it is a *sine qua non*. This would render applications of genetic alteration to gametes illegal in so far as the technology is used as a step in the process, without which reproduction would not take place. This would also cause applications of CRISPR technology to be unlawful where it aims to ‘fix’ or enhance gametes or ‘non-viable’ embryos for use in the production of a zygote by natural or artificial fertilisation (in the case of gametes), or to render them able to form into a human being (in the case of embryos).

The above interpretation is based on a plain reading of the NHA. However, as per section 39(2) of the Constitution,⁵⁹ and as confirmed in *Bato Star Fishing (Pty) Ltd v Minister of Environmental Affairs and Tourism*,⁶⁰ South Africa’s new legislative order follows a constitutional interpretation, or a purposive approach. This approach entails the advancement or application of the rights contained in the Bill of Rights. There are fundamental rights, such as reproductive freedom⁶¹ and human dignity,⁶² which could be advanced with the use of gene editing technologies like CRISPR. Whilst a full discussion of this matter is beyond the scope of this dissertation, the main point to be made is that applications of CRISPR technologies in terms of germline alterations may form part of, and be used to further, the constitutional rights mentioned above. Therefore, at the very least, it should be non-contentious to state that CRISPR technologies may be constitutionally permissible, and a constitutional interpretation of the NHA may render such gene editing technologies legal.

⁵⁸ Section 57(6)(a) of the NHA.

⁵⁹ Section 39(2) of the Constitution states that ‘[w]hen interpreting any legislation, and when developing the common law or customary law, every court, tribunal or forum must promote the spirit, purport and objects of the Bill of Rights’.

⁶⁰ 2004 (4) SA 490 (CC) para 88.

⁶¹ Section 12(2)(a) of the Constitution.

⁶² Section 10 of the Constitution.

(ii) *Construction (2)*

‘Reproduction’ relates only to human cloning – as per the title of section 57 of the NHA.⁶³ This would render illegal the alteration of gametes for the purpose of creating an exact genetic copy of a human being. Hence, the alteration of gametes for the purposes of reproduction, which are not intended to create an exact genetic copy of a human being, is permissible. Therefore, following an interpretation of both Constructions, I suggest that Construction (2) should be the preferred approach.

(c) *Somatic editing technology*

Somatic cell alterations do not result in reproductive cloning, cloning, or reproduction. This is because, as stated in Chapter 2, somatic cells refer to any differentiated cell in the body, other than reproductive cells.⁶⁴ Unless the claim of the invention involves the alteration of somatic cells,⁶⁵ which can then somehow induce reproduction (either Construction), it will not contravene the NHA.

(i) *Legality*

As mentioned above, despite the ambiguity of the NHA, a constitutional interpretation of the relevant sections could likely mean that the use of CRISPR technologies to effect germline and somatic cell edits, are legal. As the use of CRISPR technologies may fall within the ambit of the constitutional rights to human dignity and reproductive autonomy, there would need to be a justifiable limitation to their use in terms of section 36 of the Constitution in order to prevent such uses⁶⁶ – and as far as the NHA goes, there is none.

⁶³ Section 57 of the NHA is entitled ‘prohibition of reproductive cloning of human beings’.

⁶⁴ Biology Dictionary ‘Somatic cells’ available at <https://biologydictionary.net/somatic-cells/>, accessed on 10 November 2019.

⁶⁵ Such as a skin cell.

⁶⁶ Section 36 of the Constitution deals with the limitation of rights. Section 36(1) states that ‘[t]he rights in the Bill of Rights may be limited only in terms of law of general application to the extent that the limitation is reasonable and justifiable in an open and democratic society based on human dignity, equality and freedom, taking into account all relevant factors, including –

- (a) the nature of the right;
- (b) the importance of the purpose of the limitation;
- (c) the nature and extent of the limitation;
- (d) the relation between the limitation and its purpose; and
- (e) less restrictive means to achieve the purpose’.

(ii) *Patentability*

Regardless of which Construction is followed, inventions concerning germline or somatic cell editing technologies are currently patentable because South Africa has a depository patent system. Once SSE procedures are implemented, these technologies may continue to be patentable as the registrar has a discretion, and can attach notices that request alteration of the claims, or a disclaimer that the usage may be illegal.⁶⁷ Further, the wording of the claims would denote the activation of section 36(2) of the Patents Act read with section 57(6) of the NHA. If a claim reads, ‘the use of this technology to effect genetic alteration of a male spermatozoa flagellum to induce motility *for use in the effecting of natural reproduction*’, this would then activate both sections, bringing the patentability of the invention into question. However, if the claim read, ‘the use of this technology to effect genetic alteration of a spermatozoan flagellum to induce motility rendering it *capable of use in natural reproduction*’, this would then fall under section 57(6)(b) of the NHA as ‘therapeutic cloning’ which is not contrary to the NHA, and would thus not activate either Act.

VII CONCLUSION

There are many challenges in obtaining FTO for CRISPR technologies, ranging from the difficulties in ascertaining from whom licenses should be sought and the various licensing agreements, to the ethical licenses imposed by the foundational patent holders. Whilst patent pools have been a great solution in the technology industry, such models cannot simply be translated to biotechnology. These patent pools need to be optimised to suit the sui generis nature of biotechnology. Therefore, I conclude that the current CRISPR patent regime is not conducive to the public interest as FTO, especially in context of commercialisation, is restricted. From a South African perspective, the first step in the right direction would be to give effect to the public interest through an interpretation of the NHA that allows the use of CRISPR technology – within the mandate of the Constitution.

⁶⁷ This in itself means that the invention is patentable, but not able to be utilised.

CHAPTER 5

CONCLUSION AND RECOMMENDATIONS

'[B]y allowing private firms to hold exclusive rights to inventions that have been generated at public expense, it seems to require the public to pay twice for the same invention – once through taxes to support the research that yielded the invention, and then again through higher monopoly prices and restricted supply when the invention reaches the market'.¹

This dissertation focused on whether the current CRISPR-Cas9 patent regime, with regards to human therapeutics, is optimal for the public interest. Since CRISPR technologies hold great potential in relation to the prevention and treatment of various diseases, it is vital that products and processes involving these technologies are made available to benefit public health as well as society at large. However, as the US CRISPR patent dispute has shown, this is not easy. Institutions working with CRISPR have individual and profit-driven motives, and through the patenting and licensing of such technologies, the field of biotechnology and gene editing has been drastically limited. Many argue that this is due to Bayh-Dole incentivising research, which has shifted the aim of universities away from the pursuit of knowledge to a focus on patentable and licensable inventions.²

(a) What issues does the CRISPR patent and licensing regime pose to the research and commercialisation of CRISPR human therapeutic applications?

I have formulated arguments as to why the current patent regime is not conducive to both the research and commercialisation of CRISPR-based innovations. While research may not be impeded in practice, as patents tend not to bar researchers, the commercialisation of any invention is hampered. There is also much contention that patenting and licensing burdens the openness of scientific exchange in universities.³

Following the foundational CRISPR patents of Broad and UC, the patent landscape relating to this technology has grown in complexity. Currently, thousands of CRISPR-related

¹ Rebecca S Eisenberg 'Public research and private development: Patents and technology transfer in government-sponsored research' (1996) 82(8) *Virginia Law Review* 1666.

² Dovid A Kanarfogel 'Rectifying the missing costs of university patent practices: Addressing Bayh-Dole criticisms through faculty involvement' (2009) 27(2) *Cardozo Arts & Entertainment* 539.

³ The narrow focus on licensing patented inventions overlooks the fact that most financial university contributions have transpired without patents – through distribution of knowledge, discoveries, and technologies in journal publications, conference presentations, and training of students. Anthony D So et al 'Is Bayh-Dole good for developing countries? Lessons from the US experience' (2008) 6(10) *PLoS Biology* 2078 & 2082.

patent applications have been filed globally by a range of institutions.⁴ This vast number of CRISPR patents has created a confusing scenario for those wishing to invest in, or obtain licenses for, human therapeutic applications of CRISPR. Further, uncertainty regarding to whom the foundational CRISPR patents belong adds to this. This patent thicket results in higher costs associated with commercialisation, which may be a large impediment to further developments of the technology. Additionally, the CRISPR landscape may become saturated with patents, some of which may not be relevant, beneficial, or of sufficient quality. Such a situation may negatively affect the public interest in terms of health concerns and disease treatment, and raises further issues regarding the hampering of scientific progress and the development and pricing of products using CRISPR technology.⁵

Based on these considerations, I conclude that the current global patent and licensing landscape, as a result of the immense number of CRISPR patents, is suboptimal for access to, or development of, CRISPR technologies and thus, does not serve the public interest.⁶ It is hoped that once the US CRISPR patent dispute has been resolved, the outcome will provide greater clarity on the ownership and licensing of the technology. Publicly-funded CRISPR technology needs to be made more accessible for public consumption. Patent systems around the world need to be optimised in order to ensure that their CRISPR patent landscape avoids over-saturation, and that those patents which are beneficial and have the potential to play a vital role in assisting healthcare systems, and thus serve the public interest, are granted. Research on CRISPR technologies must be promoted rather than hindered, as the development of potential new products and processes for therapeutic applications could hold great benefits for public health.

(b) Are the current CRISPR licensing regimes optimal for the public interest?

The licensing and business models chosen by universities in commercialising CRISPR technologies are aligned with profiteering rather than ensuring that the healthcare potential of CRISPR is explored fully to benefit the public. Exclusive licensing prevents the widespread

⁴ The granting of such patents will result in an intricate system of patent rights – different owners will hold patents fluctuating in strength and validity, with varying similarity and international application. Marc Döring & Daniel Lim ‘Questions about CRISPR’ 2017 *Intellectual Property Magazine* 48.

⁵ Letter from James Love, Director at Knowledge Ecology International to Dr. Thomas E Price, Department of Health and Human Services 6 June 2017 available at <https://www.keionline.org/sites/default/files/CRISPR-SecPrice-6Jan2017.pdf>, accessed on 12 January 2020 1.

⁶ Additionally, the US CRISPR patent dispute highlighted a broader societal problem – the privatisation of publicly-funded research.

usage of CRISPR technology, which could prove essential in the prevention and treatment of disease. I question whether the public interest will ever be served by profit-driven surrogates.⁷

I find that the CRISPR exclusive licensing regimes hinder biotechnology,⁸ and are not optimal for the public interest due to the nature, depth, and effects of these licenses which lead to ‘bottlenecks’ and harms to welfare.⁹ They serve to limit others from entering into the market, which could adversely affect public access to CRISPR technology.¹⁰ Furthermore, in terms of publicly-funded innovation, this raises questions as to what benefit the public is actually receiving in return for financing the invention. Exorbitant licensing fees may translate into higher prices for end-products, thus burdening the public.¹¹ It seems that the corresponding benefit would be better served by non-exclusive uses.¹² Through an exploration of various arguments, the costs of exclusivity and its impact on the public interest has been demonstrated.

This is not to say that patents and exclusive licensing are completely unjustified. There may be situations where exclusive licenses are required for the commercialisation of human therapeutic applications of CRISPR, but this depends on a variety of factors such as the nature of the invention, the associated risks, and the costs involved.¹³ Certainly, where exclusive licenses are used for publicly-funded inventions, there should be evidence presented by the licensor as to why they are necessary.

For CRISPR technologies to be optimised for the public interest, there should be broad access to the products developed from public investment. Research has shown that the potential costs of even the most basic treatments remain largely unaffordable. There does not seem to be

⁷ Broad and UC have granted exclusive rights, on their CRISPR patents for therapeutic purposes, to an array of spin-outs. However, exclusivity may not be ideal, and the public interest may be better served without a patent limiting integral technology. Ian Ayres & Lisa Larrimore Ouellette ‘A market test for Bayh-Dole patents’ (2017) 102 *Cornell Law Review* 279.

⁸ Confining technology and research that requires development to a sole institution is perilous as it places control in the hands of one body. Sirpa Soini et al ‘Patenting and licensing in genetic testing: Ethical, legal and social issues’ (2008) 16 *European Journal of Human Genetics* 26.

⁹ Exclusive licensing agreements have led to a bottleneck in terms of costs, access, and innovation.

¹⁰ Exclusivity may result in a genetic monopoly, which restricts innovation and prevents new inventors from entering the market. Such licenses have been criticised for being anti-competitive. The barring of the development of CRISPR technologies without a license hinders progress, specifically in the treatment of disease. Many companies cannot afford the excessive licensing costs, leaving the development of the technology in the hands of a sole institution. This means that potential beneficial human therapeutic applications of CRISPR by other organisations may not reach the public. Soini et al op cit note 8 at 11.

¹¹ Ayres & Ouellette op cit note 7 at 279.

¹² The non-exclusive usage of CRISPR proves that exclusive licenses are superfluous in incentivising use or research using the technology. Furthermore, exclusive licenses are unsuitable as they create bottlenecks, thus preventing the development of human therapeutics. Love op cit note 5 at 11; Ayres & Ouellette op cit note 7 at 279.

¹³ Companies may be unwilling to share a license on a commercial application due to higher burdens and larger investment, and may demand exclusivity.

much in the way of public benefit for investment, which is the underlying rationale for the patent system. I question whether the patent system is achieving the core concept of technology transfer.

Granting monopoly rights over CRISPR will limit the development of better medical treatments.¹⁴ Exclusivity is certainly not always necessary to develop human therapeutic applications of CRISPR technologies. Therefore, the exclusivity model which forms part of the CRISPR patent landscape is not in line with, nor does it enhance, the public interest.

(c) Due to the patent regime, what are the challenges that South Africa faces in bringing CRISPR human therapeutic applications to the public?

Besides the aforementioned issues, there are other challenges facing South Africa in terms of bringing CRISPR technologies to market – for example, ethical restrictions precluding the granting of licenses for germline gene editing. Whilst in its infancy, germline alterations could hold great potential in the eradication of priority diseases. However, should a South African inventor wish to develop and commercialise a germline gene therapy, they would be denied a license, and should they take that therapy into clinical trials, they could face costly litigation.

Another issue is the patenting of CRISPR technologies by foreign institutions in South Africa, regardless of whether they intend to commercialise or not. It seems to be a business tactic by international institutions to maintain a monopoly on such technologies, even in areas which may not have the capability to develop these inventions, or areas in which the patent holder has no commercial intentions. This precludes countries like South Africa from creating generics, or simply using the technology for free – which would translate into accessibility and affordability for the general public. Furthermore, a patent covering eukaryotic applications of CRISPR has been applied for by Broad in South Africa – and will likely be granted due to the existing depository patent system. A South African company wishing to develop a human therapy, whether germline or somatic, would need to obtain a license, failing which they may be sued for infringement.¹⁵ Although many inventions are not optimised for usage in developing countries, such countries are also precluded from optimising inventions themselves.

¹⁴ CRISPR is illustrative of the fact that allowing non-exclusive access to vital technologies can stimulate innovation, as many researchers are utilising and refining CRISPR for a range of applications that benefit the public. *Love op cit* note 5 at 5.

¹⁵ Whether the patent holder chooses to litigate is questionable, however the challenges African countries face in science and medical technology transfer must be noted.

The challenges that South Africa faces in bringing CRISPR technology to the public relates to the unsettled legal position regarding particular applications of the technology, and the uncertainty as to whether CRISPR applications are now deemed to be obvious under patent law.¹⁶ This determination would depend on the opinion of prospective patent examiners and the interpretation of the meaning of obviousness. Heightened standards of patentability and questions of how exceptions in patent legislation are interpreted will decide whether these technologies shall remain patentable in South Africa. It is uncertain how CRISPR-related patent applications will be interpreted in South Africa with the implementation of the IP Policy.¹⁷

In terms of South Africa's challenges to research, whilst research is generally unrestricted, some patent holders or companies require written licenses for CRISPR.¹⁸ South African researchers are notorious for operating in ignorance of patent law. Therefore, this may not be an issue in reality, but researchers should be aware of the fact that there is no research exception under South African law. This may lead to a situation in which they have no defence to a court order demanding their research be halted.

(d) How can the discussed challenges be addressed to optimise CRISPR technology for the public interest?

Various solutions have been put forth in order to address the issues present in the CRISPR patenting and licensing landscape, which I will briefly discuss. Whilst a patent pool provides a potential solution in optimising CRISPR technology for the public interest, one will be hard-pressed in imagining that a patent pool, suitable for human therapeutics, would be implemented.¹⁹ Patent pooling involves the non-exclusive licensing of patents, and considering the arguments that patent holders have made in an attempt to justify exclusivity, this seems unlikely. It is possible that a patent pool model may occur in the future for other applications of CRISPR, such as agriculture. Despite the issues mentioned, I suggest that a patent pool

¹⁶ Jacob S Sherkow 'The CRISPR patent landscape: Past, present, and future' (2018) 1(1) *The CRISPR Journal* 3.

¹⁷ This encompasses inter alia SSE and patent opposition proceedings.

¹⁸ This would presumably include the payment of licensing fees.

¹⁹ Although patent pools are successful in other industries, translating that same success into the CRISPR landscape is not guaranteed. A standard model that works in one industry, may not work in another and therefore, such a patent pool cannot simply be replicated in the context of biotechnology. Patent pools need to understand the industry in which they operate in order to determine the best strategy for implementation that allows the greatest benefit at the least cost to the public. From an examination of patent pools, it can be concluded that they are not suited to technologies such as CRISPR, unless a sui generis patent pool, which lends itself to the needs of biotechnology, is created. Döring & Lim op cit note 4 at 48.

clearinghouse does pose a solution to Broad's inclusive innovation model.²⁰ MPEG LA, as an independent company, can vet business proposals and act as an intermediary between the licensor and licensee. Through this method, the information contained in business proposals can be protected.

It has been established that Bayh-Dole allows the government to revoke licenses where a patent holder has failed to commercialise an invention.²¹ This option may be utilised in terms of the commercialisation of CRISPR products and processes.²² If it is believed that CRISPR's patent licenses are too restrictive, the US Department of Health and Human Services (DHHS), of which the NIH is a part, could be petitioned in order to exercise their march-in rights.²³ As

²⁰ As illustrated, Broad's inclusive innovation model which aims to develop therapeutic applications of CRISPR that reach the public, is unsuccessful in addressing the issue of exclusivity. Rather, it does little more than act as a conduit for third party inventions to be siphoned and claimed. Therefore, the motives and effects of licensing regimes employed by research institutions do not serve the public as profit is the driving force for innovation in these non-profit institutions.

²¹ Previous petitions, requesting the exercise of march-in rights by the NIH, concerned exorbitant drug pricing. These petitions, which each related to pharmaceuticals, were *In Re Cellpro*, *In Re Norvir I*, *In Re Xalatan*, *In Re Fabrazyme*, and *In Re Norvir II*. What these petitions had in common was the view that drug pricing concerns alone were insufficient to give rise to march-in rights. Although it was alleged that the high costs of medication threatened public health and safety, 'the extraordinary remedy of march-in is not an appropriate means of controlling prices'. *In re Xalatan*. This was seen as not being related to the actual access to drugs, which is a reason why these petitions were unsuccessful. In the petition of *In re Norvir*, the NIH was requested to initiate march-in proceedings due to unreasonable pricing of HIV/AIDS treatment, which impacted on public health and safety. The NIH refused to do so as Bayh-Dole cannot determine pricing of drugs, provided that reasonable steps have been taken to commercialise. *In re Xalatan* concerned discrepancies in drug pricing between countries. The NIH refused to exercise its march-in rights as the drug had been commercialised as it was available for public use and had been so for a substantial period of time. Some of the other march-in petitions that concerned the commercialisation of pharmaceuticals were also unsuccessful because steps were being taken to solve the issue, hence negating the need to march-in as per Bayh-Dole. In the *CellPro* decision, Johns Hopkins University held a patent on a stem cell antibody. CellPro developed a drug using the antibody and thereafter obtained Food and Drug Administration (FDA) approval, and CellPro was sued for patent infringement. CellPro then requested the NIH to exercise its march-in rights as Johns Hopkins, through its lack of FDA approval, had not commercialised the invention. The NIH declined to launch march-in proceedings as Johns Hopkins University was reasonably attempting to commercialise, although more slowly. *In re Fabrazyme* involved a drug shortage as a result of manufacturing issues. The NIH refused to march in as the problems were being resolved and it was improbable that other companies would obtain FDA approval before the drug shortage was fixed. It was held that 'unrelated regulatory problems after achieving practical commercialization was an insufficient basis to march in'. David S Bloch 'Alternatives to march-in rights' (2016) 18(2) *Vand J Ent & Tech L* 255-257; John R Thomas 'March-in rights under the Bayh-Dole Act' 2016 *Congressional Research Service* 9 & 11.

²² 35 U.S.C § 203(a). Although Bayh-Dole has been admired for spurring innovation, it has simultaneously been criticised for affecting scientific standards and burdening the public with the cost of redundant patents. Ayres & Ouellette op cit note 7 at 273.

²³ As CRISPR holds enormous potential, it should be accessible by companies wishing to utilise the technology in the commercialisation of end products that aim to benefit public health. March-in rights make this possible by allowing government to bypass the requirements for licensing and decide, under certain circumstances, who should be entitled to commercialise the technology. Megan Molteni 'The long-shot bid to put CRISPR in the hands of the people' *Wired* 22 February 2017, available at <https://www.wired.com/2017/02/long-shot-bid-put-crispr-hands-people/>, accessed on 6 January 2020.

mentioned, there are many applications of CRISPR technology that are not being utilised. Therefore, the march-in provision may apply perfectly.²⁴

Despite the apparent differences between the previous failed march-in attempts, I suggest that it is unlikely that this provision will be used for CRISPR. Whilst CRISPR may meet the criteria for the utilisation of march-in rights – much like my criticism of patent pools, CRISPR technology remains experimental.²⁵ Of course, the argument then is that this provision should be used to enable broader access to develop the technology to a point whereby it is effective and safe. The US government seems cautious to tread into the private domain, and perhaps not without cause. Although exclusivity is often promoted as the preferred licensing model, other non-exclusive measures (NPI and non-exclusive licenses) exist which ensure that the development of CRISPR continues, whilst safeguarding and promoting the public interest.²⁶

I concur with Ouellette and Ayres regarding the restriction of the scope of Bayh-Dole patents. Patents under Bayh-Dole should be reserved for inventions with a market value and an intention to commercialise. One could argue that this would reduce incentive to patent, but this is simply not the case. There are other less costly incentives to stimulate innovation, such as NPI and other market-based incentives. Depending on the nature of the innovation, these incentives may work better than patents, hence safeguarding innovation. The auction model that Ouellette and Ayres put forth is also an attractive method for ascertaining the need for exclusivity, and perhaps may result in more non-exclusive licenses being granted for inventions that were previously thought to have required exclusivity. If clinical trials truly are an obstacle

²⁴ On 6 June 2017, Knowledge Ecology International (KEI) requested the DHHS to implement a policy regarding the licensing of government-funded CRISPR inventions. The KEI suggested that there is public interest in ‘open, non-discriminatory licensing of CRISPR patents on reasonable terms’. Aggressive licensing will harm the public by limiting CRISPR research and development, preventing the growth of products utilising CRISPR, and increasing prices. In response to the letter by KEI, the NIH commented on certain aspects of CRISPR, patents, and licensing, but ultimately held that ‘[a]t this time, we do not believe that a new NIH policy to address the licensing of CRISPR patented technology is necessary’. Love op cit note 5 at 1; Knowledge Ecology International ‘2017: KEI asks the Department of Health and Human Services to adopt a policy on licensing CRISPR patents’ 6 June 2017 available at <https://www.keionline.org/23370>, accessed on 12 January 2020; Letter from Carrie Wolinetz, Acting Chief of Staff and Associate Director for Science Policy at the NIH to James Love, Director at Knowledge Ecology International 21 June 2017 available at <https://www.keionline.org/23413>, accessed on 12 January 2020; National Institutes of Health, Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources, 64 Fed. Reg. (Dec. 23, 1999).

²⁵ Whether genetic alterations will result in the desired effect is unknown. There have also been reports of CRISPR alterations causing cancers. Clara Rodríguez Fernández ‘Scientists warn CRISPR therapy could cause cancer as first human trials take place’ *Labiotech* 11 June 2018, available at <https://www.labiotech.eu/medical/crispr-therapy-cancer-risk/>, accessed on 16 November 2019.

²⁶ Although exclusivity in terms of publicly-funded inventions assists in the transfer of knowledge and technology to the public, there are alternative and less costly ways of achieving this.

that cannot be overcome without exclusivity, then perhaps the solution lies in state-funded clinical trials.

In terms of South Africa, both the Patents Act and the IPRPFRA lack certain provisions, which would assist in the development and dissemination of CRISPR knowledge to the public. Regarding research, I suggest that the Patents Act and the IPRPFRA require amendment to include a clearly defined research exception, applicable to those working with CRISPR technology, in order to avoid legal liability. This would also prevent obstacles to researchers (and their publicly-funded institutions) such as the need to pay fees for research licenses.²⁷

While section 14 of the IPRPFRA does contain provisions, which are comparable to Bayh-Dole march-in rights, they are not optimised. In South Africa, only NIPMO may conduct reviews or require publicly-funded institutions to grant a license to a third party. However, under Bayh-Dole any concerned group can request the government to exercise march-in rights. I suggest that the IPRPFRA should allow any interested party to request NIPMO, or another competent authority, to exercise its state rights to protect public interests.²⁸ Furthermore, these march-in rights are created by a contractual clause in transactions. This means that the operation of these rights is contingent on, and limited to, circumstances where there is a transaction between the patent holder and a potential licensee. As South Africa is a developing country, which also protects the right to healthcare in the Constitution, it is vital that state rights in the IPRPFRA are workable, accessible, feasible, and can be reviewed to ensure the realisation of the public's right to health technologies and medicines.²⁹

Besides the various forms attached to the IPRPFRA Regulations, information on when exclusive licenses are allowed is vague.³⁰ The explanations that are required (regulation 12(7)

²⁷ Researchers should be made aware of such a research exception in order to avoid potentially beneficial research, which could serve the public interest, being halted due to their unfamiliarity with patent law.

²⁸ This will ensure that the government is held accountable and marches in when it is in the public interest to do so. Providing the public with this option will serve two purposes: (1) it would hold government accountable for failing to exercise march-in rights; and (2) it will show potential licensees that they must answer to the public when considering IP stemming from publicly-funded research or inventions. Joelle Dountio Ofimboudem 'Access to medicines implications of the South Africa Intellectual Property Rights from Publicly Financed Research and Development Act No 51, 2008' (2016) 4(1) *Intel Prop Rights* 3.

²⁹ The IPRPFRA must ensure that state rights hold practical value for the public. Public health is a major concern, especially in the South African context because of the prevalence of HIV/AIDS and tuberculosis. Due to the fact that CRISPR technologies offer a potential therapeutic solution to the health issues faced by the country, it is necessary that specific focus is given to public health and the public interest in the IPRPFRA in order to advance the commercialisation of publicly-funded research and inventions so that they may benefit society. *Ibid* at 3; Vuyisile Hobololo 'Government's walk-in rights and public access to medicines: Implications of the IPR Act on state-funded pharmaceutical R&D outcomes in South Africa' (2015) *University of Witwatersrand – Abstracts* 58.

³⁰ Schedule 2 of the IPRPFRA Regulations contains the prescribed forms.

of the IPRPFRA Regulations),³¹ such as the reason why non-exclusive licenses for commercialisation cannot work, are ambiguous. These are simply explanations that are required, with no request for specific proof of attempts at non-exclusive licensing. How would one prove that the applicant even tried to commercialise non-exclusively? There should be a requirement that the applicant provide proof of attempting to license non-exclusively, and evidence illustrating why this was not feasible. Moreover, clarity regarding the competing preferences in section 11 of the IPRPFRA is necessary.³²

Licensing practices should not cripple academic research,³³ but should rather encourage the development of new inventions that are reasonably accessible to the public.³⁴ The IPRPFRA does not contain adequate protection against all-encompassing exclusivity. For example, an exclusive license for an application of CRISPR technology covering the entire genome (Broad and UC) is currently possible. As long as there is commercialisation of one aspect of the technology, it escapes the ability of the state to intervene as per the IPRPFRA. There should be revision of the IPRPFRA that considers the sui generis nature of biotechnological inventions and the impact that they have on public health – especially when considering publicly-funded biotechnological inventions. In doing so, I suggest a sui generis biotechnology clause should be developed and adopted that ensures an appropriate balance between private and public interests.

Another potential solution would be to shift thinking and policy away from privatisation and patents as incentives for academics, towards a focus on prizes and rewards. There are other publicly-funded incentives, such as scholarships through the National Research Foundation (NRF), but even these are steppingstones to privatisation. Rewards hold numerous advantages over patents – it all depends on the nature of the innovation.

The CRISPR landscape is unclear and, as thousands of patents continue to be granted and others rejected or invalidated, the picture becomes more obscure. This complicates the licensing landscape even further. Within all of this confusion, the interests of the public seem

³¹ Regulation 12 of the IPRPFRA Regulations encompasses conditions for offshore intellectual property transactions. Regulation 12(7) of the IPRPFRA Regulations states that – ‘[a] recipient must lodge an application in prescribed Form IP5 or IP6 with NIPMO for approval of an assignment of intellectual property offshore or grant of an exclusive licence, respectively, in terms of section 12(2) of the Act in compliance with the following conditions –

(a) the application must detail compliance with section 12(2) of the Act and this sub-regulation (6); and
(b) the recipient clearly articulates the benefits of the intellectual property to the Republic’.

³² Section 11 of the IPRPFRA deals with conditions for intellectual property transactions.

³³ Soini et al op cit note 8 at 33.

³⁴ Ibid at 25.

to have taken a backseat to profits. I conclude that the public interest is not being served by the current patent system and that reform is therefore necessary.

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