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MINI–DISSERTATION FOR MASTERS IN MEDICAL LAW

Examining the role of intellectual property law, policy and management in open innovation models that facilitate innovation in and access to genomic medicine.

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My sincere gratitude to all my teachers for opening the doors to this new world, and to my mentors — Dr Thaldar and Dr Goodier — for their wisdom, support and tireless sculpting.

To my parents, my second parents, my grandmothers, and the rest of my family and friends, thank you for your love and sharing this adventure with me.

'Probably the last man who knew how it worked had been tortured to death years before. Or as soon as it was installed. Killing the creator was a traditional method of patent protection.' — Terry Pratchett, Small Gods

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Abstract

The traditional closed innovation model is largely supported by a regime where intellectual property rights (IPRs) are used to secure monopolies over inventions, with one justification being that this maximises profits for future innovation. In the pharmaceutical and related healthcare technology industries, such a regime has been criticised as impeding access to healthcare technologies and hampering cumulative innovation. One response to this criticism has been a shift towards a more open innovation model, where more permeable boundaries between organisations facilitates the flow of knowledge for innovation. In such a model, IPRs may be used to facilitate such knowledge flows rather than solely as a means of securing a monopoly, satisfying the interests of private actors to profits, public interest to access advanced technology, and private-public interest to further innovation. In this dissertation, it is explored how IPRs, particularly as patents, may be used to facilitate open collaborative innovation in the genomic medicine field. This relatively nascent field of medicine endeavours to personalise medical decisions based on an individual's genome, but in order to develop the necessary technologies, requires vast amounts of knowledge on the human genome. Many initiatives have adopted intellectual property (IP) policies that facilitate open innovation so as to accelerate knowledge flows and resulting innovation in genomic medicine. Herein, these policies are consolidated to provide a tentative IP policy framework that supports open collaborative innovation in genomic medicine, against which South Africa's Draft IP policy and the IP policy of South Africa's leading research body, the Medical Research Council, is compared. It is found that whilst other countries are directly addressing the issues of patenting in genomic medicine through legislature and case law, South Africa is yet to take comparable actions. This is reflected in its vague patent laws and IP policies regarding IP in genomic medicine. Though there may be common elements that support open innovation between the policies of international initiatives and those of South Africa, the lack of clarity in the South African instruments does not provide a strong foundation for open innovation in genomic medicine. However, as the national IP policy is still in its draft phase, and this policy recognises the value of protecting public health, there may be opportunity to amend provisions to provide the necessary direction towards open innovation in genomic medicine, especially for bodies such as the Medical Research Council.

Chapter One: An introduction to the role of intellectual property law and policy in facilitating open innovation in genomic medicine

I. Introduction

International treaties such as Universal Declaration of Human Rights (1948)[1] and the International Covenant on Economic, Social & Cultural Rights (1966),[2] as well as regional instruments such as the African Charter on Human and Peoples' Rights[3] and national legislation such as the Constitution of the Republic of South Africa 1996,[4] have recognised access to healthcare as a basic human right, in which access to medicines is encompassed. As healthcare needs evolve, new branches of medicine emerge, and require existing aspects related to healthcare, such as models of innovation, to evolve. Such a branch is that of genomic medicine.

Genomic medicine is a way to customise medical care to a person's unique genomic makeup.[5] Genomics refers to the study of genomes; a genome is the entire collective of DNA present within an individual, which includes genes.[6] Whilst each individual in a species has a standard genomic blueprint, each genome may vary structurally,[7] resulting in different characteristics between individuals. These variations are termed genomic variants, and form the basis of genomic medicine.[8] In genomic medicine, genomic variation is examined to: 1) determine predisposition to disease; 2) tailor treatments accordingly; and, consequently 3) predict response to treatments.[9] This informs personalised routes of medical care offered to patients from diagnosis of disease, to treatment and prognosis. The intention of developing such tailored care is to enhance efficiency and efficacy, thereby reducing adverse outcomes and maximising benefits of healthcare beyond what is currently achieved in conventional medicine.[10] However, when juxtaposed to conventional medicine, genomic medicine is a relatively nascent field, requiring significant amount of research and development (R&D) before it can adequately fulfil the right to health.

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[1] Universal Declaration of Human Rights (1948) Article 5.

[2] International Covenant on Economic, Social and Cultural Rights (1966) Article 12.

[3] African Charter on Human and Peoples' Rights (1981) Article 16.

[4] Constitution of the Republic of South Africa (1996) Article 27.

[5] D M Goodman, C Lymn, E H Livingston 'Genomic Medicine' (2013) 309(14) *JAMA* 1544.

[6] World Health Organization *The Ethical, Legal and Social Implications of Pharmacogenomics in Developing Countries* (2007) (Report of an International Group of Experts) 5.

[7] Ibid 3.

[8] Ibid 5.

[9] Ibid 3.

[10] Ibid 3.

The fulfilment of the right to health is aided by the *availability* of health technologies[11] as well as *accessibility* to these, as proposed by the Committee on Economic, Social and Cultural Rights.[12] Innovation enables access to a greater range of health technologies, and is therefore implicated in the fulfilment of the right to health. Innovation in science is often cumulative, meaning that innovation is built on previous innovation or knowledge.[13] Therefore, access to upstream knowledge and innovation is essential in driving the progression of innovation in genomic medicine. However, with the emergence of a globalised intellectual property (IP) regime there has been a trend to increase IP rights (IPRs) on such knowledge and technologies, which has received public outcry.[14]

A globalised regime on IP protection has emerged from the agenda of the World Trade Organisation. This has been achieved by binding member states to TRIPS, which seeks to 'reduce distortions and impediments to international trade' by harmonising the protection of IPRs.[15] The patent legislation of member states has adopted the TRIPS provisions as minima standards, despite the differing economic, social and political standing and interests between the countries.

TRIPS does recognise the need of members to 'promote the public interest in sectors of vital importance to their socio–economic and technological development'.[16] This encompasses the promotion of technological innovation and the transfer of technology, to benefit producers and users, in a way that is 'conducive to social and economic welfare',[17] and that balances 'rights and obligations'.[18] However, developing countries found that interpretation of TRIPS by developed countries did not promote their interests as developing countries in public health, despite its express provisions relating to this. Consequently, the Declaration on the TRIPS Agreement and Public Health (the Doha Declaration),[19] which also recognises the importance of IP protection in medical development, emerged largely from the disgruntlement of developing countries at the WTO Fourth Ministerial Conference in Doha. The Doha Declaration emphasises that developing countries in particular should make use of the flexibilities provided in TRIPS,[20] but to date, these have been used

[11] Used as an umbrella term to include facilities, services and goods.

[12] CESCR *General Comment No. 14: The Right to the Highest Attainable Standard of Health (Art. 12)* (2000) Article 12) Articles 12(a)–(b).

[13] Y Joly 'Open source approaches in biotechnology: Utopia Revisited' (2007) 59(2) *Maine Law Review* 391.

[14] M A Heller & R S Eisenberg 'Can Patents Deter Innovation? The Anticommons in Biomedical Research.' (1998) 280(5364) *Science*.

[15] Agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS Agreement) (1994) 320.

[16] Ibid Article 8, 323.

[17] Ibid Article 7, 323.

[18] Ibid Article 7, 323.

[19] Doha Declaration on the TRIPS Agreement and Public Health (Doha Declaration) (2001).

[20] Ibid Article 4–7.

sparsely to meet public health needs. Thus, IP governance needs to evolve under a more pragmatic model that supports public and private interests.

Pharmaceutical and biotechnology industries claim that patents allow for recoupment of high R&D costs and investment, which incentivises and stimulates further innovation in the field, which in turn may raise the standard of healthcare available to the public.[21] However, patent monopolies are likely to arise, running the risk of restricted patient access and high costs of technologies. Thus, this rationale has received criticism and public outcry, as commentators view these healthcare-based industries as having a 'unique' 'social contract with the public' to produce health technologies.[22] Consequently, the United Nations responded by consolidating the obligations of non-states actors, namely businesses, to the right to health.[23]

This claim of recouping R&D investment may be boosted in light of the consequences of stratification of consumer markets according to genomic sub-populations, to be discussed in the following chapters, and whether it is sound, it is undeniable that the costs of R&D and commercialisation are high. There are multiple results of patents, which will be discussed further in the following chapters, however, regarding innovation and access to innovation, patents have two possible effects: a) monopolies may be created where access to genomic medicine by patients is limited, and costs may be raised without competition; b) innovation in the field of genomic medicine may be stymied as R&D attempts are hindered by the threat of patent infringement, despite the claim that the promise of patenting spurs innovation. If the traditional business rationale of patenting to recoup investment for further innovation does in fact hinder R&D more than it promotes innovation, such a rationale may be untenable for the advancement of personalised healthcare. Furthermore, this traditional business rationale of patenting profusely so as to maximise profits invites contention around the issue of whether elements of the human genome, such as human genes, as shared biological features of all human organisms, are even patentable subject matter.

The Human Genome Project ignited the discussion on gene patents. The Human Genome Project regarded the discovered genomic information as a public good, and promoted open access to this information. However, competing private firms sought to privatise the genetic knowledge that they had discovered. This issue of gene patenting were considered in the United States case of

[21] Y A Vawda, B K Baker 'Achieving social justice in the human rights/intellectual property debate: Realising the goal of access to medicines' (2013) 13 *AHRLJ* 70–73.

[22] KM Lybecker 'Social, ethical and legal issues in drug development, marketing, and pricing policies: setting priorities; pharmaceuticals as private organizations and the duty to make money/maximize profits' in Cohen et al (eds) *The Power of* Pills (2006) 25–31.

[23] Special Representative of the Secretary-General *Guiding principles on business and human rights: Implementing the United Nations 'protect, respect and remedy' framework*, UN Doc A/HRC/17/31 (2011).

Association for Molecular Pathology et al v Myriad Genetics, Inc et al.[24] This case concerned the breast cancer risk genes *BRCA1* and *BRCA2* (*BRCA1/2*) that were patented by Myriad Genetics, hence limiting patient access to breast cancer diagnostics based on these genes. A clear theme underlying this debate is: to what extent must healthcare-based companies and such non-state actors fulfil their unique social responsibility in lieu of their private interests to generate a profit? Clearly, a new model for organisational R&D is required — one that promotes what will be termed as the 'triad of interests': a) the private interest in return on investments; b) the private–public interest in rapid innovation in the field of genomic medicine to deliver optimal technologies; and c), the public interest in patients' access to technologies in genomic medicine. A new R&D model that has been widely adopted by global leaders in healthcare technologies — the 'big pharma' — in an attempt to address the triad of interests, is open innovation.[25]

'Open Innovation' is a model proposed by Henry Chesbrough where 'firms can and should use external ideas as well as internal ideas, and internal and external paths to market, as the firms look to advance their technology'.[26] This contrasts the traditional 'closed innovation' model in which R&D was retained in the internal structures of an organisation, whose boundaries remained impermeable.[27] Essentially, Chesbrough calls for a bi-directional flow of knowledge — classified as either inbound, outbound, or coupled processes — through leveraging of R&D (which focuses significantly on rethinking traditional IP management).[28] Open innovation has evolved as the literature and experiential evidence around it has grown, and has even extended to 'open collaborative innovation'.[29] Nonetheless, what is retained in these divergent views is that there are 'distributed sources of knowledge for innovation',[30] a highly relevant feature of the genomic medicines industry. These 'sources', under an open innovation framework, need to network or collaborate to optimise the utility of their IP expanding innovation beyond the existing 'closed' and impermeable boundaries of the organisations. This could be highly beneficial to the advancement of innovation in genomic medicine, whilst satisfying the private interests of the entities involved.

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[24] *Association for Molecular Pathology et al v Myriad Genetics, Inc, et al* (2014) 569 USC.

[25] B H Raja, P Sambandan *Open Innovation in Pharmaceutical Industry: A case study of Eli Lilli* (Master of Science Thesis, KTH Industrial Engineering and Management, 2015).

[26] H W Chesbrough *Open innovation: The new imperative for creating and profiting from technology* (2003).

[27] H W Chesbrough & M Bogers 'Explicating Open Innovation: Clarifying an Emerging Paradigm for Understanding Innovation' in H W Chesbrough, W Vanhaverbeke, J West (eds) *New Frontiers in Open Innovation* First edition (2014) 3.

[28] Ibid 13–15.

[29] Ibid 15–16.

[30] Ibid 16.

Genomic medicine has two central facets underlying diagnostic testing and personalised, genome–based treatment — basic research of genome sequences, function and location, and downstream development of genome-based diagnostic and therapeutic technologies. These facets may be suited different approaches to IP protection, which will be explored herein, so as to facilitate sustainable innovation. Instead of using blanket approaches where IP protection is either abolished (such as in the public good argument), or where IP protection is too extensive to serve the interests of inventors (such as in closed innovation), an open innovation model may consider both the public good nature of genes and the value of downstream technologies as IP leverage in innovation. This may facilitate patient access to genomic health technologies, whilst promoting innovation in the field.

South Africa (SA) has identified through its 2013 Bio–economy Strategy that innovations in emerging knowledge economies, such as genomics, may contribute significantly to the country's future economy.[31] However, it reports that 'sustained performance of biotechnology companies has been a challenge',[32] calling for new innovation models that integrate issues, one of which it identifies as 'access to global intellectual property and knowledge pools'.[33] Thus, SA may stand to benefit from open innovation in terms of growing its biopharmaceutical and biotechnological industries, but will also need to create a favourable IP environment.

II. Rationale and research questions

As the field of genomic medicine is explored, it becomes apparent that rapid and significant innovation is needed to make available optimal technologies. However, as the contention surrounding access to conventional medicine and IPRs illustrates, researchers may face challenges in accessing knowledge and upstream innovations that are essential to advancing genomic medicine technology. However, as it will be explored, IPRs also have a role in the open innovation model. A consolidated, multi-faceted open innovation concept endeavours to expand innovation through the use of IPRs, and reduce the burden on healthcare entities such as companies and universities (where burdens may range from costs to human capital and skills), optimising the benefits to all stakeholders, including patients, and fulfilling the triad of interests posited above.

This study therefore endeavours to examine the role of IP law, policy and management in the open collaborative innovation model that facilitates innovation in and access to genomic medicine, so as to fulfil the right to health as delineated by international law. In order to achieve this, the role of IPRs under the traditional, closed innovation model that has received criticism for blocking

[31] Department of Science & Technology *The Bio-Economy Strategy* (2013).

[32] Ibid 14.

[33] Ibid 21.

essential knowledge and upstream technologies is explored. This highlights, from an IP perspective, why there is a shift to an open innovation model that uses IPRs differently. The value of open collaborative innovation in genomic medicine is substantiated using existing initiatives, and it is examined through IP policies how IPRs are used in these initiatives to create sustainable open innovation. Using these policies, a consolidated open collaborative innovation policy that can be suited to the different aspects of genomic medicine is provided.[34] This consolidated policy is then used as a reference in brief analysis of the amenability of major policy influences in SA to open collaborative innovation in genomic medicine in the country.

III. Research outline

The body of the dissertation will be constructed of five chapters, including the introductory and conclusory chapters. In Chapter One, the topic is introduced and the background and rationale of the study is presented. This is followed by a Literature Review detailing the main sources of literature — mainly primary works — that are relevant to answering the research question.

Chapter two introduces the concept of genomic medicine will be developed and juxtaposed to conventional medicine. This juxtaposition elucidates how R&D needs for innovation differs between the two, partially justifying a shift in healthcare innovation. In outlining these R&D needs, there is a concentration on the role of large–scale genomic research projects, such as the Human Genome Project, databases and biobanks in facilitating the generation of genomic knowledge that can be used to downstream R&D.

In Chapter Three, the concept of a closed innovation model and how IPRs in genomics has traditionally been used to support his model is introduced. The public good nature of genomic knowledge is also explored, and the value of limiting IPRs use so as to promote access to essential research tools such as genome sequences is highlighted. There is an examination of various cases in which patents on genomic elements, such as genes, have been challenged on the basis of hindering future innovation and restricting patient access, providing a rationale for a shift in how IPRs is used to promote innovation whilst expanding access to genomic knowledge and technologies.

In Chapter Four, the paradigm of open innovation will be explored, with a focus on open collaborative innovation. The rationale for using open collaborative innovation in the field of genomic medicine is substantiated, and there is an exploration of the IP policies of initiatives to establish how IP may be used to further the objectives of openness in genomic medicine innovation. Through this exploration of policies, a consolidated IP policy that supports open innovation is provided,[35] and used

[34] Section II (a).
[35] Ibid.

to analyse the IP policy climate within the South African context, focussing on SA's national IP policy and the IP policy of a leading body of research, the SA Medical Research Council.

The last chapter, Chapter Five, will conclude this study by listing the limitations to the study and recommendations for future researchers to consider. The conclusory remarks on the role of IP in open innovation that facilitates innovation in, and access to, genomic medicine, will be presented to close this chapter.

IV. Literature review

In this literature review, the major authoritative patent legislature and litigation in genomic medicine that illustrate the use of IPRs under a closed innovation model, and the divergent approaches to genome patenting adopted by various jurisdictions resulting from the lack of an international consensus on the matter are identified. This forms part of the substantiation for shifting to the open innovation model proposed by Chesbrough. Following this is an outline the evolution of Chesbrough's open innovation into the model of open collaborative innovation that will be used in this dissertation. The various initiatives and authoritative bodies whose IP policies are used to highlight the groundwork that is being laid for open collaborative innovation in genomic medicine are then introduced. Subsequent to the introduction of these policies, it is substantiated as to why South African has been chosen as a focus country in this dissertation as there is a paucity of IP law and policy supporting open collaborative innovation in genomic medicine in the country.

(a) The Global Intellectual Property Rights Regime

A starting point for any critique of genome patenting and its effects on innovation is the TRIPS Agreement, which binds member states to its provisions and aims to 'reduce distortions and impediments to international trade' by harmonising the protection of IPRs in a manner that does not allow these rights to hamper 'legitimate trade'.[36] The two underlying principles of TRIPS include the National Treatment and the Most–Favoured–Nation–Treatment provisions that essentially seek to harmonise the protection of IPRs amongst member states by extending state provisions to nationals of all other states. [37]

Though TRIPS arises from a trade agenda, it also recognises the need of members to 'promote the public interest in sectors of vital importance to their socio-economic and technological

[36] TRIPS Agreement (note 15 above) 320.

[37] Ibid Articles 3-4.

development', [38] which includes the public interest to protect public health.[39] This is reiterated in the Declaration on the TRIPS Agreement and Public Health (the Doha Declaration), which also recognises the importance of IP protection in medical development.[40] Both TRIPS and the Doha Declaration also emphasise the use of flexibilities to protect public health, especially regarding compulsory licensing and parallel licensing,[41] although commentary on this suggests these not are not exploited, opening the avenue for new models that facilitate technological development and address public health interests.[42]

The IPRs provisions of TRIPS are meant to be interpreted in light of its objectives of Article 8 mentioned above, but have been criticised as being open–ended, minima standards,[43] leading to divergent approaches to patenting in specific technological industries. Genome patenting is a pertinent case where it is observed that various jurisdictions have opposing views that could affect innovation in genomics differently. Two prominent examples are that of the US and the EU. The EU's Directive on the Legal Protection of Biotechnological Inventions[44] (the EU Directive) recognises the EU's primary obligations set out in TRIPS, and in its preamble, takes a pro-trade outlook, indicating the importance of IP protection in trade and industrial development. Subsequently, it provides clear grounds for the patenting of biological material, including genome sequences isolated from humans, taking a stance that promotes maximum patent–eligibility within the conditions of patentability set forth in TRIPS. [45] However, the US Patent and Trademark Office takes an opposing stance to patenting isolated genome sequences, following the judgement of the *Myriad* case in the US, where a number of claims based on the BRCA1 and BRCA2 genes were challenged on the grounds that they are not patentable subject matter under section 101 the Title 35 of the US Code, following that the isolated genes are products of nature, and thus patent-ineligible according to the law at hand.[46] These dissimilar provisions highlight the need for sound and clear patent law that

[38] Ibid Article 8, 323.

[39] TRIPS Agreement (note 15 above) Article 8.

[40] Doha Declaration (note 19 above) Article 3.

[41] TRIPS Agreement (note 15 above); Doha Declaration (note 19) Article 5.

[42] K J Strandburg 'Accommodating user innovation in the international intellectual property regime: A global administrative law approach' (2009) *Acta Juridica* 283-318.

[43] Ibid.

[44] Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions (1998).

[45] EU Directive (note 45 above) Articles 3(1), 5(2).

[46] K Sevick 'U.S. patent office floats new biotech-friendly guidelines' (19 December available at http://www.sciencemag.org/news/2014/12/us-patent-office-floats-new-biotech-friendly-guidelines), accessed on 15 April 2017.

addresses patenting of the various forms of DNA and associated molecular structures, uses of these, and associated methods claims.

A review of the literature on genome patenting, in light of TRIPS, highlights the need to a comprehensive legal international consensus on patenting in genomics that fulfils the objectives to protect public health and promote technological development as set out in TRIPS and the Doha Declaration. However, the structure of such a consensus determines how innovation will be conducted, and law and policy reform should be cognisant of the emerging models of innovation that digress from the traditional closed model.

(b) An Evolved Concept of Open Innovation

In his 2003 paper, Chesbrough introduces the concept of open innovation in the firm as that based on inbound and outbound flow of knowledge, [47] and in his subsequent work, he evolves the concept of open innovation by incorporating more recent reconceptualisations, including Gassman and Enkel's coupled innovation where knowledge is simultaneously inbound and outbound.[48] Chesbrough proposes the following definition of open innovation as 'a distributed innovation process [primarily of R&D spill–overs] based on purposively managed knowledge flows across organizational boundaries, using pecuniary and non-pecuniary mechanisms in line with the organization's business model'.[49]

Chesbrough then incorporates divergent views on open innovation that transgress his firm–centric model. These views include innovations of a public good nature that arise through 'distributed social division of labour', as proposed by von Hippel, [50] particularly termed as 'open, distributed innovation' and 'open collaborative innovation'.[51] Both open innovation and open collaborative innovation are based on the notion of 'distributed sources of knowledge for innovation'.[52] Open collaborative innovation is offered as a feasible, evolved model of open innovation in genomic medicine by various initiatives, as commentators debate the public good nature of genomic knowledge,[53] yet also recognise the need to incentivise private actors in collaborations.

[47] Chesbrough (note 26 above).

[48] Chesbrough & Bogers (note 27 above; 13).

[49] Ibid.

[50] Ibid 16.

[51] Ibid 15.

[52] Ibid 16.

[53] F Huzair & T Papaioannou 'UK Biobank: Consequences for commons and innovation' (2012) 39 *Science and Public Policy* 501.

Commentators suggest that open collaborative innovation has the potential to capture value both for private and public actors, and to accelerate the biotechnological advancement.[54]

Though there is a relative paucity of evidence of the success of open collaborative innovation in genomic medicine when compared to more established open practices in industries such as the software industry, many open initiatives in genomics have emerged that lay the foundation for future insight into the success of open collaborative innovation. Two such examples are that of CAMBIA's BIOS[55] and the 100 000 Genomes Project (100KGP). Both these initiatives emphasise in their policies the crucial role of their genomic biobanks and databases in generating meaningful genomic knowledge and allowing for knowledge flows.

Established in 2004, the BIOS initiative, based in Australia, seeks to use collective and distributed innovation to create sustainable and equitable economic and social development in the biological sciences. [56] Though its focus has largely been on agriculture, BIOS does recognise the need to address public health, and its innovation policy is worthwhile to examine as it incorporates an open innovation approach. Its objectives are seek not only to recognise public-good norms in the biological sciences, but also to 'adapt new inclusive IP sharing mechanisms' that do not allow the appropriation of public goods.[57] These two objectives indicate that BIOS does not employ a narrow view on open innovation, and endeavours to include interests to use research tools to innovate, and public and private interests to capture value from innovations through dissemination of knowledge and technologies and commercialisation. Importantly, BIOS distinguishes between research tools and downstream applications,[58] forming a crux of this dissertation — that research tools such as genome sequences should be public goods to maximise innovation of downstream technologies that need to be commercialised. BIOS seeks to achieve this commercialisation in a manner that does not restrict further access and innovation through patenting, but looks for alternative IP sharing mechanisms.

Firstly, BIOS seeks to create an understanding of the current patent IP landscape amongst its users, and has created a cost–free, public–access database of patents in the EU, US, Australia and through the Patent Cooperation Treaty (PCT) — BIOS intends to extend the range of jurisdictions. Through its patent database and informatics tools, BIOS creates a means by which to guide policy through 'analysis of patterns of IP development, protection and ownership'.[59] BIOS favours open–

[54] M Gastrow 'Open innovation in South Africa: case studies in nanotechnology, biotechnology, and open source software development' (2012) 9(1) *Journal for New Generation Sciences* 42.

[55] CAMBIA (note 57 above).

[56] A Carvalho 'The Intellectual Property and Open Source Approaches to Biological Material' in Trento Law and Technology Research Group Student Paper Series (2013) 105.

[57] CAMBIA *The CAMBIA BIOS Initiative* (2004) 3.

[58] Ibid.

[59] Ibid 9.

access licensing of CAMBIA's IP, and endeavours to identify core technologies that need to be developed.[60] To support such development, BIOS will create a cyberspace — an internet–based platform where researchers and developers can communicate to facilitate open collaborative innovation. It is for these reasons that BIOS is a suitable candidate for the study of open collaborative innovation.

The 100KGP is a genomic database established by the UK Department of Health company, Genomics England, in 2013, and is a key initiative discussed by the University of Cambridge's Centre for Science and Policy.[61] It aims to compile and own the genomic and clinical data of patients with specific diseases, and make these available for use by third parties either freely (if parties are members) or for a reasonable and fair fee.[62] Though it is not directly a platform for collaborative innovation, as with BIOS, its IP and access policy is notable as is it more aligned to a business model that seeks to generate a profit for public benefit. The IP and access policy for this project is tiered: academic and public-sectors researchers are required to join the Genomics England Clinical Interpretation Partnership ('GeCIP'), and private companies are to join the Genomics Expert Network for Enterprises ('GENE') Consortium.[63] Each tier is subject to different rules on IPRs and access, and licensing and payments. This tiered approach considers the different roles potential collaborators have, that is, whether their strengths lie in generating basic knowledge or in developing this knowledge into commercial applications, aligning with the crux of this dissertation that an innovation model needs to accommodate both the public good nature of genomic knowledge and the private good nature of its downstream applications. The 100KGP does achieve openness through fair and reasonable licensing, fully/partial open–access databases, capture of social value, and dissemination of knowledge through management of IPRs,[64] and for these reasons, is considered as a significant initiative in this dissertation topic.

These initiatives provide valuable insight into the IP policies that engender openness in collaboration, but are restricted to the boundaries of the initiative. Policy and guidelines need to extend beyond an entity to a national and even international phase, as illustrated by the OECD's *Guidelines for the Licensing of Genetic Inventions*,[65] a source which ultimately provides a platform

[60] Ibid 10.

[61] Centre for Science and Policy IP Policy Workshop Report No. 2 *Open Innovation with Large Bioresources: Goals, Challenges and Proposals* (2016) 14.

[62] Ibid.

[63] Ibid.

[64] Ibid.

[65] OECD *Guidelines for the Licensing of Genetic Inventions* (2006).

This document was endorsed by OECD's Committee for Scientific and Technological Policy meeting at ministerial level and by OECD health ministers in 2004.

for the integration and balancing of innovation, IPRs and genomic medicine. Licensing is identified by Chesbrough as a key element to open innovation,[66] and the *Guidelines* discuss best practices for licensing genetic inventions in healthcare,[67] defining 'genetic invention'[68] beyond that tackled in the case law mentioned above.[69] It explores the value of genetic innovation (which is included in genomic invention) in human healthcare and economic growth,[70] and explores the collaborative and cooperative nature of innovation. In its objective to balance the IP system, the guidelines outline licensing that: a) occurs in an 'economically–rational' manner; b) comply with competition law; and c), balance the 'interests of society, shareholders and stakeholders'.[71] The overarching themes under which 'Principles and Best Practices' are discussed all have a role in the structure of open collaborative innovation, and include: licensing generally, healthcare and genetic inventions, research freedom, commercial development, competition.[72] Whilst the premise may seem idealistic, the *Guidelines* provide further insight and solutions where possible in the 'Annotations',[73] and is a valuable foundation for national, regional or international IP policy that can foster openness in innovation.

(c) Open innovation in South Africa

South Africa is a developing country with the status of an emerging market and leader in biotechnology R&D investment, as found by Gastrow in his quantitative study of the South African biotechnology sector.[74] However, in this study, which is partially based on patent data, Gastrow finds that South Africa's biotechnology R&D profile is small by international standards, with Jordaan's concurring finding that biotechnology innovation of SA as compared to other countries has been 'modest'.[75] Furthermore, Jordaan observes an asymmetry between the involvement of the private and public sectors in biotechnological innovation, which has not been amended by prior policy revisions

[66] Chesbrough (note 26 above).

[67] OECD (note 65 above; Article 1).

[68] Ibid Article 2.

[69] *Myriad* (note 24 above).

[70] Ibid Article 3.

[71] Ibid Article 8.

[72] Ibid Part I.

[73] Ibid Part II.

[74] M Gastrow 'Great expectations: The state of biotechnology research and development in South Africa' (2008) 7(4) *African Journal of Biotechnology.*

[75] D W Jordaan 'Biotech Innovation in South Africa: Twenty Years in Review' (2016) 35(1) *Biotechnology Law Report* 41.

such as that of the 2001 National Biotechnology Strategy or the 2013 Bio-Economy Strategy.[76] As discussed above the current Bio-Economy Strategy sees the value of genomics in the economy, but reports that 'sustained performance of biotechnology companies has been a challenge',[77] calling for new innovation models that integrate issues, one of which it identifies as 'access to global intellectual property and knowledge pools'.[78] From this statement, an open innovation model may find a place in building SA's bio-economy.

In another study, Gastrow observes that literature on open innovation focussed on developed countries, and addresses this by conducting a study of open innovation in the South African nanotechnology, biotechnology and software industries.[79] He finds that whilst the biotechnology sector is 'highly networked and highly collaborative', current public policies 'do not take sufficient advantage of this', and encourages the development of public policy that supports network–building.[80] As the Draft Intellectual Property Policy of SA Phase 1 (2017)[81] is still in its early stages, and there are no major research bodies with policies geared towards open innovation in the biotechnology sector, there is a window of opportunity for SA to drive its public policy towards open innovation.

V. Research design and methods

The design of this study is based on desktop research of primary and secondary sources. Primary sources include, but are not limited to, international treaties and agreements, national legislature/policies/strategies, case law, empirical research of journal articles and original reports, and patent databases. Review of secondary sources mainly involve journal articles, reports and commentary on cases.

[76] Ibid 42.

[77] Department of Science & Technology (note 31 above; 14).

[78] Ibid 21.

[79] M Gastrow (note 54 above).

[80] Ibid 63.

[81] GN 636 of GG 41604, 25/08/2017.

Chapter Two: Understanding the Principles of Genomic Medicine

For centuries, patents as a form of IPRs have been granted for inventions in various fields of technology as a reward for innovation by private parties, and as an incentive to disclose the invention for the sake of public interest.[82] These inventions derive from the application of knowledge, for example, the principles of physics were applied to the invention of the aircraft. Over the years, knowledge has evolved, and new fields of technology have emerged. In the biological sciences, one such field is genomics, which is the study of the genomes of species and individuals. The genome is the entire DNA content found in an individual, which includes their genes — the unique set of instructions for the various functions and characteristics of an individual.[83] Genomics has led to the emergence of genomic medicine — a branch of personalised medicine where medical decisions are based on the unique characteristics of an individual's genome. As a relatively nascent field, genomic medicine requires extensive innovation that is rapid and cost-effective. Innovation begins at the stages of research and development (R&D), and extends through to the commercialisation of a product for use by the consumer.[84] Traditional proprietary-based models of innovation, loosely termed as 'closed' innovation, is when a firm is responsible for the entire innovative process, and is in this way the sole owner of any IPRs that is applied to the innovation — this will be explained further in the following chapters.[85] Though the closed model has reaped significant advancements in the past, industries have recognised the pitfalls of this type of model — namely, that it is costly and that IPRs may impede follow-on developments by blocking research and development (R&D) using patented technologies. Thus a new model of 'open' innovation, based on the flow of knowledge and technology that will be elaborated on below,[86] in which IPRs could play a more conducive role in innovation and access to emerging technologies, may be better suited to the progression of genomic medicine.

However, before it is understood how IPRs can be used in an open innovation model to further genomic medicine, the facets of the field itself will be explained, that is, what is genomic knowledge and what are its applications, and how has IPRs thus far been applied to these facets under the traditional proprietary model. In this chapter, in order to understand genomic knowledge and its applications, a brief explanation of the science of genomics and genomic medicine will first be presented. This will be followed by an exploration of the historical development of genomic

[82] TRIPS Agreement (note 15 above; Article 29(1)).
[83] N A Campbell et al *Biology* 8 ed (2008), 9.

[84] H W Chesbrough & M M Appleyard 'Open Innovation and Strategy' (2007) 50(1) *California Management Review* 57-59.

[85] Ibid.

[86] Ibid 60-62.

knowledge and its significance as a research tool in genomic medicine, and a description of the current structures that contribute to the generation of this knowledge. Following this understanding of genomic knowledge, the IPRs issues regarding genomic knowledge, and the impact this may have in a closed innovation model will be explored in Chapter Three.

I. Conceptualising genomic medicine

The field of genomic medicine is a relatively new concept in healthcare, although it is closely aligned with another field — genetic medicine — which has provided the foundation for genomic medicine. Similar to genomic medicine, genetic medicine is also a branch of personalised medicine. Genetic medicine entails the making of medical decisions regarding the treatment of a disease based on a patient's specific genes.[87] As discussed below, a gene for a particular characteristic can have many variations, such as the gene for eye colour. As it will be seen with genomic medicine, this requires genetic testing and therapies tailored to genetic variations of a patient. An example pertinent to genetic medicine would be in breast cancer, where specific variations of the breast cancers genes *BRCA1* and *BRCA2* confer a greater susceptibility to breast cancer in women.[88] Genetic medicine has, in the past few decades, garnered much attention regarding the influence of IPRs on innovation in and access to the technologies of this field.[89] Using the above example of *BRCA1* and *BRCA2*, a landmark case emerged in the US when Myriad Genetics, the company holding the patents for these genes claimed that other companies who were offering commercial genetic testing for these genes were infringing on their patents.[90] In this case, the attention centred on how these claims of infringement would affect the provision of genetic testing to the public, and further innovation in breast cancer research using the genetic data from these tests.

Genomic medicine is also raising the question of whether the traditional, proprietary-based 'closed' innovation model is sufficient to meet private and public interests. However, before answering whether a shift is needed in the innovation model, and how IP can facilitate this model, an understanding of the nature of genomic medicine and how this nature may lend itself to more 'open' innovation will be provided. 'Open' innovation is the flow of knowledge and technologies between innovation entities, changing the requirements of closed innovation from that which necessitates that an entity perform all the innovative activities (from R&D to commercialisation), to that which allows

[87] Goodman, Lymn & Livingston (note 5 above; 1544).
[88] R Cook-Deegan & A Niehaus 'After Myriad: Genetic Testing in the Wake of Recent Supreme Court Decisions about Gene Patents' (2014) 2 Curr Genet Med Rep 224.
[89] Sevick (note 46 above).
[90] *Myriad* (note 24 above).

for a networking and sharing of these activities.[91] This may be valuable in a highly complex, knowledge-based and high technology field such as genomic medicine, and will be explored in greater detail in the following chapters. In this section, a brief background into the science of genomics and genomic medicine and its link to genetics and genetic medicine will be provided, which will be reiterated in the following chapter where some of the IP issues relating to genetics will be extrapolated to genomics. The use of genomic knowledge as a research tool in downstream applications, such as pharmacogenomics, is also discussed, providing an understanding that genomic medicine comprises of essentially two facets which may lead to different approaches under an open innovation model.

(a) A scientific background to genomics

As early as 1963, an Expert Committee of the World Health Organization (WHO) noted that 'genetic considerations add a new dimension to public health work: a concern not only for the health and wellbeing of persons now living, but also for … generations yet to come'.[92] In the past few decades, genetics and genetic medicine are fields that have been deliberated at length not only by health organisations, but by intellectual property authorities as well, who have considered how IPRs should be applied in these fields. As science progressed, genetics research was taken further, and the field of genomics emerged. Both these fields are based on the gene, a concept that will be explored below.

A human being is composed of trillions of cells, each containing the same set of genes.[93] A gene encodes the 'master instructions to build, repair, and maintain humans' in a cell.[94] The cell uses these instructions to produce functional molecules, such as proteins, for specialist functions — for example, a liver cell will be instructed by a subset of genes to produce proteins that perform the functions of detoxifying ingested compounds, and a white blood cell will be instructed by a different subset of genes to produce antibodies proteins fight off infections.[95] Essentially the gene is a molecule consisting of DNA — a nucleic acid made up of nucleotides, or bases.[96] A single strand of DNA forms a structure called a chromosome within the nucleus, along which many genes are located at a specific locus on the chromosome. The four bases of DNA occur in sequences which may differ in order and length, resulting in a code; it is for this reason that genes are called 'coding' DNA.[97] This variety of sequences in the genes arises in differences in the instructions given to the machinery of a

[91] Chesbrough (note 84 above; 60-62).

[92] World Health Organization *Genetics, genomics and the patenting of DNA: review of potential implications for health in developing countries* (2005) 1.

[93] Campbell (note 83 above; 9).

[94] S Mukherjee *The Gene: An Intimate History* Kindle edition (2016) 11.

[95] Campbell (note 83 above).

[96] Campbell (note 83 above; 426-434).

[97] Ibid.

cell, a simple example being that a gene for blue eye colour instructs the relevant cells to produce a blue pigment, whereas a variation to that gene may result in a green pigment being produced. The roughly 23 000 genes of a typical human are found in the 23 pairs of chromosomes,[98] although between these genes are also stretches of 'junk' DNA — that is DNA that has no apparent coding, regulatory or structural function, and is probably the result of inefficient evolution.[99] Only about 2% of the human genome contains the genes that encode for other functional molecules such as proteins; [100] the remaining 98% is junk DNA. As each half of each chromosome pair is received from each parent's reproductive cell during sexual reproduction, genes are actually inherited and passed down to future generations.[101]

In his New York number one bestseller, *The Gene: An Intimate History*, Siddhartha Mukherjee suggests as follows regarding the concept 'gene': 'one of the most powerful…ideas in the history of science: the "gene," the fundamental unit of heredity, and the basic unit of all biological information.'[102] This is a reasonable viewpoint, as genes encode the characteristics of individuals that makes them different in how they look, behave and interact with their environment. These differences conferred by genes have been identified as the future of medicine by tailoring medical decisions based on the genetics of individuals. Now science has introduced the term 'genomics' to the concept of personalising medicine.[103] So what is the link, and what does genomics have to offer to healthcare?

As stated above, genes are coding regions of DNA, and genetics is primarily concerned with the study of these coding regions. However, the DNA of chromosomes also includes regions that do not code for specific characteristics (termed non-coding DNA, which includes junk DNA), or that is required for structural or regulatory purposes in the cell.[104] A genome consists of all the DNA in an organisms, as introduced above, which includes coding, non-coding, structural and regulatory DNA.[105] Though it is often confused with genetics, genomics differs subtly from genetics. Whereas genetics is the study of a single gene or a small number of genes and their associated functions and disorders, genomics studies the entire genetic constitution of an organism.[106] These studies include identifying the structure, function, location and evolution of the genetic elements of the genome.

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[98] World Health Organization *Medical genetic services in developing countries: The ethical, legal and social implications of genetic testing and screening* (2006) 7.

[99] E Lawrence *Henderson's Dictionary of Biology* 14 ed (2008) 344.

[100] World Health Organization (note 106 above; 15).

[101] Campbell (note 83 above; 426-434).

[102] S Mukherjee (note 94 above; 9).

[103] Goodman, Lymn & Livingston (note 5 above; 1544).

[104] Campbell (note 83 above; 426-434).

[105] Campbell (note 83 above; 426-434).

[106] World Health Organization *Genomics and World Health* (2002) 32-36.

Furthermore, genomics considers the interactions of chromosomes with each other and with other environmental factors.[107] This allows for researchers to study complex, multi-factorial diseases such as diabetes, cancer and cardiovascular diseases.[108] The study of genomes (or 'genomics') includes understanding the structure, function, mapping and evolution of genomes, which will enable scientists to understand the multiple genetic factors contributing, together with environmental interactions, to certain diseases.

Many developments in genomics have been made since the 1950s, and this field is still expanding. A critical development has been the Human Genome Project, led as a public initiative by the National Human Genome Research Institute.[109] In the Human Genome Project, researchers compiled a representative genome of the human genome by sequencing and mapping the genes of many individuals, providing a comprehensive reference database for future research.[110] Sequencing refers to uncovering the order of the bases in a gene, which codes for specific RNA and possibly proteins.[111] Mapping refers to identifying the location of genes along the chromosomes so as to produce a 'genetic map'.[112] As Mukherjee suggests, understanding genes (and by extension, genomes), 'tantalizes us with the prospect of controlling our bodies and fates'.[113] However, as will be discussed below, understanding genomes results in the development of knowledge which must be regulated. This knowledge can then be applied to produce technology that has a utility for society. How this knowledge and these applications is governed and protected, and how this protection allows for the development of the field through innovation, forms the crux of this dissertation.

(b) Understanding the nature of genomics medicine

Human genomics knowledge has been applied to the healthcare setting, resulting in the field of genomic medicine, a branch of personalised medicine, as introduced above. The inherent diversity seen between individuals of a species can be largely attributed to variations in genes. Genetic

[107] Y Farmer & B Godard 'Public Health Genomics (PHG): From Scientific Considerations to Ethical Integration' (2007) 3(3) *Genomics, Society and Policy* 15.

[108] B M Knoppers, M H Abdul-Rahman & K Bédard 'Genomic Databases and International Collaboration' (2007) 18 *King's Law Journal* 291.

[109] National Human Genome Research Institute (NHGRI) 'A Brief Guide to Genomics' (27 August 2015) available at *https://www.genome.gov/18016863/a-brief-guide-to-genomics/*, accessed on 29th August 2017.

[110] Genome News Network 'What's a genome?' (15 January 2003) available at http://www.genomenewsnetwork.org/resources/whats_a_genome/Chp4_1.shtml, accessed on 23 September 2017.

[111] NHGRI (note 109 above).

[112] NHGRI (note 109 above).

[113] Mukherjee (note 94 above) 12.

variation in humans arises from mutations and processes of sexual reproduction, where the nucleotide sequence of a gene may be altered.[114] These processes produce gene variants, or alternative forms of a gene, which may alter an instruction given for a specific function, for example, a variant may instructs that more antibodies are produced, or may instruct for the production of a dysfunctional protein.[115] Gene variants can be classified according to their effect, that is, they may be protective, neutral or risk variants.[116] Risk variants increase the susceptibility to disease, whereas protective variants decrease susceptibility to disease. Neutral variants do not appear to provide an advantage or disadvantage.[117] The study of these variants is the basis of genomic medicine. Some diseases are caused by alterations to one gene, and are called Mendelian or monogenic diseases; these are the subject of genetic studies.[118] Others are polygenic, which means the risk variants of many genes are involved in disease progression.[119] Often, polygenic diseases are multifactorial, i.e. there is a genetic component to the disease as well as an environmental component, which includes the external environment as well as the interactions that occur with noncoding DNA sequences and other molecular structures in the cell environment.[120] Examples of such diseases include heart diseases, mental illnesses, diabetes and cancer.[121] Due to the involvement of multiple genes and the cell's environmental factors, which together contribute to *genomic* variation, genomics provides a better understanding of how these genetic and environmental factors interact in the cell to cause disease, as opposed to identifying and studying these genes in isolation to each other and other factors.[122]

In genomic medicine, variations in the genome are used to optimise patient diagnosis, treatment and prognosis, and reduce side effects and risk of inefficiency.[123] This is based on the premise that the diagnosed diseases have a significant genomic basis. By understanding the genomic component of disease progression more clearly, in conjunction with patient history, presentation of symptoms and laboratory testing, a more accurate route of treatment can be chosen for the patient.[124] This may involve pharmacogenomics, where a pharmaceutical treatment is administered depending on the genomic constitution of an individual (which may affect the response to the treatment). This

[114] Campbell (note 83 above; 258-260).

[115] Campbell (note 83 above; 426-434).

[116] Coriell Institute 'Genetic Variation' available at https://cpmc.coriell.org/genetic-education/genetic-variation, accessed on 25 September 2017.

[117] Campbell (note 83 above; G-24).

[118] Ibid 276-279.

[119] Ibid.

[120] Ibid 279.

[121] Ibid.

[122] Ibid.

[123] World Health Organization (note 92 above; 4-5).

[124] Ibid.

application will be discussed further in subsequent sections. In this way, it can be seen that genomic medicine has been taken a step further than conventional medicine, which has only been able to use presentation of symptoms, patient history and laboratory tests of non-genetic factors. This means that conventional medicine has had to employ blanket, 'trial–and–error' approaches to treatment upon diagnosis, an approach which runs the risk of being ineffective or toxic to the individual.[125]

Additionally, genomic medicine also has a strong preventative medicine component — genetic testing is employed to predict the likelihood of developing a disease based on an individual's genes.[126] This enables healthcare professionals to design a route of preventative measures to delay disease onset before onset of disease; in this way, genomic medicine seeks to reduce reactive medicine (that is, treating a disease only upon presentation of symptoms), in favour of preventative medicine.[127] Conventional medicine has endeavoured to develop a preventative approach to medicine, for instance, statins are used to lower cholesterol to prevent cardiovascular disease, but genomics medicine will be able to more accurately and timeously inform the preventative interventions strategy, with less reliance on patient and family history and presentation of symptoms, which may be incomplete.[128]

The ultimate goal of genomic medicine is to have the patient's genomic profile (that is, the data on all the patient's genes and other genetic material) available to the physician so that a route of treatment can be chosen that will minimise harms and maximise benefits to the patient. Hence, it is apparent that genetic testing is a tenet of this approach. The development of genetic diagnostic technologies will have to progress simultaneously with genomic treatment technologies; that is, as new diseases emerge, or at least, as genes are identified that correlate with specific diseases and are recognised as targets in treatments,[129] there must be sufficient capability to diagnose whether an individual possesses those specific genes responsible — the example of DNA microarrays relates to this and will be discussed below. A genetic test may not be confined to only direct analysis of genetic material, but may also include testing for a gene product like protein.[130] These genes and gene products will then have to be available for ensuing R&D of genetic diagnostic technologies.

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[125] World Health Organization (note 92 above; 4-5).
[126] Ibid.
[127] Campbell (note 83 above; 258-279).

[128] World Health Organization (note 92 above; 4-5).
[129] A gene may be regarded as a 'target' as its expression may be regulated by pharmaceutical or biotechnological treatments. Consequently, functional molecules such as proteins that are encoded by DNA are may also be targets of pharmaceutical treatment. These treatments, depending on how the expression of the gene affects the diseased state, may prevent, retard or accelerate gene expression.

[130] World Health Organization (note 98 above; 15).

Whilst this focus on the patient necessitates the profiling of an individual's genome, understanding the data of this profile requires extensive R&D. The structure, function, location and evolution of genes and their variants, as well as the rest of the DNA within the genome needs to be clarified and understood in relation to diseases. As with any scientific study, this requires large-scale studies in order to derive accurate and statistically significant information. This requirement emphasises the importance of genomic databases — databases storing the information pertaining to individuals' sequenced and mapped genomes — in future medical practice. The databases, which will be discussed below, could also store information on the environmental factors to which a patient is exposed, strengthening the study of multifactorial diseases that are often the subject of genomic medicine.

What is critical to note from this discussion is the nature of genomic medicine with regard to its two technological components: genomic knowledge (such as DNA sequences and associated disease risk), and the diagnostic and therapeutic technologies that emerge downstream to this knowledge. The examples of these are briefly discussed so as to create an appreciation for the essential nature of genomic knowledge in genomic medicine innovation.

(i) Pharmacogenomics and DNA microarrays: the application of genomic knowledge

In genomic medicine, genomic knowledge can be applied to downstream diagnostic or therapeutic technologies, mentioned above. The examples of DNA microarrays and pharmacogenomics are used to illustrate the necessity of genomic knowledge in both these types of technologies, respectively.

Pharmacogenomics is the study of how genomes affect a person's response to medications in order to develop effective and safe medications, tailored to a person's genomic makeup.[131] These medications may be existing medications that are tested in different genomic sub-populations, or may be new medications that are developed using genomic knowledge. An example of this would be the highly popular medication used to prevent heart attacks and strokes, Plavix.[132] Using knowledge on the variation of the gene *CYP2C19*, researchers realised that certain variants of this gene could not metabolise Plavix, resulting in the FDA issuing a warning that patients should get tested for these variants.[133] This emphasis on genomic testing relates to the second technology, diagnostic technology.

Diagnostic technology may be used in a clinical setting where a patient's genomic profile is captured for further use in treatment decisions, or in research studies, where, using the example of pharmacogenomics, the data generated may be used in the development of downstream applications.

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[131] Genetics Home Reference 'What is pharmacogenomics? (26 September 2017) available at https://ghr.nlm.nih.gov/primer/genomicresearch/pharmacogenomics, accessed on 26 September 2017.

[132] Ibid.

[133] Ibid.

However, these diagnostic technologies rely on the incorporation of DNA sequences into their hardware.[134] An example of this is DNA microarray technology, where a collection of DNA 'spots' are placed on a solid surface. These spots are the DNA sequences of specific genes or other elements of the DNA that are under study, and are used to determine the expression of elements in, for example, disease or treatment response.[135] This will help determine how the gene influences disease progression or responds to medical treatment.

These are not the only example of how genomic knowledge is essential to the development of downstream applications — other examples include genome therapy where the genome is altered. Nonetheless, even without extensive exploration of the downstream technologies, the vital importance of genomic knowledge as a research tool can be appreciated, and it for this reason that the focus of this dissertation is on the impact of IP on genomic knowledge generation and its use.

II. Generating genomic knowledge for application: an insight into genomic databases and biobanks

As noted above, genomic knowledge is a critical component of genomic medicine, providing research tools that can be applied to addressing diseases with a genomic component. The first major step in uncovering this knowledge was seen in the Human Genome Project and in the concurrent efforts by the private company Celera Genomics, under the direction of Craig Venter, to do the same.[136] These examples are discussed below to illustrate these landmark efforts by the public and private sectors, highlighting the need for both, as critical in the advancement of genomic medicine.

(a) The Human Genome: uncovering the reference genome

The Human Genome Project was a 3-billion-dollar, 15-year public initiative,[137] 'brought about by 'international cooperation, scientific excellence and altruism' which led to the production of a 'curated and accurate' reference sequence for the *human* genome, referring to an abstraction of the

[134] R Rouse & G Hardiman 'Microarray technology- an intellectual property perspective' (2003) 4(5) *Pharmacogenomics* 1.
[135] Ibid.

[136] YourGenome 'Why was there a race to sequence the human genome' available at https://www.yourgenome.org/stories/why-was-there-a-race-to-sequence-the-human-genome, accessed on 03 September 2017.

[137] L Hood & L Rowen 'The Human Genome Project: big science transforms biology and medicine' (2013) 5(79) *Genome Medicine* 1.

typical genome of a human being.[138] This led to the cataloguing of a 'parts list 'of most human genes, and thus most human proteins and other important elements, integral for this understanding of system biology.[139] The *human* genome thus described is a mosaic of the genomes of many research participants, and whilst each and every individual has their own unique genome, what the Human Genome Project and other similar projects demonstrated is that individuals of the human species shared distinct elements.[140] Individuals have different variations of genes, which confer varying characteristics, but the location and function of these genes in a normal human profile is the same.[141] Thus, whilst genomic medicine relies on the sequencing of an individual's genes, it is the 'master' information on gene location and function provided by projects such as the Human Genome Project that allows for the holistic application of this sequencing data in genomic medicine. However, the information provided by the Human Genome Project alone is not sufficient for the translation of genomic data.[142] Further data needs to be collected especially on gaps left in the Human Genome Project, such as undiscovered variants, and experimental analyses needs to be conducted to adequately annotate the genome (that is, to indicate the particular gene variant sequenced in the genome, the chromosomal environment, and the functional implications of these factors on the production of downstream molecules).[143]

Genomic medicine focusses on genomic sub-populations that are characterised according to their genomic variation. In both conventional medicine and genomic medicine, studies have statistical power when the sample sizes of the studies are large enough. The statistical power of a test in a study is the probability that the test will correctly detect a difference, if the difference actually exists.[144]

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[138] Ibid.

[139] Ibid.

[140] D R Bentley 'Genomes for medicine' (2004) 429 *Nature* 445.

[141] This is to say that even although a mutant gene may disrupt a particular cellular function by causing the aberrant production of a protein, the cellular function still remains central in the identity of the gene mutation.

[142] Bentley (note 140 above; 445).

[143] Ibid.

[144] The power of a test is influenced by the design of the test and by the sample size. A simple example of this would be flipping a coin. It is already known that there are two options, and in an unrigged coin, there is an equal (50%) chance of getting either tails or heads. However, if ten coins are flipped, it is unlikely that 5 will land on heads and 5 will land on tails. The number of coins will have to be increased until a 50:50 ratio is observed. Thus, a small sample size runs a higher risk of not detecting what *should* be detected, and thus has a lower statistical power. This means that it is unlikely the same results will occur when the experiment is repeated.

An example in genomics medicine could be in a study of whether gene variant X influences progression of disease Y. In a small sample of 10 individuals with X, 9 may have Y. This suggests that X influences progression of Y. But in a much larger sample of 1000 individuals, only 300 may have Y. An appropriate sample size would be one that yields a result that will be seen even if the sample size is

However, due to the blanket, 'one–size fits all' nature of conventional medicine, this is much easier to achieve — often study cohorts are selected from a provincial or national region. In genomic medicine, variations in genes and possible other factors that affect genome function stratify research samples into variant sub-populations. This may mean that research has to extend to a national or global scale to achieve significant statistical power.[145] Additionally, research that is performed at a global level could identify links between diseases and smaller genomic sub-populations — links that may otherwise remain undetected in smaller scale research. To facilitate such genomic research, as seen in the Human Genome Project, 'a powerful new set of research tools, resources and supporting technologies' is needed.[146] This includes not only sample data, but also 'highly sophisticated, substantial database infrastructures'.[147] Therefore, countries and global consortia have created mechanisms like genomic biobanks and databases to collect, store and use genomic data samples. Essentially, these databases contain upstream technologies (or research tools) which will facilitate innovation in downstream technologies such as pharmacogenomics.

The Human Genome Project followed an open approach to data sharing and used open source software.[148] The international cooperation and altruism of this project has been praised by those who maintain that genomic data should be placed in the public domain and should not be privatised.[149]

Proponents of this stance maintain that the human genome is part of the common human heritage and belongs to all people, and should be made freely accessible to the public.[150] This claim will be explored further in the following chapter. However, much has to be said about the privately–run human genome project led by Craig Venter and his team in Celera Genomics. In 1998, Venter started Celera Genomics and announced that his company would also sequence the human genome using a different, newer sequencing technique, as he felt the efforts of the Human Genome Project was too costly and was taking longer than necessary.[151] Unlike the Human Genome Project, Celera intended to privatise its genome sequences granting access to these data only to paying customers, [152] and through patenting roughly 100–300 genes that were important to drug development, although

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increased. And unlike with a coin that has only two options, potentially thousands of genes could be associated with a specific disease, requiring much larger sample sizes.

[145] Farmer & Godard (note 107 above; 16).

[146] Knoppers, Abdul-Rahman & Bédard (note 108 above; 292).

[147] Ibid.

[148] Hood & Rowen (note 137 above).

[149] Ibid.

[150] Ibid.

[151] YourGenome (note 136 above).

[152] Ibid

approximately 6 500 place-holder patent applications were initially filed (and later relinquished).[153] As this was contrary to the public-spiritedness of the Human Genome Project, the race was on to complete the sequencing of the human genome.

In the beginning of 2000, both Celera and the Human Genome Project made a joint public announcement that they had each completed a working draft of the human genome, although there were still gaps to be filled by both contenders.[154] This announcement was made together with the joint declaration by US President Bill Clinton and British Prime Minister Tony Blair that all genome information should be free to the public.[155] In 2001, the Human Genome Project published its findings in *Nature*, with Celera publishing its findings a day later in *Science*.[156] By 2003, The Human Genome Project had completed its final draft of the human genome, and Celera agreed to make its sequences available for non-commercial use, although it limited the amount of data that could be downloaded at any given time.[157] Unfortunately, in 2002, Venter was removed from his presidency at Celera, and pursued improving the application of personalised medicine through sequencing his own genome with a slightly different goal to Celera or the Human Genome project.[158] Whereas Celera and the Human Genome Project concentrated on sequencing one chromosome of each pair of chromosomes in the complete set, Venter decided to sequence both chromosomes in the 23 pairs.[159]

This entry of a private competitor may well have galvanised the efforts of the Human Genome Project, suggesting that private entities could have a necessary role in creating sustainable models to undertake extensive, time-consuming and costly R&D needed before genomics medicine can become a primary route of medical care.[160] As stated by Venter, 'business is the way to drive science forward, and people are finding there's no difference in the goals or outcomes, because for science to impact society, it has to be economically viable'.[161] Celera and the Human Genome Project ran parallel to each other, yet it is likely that they influenced the accomplishment of each other's goals. It is possible that creating a symbiosis between the public and private domains through an open innovation model

[153] BBC News 'Human Gene Patents Defended' (27 October 1999) available at *http://news.bbc.co.uk/2/hi/science/nature/487773.stm*, accessed on 11 December 2017.

[154] M A Shampo & R A Kyle 'J. Craig Venter — the Human Genome Project' (2011) 86(4) *Mayo Clinic Proc* e27.

[155] Ibid.

[156] Ibid.

[157] Wikipedia 'Celera Corporation' (28 November 2017) available at *https://en.wikipedia.org/wiki/Celera_Corporation*, accessed on 11 December 2017.

[158] E Singer 'Craig Venter's Genome' (4 September 2007) available at *https://www.technologyreview.com/s/408606/craig-venters-genome/*, accessed on 11 December 2017.

[159] Ibid.

[160] A Beard 'Life's Work: An interview with J. Craig Venter' (September 2014) available at *https://hbr.org/2014/09/j-craig-venter*, accessed on 11 December 2017.

[161] Ibid.

could accelerate the field of genomics medicine even more. This will be explored further in Chapter Four. However, before exploring the innovation model that may accelerate the field, the aspects that individually contribute to the development of genomic medicine are identified in the following sub-section.

(b) Genomic databases and biobanks: creating research tools for innovation

When considering that the roughly 23 000 genes of the human genome is only about 2% of the genome,[162] and considering the multitude of diseases implicated in genomic medicine, it is not difficult to acknowledge the amount of R&D that will be needed to develop this medical field. This R&D will require an extensive amount of genomic data and samples from which this data can be obtained. The infrastructural requirement to capture and store such data and their associated samples may be 'huge'.[163] It is likely that it is on these grounds that biobanks and large genomic databases have secured a place in the field of genomics research.

Biobanks are repositories of samples from living organisms, which are used in studies to generate information that is stored in databases. This may include genomic data on gene variants and other genome-related molecules, as well as non-genomic data such as environmental factors and epidemiological information, all of which may have a bearing on genomic variation to influence disease progression.[164] These structures are usually based in a regional or national population, for example, the Framingham Heart study is based in Framingham, Massachusetts, and more large-scale initiatives have been established, such as the UK Biobank, the National Biobank of Korea,[165] the Estonia Genome Project and the Icelandic Health Sector Database.[166] However, as it will be discussed below under global consortia, efforts are being to globalise these databases and biobank-related research through networking.

Both biobanks and databases are 'huge infrastructural development[s]', and necessitate 'ongoing governance and management for sample collection, storage and use'.[167] As raised by Huzair and Papaionnou, regarding the UK Biobank, there is the question of 'who should invest to support pharmaceutical innovation…and serve the public interest.'[168] Currently, approximately 60% of

[162] World Health Organisation (note 106 above).

[163] Huzair & Papaioannou (note 53 above; 500).

[164] R Chadwick & S Wilson 'Genomic databases as global public goods' (2004) 10 *Res Publica* 124.

[165] Ibid 211.

[166] Farmer & Godard (note 107 above; 17).

[167] Huzair & Papaioannou (note 53 above; 500).

[168] Ibid.

sponsors for biobanks are government institutions,[169] yet pharmaceutical companies benefit from these resources by developing commercial technologies from their related studies. The CAMBIA BIOS initiative[170] recognises the distinction between the tools for innovation generated by biobanks and stored in databases, and the products of innovation, such as the downstream applications of diagnostics or therapeutic technologies, often produce by private actors.[171] This initiative seeks to create an open, networking platform that addresses how IP may be used in open innovation in biological sciences, including genomics. This type of networking between public and private actors endeavours to alleviate the challenges of the substantial time, investment, research participation and expertise that is involved in creating and applying genomic knowledge so as to 'fully to address all of the complexities of the common disease risk'.[172] Collaborative initiatives involving biobanks and databases, including CAMBIA BIOS,[173] are explored in Chapter Four to assess how their IP policies and structure contribute to open innovation in genomic medicine.

III. Conclusion

WHO states that 'in the long–term, [information generated by genomics will] have major benefits for the prevention, diagnosis and management of many diseases which hitherto have been difficult or impossible to control.'[174] It is for this reason that special attention should be given to the progress and development of genomics, which includes innovation in genomic medicine and access to its technologies.

Genomic medicine requires the genomic profile of an individual in order to inform medical decisions. This profiling requires genomic testing, but a profile alone cannot aid in directing medical decisions if the significance of genomic variants in disease progression is not understood. Thus, an understanding the complexity of the human genome is critical. The development of genetic technologies used to understand human genes is not a new endeavour, however the human genome, in all its complexity, poses a more complicated, and possibly more expensive challenge. A projection of the costs of sequencing an individual genome shows that there has been a dramatic decline in the cost, starting at roughly $100 million in 2001, to approximately $1000 in 2015.[175] This is promising,

[169] Ibid 212.

[170] CAMBIA (note 57 above).

[171] CAMBIA (note 57 above).

[172] Knoppers, Abdul-Rahman & Bédard (note 108 above; 293).

[173] CAMBIA (note 57 above).

[174] World Health Organization (note 106 above; 5).

[175] NHGRI 'DNA Sequencing Costs: Data' (24 May 2016) available at https://www.genome.gov/27541954/dna-sequencing-costs-data/, accessed 26 September 2017.

however if the resulting genomic knowledge is protected by IPRs, further R&D may be expensive — this is discussed in the next chapter. Furthermore, to fully annotate the human genome and develop downstream technologies, significant expertise is needed. Thus, biobanks and genomic databases as components of larger networking initiatives, could be critical structures in accelerating research, whilst addressing these issues of cost and capacity.

It is for this reason that a better model that facilitates access to research tools for innovation in downstream applications should be developed and employed. Intellectual property will have a role in this model, which should allow for both open collaboration and maintaining a sustainable industry. Thus it is important to answer the questions of who should own such genomic knowledge, and how can IPRs be used to facilitate R&D in genomic medicine for further innovation. These questions will be discussed in the following chapters on: a) IPRs pertaining to genomic knowledge; and, b) the open innovation models of biobanks and databases that facilitate innovation in genomic medicine.

Chapter Three: understanding the current IP landscape in genomic medicine

'Light bulb moments' are synonymous with an ingenious, innovative idea. However, innovation is not just a moment; it is a process of many stages. A simplified innovative process begins with an idea, discovery or emergence of new knowledge. These are then used in the design of new technologies, which may occur by tying in old knowledge or inventions, by experimental trial-and-error, or both. Following the invention of the new technology, the technology has to be marketed and commercialised so as to create a consumer market, satisfy this market, and, regarding profit-driven entities, generate a profit. If the technologies are health-related, there may be an additional, regulatory step prior to commercialisation. This multi-step process can be laborious and expensive depending on how many steps an entity controls.

In traditional closed innovation, an entity will control the entire process, incurring significant costs. IPRs then play an important role in securing financial gains for the inventors by limiting the amount of competitors in the market. In this way, securing markets captures value for the inventors from the invention. Thus, an important aspect of closed innovation is the protection and management of IP. However, there has been a shift in the innovation models of certain industries, particularly in the biotechnology and software industries.[176] Escalating costs and burden of resources, which will be discussed further in Chapter Four, are compelling actors in certain industries to limit their activities to fewer steps in the innovation chain.[177] This division of the innovation chain falls under the model of open collaborative innovation, which will be explored in the next chapter. However, this shift does not make IPRs obsolete. In fact, IPRs now adopt an additional role to being an incentive to invent and reward — the role of being an incentive to network with another entity to gain external knowledge for one's own innovation chain.

However, especially in the health-related industries of pharmaceuticals and biotechnology, IPRs, especially in the form of patents, have received criticism for two broad effects: blocking further innovation, and hampering consumer access through trade barriers.[178] The latter will not be discussed herein, as this would require discussion that is too extensive for this dissertation. Instead, the impact of IPRs on innovation will be explored. Through this exploration it will be ascertained how the current IP regime, which has been used to support a closed innovation model, could hinder scientists in accessing upstream technologies for further innovation and so reduce both the scientific progress for public benefit and potential economic gains of the related private sector. The discussion will focus

[176] Gastrow (note 54 above).

[177] Ibid 42.

[178] Vawda & Baker (note 21 above; 73-76).

on patents as these are the main form of IPRs used by biotechnology and pharmaceutical industries. It will be assessed whether patents on parts of the genome (such as gene sequences and non-coding DNA) should be allowed under international and national patent law, considering the value of this knowledge as research tools and the nature of this knowledge as a public good. Using this assessment, the amendment of patent law and how these amendments may facilitate open innovation between the public and private sectors will be recommended.

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I. A brief understanding of patents

Intellectual property refers to 'creations of the mind: inventions; literary and artistic works; and symbols, names and images used in commerce'.[179] Intellectual property rights, in the form of patents, copyrights and trademarks, are rights to ownership of intellectual property, and are enshrined by Article 27(2) of the Universal Declaration on Human Rights which states that:

> 'Everyone has the right to the protection of the moral and material interests resulting from any scientific, literary or artistic production of which he is the author'.[180]

Patents are government-granted privileges that provide exclusive rights to the patent holder to make, use, sell and trade in the patented invention within a particular jurisdiction,[181] usually for a term of 20 years.[182] An invention, as stipulated by Article of 27(1) of TRIPS, is that which is: a) novel (it does not exist in prior art, which is the body of existing knowledge); b) non-obvious (or inventive, as termed some jurisdictions), meaning that it is not obvious to a person skilled in the art to create the invention from prior art; and c), useful or capable of industrial application.[183] Patents may apply to products, processes of manufacture or uses of an invention.[184]

Patents operate under a *quid pro quo* system — they seek to reward the inventor through exclusive rights that will enable him to recoup the costs of inventing, but also for the obligatory disclosure of his invention to the public in a sufficiently detailed manner so as to enable a person skilled in the art to replicate in the invention.[185] With this knowledge, others may apply for a licence

[179] WIPO Publication No.450(E) *What is Intellectual Property* 2.

[180] Universal Declaration (note 1 above; Article 27(2)).

[181] TRIPS Agreement (note 15 above; Article 28(1)).

[182] Ibid Article 27(1)).

[183] Ibid Article 33).

[184] WIPO (note 179 above; 5).

[185] TRIPS Agreement (note 15 above; Article 29).

to use the invention within the patent term, 'invent around' the claims of the patent, or choose to use it once the patent has lapsed.[186] Thus, this information may be used in further innovation that makes a greater range of technologies available for public consumption, and in doing so, may significantly boost economic activity.[187] As set out in Article 7 of TRIPS to be discussed below, the objectives of IP protection are as follows:

> 'promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations.'[188]

This disclosure through patents is juxtaposed to trade secrets, which are based in private law, where information of an invention is not publically disclosed, preventing the public from using this information in further innovation until the trade secret is shared either through private contract or unauthorised disclosure.[189] In this scenario, information may remain undisclosed for an indefinite period of time, which would not support further innovation. Contrary to this, patents attempt to balance the social cost of exclusion to use an invention with the social benefit to information about the invention for further use and innovation. However, contention arises as to whether patent law does actually achieve this balance, and whether patents do not in fact 'deter' innovation.[190] This debate, particularly in the context of genomic medicine, will be explored in the following sections.

II. The impact of patents on genomic medicine: a focus on genomic knowledge

The impact of patents on access to technologies by researchers and consumers has been widely debated over the past decades, especially after the rise of human-rights based litigation challenging pharmaceutical patents.[191] Whilst patents have an economic justification as a reward for the labour and costs incurred by inventors, these also have the potential to create monopolies that prevent access to patented technologies, stifling further innovation along the innovation chain.

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[186] Here the term 'use' refers to the activities mentioned TRIPS.

[187] M B Guaragna *Stimulating innovation in Brazil: a study of intellectual property law, biotechnology and open scientific innovation* (DPhil in Law, Queen Mary University of London, 2016) 70.

[188] TRIPS Agreement (note 15 above; Article 7).

[189] Heller & Eisenberg (note 14 above; 698).

[190] Heller & Eisenberg (note 14 above; 698-699).

[191] *Myriad* (note 24 above).

On the note of research, genomic technologies are heavily reliant on upstream research tools, such as DNA sequences, for their R&D. This was illustrated in the examples of DNA microarrays and pharmacogenomics in Chapter Two. As critical research tools, the privatisation of these sequences through patents may result in their underuse, a phenomenon described as the 'tragedy of the anti-commons' by Eisenberg and Heller.[192] Furthermore, DNA sequences form part of a critical facet of genomic knowledge, which some argue is a public good that should not be privatised.[193] The effect of patents on genomic medicine innovation will be discussed in light of these two arguments.

(a) Genomic knowledge as a public good

As proposed by Clark and Turner, 'knowledge is at the heart of innovation'.[194] This is exemplified by the biotechnology industry, which is a knowledge-based industry where knowledge is derived from research and developed into applications.[195] Both the knowledge and the applications capture not only social value from use in health systems, but also financial value from IP protection and consumer markets (where for-profit entities are concerned). In genomic medicine, the foundational knowledge is that of genomic variants and their role in disease progression. Such knowledge, as research tools, has allowed for a plethora of downstream applications in diagnostics and therapeutics to emerge, justifying the above statement by Clark and Turner. However, knowledge is also regarded as the archetypal public good,[196] and the human genome may be regarded as our 'common human heritage'.[197] As such, genomic knowledge regarding the genome sequences may be considered as a public good, which should benefit the public and not be privatised — this will be explored below.

The nature of goods as public or private has been defined by politics and economics. In a political sense, public goods are defined as 'interests or goods which are associated with a multiplicity of people or communities'.[198] Though this dissertation focuses more on the economic ramifications of IP on genomic medicine innovation, this political definition cannot be discarded as genomics relates to it in two ways: a) research projects like the Human Genome Project require several groups

[192] Eisenberg & Heller (note 14 above).

[193] Huzair & Papaioannou (note 53 above; 500-501).

[194] J L Clark & P Turner 'Extending the Knowledge-based View: An Examination of Intellectual Property Strategies in Australian Biotechnology Firms' (2003) 21(1) *Prometheus* 96.

[195] Ibid 88.

[196] E Dowdeswell et al 'Realising the promise of genomics: exploring governance' (2006) 8(1/2) *Int J Biotechnology* 135.

[197] P N Ossorio 'The Human genome as Common Human Heritage: Common Sense or Legal Nonsense?' (2007) *Journal of Law, Medicine & Ethics* 425.

[198] Huzair & Papaioannou (note 53 above; 501).

of participants from different communities in order for the research to be translated into effective and viable applications that address multiple interests groups, for example, analysing the variations in the genome across ethnicities could highlight which ethnic groups are more susceptible to onset of certain diseases; and b), in such public initiatives, the involved scientists and related personnel may come from many different national background and sectors. Therefore, groups have argued that the human genome (as genomic knowledge) is a public good, and because it is shared amongst people and inherited through generations, is also part of the 'common human heritage'.[199] The Human Genome Organisation (HUGO) Ethics Committee Statement on Human Genomic Databases is one such proponent, taking the view that such databases are 'global public goods', and so should be treated as public resources to promote the access and flow of information.[200] It is for this reason that these groups argue against patenting the parts of the human genome, such as DNA sequences. This is a strong argument, but fails to evaluate genomic knowledge as a tool in the innovation process. Certainly the sentiment of a 'common human heritage' calls for unhindered access to genomic knowledge, but this fails to address how innovation can be derived from genomic knowledge sans the traditional incentive of IPRs. Thus, the economic definition of private and public goods must be applied to genomic knowledge to evaluate to what extent this knowledge should reside in the public domain or be privatised.

From an economics perspective, public goods are non-excludable, meaning that no person can be 'effectively excluded from using the good'.[201] Public goods are also non-rivalrous, meaning that the use of the good by one person does not reduce the availability of the good for use by another.[202] Knowledge is considered the archetypal public good,[203] but this stance is evolving as throughout the decades, knowledge, and not merely the applications deriving from knowledge, have been subjected to privatisation by patents, making such knowledge excludable. Indeed, holding knowledge as a trade secret excludes others from using it, and so knowledge may not actually be a pure public good. In this case, where a good is excludable and non-rivalrous, it is considered as a 'club good'.[204]

Biobanks and genomic databases, specifically those associated with consortia, as mentioned in Chapter Two, govern common pool resources, that is, samples are rivalrous (they can be depleted or be made unavailable through use), but are intended to be non-excludable (available to all researchers, often pending research approval). However the knowledge that is generated, which

[199] Knoppers, Abdul-Rahman & Bédard (note 108 above).
[200] Ibid.

[201] Huzair & Papaioannou (note 53 above; 501).

[202] Ibid.

[203] Dowdeswell et al (note 196 above; 135).

[204] Huzair & Papaioannou (note 53 above; 502).

includes genomic knowledge, is non-rivalrous and does not necessarily have to be excludable.[205] In many cases, public (or semi-public) biobanks and databases endeavour to protect the non-excludability of knowledge, that is, the knowledge generated from research on the samples is kept in the public domain for others to access.[206] This is mainly because samples from which this knowledge is obtained are donated by the public, and so the public interest to access this knowledge and avail it for future beneficial innovation is considered.

However, generating knowledge, especially in risky and high-technology fields such as genomics, is expensive, and so it is unrealistic to assume that continued production of genomic knowledge will continue without a means to guarantee a profit. Public initiatives and government intervention shoulder these costs to keep the knowledge in the public domain to satisfy all interests to access and demand, but looking at the cost of the Human Genome Project, listed in chapter two, it may be unwise to rely on these for the future of genomic research. This does not necessarily mean that privatisation of genomic knowledge is the solution, as will be discussed further on, although the private sector may have access to greater resources for the generation of genomic knowledge. Thus, what may be needed are collaborations between the private and public sectors where genomic knowledge is generated in the public domain and used to develop technologies for privatisation. As biobanks and related consortia already face the dilemma of whether the privatisation of the downstream technologies, derived from public participation should be condoned,[207] what is needed are clear IP policies on genomic knowledge, downstream innovation and collaboration. However, as policy is informed by law, patent law, which will be discussed below, is critical in determining whether genomic knowledge remains in the public domain, and how it is used as research tools if it is privatised. The impact of patents on genomic knowledge as a research tool will be discussed below.

(b) The tragedy of the anti-commons: the underuse of genomic knowledge as research tools

As drawn from the *Ligand Pharmaceuticals v. La Jolla Research* case,[208] research tools have significant impacts on basic research activities and on commercial treatment discovery. Science innovation is a cumulative process where inventions or knowledge are constantly improved or used to create new inventions.[209] For this to occur, scientists need to be able to access and use the inventions

[205] Ibid.

[206] Knoppers, Abdul-Rahman & Bédard (note 108 above).

[207] Umea University's biobank in Sweden and the Type 1 Diabetes Genetic Consortium.

[208] *Ligand Pharms, Inc v La Jolla Cancer Research Found,* (1993) No. 93-01895 S.D. Cal.

[209] J Pénin 'More open than open innovation? Rethinking the concept of openness in innovation studies' (2008) 18 *Juillet* 8.

or knowledge generated by others. Premarket, upstream research yields knowledge that can be used as research tools in the further development of a technology. Genomic knowledge, such as sequences of coding and non-coding DNA regions, is valuable as research tools and a foundation for further innovation in genomic medicine, for example, gene sequences can be used in creating DNA microarrays for genome testing as discussed in Chapter Two.

Biomedical research, which includes pharmaceutical and biotechnology research, has traditionally existed in the public sector,[210] with universities as prolific hubs of research. Governments frequently funded such research, especially at universities, and the results were placed in the public domain through publication.[211] However, in recent years, the promise of such research to yield profitable products has been recognised, and a shift has occurred in universities to patent the products of their research and not only to publish their results. Some countries even have legislation that supports this, such as the Patent and Trademark Law Amendments Act (commonly referred to as the Bayh-Doyle Act)[212] in the US and the Intellectual Property Rights Act in South Africa,[213] possibly to encourage accelerated growth of sectors — these will be examined below. This shift towards privatising knowledge that may otherwise have existed in the public domain potentially reduces the access and use of important upstream resources — a phenomenon called 'the tragedy of the anti-commons'.[214]

In their article, Eisenberg and Heller propose the 'tragedy of the anti-commons' in biomedical research.[215] The tragedy of the anti-commons derives from the contrasting proposition of the 'tragedy of the commons'. The latter was a theory proposed by ecologist Garrett Hardin which states that people overuse resources they commonly own to satisfy their self–interests, which results in the depletion of the resource, contrary to the common of all users,[216] for example, communal land may be farmed excessively. This occurs because there are no private rights to protect how the resource is used, and is analogous to tangible goods, such as biological samples, placed in the public domain.[217] Thus, to protect common resources from overuse and exploitation, private rights to these resources were granted in hopes of conserving these resources. Knowledge has been included as a resource that

[210] D Nicol & J Nielsen 'The Australian Medical Biotechnology Industry and Access to Intellectual Property: Issues for Patent Law Development' (2001) 23(347) *Sydney LawReview* 353.

[211] Ibid.

[212] Patent and Trademark Law Amendments (1980).

[213] Intellectual Property Rights From Publicly Financed Research and Development Act No. 51 of 2008.

[214] Eisenberg & Heller (note 14 above; 698).

[215] Ibid.

[216] G Hardin 'The Tragedy of the Commons' (1968) 162 (3859) *Science* 1243–1248.

[217] Ibid.

requires protection, but as it will be substantiated further on, knowledge cannot be depleted as it is used, nullifying the justification that knowledge should be privatised to conserve it.

The tragedy of the anti-commons posits that at present resources have been privatised too extensively, preventing access to these resources, and effectively underusing them. This is not limited to the patenting activities of universities, but these entities are prolific hubs of premarket, upstream scientific research, and are usually publically-funded. This proposed tragedy underlies the rationale for the Bermuda Principles[218] signed by the Human Genome Project consortia to place primary gene sequences in the public domain, discussed in chapter two. In this way, the consortia sought to maximise the use of this basic scientific resource, and so was jolted by Celera's threat to privatise their own corresponding genomic research.[219]

In biomedical science, including biotechnology, Eisenberg and Heller propose that extensive patenting leads to 'patent thickets', that is, when many patents are held for a particular technology.[220] In order to access this technology for use in R&D or in a clinical setting, the potential user would have to gain licenses for a number of patents, or risk infringements.[221] This may be a time-consuming and expensive task, and may deter R&D and use of the invention. Furthermore, where there is fragmentation of patents, that is, each of the many patents on a technology are held by multiple holders, license negotiations may be more arduous and costly, and there is no guarantee that every patent holder will agree to licensing out their patent.

In the context of biotechnology, the tragedy of the anti-commons can be discussed in terms of concurrent fragments and stacking licenses. Concurrent fragments of IPRs refers to when multiple patents required for a technology are held by many different patent holders, requiring extensive licensing agreements to avoid infringement. Eisenberg and Heller propose that as more patents exist for a technology, the risk of infringement increases, and it is more likely to deter potential innovation.[222] This is of particular interest in genomic diagnostic and therapeutic technologies, whose R&D require multiple gene sequences to be used simultaneously. Using the example of genomic microarray technology for diabetes, if a microarray for this multifactorial disease was to be developed, many genes of the genome, and possibly non-coding regions, would be required to develop the technology. If each of these genes and non-coding regions are patented, a developer would have to negotiate multiple licenses before being able to develop the microarray technology.[223] This may be a formidable task in terms of time and costs, and could deter the envisioned innovation.

[218] Bermuda Principles (1996).
[219] YourGenome (note 136 above).
[220] Ibid.
[221] Ibid.
[222] Ibid.
[223] Rouse & Hardiman (note 134 above; 1).

Additionally, depending on the contract of the licenses, selling and use of the microarray technology may be subject to additional royalty payments, as it will be discussed below under stacked licenses.

A particular incident highlights the challenge of concurrent fragments in genomic technologies. In 1991, the (National Institutes of Health) NIH filed patents for expressed sequence tags (ESTs), which are gene fragments that signal how genes are expressed, and are used in genomics to identify genes and families of genes, and map these.[224] Unlike with the case of Myriad Genetics discussed below,[225] the outcry was not necessarily that gene sequences were being patented, but that the function of these ESTs were largely unknown.[226] As ESTs were correctly thought to be powerful research tools in genome analysis, patenting these ESTs potentially had the effect of hindering efficient genomic research as in many cases ESTs were not yet corresponded to their particular genes, and even if they were, the patents would prevent further R&D in the absence of licenses. The NIH abandoned their attempt to patent these tools, although private firms continued to patent ESTs and genes whose function were unknown.[227] In the development of genomic technologies for genomic medicine, patenting many ESTs and their associated genes could hinder R&D for a particular application, for example the microarray for diabetes, as licenses for each of the multiple ESTs and related genes may be needed before R&D can ensue.[228] This further translates to the use of the technology, which will be discussed under stacking licenses.

A stacked license is that which goes beyond the patented, licensed research tool to the ensuing downstream technologies.[229] In many cases, research tools enable the development of valuable commercial technologies, but because the research tool may not be directly be incorporated into the technology, the patent holder of the research tool does not reap the downstream value his tool helped create. An example of this would be in pharmacogenomics, where genomes sequences would be used to research a medical treatment, but the actual sequences are not in the medication. In this case, patent holders of the sequences will only receive a once-off payment by licensees for use in research, and will not reap the commercial benefits of the medical treatment. A stacked license is a creative attempt to transfer some of these benefits of patent holders of upstream technologies. An example of a stacked license is a reach-through licensing agreement (RTLA).[230] An RTLA gives the patent holder rights to the downstream technology developed by the licensee.[231] These rights may be exclusive or non-

[224] Eisenberg & Heller (note 14 above; 699).
[225] *Myriad* (note 24 above).
[226] Eisenberg & Heller (note 14 above; 699).
[227] Ibid.
[228] Ibid.
[229] Ibid.
[230] Ibid.
[231] Ibid.

exclusive licenses to use the technology (to be explained in Chapter Four), and/or royalty rights. Where the RTLA stipulates exclusive licensing to the licensor, future innovation or use of the technology may be blocked as licensors now have bargaining power over the downstream technology, which may fall beyond the scope of their actual patents.[232]

However, RTLAs do provide a potential loophole to pursue otherwise costly research — licensors may only ask for a small upfront fee in anticipation of receiving royalties on the downstream technology, instead of asking for a larger, once-off payment for the license and receiving no further royalties.[233] This simplifies the initiation of the R&D by the licensee. Although where a downstream technology requires many research tools, and thus incurs multiple RTLAs, this may not be a feasible solution, especially if the expected commercial value is low, as may be the case in stratified markets. In this case, royalties must be paid to many licensors, and is termed 'royalty stacking'.[234] Cetus Corporation attempted to stack royalties on all products developed from their licensed technology called polymerase chain reaction, an integral technology in genome analysis, but was met with resistance.[235]

A particular challenge arises in negotiating licenses in genomic technologies due to the nature of the upstream research tools and technologies. Genes and non-coding regions of the genome, which are critical components of the research into and hardware of diagnostic and therapeutic technologies of genomic medicine, are non-substitutable. This exponentially increases the bargaining power of patent holders, who may hold out on licensing until satisfactory terms and conditions are applied. Furthermore, it is difficult to successfully 'invent around' DNA sequences, especially if the patent claims are broad.[236] Using the example of the human erythropoietin protein in the case of *Amgen, Inc v Chugai Pharm Co,*[237] the claims to the erythropoietin protein (traded as EPOGEN) were broad, as it covered *any* 'purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin', which would include chemically synthesised DNA and naturally-occurring DNA. These were found by the court to be valid and infringed by Chugai Pharm Co, forcing competitors to 'invent around' the product claims, for example the private company Hoffman–La

[232] Ibid 698.

[233] Ibid.

[234] E van Zimmeren et al 'Patent pool and clearinghouses in the life science' (2011) 29(11) *Trends in Biotechnology Trends in Biotechnology* 569.

[235] Eisenberg & Heller (note 14 above; 699).

[236] D Nicol 'Cooperative Intellectual Property in Biotechnology' (2007) 4(1) *SCRIPT-ed* 139.

[237] *Amgen, Inc v Chugai Pharm Co,* 706 (1989) F. Supp. 94, 94 D. Mass.

Roche chemically altered its erythropoietin protein by conjugating it to another compound.[238] However, as Roche still uses the DNA sequence in producing the erythropoietin protein prior to conjugation, Amgen sued the company,[239] and Roche was ordered by the district court not to import its product to the US.[240] As mentioned in the above section, infringement may be avoided by public sector researchers using research or experimental exemption, although this is not always clear. Additionally, if a technology resulting from such research were to be commercialised, and if it is clear that patented technology was used, inventors run this risk of infringement, as will be discussed under the *Myriad* case.[241]

These examples illustrate the tragedy of the anti–commons, but Heller and Eisenberg do concede that privatisation through IPRs may fortify the incentive to undertake risky and high–investment research, and could allow for the distribution of profits more equitably as the rights clearly delineate who is to reap according to what he has sown.[242] Furthermore, there are means to circumvent the challenges of multiple negotiations. Developers have the option of employing experienced and knowledgeable lawyers to expedite the negotiation process, however, this is only feasible if the developers have the financial means to do so. Compulsory licenses, whereby the government instructs that the patent–holders to grant the developers the right to use the patented technology, may also be used.[243] The debate on the effectiveness of compulsory licensing is extensive, and will not be discussed here, but what is noteworthy is that it is a measure to be used only after negotiations with the patent owner have failed, [244] and it is relatively rarely used, so it may not be an effective solution.[245]

Moreover, there is the argument that there is little evidence that the anti–commons is prevalence problem that will persist in biomedical sciences. Whilst Gold observes that in the pharmaceutical industry, there are fewer new medications produced each year, which he attributes to heightened patenting,[246] in Kaplan's review of studies on the anti–commons effect, he finds there is

[238] R Cook-Deegan & C Heaney 'Patents in Genomics and Human Genetics' (2010) 11 *Annu Rev Hum Genet* 396–397.

[239] Ibid.

[240] Ibid.

[241] *Myriad* (note 24 above).

[242] Heller & Eisenberg (note 14 above; 698).

[243] TRIPS Agreement (note 15 above; Article 31).

[244] E R Gold et al 'Are Patents Impeding Medical Care and Innovation?' (2009) 7(1) *PLoS Medicine* 2.

[245] R Beall & R Kuhn 'Trends in Compulsory Licensing of Pharmaceuticals Since the Doha Declaration: A Database Analysis' (2012) 9(1) *PLoS Medicine* e1001154.

[246] Gold et al (note 244 above; 2).

little conclusive evidence on the existence of this tragedy in the biomedical sciences.[247] Heller and Eisenberg note that private arrangements have been created to reduce the potential obstacles of multiple, overlapping IPRs, and such arrangements include bundling of licenses, clearinghouses and patent pools, as well as practicing non–exclusive licensing, all of which are discussed further on.[248] As these become more established in the industry, negotiating licenses may become simpler, enabling wider use of the patented resource. The feasibility of such arrangements will be explored further in ensuing sections.

(i) Merck and the SNP Consortium: the private sector's attempts to counter the anti-commons

As mentioned above, IPRs owners may devise an arrangement to alleviate the obstacles of privatisation. And so, although private actors are often accused of placing profit before public interest, contributing to the perceived anti-commons at the expense of further innovation, this is not always the case, as demonstrated by the following actions of private actors. One such action, important event in the timeline of genomics development, is that of the Merck Gene Index. In 1994, Merck, a private pharmaceutical company, together with the Gene Sequencing Center at Washington University, initiated a project to identify gene sequences and place these in the public domain.[249] Four years later, over 800 000 gene sequences had been released into the public domain where any interested researcher could access the data.[250] This move was not purely philanthropic, although it did enable open access to the data.[251] By building this database in the public domain, Merck effectively prevented other entities from privatising the same knowledge, meaning that Merck would not have to enter into license negotiations as a licensee and incur license and transaction costs.[252]

The success of this pre-emption in bolstering genomic research prompted further initiatives, such as the SNP consortium, where eleven pharmaceutical companies and the Wellcome Trust collaborated to share data on research into genome variations called single nucleotide polymorphisms (SNP) and disease associations.[253] Though the data was placed in the public domain, the consortium initially filed patents to protect data that was at high risk of being patented by other entities. These

[247] Ibid 3.

[248] Heller & Eisenberg (note 14 above; 700).

[249] Chesbrough & Appleyard (note 84 above; 72).

[250] B M Frishmann, M J Madison, K J Strandburg *Governing Knowledge Commons* (2014) 121.

[251] Ibid.

[252] Ibid.

[253] Ibid.

patents were then abandoned once the consortium placed the data in the public domain. This is a good example of IP strategy used to protect genomic knowledge.[254]

These two examples illustrate how valuable genomic knowledge is for commercial prospects — companies are willing to forgo IPRs and enter into collaborations to protect their interests to innovation down the line, and so openness is not only a model for public actors to share their scientific endeavours and avail it to the public for use. These collaborative efforts between private and public entities could be regarded as a foundation for openness in the genomics world, and more recent initiatives will be explored in the following chapter.

(c) IPRs on publically-funded technologies: the private rights granted to genomic knowledge generators

The anti-commons is by no means restricted to the patenting activities of large companies in the private sector. Publically-funded entities, such as universities and research institutes, biotechnology start-ups and non-profit organisations are prolific generators of genomic knowledge, and as such, may contribute to the anti-commons through their own patenting activities. As these entities are often driven by state-funding, it is questioned whether the results of their research should not be placed in the public domain to be used for the benefit of the public. Two ground-breaking additions to national legislature were made regarding this question in the US and SA with the Bayh-Dole Act[255] and the IPR Act[256] respectively. These statutes changed the IP activities of publically-funded entities to promote the ownership of inventions by these entities rather than the state. By granting universities, small businesses and non-profit organisations rights to their state-funded inventions, these Acts endeavour to encourage these entities to transfer their technologies from the laboratory to the market through commercialisation, as governments may not have the resources to commercialise all the projects they fund.[257] In this way, the tragedy of the anti-commons and underusing inventions is lessened as inventions are commercialised for utilisation by the public.[258] Importantly, the goal of such legislation is to promote scientific progress by unifying the policy on government-funded inventions. As these two Acts share many similarities, they will be discussed simultaneously below

[254] Cook-Deegan & Heaney (note 238 above; 401).

[255] Patent and Trademark Law Amendments (note 212 above).

[256] IPR Act (note 213 above).

[257] A Barratt 'Lessons from Bayh-Dole: Reflections on the *Intellectual Property Rights from Publicly Financed Research and Development Act*' (2010) 35(2) *Journal for Juridical Science* 31.

[258] IPR Act (note 213 above; s 2(1)).

to determine how they may influence the privatisation of genomic knowledge and the collaboration between private and public sectors.

In the US, two of the objectives of the Bayh-Dole Act are:

> 'to promote *collaboration* between commercial concerns and non-profit organizations, including universities; to ensure that inventions made by non-profit organizations and small business firms are used in a manner to promote free competition and enterprise *without unduly encumbering future research and discovery*'[259] (emphasis added)

Though these objectives are not explicitly stated in the IPR Act, the provisions of the IPR Act mirror those of the Bayh-Dole Act that seek to address these objectives.

In section 202(c)(3) of the Bayh-Dole Act, the above-mentioned entities are required to patent any state-funded invention that they intend to own and commercialise.[260] The IPR Act also stipulates that IP must be protected from appropriation, although it does not explicitly state that this must be done through patenting.[261] It is assumed that a patent encourages commercialisation as it secures a market for the entity, and it also allows for the dissemination of knowledge through disclosure and licensing. Concerning licensing, both Acts stipulate that priority must be given to small businesses,[262] with the IPR Act preferring non-exclusive licensing.[263] The Bayh-Dole Act states that the state must be granted a non-exclusive, irrevocable, non-transferrable, paid-up license.[264] This is mirrored by the IPR Act, which stipulates that an irrevocable, royalty-free license must be granted to the state.[265]

Through these licensing provisions, it seems that the objectives of collaboration between the two sectors, and free competition and enterprise is being promoted. Furthermore, under the Bayh-Dole Act, if entities agree to license these inventions, royalties have to be shared with the state, and a percentage has to be invested to further scientific R&D, thus attempting to satisfy the second objective listed above.[266] The IPR Act also calls for a portion of the resulting revenue to be allocated for further scientific development.[267] However, for these licensing provisions to be effective in

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[259] Title 35 of the United States Code (USC) s 200.

[260] Ibid s 202(c)(3).

[261] IPR Act (note 258 above; s 2(2)(b)).

[262] USC (note 259 above; s 202(c)(7)); IPR Act (note 258 above; s 11(1)(b)).

[263] IPR Act (note 258 above; s 11(1)(a)).

[264] USC (note 259 above; s 202(c)(7)).

[265] IPR Act (note 258 above; s 11(1)(e)).

[266] Ibid.

[267] Ibid s 10(5)(a).

transferring technology from the laboratory to market, small businesses must be able to commercialise these technologies maximally. The sentiment of collaboration between state-funded entities should not rule out the possibility that larger private actors may more effectively achieve the objective of utilising the invention. Though the Bayh-Dole Act does not lean towards the involvement of larger private entities through its provisions, the IPR Act does recognise that:

> 'A private entity or organisation may become an exclusive licensee of intellectual property emanating from publicly financed research and development undertaken at an institution if such private entity or organisation has the capacity to manage and commercialise the intellectual property in a manner that benefits the Republic.'[268]

Thus, whilst the Bayh-Dole Act makes collaboration an objective, it is actually the provisions of the IPR Act that may allow for more feasible collaborations for the commercialisation of technology. Therefore, policy on state-funded inventions should encourage collaboration that encompasses a diversity of actors so as to provide an even more regulated approach to openness.

As universities, biotechnology start-ups and non-profit organisations are primary contributors to the generation of genomic knowledge, it could be assumed that, in the absence of clear patent laws regarding DNA sequences and uses in research methods, which will be discussed below, these entities may ring-fence valuable knowledge needed for downstream applications by other entities through patenting. Whether this has indeed been the case requires further research beyond the scope of this dissertation.

In their study, Huang and Murray find that gene patenting decreases public genetic knowledge, an effect that is exacerbated by increasing patent scope, private sector ownership, thickets and fragmented patent ownership.[269] However, Eisenberg and Heller do acknowledge the potential role of privatisation in upstream research, noting that it 'fortif[ies] incentives to undertake risky research projects'.[270] Furthermore, Kaplan observes that 'there is little empirical evidence that an anti-commons problem is impeding innovation'.[271] These diverging viewpoints on the pervasiveness of the anti-commons tragedy suggest that as yet patents can neither be absolved of their posited impediment to innovation, nor can they be prohibited on the basis of the anti-commons. Rather, it is recommended that more industry- and sector-specific research be conducted regarding the anti-

[268] Ibid s 15.
[269] Ibid.
[270] Eisenberg & Heller (note 14215 above; 698).
[271] Gold et al (note 244 above; 2).

commons effect created by the patenting upstream research tools such as genome sequences, which will be discussed below.

III. Patenting Genome Sequences

When Celera announced its intent to patent the genomic sequences it uncovered, the Human Genome Project responded by accelerating its efforts so as to win the race and place its reference genome in the public domain (as elaborated on in the previous chapter). Since this race, patenting of genes has garnered global attention, with a simultaneous rise in litigation against DNA patents, mostly in developed countries. Indeed, in the US, there was a motion to pass the Genomic Research and Accessibility Act, which would end patenting of genes.[272] The number of DNA patents, on full or partial sequences, has increased over the years in the countries producing the most biomedical innovations. Thus GeneWatch UK noticed an upward trend in gene patenting in the UK.[273] However, investigators analysing gene patenting in the US should observe a decline in gene patents since the judgement of *Myriad*[274] where patents on natural DNA sequences were declared non-patentable (to be discussed below). These discrepancies arise from the fact that international and national patent laws are either not clear on the subject of DNA patenting, or that they are not aligned. The laws on these research tools will affect the IP policies created for open innovation initiatives by consortia involving biobanks and genomic databases, as well as downstream developers, and will be explored in Chapter Four. Thus, the legal instruments — in particular, TRIPS, and the national or regional patent laws of the US, the EU and SA— as well as relevant litigation on DNA patenting and further innovation will be examined. Based on this, recommendations on how these laws can be amended so as to facilitate IP policies that align with open innovation principles will be made.

(a) Examining international patent law: the TRIPS agreement

The examination begins with an international legal instrument, the TRIPS agreement, which binds 162 member states, and thus has a significant influence on the global landscape of IPRs. The standards provisions of patents, relating to patent term and invention criteria, enclosed in TRIPS have been outlined in the above section. Though TRIPS seeks to harmonise IP law across states, the language of certain provisions allows for flexibility in interpretation. The most pertinent of such provisions to this discussion of DNA patenting are those of Article 27. Whilst Articles 27(2) and (3) allows

[272] C M Holman 'The impact of human gene patents on innovation and access: a survey of human gene patent litigation' (2007) 76(2) *eScholarship UC Berkeley* 295–296.

[273] Nicol & Nielsen (note 210 above; 360).

[274] *Myriad* (note 24 above).

members to exclude certain subject matter from patentability, it is neither specific in its exclusions, not are member states obliged to do so. Indeed, *methods* of diagnosis, therapy and surgery of humans may be excluded, but this in itself does not exclude diagnostic or therapeutic genomic technologies.[275] The gene patent debate more likely hinges on the interpretation of Articles 27(1) and (2). Where Article 27(1) states that there may be no discrimination in the fields of technology on what is patentable,[276] two overarching stipulations apply that may be used to challenge patents in genomic technologies. Firstly, the invention claimed must fulfil the criteria of inventiveness, novelty and industrial application.[277] Litigants have challenged human gene patents based on these grounds. Secondly, members may exclude inventions from patentability if they are contrary to public policy or if the inventions protect human health.[278] Considering the global public good nature of genomic knowledge, discussed above, it may be seen as contrary to public policy to patent genes as inventions. A second argument could be made that it is contrary to public health to patent basic science that is critical as a research tool.

Article 8, which outlines the principles of TRIPS, grants members the freedom to adopt measures that 'protect public health', 'promote the public interest in sectors of vital importance to their socio-economic and technological development', and 'prevent the abuse of intellectual property rights by right holders'.[279] In light of these freedoms, the national/regional patent law of the US, the EU and SA, the choice of which has been justified in Chapter One, will be examined. These laws will be explored with reference to the landmark precedent set by the US *Myriad* case[280] that led to a revision of United States Patent and Trademark Office (USPTO) guidelines.[281]

(b) The role of *Myriad* in patent office practice

Myriad Genetics is a US-based molecular diagnostic company that held patents for the breast cancer genes, *BRCA1* and *BRCA2*. Under the prior USPTO guidelines, genes were patentable as they were regarded as 'compositions of matter'.[282] The company offered testing for the variants of these genes, some of which are associated with higher incidences of breast and ovarian cancer in women, but was

[275] TRIPS Agreement (note 15 above; Article 27(3)).

[276] Ibid Article 27(1).

[277] Ibid Article 27(1).

[278] Ibid Article 27(2).

[279] Ibid Article 8.

[280] *Myriad* (note 24 above).

[281] USPTO Memorandum *Supreme Court Decision in Association for Molecular Pathology v. Myriad Genetics, Inc.* (13 June 2013).

[282] USC (note 259 above; s 101).

not the only provider which used these genes in their diagnostic testing. In the ensuing litigation, Myriad challenged competing providers in attempts to secure a monopoly over the diagnostic service.[283] This began with litigation against OncorMed[284] and the University of Pennsylvania[285] that forced both competitors agreed to leave the commercial testing market and created a monopoly over the testing for these genes by Myriad. In this instance, the use of the genes in non-commercial research was not challenged. The risks of a monopoly are that: a) costs of services or products can be raised; b) logistics may hinder patient access; c) the company can deny access to goods; d) there is less incentive for a company to improve on the existing technology;[286] and, e) all the information about the gene variants is controlled by one entity, which is not necessarily unbeneficial if the company has interests in maximally developing this information. The threat of these risks led to the landmark case *Association for Molecular Pathology v Myriad Genetics, Inc*[287] where a precedent was set regarding the patentability of naturally-occurring DNA sequences,[288] which led to a revision of the USPTO guidelines.[289]

In the above case, the plaintiff, the Association for Molecular Pathology (AMP), challenged many claims of the *BRCA1/2* patents, including the validity of patenting gene sequences, diagnostic methods claims and drug screening claims. Of particular interest to this chapter is the validity of gene patents as patentable subject matter, based on §101 of Title 35 of the Unites States Code (regarding patent law) which states that:

> 'Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.'[290]

The plaintiff argued that the patents restricted research for clinicians and limited scientific progress, which is at the heart of this discussion. Additionally, the plaintiff argued that the patent

[283] Myriad engaged in similar litigation in Australia. Though the limitations of this dissertation do not allow an in-depth discussion of this case, the High Court of Australia concurred with the US Supreme Court's ruling on isolate DNA sequences, based on analogous statutory provisions in patent subject matter.

[284] *Myriad Genetics, Inc v OncorMed, Inc,* (1997) No. 97-922 D. Utah.

[285] *Myriad Genetics, Inc v Univ of Pa,* (1999) No. 98-829 D.C. Utah.

[286] Vawda & Baker (note 21 above).

[287] *Myriad* (note 24 above)

[288] USPTO Memorandum *Supreme Court Decision in Association for Molecular Pathology v. Myriad Genetics, Inc.* (13 June 2013).

[289] Ibid.

[290] USC (note 259 above; s 101).

made it impossible for patients to receive second opinions, and they were subjected to high costs of the testing service. The defendant, Myriad Genetics, countered that the 'isolated sequences' were analogous to other chemical compounds, which were patentable under the USPTO provided they were novel and thus different from sequences found in the body. Myriad argued that the isolation procedure sufficiently altered the chemical composition of the isolated sequences. Patent law is the US, in line with the guidelines of TRIPS (to be discussed below) excludes laws of nature from patent eligibility, and the Supreme Court judges in the *Myriad* case cited *Diamond v Chakrabarty* in determining whether the isolated genes had 'markedly different characteristics from any found in nature'.[291] It was found that merely isolating and purifying the two genes did not markedly alter their genetic information, and these patents did not claim for 'new compositions of matter', and were thus ineligible.[292] This led to a revision of the USPTO guidelines, which states that 'examiners should now reject product claims drawn solely to naturally occurring nucleic acids or fragments thereof, whether isolated or not'.[293]

Another claim that was challenged by the plaintiffs was the sequences to cDNA (complementary DNA) of the above genes. Genes contain regions that are coding and non-coding, called exons and introns, respectively.[294] The introns do not code for the gene's functional product (such as a protein), but are involved in the regulation of gene expression in the cell. In a laboratory setting, these introns are unnecessary and removed to form cDNA — a refined form of the isolated DNA.[295] As with natural DNA sequences, cDNA is also an important research tool, often used in place of naturally-occurring sequences, as introns may be redundant to the research.[296] On this matter, the judges found that cDNA is 'not a "product of nature"', and must be created in a laboratory by removing intron sequences, and thus it is patent eligible according to US patent law.[297] However, it must be pointed out that whilst cDNA is produced by removing intron sequences, this is mirrored by machinery in the cell that creates templates of the DNA to be used in making the final product, such as a protein.[298] These templates are also void of introns sequences, these having been removed by the cell machinery. Thus, it is felt that this step is part of existing knowledge and an obvious step, and should render cDNA patent ineligible.

[291] *Diamond v Chakrabarty* 447 U.S. 303.

[292] *Myriad* (note 24 above).

[293] USPTO (note 288 above).

[294] Campbell (note 83 above; 426-479).

[295] Ibid.

[296] Ibid.

[297] *Myriad* (note 24 above).

[298] Campbell (note 83 above; 426-479).

Nonetheless, the judgement on naturally-occurring DNA sequences has been celebrated by the public and scientific community. A key feature of this case is that the judges recognised that patent protection must balance creating incentives for innovation, and should not 'imped[e] the flow of information' that might lead to innovation.[299] Furthermore, they highlighted that Myriad could not rely on that fact that it was the practice of the patent office in the past to grant gene patents.[300] This is a promising stance that invites reconsideration of what may be an outdated system for genomic technologies, as it has already been incorporated into the USPTO guidelines.

(ii) Patenting methods of using research tools: the GTG controversy on non-coding DNA

Literature on DNA patenting has focussed on gene patenting, and little attention has been placed on the patents of non-coding DNA (as explained above, DNA that does not form genes, which code for cell processes). Non-coding DNA is also being recognised as a valuable diagnostics research tool in genomic medicine as it enables the identification and analysis of genes that may be associated with diseases. Recent cases have emerged with a leading firm in non-coding DNA research, Genetic Technologies (GTG), and have highlighted the function of non-coding DNA sequences in identifying gene sequences.

Non-coding sequences and genes are linked, which means that they are inherited together. Therefore, to identify a specific genetic variation, one can look for the non-coding region, which is often a shorter sequence, rather than looking for the longer gene sequence.[301] In many of the GTG cases, the company claimed that other pharmaceutical and biotechnology firms were infringing on their patented methods of detecting genes using the non-coding DNA, such as in the US case of *Genetic Technologies Ltd v Merial LLC.*[302] Here the Federal Court used the two-step test for patent-eligibility. In the first step they determined whether the disputed claim was directed toward patent-ineligible subject matter, and found that GTG's patent was 'directed toward a law of nature'— that is, the linkages between the non-coding and coding regions of DNA was naturally-occurring — which is a patent-ineligible concept.[303] In the second step, the court assessed whether an inventive concept was used that sufficiently transformed the patent-ineligible law of nature into a patent-eligible application.

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[299] Ibid.

[300] Ibid.

[301] Campbell (note 83 above; 426-479).

[302] *Genetic Technologies Ltd. v Merial LLC (Fed. Cir 2016) Nos. 2015–1202, 2015–1203.*

[303] USC (note 259 above; s 101).

The court found that the steps of 'amplification and analysis of the amplified [non-coding] DNA' did not constitute an inventive concept, as these steps were 'well-known, routine and conventional' activity.[304] Furthermore, the court found that analysing the non-coding DNA to detect the coding region was a mental process, which is regarded as patent-ineligible because 'computational methods which can be performed entirely in the human mind are the types of methods that embody the basic tools of scientific and technological work that are free to all men and reserved exclusively to none'.[305] Thus, the patent was declared invalid under 35 USC s 101,[306] setting a precedent for methods that use non-coding DNA as a research tool for genomic analysis.[307] However, this only applied in the US. Other countries have not yet raised the issue of patents on non-coding DNA sequences or how these are used, leaving GTG as a chief patent-holder in non-coding DNA technology. Additionally, the patenting of the sequences was not been challenged as in *Myriad*,[308] although it is likely that non-coding DNA will be treated the same as naturally-occurring isolated gene sequences. This is because the only difference between these two structures is their function, not their chemical structures. Thus, these implications for gene patents would hold for non-coding DNA sequence patents as well.

GTG, as such a leader in non-coding DNA technology, is in a prime position to expand its licensing potential globally. Unlike with the Merck Gene Index,[309] GTG seeks to capture value through licensing patents to increase their revenue for further projects, even extending licensing to academic institutions who stand to benefit commercially from their R&D using non-coding DNA.[310] However, in light of the *Genetic Technologies* case (and similar litigation), it is questionable whether its patents are necessarily valid. If these patents are not valid, GTG's extensive licensing, costing from $75,000 for commercial firms, is an expensive obstacle in the R&D cycle of firms and academic institutions.[311] Nonetheless, in the absence of legal precedent and clarity in the patent law, GTG is primed to expand its licensing program with private and public entities engaged in genomic research. Mervyn Jacobson, executive chairman of GTG says that the licenses for academic institutions are a flat license arrangement of $1 000, which is minimal, and that GTG tries 'to be helpful to publicly

[304] Ibid.

[305] *Genetic Technologies Ltd* (note 302 above).

[306] USC (note 259 above; s 101).

[307] Ibid.

[308] *Myriad* (note 24 above).

[309] Chesbrough & Appleyard (note 84 above; 72).

[310] Bio-IT World 'GTG Primed to Expand Non-coding DNA Licensing' (26 January 2006) available at *http://www.bio-itworld.com/newsitems/2006/january/01-26-06-news-gtg/* accessed on 04 November 2017.

[311] Ibid.

funded organizations'.[312] Future research will determine whether this approach is indeed beneficial, or if the GTG extensive licensing program needs more development under an open innovation paradigm, assuming GTG will not adopt an open access approach like Merck and that patent law or case law will not address the patent-eligibility of non-coding DNA sequences or the methods of gene detection in which they are used.[313]

(c) Examining the patent law of the EU and South Africa

The above cases, and those that were used in deciding their judgements, have set precedents in the US. However, not all jurisdictions concur with these guidelines, as seen in the EU. Under the EU Directive on the legal protection of biotechnological inventions, inventions are still eligible to patent 'even if the structure of that element is identical to that of a natural element', such as isolated DNA.[314] As products of nature, these were recognised as 'basic tools of scientific and technological work' beyond patent protection in *Myriad*, which were required for future innovation.[315] The Directive holds the view that private business interests and public health interests should be considered, and acknowledges that high-risk investment in the fields related to genomics must be rewarded to encourage further investment and industrial development, without creating barriers to trade.[316] Although the Directive does acknowledge the need to protect public health,[317] which may be a gateway should a situation arise where genome patents threaten the interest of the public in genomic healthcare technologies, its current provisions allow genome sequences (natural, isolated or cDNA) to be privatised and kept out of the reach of the public domain, which may not favour open access, as envisioned by certain open innovation practices. However, open innovation does not rely on open access alone, with licensing of IP an integral part of certain practices under this paradigm. Therefore, at least with these clear legal guidelines, IP policies that favour open innovation may still be more easily developed as opposed to countries that do not have clear guidelines, such as SA.

SA is an example of a country that, despite adopting Article 27(1) of TRIPS in its Patents Act No. 57 of 1978[318] (hereafter the Patents Act), does not apply the subject patentability criteria of novelty, inventiveness and utility when granting patents. The European Patent Office, on the other

[312] Ibid.

[313] Ibid.

[314] EU Directive (note 44 above; Article 5(2))

[315] *Myriad* (note 24 above).

[316] EU Directive (note 44 above).

[317] Ibid.

[318] Patents Act No. 57 of 1978 s 25.

hand, follows Article 3 of the EU Directive which lists these criteria. Unlike in the US, the SA patent authority does not issue guidelines that are used to assess patentability, so it could well occur that patent claims on naturally-occurring DNA sequences or otherwise may slip under the radar, left to be challenged in the courts. Nonetheless, this is not entirely ominous as this deficit of direction leaves a space to develop patent law, judicial guidelines or policy that could call for the proper application of the invention criteria (as will be discussed in Chapter Four under the national IP policy of SA). It is suggested that firstly, SA draws on the judgement of *Myriad*[319] to exclude naturally-occurring DNA sequences, isolated or not, and defines what is 'markedly different' to nature, and in the process reviews the decision made on cDNA. Secondly, SA should employ a search-and-examination system where the patent authorities will grant a patent based on the criteria of novelty, inventiveness and utility. This will be explored under SA IP policy reform in the next chapter. By implementing these measures, SA and other countries that follow suit, may create a healthier IP environment for open innovation initiatives.

Certainly, when looking at global consortia, such as the SNP Consortium or the Human Genome Project, international harmonisation regarding patent law and policy is favourable, regardless of the innovation model they employ. TRIPS is in an ideal position to initiate this, given the number of signatories, its objective to harmonise patent law, and the fact that its provisions were adopted into legislation in several countries. Commentators argue that perhaps the World Intellectual Property Organization (WIPO), free from the trade agenda of TRIPS, is a better platform for issues of intellectual property harmonisation.[320] An international consensus on patent law and policy would ease the task of global consortia in advancing genomic health. However, as already seen by the contrasting provisions between the USPTO guidelines and the EU Directive, such a consensus on genomic issues, especially DNA patenting, may be challenging. Furthermore, natural genome sequences are only one aspect of the genomic research tool arsenal. As highlighted in the *Myriad* judgement, a distinction can be made between man-made and naturally occurring sequences, although this is also contentious. Additionally, a lack of IPRs may discourage discovery of these research tools in the private sector, placing the task on the public sector, which may lack the necessary resources. IP law may need to evolve to encompass these issues before solid IP policies of open initiatives can progress smoothly to address public and private interests in innovation.

[319] *Myriad* (note 24 above).
[320] Strandburg (note 42 above).

IV. The benefits of patents on the human genome

In the above sections, the potential of patents on genomic knowledge to hinder scientific progress, however this is a one-sided perspective has been explored. Patents may also have a valuable role to play in managing the flow of information and optimising the use of knowledge. These benefits will be discussed under Burk's theory of patents as data aggregators, and under the practice of licensing in open innovation.

Burk theorises that patents on technologies that contribute to genomic knowledge application, such as genomic testing technologies, act as data aggregators.[321] In his theory, Burk posits that as patents can restrict the number of gene/genome testing providers, data resulting from these genetic tests will accrue within fewer companies' databases. Myriad Genetics is a good example of this as by monopolising the genetic testing of *BRCA1/2*, it received all the data on the possible variants and associated disease information from its patients. As genomic medicine is tethered to the in-depth understanding of these variants, Burk suggests that patents allow for the data to be coordinated at one point (in the case of single provider) rather than being dispersed among competitors as incomplete pockets of data. Thus, he proposes that the amount and diversity of useful data held by a firm decreases as more competitors enter a market, in the absence of licensing agreements and networking, leading to reduced innovative output.

In a closed innovation model, a patent monopoly favours data aggregation, but limits the R&D capabilities of other interested researchers who do not hold the patent rights through licensing. In open innovation, the flow of knowledge will require either open access to data or extensive licensing, both of which will be discussed in Chapter Four. Patents are integral to licensing, as these are licensed out or in, and in this way technology is transferred and a profit may be generated. Currently, licensing practices are modelled under a closed innovation approach, but are essential in Chesbrough's open innovation model to be explored in Chapter Four. But patents are not only a passive means of securing profits through monopolies or licensing, but are also used as indicators of a firm's expertise and potential.[322] This is particularly relevant to Small and Medium Enterprises (SMEs) who may proactively use patent portfolios to attract the partnership or investment of large corporations, or may establish themselves as prolific innovators from whom large companies can buy the patented technologies or agree to licenses. This is especially the case in cross-licensing,[323] where SMEs (or any actor) can use their IPRs as a form of leverage. In all these cases, IPRs are used to confer a

[321] D L Burk 'Patents as data aggregators in personalized medicine' (2015) available at https://intranet.law.ox.ac.uk/ckfinder/userfiles/files/Alleles_%20D%20Burkdocx.pdf, accessed 24 April 2017.

[322] Nicol & Nielsen (note 210 above; 355).

[323] Ibid 355-356.

competitive advantage.[324] Furthermore, the evolution of these inter-firm relationships could pave the way for more open models of innovation using IPRs and strengthening the pro-IPRs stance largely adopted by the private sector of the biotechnology and pharmaceutical industries. The use of IPRs in open innovation through licensing will be discussed in the following chapter.

V. Conclusion

Genomic knowledge generates critical R&D tools, such as DNA sequences, for downstream innovation in genomic medicine, but this knowledge, despite it being argued that it is a public good, may be privatised through IPRs such as patenting. This necessitates licenses for further innovation, which may be costly and difficult to negotiate, especially where a patented technology incorporates claims to many research tools, or where innovation requires multiple research tools held by different patent holders (concurrent fragments). Using the *Myriad*[325] case as precedent, some may argue that patents on DNA sequences should be prohibited, and whilst this is sentiment is shared by the author, the lack of clarity from TRIPS, and the conflicting views of jurisdictions may not enable a global transition to this provision. Furthermore, although these measures will open up these critical research tools for further innovation, these will not enable value capture for private interests groups, as these research tools alone are merely chips of knowledge that need to be translated into useful, commercial medical technologies. What is needed is a governance mechanism that promotes innovation in genomic medicine and 'maintains a balance between the global public goods characteristics of genomics knowledge and the private goods nature of its application'.[326] This mechanism, facilitated by coherent IP law and policy on patenting and licensing in the public and private sectors, needs to allow for the 'continuous circulation of knowledge' for downstream innovation.[327]

Innovation systems need to be constructed so as to 'create and distribute benefits from a public resource without being captured through patents and private appropriation of value'.[328] There should be an innovation system that does not rely on patent monopolies and excessive license fees, but in doing so, does not minimise the economic profits to potential 'research partners' of biobanks and public initiatives to that which is unappealing and unsustainable. Thus private actors must be incentivised to produce public goods, that are not rendered excludable by IP, or public actors must be

[324] An interesting use of IP has also been as part of a company's defence strategy when facing claims of infringement. In the case of *Incyte Genomics, Inc. v. Invitrogen Corp.* , the lawsuit seems to have been filed in retaliation to a patent infringement lawsuit filed by Invitrogen against Incyte previously.

[325] *Myriad* (note 24 above).

[326] Dowdeswell (note 196 above; 132).

[327] Guaragna (note 187 above; 69).

[328] Huzair & Papaioannou (note 53 above; 508).

supported to undertake risky, high investment ventures.[329] One means of doing this would be to nationalise IP at market prices, which means that privately–owned IP would be sold to the state and the IP would exist under state control and become a public asset. This provides private actors with a more dependable source of profit in lieu of profiting off their patents, and allows the state to use the IP as a public good to meet the demands of the concerned sectors. The 100 000 Genomes Project, which is explored in the following chapter, employs a similar structure where a state–owned company largely controls the publically– or privately–generated IP developed from the genomic information it holds.

This model has economic ramifications that may affect the subsequent willingness of the private sector to engage in this type of arrangement where IPRs are traded for a dependable income source, however, these ramifications are beyond the scope of this dissertation. Instead what this arrangement emphasises is the centralisation of IP ownership. As the state concerns itself with meeting public demands, it is a prime candidate to act as a governing body over the relevant IP. However, the state may not be the only actor capable of coordinating IP through ownership — independent, private initiatives also have this capacity, such as with the BIOS initiative to be explored in the following chapter. Ideally what such centralisation offers is a control over how knowledge flows are created, fostering an environment for partnerships or networks between public and private actors that have similar R&D goals but different interests.[330] Rischard[331] summarises the potential of networks below as follows:

> 'On our increasingly small and interconnected planet…global problems cannot be solved within any one nationstate. They call for collective and collaborative action….The current international system is simply not effective enough – or at least fast enough – to solve these problems.'[332]

Though Rischard is referring to networking between nations, and Dowdeswell et al[333] use this in support of government-led networks (for legitimacy and accountability), the latter agree that the potential of this system could be extrapolated to public-private sectors networks as well (which involve international organisations, non-governmental organisations, corporations, and other

[329] Ibid.

[330] Ibid.

[331] J F Rischard 'High noon: we need new approaches to global problem solving, fast' (2001) 4 *Journal of International Economic Law*.

[332] Ibid.

[333] Dowdeswell (note 196 above; 138).

interested parties), such as BIOS,[334] although this requires further substantive evidence. These networks require a flow of knowledge and technology, facilitated by a model such as that of open innovation. In the following chapter, open innovation in genomic medicine will be explored, and the openness of the IP policies of three genomics-related initiatives that involve the public and private sectors will be compared.

[334] Ibid.

Chapter Four: The role of IP policy on open collaborative innovation in genomic medicine

As proposed by Peter Drucker, an eminent management theorist of the 20th century, 'The corporation as we know it is … unlikely to survive the next 25 years. Legally and financially, yes. But not structurally and economically', as the economy becomes based in rapidly evolving knowledge.[335] Companies operating under traditional internally-focussed, closed innovation models — in which producers control the entire innovation chain, from discovery to marketing, and act in isolation[336] — are realising that this business model is becoming obsolete[337] as it struggles to produce and use knowledge at sufficient pace, leading to declining R&D productivity and competitive advantage.[338] This has led to the concept of 'openness' in innovation, which relies on strategic alliances based on strengths, and models where knowledge can rapidly flow to enhance productivity and commercialisation of innovation. In this chapter, the concept of open innovation, focussing on open collaborative innovation as framed in Chapter One will be discussed. This will be followed by a discussion on the shift from closed to open innovation models in genomic medicine, drawing on the arguments made in Chapter Three to highlight the role of IPRs in this shift. In the next section, the various IP policies of collaborative initiatives, as substantiated in Chapter One, will be consolidated into a comprehensive IP policy that promotes open innovation. The Draft Intellectual Property Policy of SA Phase 1 (2017)[339] and the SA Medical Research Council's (MRC) IP policy[340] will be examined in juxtaposition to the consolidated IP policy on open collaborative innovation.

I. The principles of open innovation in genomic medicine

(a) The foundation of open innovation: purposive knowledge flows

Science has traditionally been associated with the 'ideal of free and open dissemination of scientific knowledge' that enables cumulative innovation by producers and users of inventions.[341] However, as industries emerged and grew, the interest arose to capture value from scientific pursuits for future

[335] J Daly 'Peter Drucker' (22 August 2000) available at *http://www.ghandchi.com/iranscope/Anthology/Drucker-SageAdvice.htm*, accessed on 15 November 2017.

[336] B Hughes & J Wareham 'Knowledge arbitrage in global pharma: a synthetic view of absorptive capacity and open innovation' (2010) 40(3) *R&D Management* 325.

[337] M Goldman 'The Innovative Medicines Initiative: A European Response to the Innovation Challenge' (2012) 9(3) *Clinical Pharmacology & Therapeutics* 418.

[338] Gastrow (note 54 above; 42).

[339] Draft IP Policy (note 81 above).

[340] South African Medical Research Council *Management and Commercialisation of Intellectual Property Policy* (2013).

[341] Joly (note 13 above; 391).

innovation and to satisfy investments. As knowledge was recognised as the heart of innovation and competitiveness,[342] and a firm's competitive advantage stemmed from its 'unique knowledge and how it manage[d] that knowledge'[343] industries sought to control knowledge and resources in the innovation chain, from discovery to commercialisation to avoid incurring external costs for resources and skills, and to secure monopolies and fees from licensing.[344] This control required the boundaries of the firm (or other profit–seeking entities) to be closed and impermeable; knowledge and innovation was kept within the firm, and was sourced in as this would require the firm to enter costly licensing agreements, whose upfront payments or royalties would reduce the profit margins of the firm.[345] Especially in the past few decades, IPRs, as discussed in Chapter Three, have dominated the innovation landscape as means of creating competitive advantage and capturing value through closing the boundaries of an entity,[346] and IP policies based on patent and contract law have been integral in the business model of profit-seeking entities, as well as the models of public-based organisations that seek to capture social value of healthcare, such as medical research councils or national biobanks, or initiatives, such as the Human Genome Project. Additionally, IPRs are not only a passive means of securing profits through monopolies or licensing, but are also used as indicators of a firm's expertise and potential.[347] This is particularly relevant to SMEs who may proactively use patent portfolios to attract the partnership or investment of large corporations, or may establish themselves as prolific innovators from whom large companies can buy the patented technologies or agree to licenses.

However, arguments have been raised that enclosing scientific knowledge is contrary to the communalism ideal of science mentioned above,[348] and that a new model of innovation is needed that balances the ideals of science with the private interests of participants. This model should allow for the dissemination of knowledge and technology, aligned with the principles of international instruments such as the Universal Declaration of Human Rights[349] or the TRIPS Agreement,[350] to be

[342] Clark & Turner (note 194 above; 96).

[343] Ibid 85.

[344] Ibid.

[345] Ibid.

[346] Whilst the emphasis of closed boundaries is firm–centric herein, it would also stand to reason that the public sector would also practice closed innovation with the intent of maximising the capture of social value, for example, if a vaccine for TB could be researched, developed, mass produced and distributed by a governmental body, public health would stand to benefit greatly. However, this is not a practical expectation for a majority of public entities as the costs of executing the entire innovation chain that is publically–funded entity may be too high.

[347] Nicol & Nielsen (note 210 above; 355).

[348] Joly (note 13 above; 391).

[349] Universal Declaration (note 1 above; Article 27).

[350] TRIPS Agreement (note 15 above; Articles 7-8).

used for further scientific pursuit. For knowledge to flow optimally, the boundaries of entities have to be permeable, leading to the model of open innovation. Before the potential of this model is explored, open innovation has to be defined within the context of this dissertation. In Chapter One, the open innovation model that will be explored has been outlined, and will be elaborated on in this section.

The concept of open innovation is based on the principle that knowledge relevant for innovation is abundantly dispersed outside the firm, and external knowledge can be used to improve internal innovation.[351] A strong public knowledge base is highlighted as a factor promulgating the shift to open innovation,[352] as the abundance of external knowledge that will be available to competitors is extensive. Knowledge–based economies are suited to open innovation and the nature of knowledge itself supports openness — whereas physical goods are protected from overuse by privatisation, as discussed under the tragedy of the commons, knowledge is intangible and non–rival, that is, it can be reused and applied to generate increasing returns without being diminished.[353] In this way, knowledge can flow easily between entities and be used without creating obstacles of access for each entity. For example, two diagnostics firms may use the same gene information to independently develop diagnostic technologies, and the knowledge will still be available for further use. This is juxtaposed to a scenario where two soft drink companies have to compete for an exhaustible supply of water. This concept of purposive in–flows and out–flows of knowledge is based on the work of Henry Chesbrough, as discussed in Chapter One. Chesbrough delineates open innovation as being inbound or outbound, with knowledge being internalised from external parties, or outsourced to external parties, respectively.[354] Synonymous phrases used to describe such flow of knowledge include outside–in and inside–out, respectively.[355] In the following sub–section, the means by which knowledge flow is created in the firm–centric open innovation model envisioned by Chesbrough will be described, and further on the evolution of this model beyond the firm to a more collaborative approach between a variety of actors will be explained.

[351] F T Piller & J West 'Firms, Users, and Innovation: An Interactive Model of Coupled Open Innovation' in H Chesbrough, W Vanhaverbeke and J West (eds*) New Frontiers in Open Innovation* (2014) 29.

[352] Chesbrough & Bogers (note 27 above; 10).

[353] Chesbrough & Appleyard (note 84 above; 62).

[354] Chesbrough & Bogers (note 27 above; 8).

[355] Ibid.

(i) Inbound and outbound licensing

Licensing is a means of creating knowledge flow, and knowledge may be licensed in from an external source, or licensed out. Generally, IP is licensed out by a licensor to a licensee for a fee, although in a cross–license, each party acts as a licensor and a licensee, trading in IP licenses. Licensing incurs transactions costs, and high upfront fees or royalties, which may be prohibitive to the practice. The OECD addresses best licensing practices in its *Guidelines for the Licensing of Genetic Inventions* (*Guidelines*)[356] (to be discussed below under the section on the consolidated policy framework). There are three types of licenses, each dictating the number of potential licensees and third party involvement: exclusive, semi–exclusive and non–exclusive. In an exclusive licence agreement, the licensee has exclusive rights to use the licensed technology and the associated IPRs, and the licensor itself does not retain these and must refrain from granting licences to third parties.[357] The semi-exclusive licence agreement assigns the same rights to the licensee as the exclusive license, however the licensor may retain the right to exploit the technology, although it may not license out to third parties.[358] In a non-exclusive licence agreement, the licensee and licensor are assigned the same rights as in the semi–exclusive license, but the licensor retains the right to grant other licences to third parties.[359]

The benefits of licensing in knowledge is that it reduces the amount of human and financial capital required by a single firm to generate the same knowledge, and diminishes duplication and risks of failure.[360] Moreover, it may provide new directions to the existing knowledge base. Licensing out is also beneficial to a firm, especially in light of knowledge spill–overs, that is, knowledge that is generated by the firm but is not directly useful for its core purposes but can be used by others.[361] These knowledge spill–overs contribute to external knowledge, and are useful as leverage in the open innovation model, where one party trades their knowledge for that of another.[362] Licensing out provides financial revenue, and in some cases, builds a reputation for the firm. An evolution of licensing practice to cross–licensing, may reduce transaction costs, upfront payments and royalties,

[356] OECD (note 65 above).

[357] Ibid 14.

[358] Ibid.

[359] Ibid.

[360] Chesbrough & Bogers (note 27 above; 12-14).

[361] Ibid.

[362] Ibid.

but this is only feasible if both parties have equally valuable licenses, which is not necessarily easy to evaluate objectively.[363]

Licenses do not have to be for patented technology. In fact, an OECD report states that 'in several countries most licences are for non-patented intellectual property, such as biological research material or copyrighted works'.[364] However, as the focus on this dissertation on the role of IPRs, particularly patents, in open innovation, licensing will henceforth concern patented knowledge and technologies, unless otherwise stated.

To maximise the diffusion of knowledge, licensing may follow FRAND licensing policy.[365] FRAND policy requires that licensing is fair, reasonable and non-discriminatory.[366] However, the challenge is determining what constitutes the FRAND principles. Often, these terms are defined by standard bodies that oversee licensing in a particular technology. Genomic medicine does not seem to have such bodies, without which the articulation of FRAND policy is difficult to achieve. Policies regarding IP that intend to favour open innovation, or any licensing practice, should address both the issue of FRAND definitions and oversight standard bodies. The three following examples of licensing in genomic diagnostics illustrates this challenge. Firstly, genes patented by research institutions can be freely accessed for diagnostic testing, but royalties must be paid when the genes are used in commercial tests, and these payments should not be prohibitive.[367] Secondly, firms may also choose to license out their patents on diagnostic testing on condition that competitors mark their cost-price higher than the patent holder. This, however, may not benefit consumers if the patent holder chooses to set this baseline cost quite high. A third strategy, as employed by Myriad regarding the BRCA genes, is that licenses may be granted for a subset of the gene mutations, with the patent holder retaining the rights to test for the entire set of genetic mutations. Again, patient access to services is impeded by this model of commercialisation, and as seen from these examples. What is needed is a model of innovation that creates more openness for researchers and consumers to enjoy the scientific benefits.

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[363] G Van Overwalle et al 'Models for facilitating access to patents on genetic inventions' (2006) 7 *Nature Reviews Genetics* 144.

[364] OECD *Patents and innovation: trends and policy challenges* (2004) 20.

[365] R N A Bekkers, E Iverson & K Blind 'Patent pools and non-assertion agreements: coordination mechanisms for multi-party IPR holders in standardization' in Proceedings of the European Association for the Study of Science and Technology (EASST) 2006 conference (2006) 8.

[366] Ibid.

[367] Van Overwalle et al (note 363 above; 144)

(b) The evolution of open innovation through democratisation and collaboration

The open innovation model proposed by Chesbrough is a firm-centric paradigm where firms form strategic alliances to barter knowledge, but this knowledge remains within a closed circuit of the few networked parties. [368] Over the years, others have developed the model to extend beyond the firm, retaining the principle of knowledge flows between actors, claiming that certain knowledge such as research tools, must not just flow in a closed circuit, as in Chesbrough's firm-centric model as this may impede cumulative innovation.[369] For example, knowledge on genomic sequences should be available as widely as possible, with the option of improving on the knowledge base through annotation, and re–entering this modified knowledge into a commons. As mentioned in Chapter One, of particular note is the open distributed innovation model proposed by Von Hippel — which incorporates the public good nature of genomic knowledge —[370] and Gassman and Enkel's interactive coupled innovation model,[371] which builds on Chesbrough's model. In the latter model, inside–out and outside–in processes are combined in strategic networks of complementary partners, which distributes the innovation process as suggested by Von Hippel.[372]

This distributed innovation, also known as democratised innovation,[373] is where knowledge is disseminated (through means discussed below) through society so that the tasks of innovation are shared by partners. [374] These partners may include other firms, non-profit organisations, universities, and individuals (such as users and inventors)[375] which may differ in what they produce and how they commercialise their innovations, that is, these entities may have different innovation strengths and approaches to disseminating innovation.[376] For example, universities are rich sources of basic research;[377] core biotechnology firms are rich sources of complementary knowledge, creativity and entrepreneurship; [378] and large companies offer 'management organisation and technology'. [379] These

[368] Pénin (note 209 above; 8).

[369] Chesbrough & Bogers (note 27 above; 15).

[370] Ibid.

[371] Ibid 13.

[372] Piller & West (note 351 above; 37).

[373] Chesbrough & Bogers (note 27 above; 16).

[374] Centre for Science and Policy (note 61 above; 7).

[375] Piller & West (note 351 above; 39).

[376] Ibid 37.

[377] K Asakawa, H Nakamura & N Sawada 'Firm's open innovation policies, laboratories' external collaboration, and laboratories' R&D performance' (2010) 40(2) *R&D Management* 112.

[378] Ibid 111.

[379] Goldman (note 337 above; 420).

principles of purposeful, reciprocal and strategic flows of knowledge between parties aims 'for the benefit of all by coordinating activities and communicating information within an environment of trust and transparency', leading to an overall model of open collaboration.[380] In such a model, the locus of innovation shifts from being within each organisation to being jointly created outside the collaborating organisations.[381]

The open collaborative model explored here is based on the flow of public and privatised knowledge between the private and public actors. UNESCO's Universal Declaration on the Human Genome & Human Rights[382] states that scientific benefits should be shared,[383] calling for the exchange of scientific knowledge and information between cooperating organisations and states.[384] As discussed in the previous chapter, whilst knowledge is regarded as the archetypal public good, knowledge as IP can be protected. Thus, as highlighted in Chapter Three, the crux is the balance between keeping knowledge in the public domain and privatising it so as to maximise its distribution for further innovation. The UK MRC's Data Sharing Policy[385] encapsulates this duality in both its mandate on commercialisation and public–private collaboration, and the view that publically–funded research data is a public good, to which access should be as unrestricted as possible.[386] Placing knowledge in the public domain does have the potential to optimise its diffusion for further scientific innovation as the knowledge is freely accessible. However, as explored in the previous chapter, privatising knowledge attracts commercialisation that also allows for diffusion of innovation in the interests of the consumer. In the sub–sections below, the various models of open innovation that can be incorporated into open collaborative innovation will be described.

At this juncture it is important to emphasise that open collaboration here does not necessarily mean parties have a common research or development goal – some, such as the SNP Consortium or the severe acute respiratory syndrome (SARS) vaccine pool, may concentrate on a particular disease or task, but others may simply have an overall goal to promote information flow to enable the goals of individual parties. Moreover, open collaboration is not necessarily synonymous with altruism or free–for–all access without IP protection. [387] 'Open' in this context does not stipulate 'free' in terms

[380] J Shuman & J Twombly *Innovation and Growth through Collaborative Networks* The Rhythm of Business, Inc (2008) 12.

[381] Piller & West (note 351 above; 39).

[382] Universal Declaration on the Human Genome and Human Rights (1997).

[383] Universal Declaration on the Human Genome and Human Rights (1997) Article 12.

[384] Ibid Article 19.

[385] UK Medical Research Council *Data Sharing Policy* (2005).

[386] T Caulfield, S H E Harmon & Y Joly 'Open science versus commercialisation: a modern research conflict?' (2012) 4(17) *Genome Medicine* 5.

[387] Shuman & Twombly (note 380 above; 13).

of access or cost. As Cohen and Walsh state, 'any positive price for access to intellectual property potentially restricts access',[388] however, if the price is reasonable and non–discriminatory, analogous to the FRAND principles above, the knowledge is regarded as being open in a 'weak' sense.[389] Openness rather refers to the unimpeded flow of knowledge via networks of strategic alliances through which knowledge is diffused to meet innovation needs. These alliances are often based on contractual tools or cooperative strategies,[390] which may involve protected IP, or may operate through a knowledge commons or public domain.

At the centre of my dissertation, as delineated in Chapter Two, are two ideas: a) knowledge of research tools stemming from precompetitive research, often enabled by biobanks and databases, should be made widely available through the public domain; and, b) downstream applications of knowledge may need to be protected to satisfy private interests, which may in turn lead to public benefit as technologies are made available. In the following sub–sections, it is explored how the public domain and knowledge commons, as well as specialised practices of licensing IP may be used to promote open collaboration. These mechanisms have been incorporated into the policies that will be examined further on and used to consolidate an overall policy on which to base open collaborative innovation.

(i) Collaboration through the public domain and knowledge commons

The concepts of the public domain, knowledge commons and open access have been explored in Chapter Two under the Human Genome Project and in Chapter Three. To summarise, anything that is placed in the public domain can be accessed, used and distributed by the public, and is without IP protection or licensing agreements.[391] This is regarded as the most open type of access arrangement, and any collaborator of member of the public is able to access and use the knowledge for innovation, such as in the Human Genome Project. The OECD states that data from publically–funded research should fall under an open–access model as an international norm.[392]

Another means by which open access is created is through a knowledge commons, which is similar to the public domain but partially addresses the issue of free–riding of public goods.[393] Free–riding occurs where those who benefit from a resource do not pay for it, leading to an under–

[388] In Pénin (note 209 above; 6).
[389] Pénin (note 209 above; 6).

[390] Joly (note 13 above; 387).

[391] Stanford University Libraries 'The Public Domain' available at *https://fairuse.stanford.edu/overview/public-domain/welcome/*, accessed on 14 November 2017.

[392] OECD *Principles and Guidelines for Access to Research Data from Public Funding* (2007) 15.

[393] Carvalho (note 56 above; 105).

production of that resource, or an over–consumption.[394] Knowledge is non–rival and so does not deplete through use, and so cannot be over–consumed like a physical good. However, there is a disincentive to produce knowledge if there is no commercial incentive to do so, or if the modifications of that knowledge are enclosed by property rights. For example, a genome sequence may be placed in the public domain, but a firm may develop and patent a diagnostic test using that sequence, diminishing the public benefit of that sequence. A knowledge commons, such as that of BIOS[395] to be discussed below, may stipulate that users are bound to a copyleft license, that is, any cumulative innovation based on the knowledge of the commons must be placed in the commons for its users to access and use without restriction, and each user's input will add to the value of the goods.[396] A knowledge commons, such as BIOS[397], may also be created within a certain community, in which parties may have to pay membership fees for open access, reiterating that 'open' is not synonymous with free of cost. The aim of this measure is not to restrict access, but rather to create sustainability of the commons. It may also be that only members of the commons enjoy unrestricted use of the IP through copyleft licensing,[398] whilst other users may have separate arrangements with the licensor, allowing for financial gain. This would encourage entities to become members, increasing the pool of knowledge and subsequent benefits to scientific progress.

These models of open access suit precompetitive research where commercial entities are more willing to waive their IPRs to participate with public entities and develop a strong foundation for future innovation, such as in the Innovative Medicines Initiative (IMI). However, to translate such research into viable downstream technologies is highly risky, costly and requires clinical trials and regulation. For these reasons, without a means of capturing financial value, commercial entities may be unwilling to collaborate in purely open access initiatives, without IP protection for downstream technologies. Recognising this, protected IP may still be used as a specialised tool for co-ordinating collaborations.[399] For example, many national policies and guidelines from state health departments and funding bodies encourage the commercialisation of technology by the traditional basic science hubs — academia and the public–sector — through exploitation of IPRs,[400] and through collaboration

[394] Wikipedia 'Free rider problem' available at *https://en.wikipedia.org/wiki/Free-rider_problem*, accessed on 22 November 2017.

[395] CAMBIA (note 57 above).

[396] Carvalho (note 56 above; 105).

[397] CAMBIA (note 57 above).

[398] Ibid.

[399] Centre for Science and Policy (note 61 above; 8).

[400] Caulfield, Harmon & Joly (note 386 above; 3).

with industry.[401] Two such tools – patent pools and clearing houses –[402] will be discussed below as a means of coordinating collaboration whilst retaining capture of financial value for licensors of IP. However, without an effective open strategy to guide this process, knowledge can be hedged in and its benefits to a wider population reduced. Thus it is important for entities to consider how an IP strategy may be used to sustain open innovation, in which value is created and captured by many, not just a single entity.

(ii) Patent Pools and clearinghouses

The characteristics of the various licenses used in transferring knowledge and technology has been described above. To reiterate, licenses may be exclusive, semi–exclusive or non–exclusive in nature, which determine to what rights licensees and licensors are entitled. The practice of licensing has been used in the closed model of innovation, and is a vital practice of Chesbrough's firm–centric open innovation.[403] Open collaborative innovation initiatives, such as BIOS[404] or 100KGP[405], also use licensing to create openness. Licenses create openness when the knowledge flow is maximised, which occurs when multiple licensees are allowed by the licensing structure, as in a non–exclusive license, and when the total costs of the license are not prohibitive. Patent pools and clearinghouses have the potential to maximise the licensing of knowledge and technologies whilst reducing the overall costs to licensees, as will be explored below.

Patent pools and clearinghouses, often referred to as collaborative licensing models, are intermediary tools that enable access to multiple inventions through aggregating information and technologies, thus reducing search and transaction costs and streamlining the licensing process.[406] These tools involve numerous licensors and licensees, as opposed to only a few as in bilateral licensing.[407] In a patent pool, licensors may license their patents out to each other by way of a multi–party agreement, and then bundle their patents and license out the bundle to a third party. As a one-stop license, these mechanisms reduce the number and complexity of negotiations and the high transactions costs incurred through multiple bilateral licenses, and may standardise license terms to provide greater legal certainty.[408] A prudent pool would also vet the patents that are pooled to verify

[401] Ibid.

[402] R Aoki & A Schiff 'Promoting access to intellectual property: patent pools, copyright collectives, and clearinghouses' (2008) 38(2) *R&D Management* 192.

[403] Chesbrough (note 26 above).

[404] CAMBIA (note 57 above).

[405] Genomics England *Genomics England Intellectual Property Policy* (2017) Article 3.6.

[406] Ibid.

[407] Van Zimmeren (note 234 above; 570).

[408] Ibid 569.

that these are valid and enforceable to prevent unnecessary litigation. Additionally, a patent pool consists of complementary technologies or information, rather than those that are competing or are substitutes for each other.[409]

Over the years, patent pools have emerged involving public and private actors, many of which targeted the treatment or prevention of infectious diseases such as malaria (Medicines Patent Pool) or neglected tropical diseases (BIO Ventures for Global Health pool). Though not directly related to human genomic medicine, these pools will need to include parties that have an understanding of the genomes of the infectious agents, as in the Severe Acute Respiratory Syndrome (SARS) pool. However, although private and public actors are involved, these pools are humanitarian in their objectives, and it is yet to be seen how pools in genomic medicine that incorporate private interests will work.

A clearinghouse is an intermediate platform that acts as a matchmaker service between licensors and licensees to exchange information or technology. As a neutral intermediary service that standardises licensing terms, such as the Science Commons,[410] and that may bundle licenses, the clearinghouse eliminates engagement between the licensors and licensees.[411] This reduces negotiations and transaction costs, provides visibility for licensors, and cuts down on the searching process by licensees.[412] Clearinghouses may also engage in other activities, such as royalty collection and dispute management.[413]

Two pertinent examples of clearinghouses include MPEG LA's Librassay[414] and DSM's SNP Nutrigenomics.[415] Librassay aims to aggregate patents for existing and emerging diagnostic tests that bear on personalised treatment of diseases, and non-exclusively license out this bundle for diagnostic use.[416] The success of the clearinghouses is still to be established. DSM, through its SNP Nutrigenomics clearinghouse seeks to reduce patent thickets around genetic variations called SNPs, particularly regarding personalised nutrition. By providing standard licenses, it hopes to encourage companies to develop genetic tests for personalised nutrition, but the uncertainty of such a market has discouraged potential parties from collaborating.[417] This suggests that whilst patent pools and clearinghouses have promise as mechanisms of open innovation, they are heavily dependent on the

[409] Aoki (note 406 above; 194).

[410] Van Overwalle (note 363 above; 145).

[411] Ibid.

[412] Van Zimmeren (note 234 above; 570).

[413] Aoki (note 406 above; 194).

[414] Van Zimmeren (note 234 above; 571).

[415] Ibid.

[416] Ibid.

[417] Ibid 572.

willingness of actors to participate to create a critical mass of information and technology that makes the platform viable.[418]

By enabling access to multiple inventions, patent pools and clearinghouses may overcome the problems of patent thicketing as all relevant patents may be included in a bundle of rights, especially where the development of an innovation is dependent on using multiple research tools like genomic sequences. Both patent pools and clearinghouses are mechanisms to enhance the licensing process needed in open innovation models. However, these simplify the process of licensing, and may not necessarily lead to technology transfer and distribution without suitable policy that promotes these aims.[419] Furthermore, the interests of parties that may be from different sectors must be aligned, and competing technologies should not be included in the same pool.[420] And as other commentators have noted, patent pooling can tend towards anti-competitive practices. To keep within the IP law focus of this dissertation, this will not be discussed further, but future policy should consider this. As yet, neither mechanism has seen extensive and broad success in the life sciences or genomic medicine, in particular. Although as models that require broad licensing, such open collaborative innovation, are more frequently adopted, these tools may be refined and used more widely, which would need to be pre-empted by policy.

(d) The shift to open collaborative innovation

Pharmaceutical companies, core biotechnology firms (such as SMEs) and public research institutes (such as universities and NPOs) are looking to expand their current operations in personalised medicine activities, which would benefit public health interests. Pharmaceutical companies have largely relied on blockbuster models of innovation in conventional medicine, where incremental changes are made to an existing, successful invention.[421] But the field of genomic medicine is nascent and different from conventional medicine, as discussed in Chapter Two, and requires breakthrough innovations to capture consumer interest and meet their needs. To bring about such breakthroughs, the following activities are critical in the innovation chains: extensive precompetitive research and discovery of genomic knowledge; innovative application of this knowledge to generate inventions; and effective distribution of these inventions to satisfy consumer interests. This highlights the importance of knowledge in driving genomic medicine. However, under a closed innovation model,

[418] Van Overwalle (note 363 above; 146).

[419] Guaragna (note 187 above; 196).

[420] Ibid 196-197.

[421] T Melese et al 'Open innovation networks between academia and industry: an imperative for breakthrough therapies' (2009) (15(5) *Nature Medicine* 502.

these entities are faced with stagnated knowledge — either knowledge that is obsolete, or knowledge that cannot be translated into useful innovation by that entity because the boundaries of these entities are closed. In this way, knowledge cannot flow to where it would be used most effectively, for example, key information on genome variants associated with a disease discovered by a university may enable an SME to develop a genomic test. To assist these knowledge flows, the boundaries of these entities need to become more permeable, which may be facilitated by strategic alliances and collaborations,[422] for example, Merck's Gene Index[423] discussed in the previous chapter. In this dissertation, the main focus is on the collaboration between public and private sectors, with an emphasis on public biobanks and databases.

Clarke and Turner[424] note that a salient characteristic of the biotechnology industry is that of collaborations between various actors such as universities, biotechnology SMEs and large companies (often pharmaceutical-based) and not-for-profit organisations.[425] The alliances within collaborations may be vertical, which brings in new upstream knowledge and allows for commercialisation downstream, or horizontal, which brings in the complementary knowledge of competitors. Networking arising from webs of vertical and horizontal alliances is also powerful, as Powell notes, in the biotechnology industry, innovation is a result of networks, not individual firms.[426] The Diabetes Genetics Initiative[427] is a pertinent example of collaboration between the Broad Institute of Massachusetts Institute of Technology (MIT) and Harvard, Lund University, and Novartis Institutes for BioMedical Research where the expertise and resources of these collaborators are combined to collect and analyse the genomes of diabetic patients so as to understand the genomic variants contributing to Type 2 Diabetes.[428]

The importance of collaborative innovation in genomic medicine can be attributed to various reasons, as outlined below, many of which are proposed by the Genomic Medicine Colloquium[429] – the overall reasoning is very few firms have the internal capacity to take a product through from research to commercialisation, for reasons of time, cost, resources and regulatory approval.[430]. Firstly, genomic medicine is dependent on highly complex technologies in both diagnostics and therapeutics,

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[422] Ibid 503-505.

[423] Chesbrough & Appleyard (note 84 above; 72).
[424] Clark & Turner (note 194 above; 90).
[425] Ibid.

[426] Ibid.

[427] Broad Institute 'Diabetes Genetic Initiative' available at *https://www.broadinstitute.org/diabetes/diabetes-genetics-initiative*, accessed on 30 October 2017.
[428] Ibid.

[429] Clark & Turner (note 194 above; 90).
[430] Clark & Turner (note 194 above; 90).

which should be developed together to optimise their benefits. This complexity is partially attribute to the nature of genomics — to understand a single disease through genomics, a web of multiple genomic elements may have to be studied. This complexity calls for greater human and financial resources than a single firm may be able to provide. [431] Open collaboration creates networks of partners and transparency, and where initiatives are geared towards a common R&D goal, [432] the activities of innovation may be democratised, reducing overlapping research and duplication. [433] Such transparency and distribution of tasks will also enable collaborators to work on cumulative innovation and concurrent technologies and accelerate development in the field. Furthermore, as the focus shifts away from only producers to include users of technologies, diagnostic and therapeutic technologies can be customised within the collaborative initiative, potentially expanding the range of user of the downstream technologies. [434] A hypothetical example would be where a collaborating commercial laboratory finds that testing for breast and ovarian cancer is more appealing to patients than only testing for one type of cancer, and uses the network to communicate this to producers of the test. The networks of collaboration creates a platform not only to share IP and funding, but also expertise and skills in applying new knowledge.[435] Balancing the development of resources and relations is needed in such a highly complex field that requires interoperability and convergence of technologies and knowledge to address the needs in diagnostics and therapeutics. [436] Companies, like Roche, are recognising that collaboration may aid them in achieving breakthrough inventions and assisting the shift from the blockbuster model that relies on incremental adjustments to existing technologies. [437]

Secondly, the tools used and the technologies required by the field undergo rapid evolution may be too costly for a single entity to constantly update their tools and develop new technologies. As with other branches of medicine, genomic medicine is a high–investment and high–risk field that requires value capture, although private entities are observing that patenting may not always result in such capture, as explained by the 'Valley of Death' phenomenon.[438] In this phenomenon it is observed that patented inventions do not necessarily become commercialised. This may fall into an abyss

[431] T A Manolio et al 'Implementing genomic medicine in the clinic: the future is here' (2013) (15(4) *Genetics in Medicine* 258.

[432] Joly (note 13 above; 399).

[433] Ibid 393.

[434] Ibid 402.

[435] H W Chesbrough *From Open Science to Open Innovation* (2015) 8.

[436] European Patent Office (EPO) *Scenarios for the future* (2007) 93.

[437] P Nakagaki, J Aber & T Fetterhoff 'The Challenges in implementing open innovation in a global innovation–driven corporation' 2012 *Research–Technology Management* 32.

[438] A K Rai et al 'Pathways Across the Valley of Death: Novel Intellectual Property Strategies for Accelerated Drug Discovery' (2008) 8 *Yale Journal of Health Policy, Law, and Ethics* 53-89.

because the costs between the processes of patenting and commercialisation in the medical field is higher than in other fields of technology (noting the additional step of regulation). Moreover, as populations are stratified according to genomic sub-populations, there is a risk of market failure as the consumer bracket for a product becomes smaller as compared to the larger populations for which conventional medicine caters. Collaborative efforts, whether by private or public actors, or both, share these risks and investments, as discussed in the previous section, and can pool resources and reduce transactions costs and time–consuming negotiations,[439] especially regarding the use of patent pools.

Thirdly, genomics is also highly susceptible to the effects of patent thickets, as genome sequences cannot be substituted.[440] Open collaborative innovation that creates more open access through specialised licensing agreements, such as copyleft licenses or patent pools, or stipulations to preserve the knowledge in the public domain, can reduce the number of patents placed on essential research tools that are needed for precompetitive research, such as in the Merck Gene Index.[441] Such preservation of the public domain or knowledge commons reduces the threat of patent infringement and litigation, and attracts scientists to the field. Open collaborative innovation lessens the uncertainty of research exemptions, whereby scientists in public research institutes may be hesitant to engage in precompetitive research as countries either do not have explicit laws or guidelines, or in some cases have very strict rulings from courts. For example, the US federal court ruled that research exemptions should only apply 'when research is solely for amusement, to satisfy idle curiosity, or for strict philosophical inquiry'.[442] Such a narrow view of this exemption is possibly influenced by legislation such as the Bayh-Dole Act[443] that promotes publically-funded bodies to patent inventions. Narrowing the scope prevents public entities from exploiting the exemption to further their commercial interests without proper due compensation for the patent holder. Collaborative networks that are based on private contracts between parties, informed by policy and law, provide an opportunity for researchers and patent holders to communicate the terms of research exemptions.

Lastly, open collaborative innovation engenders social responsibility by firms in terms of patenting and licensing practices by facilitating greater access for further innovation and social benefit without jeopardising the firm's sustainability. In such open innovation, where the boundaries of a firm are willingly made more permeable, commercial entities agree to avoid strategies of secrecy in precompetitive stages to maintain a competitive advantage downstream. As suggested by Melese et

[439] A Kapczynski et al 'Addressing Global Health Inequalities: an open licensing approach for university innovations' (2005) 20(1031) *Berkeley Technology Law Journal* 1077.

[440] Joly (note 13 above; 390).

[441] Frishmann, Madison & Strandburg (note 250 above; 121).

[442] OECD (note 364 above; 18).

[443] Patent and Trademark Law Amendments (note 212 above).

al ,'Establishing areas of precompetitive research, with open standards and protocols, would enable companies to pool their knowledge and resources to fill current technology gaps'.[444]

II. The role of IP policy in open collaborative innovation

(a) A consolidation of IP Policies to promote open collaborative innovation in genomic medicine

As explained in Chapter Two, biobanks and genomic databases are essential in generating genomic knowledge and in supporting precompetitive research. A primary mission of many large–scale public biobanks is to make these data accessible to the scientific community so as to maximise the research output for downstream innovation.[445] The approach of sharing data on DNA sequences was endorsed by the Bermuda Principles,[446] and the role of resource producers, users and funding agencies in doing so was reiterated by the scientific community in 2003.[447] These are rich sources of primary knowledge and expertise, databases and biobanks are valuable as platforms for private–public partnerships and collaborations, which are useful in decentralising the innovation process and accelerating the generation and translation of genomic knowledge into applications for patient benefit.[448]

However, the heterogeneity of collaborative partners from public and private sectors leads to diverse views on: a) how samples and databases should be accessed; b) whether IP should be granted to inventions stemming from research on their samples; and c) how such IP should then be governed, considering the public good nature of the knowledge in databases discussed in Chapter Three. Currently, there is no binding international consensus or comprehensive framework, as found in an OECD report on the 'issues of ownership, commercialisation, exclusive licensing, access for researchers, benefit sharing and other issues' regarding population databases,[449] thus leaving these issues to the policy–makers of the biobanks and databases. The Universal Declaration on the Human Genome and Human Rights states that human genome in its natural state will not give rise to financial

[444] Melese et al (note 421 above; 507).

[445] S Fortin et al '"Access Arrangements" for Biobanks: A Fine Line between Facilitating and Hindering Collaboration' (2011) 14 *Public Health Genomics* 105.

[446] Bermuda Principles (note 218 above).

[447] Ibid 106.

[448] P Hofman et al 'Public–private relationships in biobanking: a still underestimated key component of open innovation' (2014) 464 *Virchows Arch* 3.

[449] OECD *Creation and Governance of Human Genetic Research Databases* (2006) 61.

gains,[450] and favours free access to and sharing of data under a collaborative framework. However, this declaration pays little attention to the translation of such data in useful medical applications. Biobanks and genomic databases, such as the 100KGP,[451] have acknowledged that IP frameworks are essential in their governance of common pool resources used in research, especially where there are private participants and commercialisation is essential to the distribution of innovation. IP policy must capture the full potential of collaborative relationships between the different sectors, and close the gap between basic research and its clinical translation. In this section, the policies of various open collaborative initiatives related to genomics that have been introduced in Chapter One, such as the BIOS initiative,[452] the 100KGP,[453] and the Diabetes Genetics Initiative, as well the OECD's *Guidelines*,[454] will be drawn on to create a framework for IP policy that can be applied in an open collaborative model of innovation.[455]

The open collaborative model, highlighted in the above section, is a modification of Chesbrough's firm–centric open innovation model; the former incorporates a mixture of actors from the private and public sectors. This means that innovation policies, which include IP policies, should also be modified to fit the objectives of collaboration, that is, where there is a network of actors who benefit jointly from the collaboration, even if they do not have a common research goal. Thus, policy should encourage the development of open strategy where collaborators 'actively shape the external conditions to facilitate the development of a joint innovation strategy where all partners can benefit'[456], rather than a system of immediate bartering knowledge for a short–term open innovation effort. Partners from different sectors have different interests, as discussed throughout this dissertation, all of which must be met by policy to promote the sustainability of the open collaboration by attracting contributors,[457] aligning research agendas, disseminating collaboration results, or using IP strategies to promote further innovation and prevent unsuitable appropriation of the results emerging from the collaboration.[458] A good example of open strategy is the Merck Gene Index[459]

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[450] Universal Declaration on the Human Genome and Human Rights (note 383 above; Article 4).

[451] Genomics England (note 405 above).

[452] CAMBIA (note 57 above).

[453] Genomics England (note 405 above).

[454] These guidelines address licensing practices crafted to meet public health needs in member and non–member countries, and recognise the input and potential of private–public collaboration.

[455] It must be noted that IP is only one aspect bearing on innovation, and should be considered together with policies on other areas in a more comprehensive study.

[456] W Vanhaverbeke, N Roijakkers, H W Chesbrough 'The Importance of Connecting Open Innovation to Strategy' in N Pfeffermann & J Gould (eds) *Strategy and Communication for Innovation: Integrative Perspective on Innovation in the Digital Economy* 8.

[457] Chesbrough & Appleyard (note 84 above; 69).

[458] Vanhaverbeke, Roijakkers & Chesbrough (note 456 above; 9-10).

[459] Chesbrough & Appleyard (note 84 above; 72).

discussed in the previous chapter. Philanthropy aside, Merck attracted partners using the bait of a common objective — to prevent the appropriation of valuable knowledge that would influence their independent commercial activities downstream. In doing this, whilst Merck relinquished any rights to the genetic markers in the index, it also encouraged others to do the same, creating a valuable knowledge commons that would enable greater downstream innovation and value capture, rather than only capturing value on a few patented genes. This initiative upheld the tenets of open collaboration by encouraging entities to make their boundaries permeable to allow knowledge to *flow* out (into a commons) for use by others, promoting the *democratisation* of precompetitive research and enabling the *diffusion of knowledge* for further innovation whose social and financial *value may be captured*.[460] Based on these principles, encapsulated by many IP and licensing policies of guiding bodies, such as the OECD, and collaborative initiatives by biobanks and databases, and how IP policy should be framed so as to promote open collaborative innovation will be outlined.

In the previous section, there is an exploration of how knowledge flows are created in open collaborative innovation through the public domain and knowledge commons and specialised licensing that endeavours to preserve open access to knowledge. As mentioned in that discussion, IPRs do not necessarily have to be negated, but must be used creatively to avoid creating obstacles to accessing knowledge, as IPRs still have a role in attracting venture capital and external investment, as well as commercial entities such as large pharmaceutical companies.[461] IPRs for research tools (although this is not ideal, as discussed in Chapter Three) or downstream innovations should not be disproportionately allocated in collaborations; collaborators should receive the rights according to their contribution.

Many collaborations, especially those initiated by the public sector, such as health departments or the MRC, include universities and public research institutions. These are regarded as prolific producers of basic research that can be licensed out in accordance with open policy that encourages data–sharing.[462] The policies of these national bodies should balance commercialisation needs with open access, and should stipulate that collaborators incorporate data–sharing plans in their research proposals. [463] In cases where exclusive licensing is preferable, such as when considerable investment is needed to distribute a technology, policy should include an agreement that licensees fulfil the requirement to exploit the invention and agree to milestones in the event of

[460] Centre for Science and Policy (note 61 above; 7).

[461] S J Herstad et al 'National innovation policy and global open innovation: exploring balances, tradeoffs and complementaries' (2010) 37(2) *Science and Public Policy* 120.

[462] Caulfield, Harmon & Joly (note 386 above; 2).

[463] Caulfield, Harmon & Joly (note 386 above; 6)

commercialisation.[464] Furthermore, where national legislature or policy prefer licenses held by research institutions to be granted to NPOs and SMEs,[465] such provisions must not hamper the flow of knowledge to other actors such as large pharmaceutical companies, which could adversely affect the distribution of goods in genomic medicine as commercialisation may not be optimally executed.

To create sustainability and promote open access, national policy could instruct publically-funded bodies to dedicate a percentage of their output to the public domain where it is applicable.[466] Policies of individual collaborative initiatives have also recognised the value of preserving a commons for research tools, for example, the Diabetes Genetics Initiative aims to make its work readily available at no cost to academic institutions and NPOs,[467] and BIOS states that 'enclosure rarely ensure[s] a sustainable competitive advantage'.[468] This implies that a fragmented hegemony on critical tools does not actually benefit firms, and is a waste of innovation resources, for example, if various genome sequences involved in diabetes are patented by different firms, a single firm will not be able to develop effective technologies without licensing-in other patents. For research tools to be effective in innovation, broad access, in which multiple components are publically accessible, needs to be realised. In his theory on patents as data aggregators, explored in Chapter Three, Burk highlights that genomic data is more powerful when coordinated at one point, for example, if Myriad held all the data on the *BRCA* gene variations, instead of the dataset being fragmented, this single firm would be able to develop more impactful diagnostics tests.[469] Burk suggests that patents are key in allowing this aggregation of data at a single point, or even to control the coordination points through licensing. In a closed innovation model, a patent monopoly favours data aggregation, but limits the R&D capabilities of other interested researchers who do not hold the patent rights through licensing. In open innovation, the flow of knowledge will require either open access to data or extensive licensing. In moving away from closed innovation, large–scale biobanks and databases that pool resources into a commons or in the public domain, may also function as coordination points as they provide robust sample sets and datasets for research, and can adopt open licensing practices.

Although, merely placing knowledge in the public domain may not prevent others from appropriating the data by combining it in their own cumulative innovation; BIOS[470] recognises that

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[464] OECD (note 364 above; 21).

[465] IPR Act (note 258 above; s 11).

[466] Kapczynski (note 439 above; 1064).

[467] Broad Institute 'Diabetes Genetic Initiative' available at *https://www.broadinstitute.org/principles-disseminating-scientific-innovations*, accessed 30 October 2017.

[468] CAMBIA (note 57 above; 4).

[469] Burk (note 321 above).

[470] CAMBIA (note 57 above; 4).

genome sequences placed in the public domain may be captured by 'converting that information into economically valuable goods and services'.[471] BIOS proposes the solution of a copyleft licensing obligation, discussed above, in its open licensing agreements to grant rights to BIOS in any improvements made on the licensed technology, which will be placed in a protected commons to prevent those who incrementally improve on a technology from enclosing that technology in a patent. Thus, licensees may not appropriate developments to technologies licensed out by BIOS and prevent access by others or fostering of growth of the knowledge commons.[472] The HapMap project, which seeks to identify shared genetic variations across populations, also addresses this problem of commons appropriation using a click-wrap license where users have to click to agree to the terms of the project before being able to use the information — these terms include users agreeing not to combine the data of the project with their own results and enclose the project's data in a patent.[473]

However, although a commons model and the public domain may be suitable for precompetitive knowledge and vital research tools, this may not always be a feasible option to incentivise participation in a collaboration; IPRs may still be regarded as essential to value capture from downstream innovation. It is my suggestion that IPRs only be used to capture value from downstream applications, and appropriation is deferred until is in undeniable that the invention meets the criterion of patentability, which needs to be clarified by TRIPS or national policy and legislation, as discussed in Chapter Three.[474] Policy should ensure that IPRs promote knowledge flow through open licensing practices, as used by BIOS[475] and the Diabetes Genetics Initiative which follow the FRAND principles discussed above, and favour non–exclusive licensing. Before open licensing becomes attainable, there must be clarity as to how IPRs are assigned to collaborators. This is especially pertinent considering that national legislation in some countries, such as the US and SA, encourages patenting of publically–funded research by assigning IPRs to public actors such as universities, as discussed in Chapter Three. Policy should clarify how the IPRs on the collaboration's results are to be assigned between collaborators, and how non–holders may use the IP post–termination of the collaboration.[476] Open collaborations should differentiate between precompetitive, non–commercial research, and competitive, commercial R&D. This may allow for a tiered system of

[471] CAMBIA (note 57 above; 7).

[472] Pénin (note 209368 above; 15).

[473] Kapczynski (note 439 above; 1071).

[474] M Allarakhia, D M Kilgour & J D Fuller 'Modelling the incentive to participate in open source biopharmaceutical innovation' (2010) 40 *R&D Management* 61.

[475] CAMBIA (note 57 above).

[476] G Slowinski & K W Zerby 'Protecting IP in collaborating research' 2008 *Research Technology Management* 58–65.

IPRs, as seen in the 100KGP,[477] where non–commercial academic researchers assign all IPRs to the 100KGP parent body, Genomics England, to avoid a fragmentation of rights and to create a knowledge coordination point. Should researchers intend to commercialise any technologies using Genomics England IP, the two parties will negotiate a 'fair and reasonable' license.[478] Genomics England will also share any profits with institutions that contributed to the IP enclosed in the license.[479] However, forgoing any IPRs as an academic institution may not always seem appealing, especially when IPRs are used to attract investment or commercial partners, or build a reputation.

Genomics England also has an IP policy for commercial entities, which are tiered according to size. Where companies collaborate in 100KGP,[480] any IP that arises will be owned by Genomics England, but where companies solely develop technologies using Genomics England information, without collaboration, the company retains all IPRs. In the former scenario, such a policy may deter commercial collaborators as IPRs have to be relinquished, although it does create a strong knowledge base for 100KGP. In the latter, openness is substituted for sustainability as IPRs holders either have to pay royalties or a larger upfront fee, depending on their size. [481] This business model approach to collaboration, where profits are derived from IP, may certainly support sustainability, however commentators at the IP Policy Workshop held by the Centre for Science and Policy, Cambridge,[482] have queried whether a government–based initiative should support the capture of financial value, instead of the traditional focus in supporting innovation through infrastructure and funding. From this arises the concern of how to balance openness with value capture so as to cater for public and private interests, which are dependent on the nature of the collaborators, the complexity and potential of the field, and the long–term goals of the collaboration.

Another option to keep the boundaries of collaborators permeable and maintain a knowledge flow is where IPRs are jointly held by collaborators, and in the cases where a collaborator cannot hold the IPRs, open licensing should enable them to access the information easily, encouraging their participation in the initiative. Creative licensing agreements could also be used to prevent a hegemony over knowledge, for example, jointly–held IPRs or exclusive licenses could be licensed according to geography, field of use and time, without infringing competition law[483], as recommended by the IP policy for 100KGP. [484] Hypothetically, companies A and B could each hold IPRs in different

[477] Genomics England (note 405 above).
[478] Centre for Science and Policy (note 61 above; 14).

[479] Ibid.

[480] Genomics England (note 405 above).
[481] CSaP Workshop Report *Realising Genomic Medicine: Intellectual Property Issues* (2015) 8.

[482] Ibid.
[483] Allarakhia, Kilgour & Fuller (note 474 above; 63-64)

[484] Genomics England (note 405 above).

countries simultaneously, or hold IPRs in the same country at different times. Where a technology has patents on multiple uses, such as a diagnostic test for breast and ovarian cancers, A could hold the IPRs for the use of the test in breast cancer diagnosis, whilst B could hold the IPRs for ovarian cancer diagnosis.

Furthermore, open collaborative initiatives should make core external knowledge available for licensing if it is not already in the public domain. This knowledge is not the IP of the initiative, but is externally sourced from third parties by collaborators in order to innovate. For example, Genomics England, a subsidiary of the UK Department of Health, may claim ownership of whole genome sequence datasets of third parties if these datasets are used by 100KGP academic researchers in creating their own IP for a hypothetical invention 'C', depending on whether the datasets were created using public funds.[485] By doing this, Genomics England ensures that licensees who seek to use C for further innovation can acquire critical research tools to fully understand C and optimise innovation without having to enter negotiations with the third party and pay exorbitant transactions costs.[486] However, before adopting such measures, policy–makers need to evaluate whether this appropriation of external IP does not discourage third parties from allowing collaborators to use their data. As this data is publically–funded, funding bodies should clearly communicate in their own IP policy the possibility of a governmental subsidiary claiming ownership of core data.

Open licensing should be available to third parties so as to maintain a flow of knowledge, and where IPRs align in research, patent pools could be orchestrated to facilitate licensing within the collaboration and with third parties. Again, the assignment of the resultant IP from third party collaboration should be clearly guided by policy.[487] In Nicol's analysis of cooperative IPRs in biotechnology, [488] it is suggested that databases and biobanks such as BIOS or 100KGP act as coordination points of knowledge, and through their IP policy, can act as patent pools.[489] Open collaborations could also participate in clearinghouses to maximise the dissemination of their IP, and policy would have to address how this may be conducted. Clearinghouses and technology transfer offices, or similar mechanisms within a collaboration, should be used to correctly evaluate IP for fair licensing. [490] However, for patent pools and clearinghouses to be effectively formed, policy would also need to address the possibly negative perception entities have of patent trolls and clearinghouses that may have thus far contributed to the slow growth of these mechanisms, for example parties

[485] Ibid.
[486] Ibid.
[487] OECD (note 65 above).
[488] D Nicol (note 236 above).
[489] Ibid.
[490] J P J de Jong, T Klavet & W Vanhaverbeke 'Exporing a theoretical framework to structure the public policy implication of open innovation' (2010) 22(8) *Technology Analysis & Strategic Management* 888.

believe that they will lose control over the bargaining process, to their determines.[491] Furthermore, in genomic medicine, these mechanisms would need to assemble multiple key patented technologies, which would need to be clearly marketed to prospective licensees. If these technologies are not verifiably critical to further innovation, prospective licensees may fear wasting financial and human resources on buying into these license bundles, and attempting to develop using these patented technologies. Effective policy would appease these licensees if it articulated clear instructions on how patent pools and clearinghouses vet patented technologies, although achieving this may be unrealistic as it is not always easy to evaluate a technology. Furthermore, licensors may fear that their technologies are undervalued, discouraging their participation.

Licensing of IP is an important means of knowledge diffusion and distribution of applicable technologies. The OECD *Guidelines*[492] provide best practices that would enable diffusion of knowledge and financial and social value capture to satisfy private and public interests. The objective of the *Guidelines* is to foster innovation and make this readily available for maximum utilisation through non–exclusive licensing to promote a healthy competitive environment that would meet the commercialisation needs of public demand, [493] and would enable licensors and licensees to obtain returns on their investment. [494] In accordance with the principle of reasonableness in FRAND licensing, the *Guidelines* recommend that best practice minimise the burden of royalties, upfront fees and transaction costs, and reach–through licenses, discussed in Chapter Three, as these may hinder access to downstream innovation and discourage inventors. [495]

Particularly in relation to research activities, which would encompass the agendas of genomic databases and biobanks, the *Guidelines* recommend that information, particularly foundational genetic inventions,[496] is rapidly disseminated through broad licensing and unrestricted access to databases. Where research results are kept confidential for patenting, this should not unduly hamper the eventual publication of such results in the public domain or knowledge commons.[497]

In the event that IPRs are not used to capture financial value through monopolies and social value through dissemination of innovation, policies should consider how value is to be captured, and how knowledge spill–overs are to be patented or otherwise treated as public goods. [498] Where

[491] Van Zimmeren et al (note 234 above; 573-574).

[492] OECD (note 65 above).

[493] OECD (note 65 above; Articles 1.A, 5.A, 5.3).

[494] Ibid Article 1.C.

[495] Ibid Articles 4.1-4.4.

[496] Ibid Article 4.A.

[497] Ibid Articles 3.1-3.5.

[498] Jong, Kalvet, Vanhaverbeke (note 490 above; 881).

knowledge flow is encouraged through open access that reduces a commercial entity's ability to derive profit from IP protection, there must be an alternative rewards system. These rewards may still be pecuniary, as in prizes for open innovation, or could be non–pecuniary, as in social rewards.[499] The latter could include prestige and recognition derived from open challenges, a reputation of openness, refinement of skills and gain in expertise through peer interactions and exposure to new ideas.[500] A significant development in this area of alternative rewards systems is in the InnoCentive open initiative where solutions are sourced from the public knowledge flows, termed crowdsourcing, and rewarded socially and monetarily. Policy must clearly outline these rewards for sharing IP and create realistic paths for participants to gain these.

Collaboration policy offers a platform for standardising activities that are not clearly legislated or regulated by national policy. Ideally, national policy and open collaboration policy should standardise research exemption licenses to clarify how research may be conducted in collaborative innovation. This would reduce uncertainty about facing infringement litigation. On that point, IP policy should provide clear IP dispute resolution mechanisms.

The policy guidelines,[501] consolidated from various sources, attempt to promote the principles of open collaborative innovation discussed in this chapter. Policy is dependent on national laws, but can also provide certainty in areas that the law does not address. The innovation policies of individual collaborations or overarching bodies, such as the Medical Research Council (MRC) can be more specific in how IP is managed in particular fields, for example, whether genomic research tools can be patented. In its IP policy, Genomics England states that it does not intend to own the genomes of any individual, [502] or patent isolated sequences,[503] nor does it support patenting overly broad claims that may hinder further innovation.[504] Overarching bodies, such as medical research councils or national research foundations, play a critical role in promoting a research agenda that addresses public health needs through the collaboration of the public and private sectors – for example, funding bodies could stipulate that grant–holders engage in open collaborative practices. The IP policies of these national bodies should favour governmental health services, as seen in the 100KGP[505] where a particularly favourable licensing regime will be considered for the National Health Service in

[499] Chesbrough & Bogers (note 27 above; 16)

[500] Joly (note 13 above; 399).

[501] Section II (a) above.

[502] Genomics England (note 484 above; Article 2.3).

[503] Ibid Article 3.2.1.

[504] Ibid Article 3.2.2

[505] Genomics England (note 484 above).

alignment with the 100KGP objectives to 'bring benefit to NHS patients'.[506] Using the case of the South African MRC, the role of its IP policy in fostering open collaborative innovation will be explored, juxtaposing its policy with the consolidated framework above.[507] However, as open collaborative innovation develops, and healthcare needs change, a single, static framework would not be advantageous. As suggested in the preface of the OECD *Guidelines,*[508] guidelines and policy should be dynamic, evolving in light of scientific progression, and changes in business practice and societal needs.[509]

(b) The promise of South African IP policy in open collaborative innovation

According to the OECD, SA is 'the continent's leading economy, with strong research–based industries'[510] and 'related knowledge–intensive business services' and 'knowledge infrastructure'.[511] Research and innovation are significantly influenced by domestic industry–academic networks,[512] and as Gastrow finds, these networks are incorporating open innovation.[513] Furthermore, international collaboration has a role in scientific publication and patenting, as per the OECD's findings, indicating that knowledge flow is occurring on the domestic and international fronts. However, despite these positive indicators, there is an imbalance in the participation of the private and public sectors in the biotechnology industry — the OECD reports that whilst government funding of R&D doubled, the figure by businesses hardly increased.[514] Jordaan suggests that public policy on the level of national strategy, which largely excludes the private sector, contributes to the reluctance of private sector to contribute to the industry.[515] This imbalance has the potential to impede the growth of a strong genomic knowledge base and, more pertinently, to hinder the translation of this knowledge into downstream technologies and the distribution of these technologies to capture their value. At a meeting convened by SA's Council for Scientific and Industrial Research (CSIR), policymakers and leading researchers identified that in order to create affordable products and services, universities,

[506] Ibid Article 1.1.1

[507] Section II (a).

[508] OECD (note 65 above).

[509] OECD (note 65 above; Article 5).

[510] OECD *OECD Science, technology and industry outlook* (2012) 380.

[511] OECD *OECD Reviews of Innovation Policy: South Africa* (2007) 11.

[512] OECD (note 510 above; 380).

[513] Gastrow (note 54 above).

[514] OECD (note 511 above; 1).

[515] D W Jordaan 'Biotech innovation in South Africa: twenty years in review' (2016) 35(1) *Law Report* 42.

research councils and industry must closely network,[516] and called for a policy that promotes not only networking, but the growth of these sectors, possibly assisted by collaboration. Thus, it is critical to understand the current public policy landscape to determine how the innovation chain in genomic medicine may be hampered, looking at this through the lens of open collaborative innovation. In Chapter One, the past national strategies aimed at building the biotechnology industry in South Africa were briefly outlined, and in this section, the focus is on two current IP policies that have a bearing on innovation in this field: the Draft Intellectual Property Policy of SA Phase 1 (2017),[517] and the Medical Research Council's IP Policy.[518]

(i) The Draft Intellectual Property Policy of SA Phase 1 (2017)

In the Draft Intellectual Property Policy of SA Phase 1 (2017) (Draft Policy),[519] under the Department of Trade and Industry, IP is recognised as an important policy instrument in 'promoting innovation, technology transfer, research and development (R &D), creative expression, consumer protection, industrial development and more broadly, economic growth'.[520] The Draft Policy also aims to transition from an 'over-reliance'[521] on natural resources to a knowledge economy. Though public health is given more attention, with this policy intending to 'strike a balance between owners and users of IP',[522] SA still lags behind other jurisdictions which have specific public policies addressing genomics in public health, such as the EU Directive.[523] This section examines how the provisions of this policy promote open collaborative innovation between the public and private sectors in genomic medicine — although its phase 2 intends to address biotechnology, this seems to be limited to agricultural resources.[524]

As the Draft Policy seeks to promote the growth of domestic industry,[525] it is important to determine its reliance on national and international linkages to do this, that is, to determine whether a global openness is fostered. As demonstrated by the Human Genome Project and subsequent genomic research initiatives, the nature of research and development in genomic medicine is global

[516] C A Gardener, T Acharya & D Yach 'Technological and Social Innovation: A Unifying New Paradigm For Global Health' (2007) 26(4) *Health Affairs* 1057.

[517] Draft IP Policy (note 81 above).
[518] South African Medical Research Council (note 340 above).
[519] Draft IP Policy (note 81 above).
[520] Draft IP Policy (note 81 above; 318).

[521] Ibid.

[522] Ibid 324.

[523] EU Directive (note 45 above).
[524] Ibid 351.

[525] Ibid 321.

— research participants, and researchers and developers from around the world engage in these initiatives to maximise the potential of the genomic knowledge generated so as to benefit a wider range of genomic sub–populations. Therefore, there is a need for a national policy to facilitate international networking so as to access globally distributed knowledge networks that can support such initiatives by the public and private sectors.[526] Gastrow notes that public policy does not currently promote the formation of global innovation networks.[527] These linkages are essential in a field like genomic medicine, which relies on cumulative innovation and is highly complex in terms of its technological content,[528] requiring diagnostic and therapeutic goods for a multitude of genomic sub-populations. As Herstad et al note, the 'more *complex* knowledge bases, products or processes become, the higher is the direct or indirect dependence on various external sources of information, ideas and knowledge'.[529] Open innovation on a global scale can enable broader knowledge diffusion, and allow domestic actors to in-source knowledge and technologies to build their R&D capacity in a highly complex area such as genomic medicine, especially in the cases of developing countries. Furthermore, these international linkages may contribute to knowledge spill-overs, which can be transformed by domestic actors into useful technologies, if supported by policy that encourages networking and permeability for the flow of information.

However, the globalisation of genomic research does not detract from the requirements of domestic industries to develop. As Herstad et al observe,[530] Chesbrough emphasises the use of these knowledge spill-overs from the knowledge commons, but this may in fact reduce domestic capability in the long run. If there is a perpetual dependence on external sources, domestic industries are less likely to invest in their own R&D, which would mean that in the long-run, knowledge flow will become unidirectional as opposed to bi-directional, and capacity to absorb from external sources will not increase dynamically in these industries.[531] Cohen and Levinthal define absorptive capacity as 'the ability to recognize the value of new information, assimilate it, and apply it to commercial ends'.[532] Hence, prior knowledge created by internal R&D is essential in increasing absorptive capacity, and an open innovation model should accommodate both in-sourcing and internal

[526] Herstad (note 461 above; 114).

[527] Gastrow (note 54 above; 58).

[528] Herstad (note 461 above; 115).

[529] Ibid.

[530] Ibid.

[531] Herstad (note 461 above; 115-117).

[532] W M Cohen & D A Levinthal 'Absorptive capacity: a new perspective on learning and innovation.' (1990) 35 *Administrative*

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development, which may contribute to out-sourcing later on. Thus, if the Draft Policy should seek to foster open innovative practice, it would need to balance the formation of international linkages with that of domestic networking and growth.[533] Currently, although the Draft Policy is unclear about how it would foster international linkages to achieve this balance, like the Bayh-Dole Act[534] of the US, SA's IPR Act articulates the need to support domestic firms, especially SMEs, and the need to develop policies that prioritise national linkages. Therefore, when focussing on the field of genomic medicine, the Draft Policy should appoint a focus group that identifies: a) how the biotechnology industry of SA is formed and how productive it is; b) what are the current international influences; c) how have comparator countries addressed the issues of domestic and international linkages in the industry; and d), how should SA address the same issues.

A key reform introduce by the Draft Policy is the application of a substantive search–and–examination (SSE) process to stimulate 'genuine innovation',[535] as the Draft recognises that whilst SA patent law provides for SSE, as discussed in Chapter Three, limited human and financial resources in the past have curtailed efforts to effectively apply such a process.[536] Currently, only a depository system is employed, with SSE only be applied if the patent is challenged in litigation. This allows for a significant difference in patenting trends in SA as compared to comparator countries such as Indian or Brazil. According to a study by researchers from Harvard and Columbia, SA grants 93% of the patents applications, compared to India's 19% or Brazil's 14%. Even the US, a country which promulgates strong patent law, only grants 61% of the patent applications. This is an important flexibility that may prevent the patenting of subject matter that does not fit the criteria of inventions, such as isolated DNA sequences (referring to *Myriad*[537] from the previous chapter). In this way, genomic sequences, research tools and inventions that do not fit the criteria may be placed in the public domain or in knowledge commons, but it is important that policy considers the role of secrecy in lieu of patenting. There must be sufficient incentive, generated by clearly–defined means of value capture, to share IP in collaborations otherwise entities may not publically disclose their results and inventions as in done patenting *quid pro quo*.

The Draft Policy also intends TRIPS flexibilities to be used optimally to meet public health needs. As discussed in Chapter Three, apart from the actual flexibilities stated in TRIPS, there may be significant room for the interpretation of its provisions, especially regarding interpreting patentable

[533] Herstad (note 461 above; 113).

[534] Patent and Trademark Law Amendments (note 212 above).

[535] Draft IP Policy (note 81 above; 319).

[536] Ibid 330.

[537] *Myriad* (note 24 above).

subject matter criteria.[538] The Draft Policy suggests that there may be a way to interpret TRIPS so as to allow for SSE limited to certain fields of public interests so as to accommodate for capacity constraints. Whilst Article 27.1 of TRIPS states that all fields of technology should enjoy patent rights, this does not mean that rights have to be granted through a depository system. As long as an alternative system, such as SSE, is used that potentially allows patents in the field, this article is not violated.

The Draft Policy also values voluntary licensing to third parties. To optimise the impact of voluntary licensing that promotes access and innovation through technology and information transfer, the Draft Policy calls for transparency regarding the terms and conditions of the licensing contract. The Draft Policy concurs with the IPR Act[539] of SA on how publically–funded IP should be licensed, preferring non–exclusive licensing to SMEs and Broad–Based Black Empowerment Enterprises (BBEEE),[540] but these preferences may not always be feasible, for example, where exclusive licensing may be better suited (as identified above by 100KGP)[541], or where large firms are necessary for innovation. As the IP Policy of SA intends to propagate the ideals of the IPR Act, and promote the conditions of 'fair' licensing,[542] possibly modelled on FRAND terms, the policy itself should delineate what these conditions are and how they can be achieved. By doing so, the policy will engender a national protocol on licensing that will improve technology transfer and knowledge flows through the public and private sector collaborators.

In a study conducted by Gastrow, he observed that firms, universities and public science institutes are all active collaborators, with evidence of open innovation.[543] He also found that there was a great propensity to collaborate with other domestic firms or within the firm, or to collaborate with international firms, as well as government organisations.[544] However, he finds that the greatest single mode of collaboration is the industry–university linkage, particularly with foreign universities.[545] A pertinent issue to this type of linkage is that of research exemptions on patented inventions. The Draft Policy recognises that to promote the dissemination and advancement of knowledge, and 'preserve the scope of researchers'[546] provisions on research exception and

[538] Ibid 333.

[539] IPR Act (note 213 above).

[540] Ibid 338.

[541] Genomics England (note 405 above).

[542] Ibid 338.

[543] Gastrow (note 54 above; 53).

[544] Gastrow (note 54 above; 56).

[545] Gastrow (note 54 above; 56).

[546] Draft IP Policy (note 81 above; 338).

experimental use must be clarified.[547] This clarification will ease the flow of knowledge through research, necessary for openness in innovation.

The Draft Policy, although not explicitly geared towards open innovation, recognises the importance of allowing knowledge to flow between the public and private sectors. Its provisions on granting of patents, licensing practices and research exemptions are foundational for future open collaboration, although the policy does not fully address the potential of patent pools and clearinghouses in promoting innovation. Moreover, as a national policy, there is a stronger focus on domestic linkages than international linkages, which may be detrimental in a global field like genomics. However, this policy is promising, and, together with the law, will inform how national bodies create innovative practices. One such body, the Medical Research Council, will be discussed below regarding how well suited its IP policy is to fostering open collaborative innovation.

(ii) The Medical Research Council

The South African Medical Research Council (MRC) is a national research body, mentioned in Chapter One, which includes research, development and technology transfer in its mandate on the improvement of public health.[548] Through its Technology Transfer Unit and its Strategic Health Innovation Partnerships (SHIP), the MRC endeavours to partner with local universities, science councils and the private sector to translate its research into applications that can improve healthcare.[549] These partnerships, occurring at different stages of the innovation chain, are indicative of openness in the MRC's innovation, but the body's IP policy will determine the level of open collaboration engendered by the MRC.

In its *Management and Commercialisation of Intellectual Property Policy*, the MRC identifies IP as a key asset,[550] and sets out to identify, protect, utilise and commercialise IP emerging from its research, for public benefit,[551] and to reward relevant stakeholders to encourage further investment.[552] As with the policy framework above, and in line with the concept of balancing heterogeneous interests, the policy recognises the need to achieve a 'balance between research excellence, academic freedom and capacity development and the need to commercialise inventions through innovative and

[547] Ibid 337.

[548] SAMRC 'Overview' (2017) available at *http://www.mrc.ac.za/*, accessed on 02 November 2017.

[549] SAMRC 'Strategic Health Innovation Partnerships' (2017) available at *http://www.mrc.ac.za/*, accessed on 02 November 2017.

[550] South African Medical Research Council (note 340 above; Article 3.2).

[551] Ibid 2.3.

[552] Ibid 2.4.

entrepreneurial endeavour' through the involvement of multiple actors, including the MRC, industry, society and IP creators.[553]

The policy aligns with the policy framework for open innovation provided above in that it seeks to create a flow of information through 'open dissemination and free exchange of research results',[554] but like with BIOS[555] and 100KGP[556], values the protection and management of IP in this process.[557] In its policy, the MRC sets out how IP ownership should occur and how benefits from its commercialisation should be shared between the MRC and member institutions. Unlike with 100KGP[558], the MRC is more willing to vest IPRs in the participating institutions, or to jointly own IP.[559] The MRC is also willing to share or vest complete IP ownership with sponsors or private funding organisations, especially where the MRC is unable to commercialise the IP. This willingness to share IP ownership may be inviting for potential MRC collaborators, and could facilitate wider commercialisation of technologies. Moreover, the MRC will ensure that the MRC and IP creators are not prevented from using the IP for further research, thus maintaining a knowledge flow for cumulative innovation.[560] The policy also provides for the exclusive or non–exclusive licensing of IP to third parties for commercialisation that will benefit the public, increasing the value of resources to consumers. Importantly, if the licensee fails to exploit the IP adequately, the MRC retains the right to exploit the IP itself or contract another organisation to do so, thus ensuring innovation is optimised.

In terms of its licensing policy, the MRC, like the initiatives examined in the above sub-section, has a preference for non–exclusive licensing, promoting the involvement of more parties, and encouraging a wider dissemination of knowledge.[561] The MRC also intends to limit licenses according to geographic location, a particular market or sector, and/or field of use, as explained in the policy framework above.[562] Furthermore, diligence and performance clauses are attached to exclusive licenses to optimise their benefits.[563] The MRC policy is also aligned to the IPR Act, which delineates the rights of the state regarding licensing and march-in rights, and which gives preference to SMEs and BBBEE firms, as discussed in the previous chapter, widening the range of potential

[553] Ibid 3.1.

[554] Ibid 3.2.2.

[555] CAMBIA (note 57 above).

[556] Genomics England (note 405 above).

[557] South African Medical Research Council (note 340 above; Article 3.2.3).

[558] Genomics England (note 405 above).

[559] South African Medical Research Council (note 340 above; Articles 3.3.1 – 3.3.5).

[560] Ibid 3.3.9, 3.3.17.

[561] Ibid 3.10.1.1-3.10.1.2.

[562] Ibid 3.10.1.1.

[563] Ibid 3.10.1.3.

collaborators.[564] However, the preferences to license to the SA government, or to firms (including joint ventures and spin–outs)[565] domiciled in SA encourages national linkages over international linkages, which may be detrimental in the long run, as discussed under the Draft Policy.

To further allow for the dissemination of knowledge, the MRC does not claim ownership of not–for–profit academic works, but does specify that it should have indefinite, free, non–exclusive use of such material.[566] However, commercial IP, such as databases or electronic data, which may be appropriated by external entities and marketed at costs that are prohibitive to knowledge dissemination, will be owned by the MRC unless otherwise negotiated (in which case the MRC retains the right to use such IP).[567] Like with BIOS[568] and 100KGP[569], this will prevent a hegemony over valuable information needed for further innovation, creating a more open access environment.

The MRC also promotes publication of research results in line with the principles of open science discussed above. However, where commercial potential exists, the MRC encourages patent applications to be filed before results are openly communicated.[570] This is not an indefinite inhibition of open communication of results, but to ensure that IP can be commercialised to more effectively benefit the public in appropriate circumstances. This commercialisation is further supported by the inclusion of spin–out companies and joint ventures in the IP policy, as well as licensing and placing invention in the public domain for open access where suitable and approved by the National Intellectual Property Management Office (NIPMO).[571] If regulated appropriately, these commercial entities could strategically engage with industry and the public sector to create a network of open innovation to maximise the application and benefit of IP.[572] The MRC, like the 100KGP,[573] also intends on commercialising IP to generate income, which will be shared accordingly with involved MRC members.[574] This may encourage participation in MRC research projects and may create sustainability for future innovation.

The provisions of the MRC IP policy align with the main purpose of the consolidated framework provided in sub-section II (a) — to create open dissemination of knowledge and free

[564] Ibid 3.10.1.5.

[565] Ibid 3.10.2.-3.10.3.

[566] Ibid 3.3.14.

[567] Ibid 3.3.14.

[568] CAMBIA (note 57 above).

[569] Genomics England (note 405 above).

[570] South African Medical Research Council (note 340 above; Article 3.8).

[571] Ibid 3.9, 3.10.5.

[572] Ibid 3.10.

[573] Genomics England (note 405 above).

[574] South African Medical Research Council (note 340 above; Article 3.12).

exchange of research. However, the MRC, unlike the biobanks and databases examined above, does not have an explicit stance on creating open access databases and knowledge commons, either by acting as a platform, or by stipulating that collaborators do so. The MRC could take a firmer stance on the data–sharing responsibilities of collaborators, and could include provisions on creative licensing such as copyleft licensing that promotes open access. The MRC, like the Draft Policy, offers sparse direction on patent pooling and clearinghouses, and there is a stronger focus on domestic rather than international linkages. However, the MRC recognises the need to create knowledge flow and to capture the social and financial interests of the different actors, and sets a strong foundation for open collaborative innovation between the public and private sectors. With time it will be seen how the MRC intends to engage in innovation in genomics medicine, and whether it develops its IP policy to build on the foundations of open collaborative innovation it has built.

III. Conclusion

Open innovation as conceptualised by Chesbrough has evolved and includes the model of open collaborative innovation – a model that is highly suitable to meeting the demands of the complex, global and rapidly transforming field of genomic medicine. 'If an organisation lacks the ability to collaborate, it lacks the ability to innovate and grow'.[575] This transition of the genomics field from closed to open innovation requires entities to revise their policies on innovation, including their IP policies. In this chapter, a consolidated IP policy framework geared towards open collaborative innovation is provided in section II (a), and is used as basis for examining the national Draft IP policy of SA and its MRC. From this comparison it appears that both the Draft Policy and the MRC recognise both the importance of knowledge dissemination and translation into useful applications to satisfy public and private interests to innovation and capture value — the licensing practices of these instruments align with the OECD's *Guidelines*[576] and of more open collaborations, such as 100KGP[577] and BIOS[578], included in the consolidated framework provided above. However, neither offer guidance on optimising alternative mechanisms for more open collaborative knowledge transfer, such as patent pooling and clearinghouses. Without clear guidance, these mechanisms may not be considered by domestic and international actors in the industry, and may not be used optimally to reduce transaction and licensing costs so as to promote the maximum use of resources in innovation. Additionally, lack of guidance may result in intentional or unintentional anti–competitive practices

[575] Shuman & Twombly (note 380 above; 24).

[576] OECD (note 65 above).
[577] Genomics England (note 405 above).
[578] CAMBIA (note 57 above).

in those patent pools and clearinghouses that emerge, which could be deleterious to the effectiveness of the mechanism and could cause its premature termination by the state.

Moreover, although they mention opening access to information, neither the Draft Policy nor the MRC commit to initiating a strong scientific knowledge base, either in the public domain or as a knowledge commons through databases or biobanks. Rather, as found in a closed innovation model, there is a stronger focus on using IP for the purposes of commercialisation, rather than examining its role in growing knowledge bases. The provisions in the Draft Policy[579] and the MRC IP Policy[580] place emphasis on how commercialisation may be promoted through domestic and international linkages, and through national patent law amendments, such as the review of the SSE process in South Africa or the IPR Act to support the dissemination of publically-funded inventions. This is promising for established industries that are on the precipice of commercialising their innovations. However, in a nascent industry like genomic medicine, where innovation must still occur at the R&D stages prior to commercialisation, what is first needed is the development of a strong knowledge base that can serve the R&D needs of the industry. Both the Draft Policy[581] and the MRC IP Policy[582] omit specific provisions on how to develop this knowledge base either at a national level or through international linkages. Both these policies should address how IP may be used to promote collaboration in R&D, and should pay greater attention to structures such as open access databases, patent pools and clearinghouses on a domestic and global level that could facilitate open collaboration prior to commercialisation. In a globalised knowledge economy, and especially in the knowledge-intensive field of genomic medicine, neglecting collaborative innovation in R&D that generates knowledge may retard long term social and financial value capture as the knowledge available to the local industries to innovate is diminished.

South Africa could draw on the experience of the UK — where the UK Department of Health created the subsidiary body, Genomics England, to establish and govern its 100KGP biobanks and database.[583] South Africa similarly needs to appoint a governing body that can either oversee a national, publically-accessible biobank and database, or coordinate multiple fragmented databases and biobanks. Without engaging in an extensive discussion that is beyond the scope of this dissertation, it is proposed that the MRC is a possible candidate, being a national research body. However, other institutions, such as universities, or an independent conglomeration of private and public actors acting in concert with the state, could also be oversight bodies in the nationalisation of genomic knowledge.

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[579] Draft IP Policy (note 81 above).
[580] South African Medical Research Council (note 340 above).
[581] Draft IP Policy (note 81 above).
[582] South African Medical Research Council (note 340 above).
[583] Genomics England (note 405 above).

Policy can be used to elaborate on the unclarified areas of the law, such as genome patenting for the benefit of public health. The Draft Policy intends to focus on public health, but its biotechnology focus seems to angle towards agriculture, with public policy on genomics left undeveloped. The gap could be addressed by the MRC, a major national research body, but its IP policy is vague regarding the patenting of research tools in genomics, such as genomes sequences. Though the limitations of this dissertation preclude a comparison with IP policies of organisations similar to the MRC in other countries, it would be valuable to compare their provisions of patenting in genomics. It is suggested that the MRC clarifies its position on genomes patenting so that collaborators are not deterred by uncertainty on this matter.

On the point of collaboration, both the Draft Policy and the MRC, like the IPR Act,[584] focus on domestic linkages, especially regarding the public sector and small businesses. There is uncertainty as to how large domestic private companies are regarded in the hierarchy over the licensing policies, which may exclude these entities from participating in the knowledge flow and technology transfer required for open collaboration. From the provisions of both the policies, the preference given to SMEs and BBEEE firms, combined with the lack of direction regarding large multinationals, may also exclude these multinational firms from collaborating. It is recommended that both policies encourage the inclusion of these entities in collaborations, and afford greater attention to fostering global linkages.

As the policies of both the MRC and state have significant bearing on the innovation landscape of South Africa, their IP policies could be used to promote the principles of open collaborative innovation so as to satisfy private and public interests in innovation in genomic medicine. Both the MRC's IP policy and the Draft Policy have laid a foundation for open innovation through their recognition of the importance of dissemination of knowledge and optimal distribution of innovation, and their provisions on licensing align significantly with those of initiatives based in open innovation, as discussed under the consolidated policy framework.[585] However, neither body explicitly identifies the value of open collaborative innovation in a field like genomics, where considerable R&D is necessary and would benefit not only from the growth of the domestic industry, but also from networking with international players. As key industry players, such as the large multinationals, are recognising the value of open collaborative innovation in fulfilling their own private interests in profit, as well as the public interest in relation to advancement in the field, the existing policies should adopt a firmer stance on promoting open innovation in the genomic industry. The Draft Policy is a national instrument, and so addressing the specific topic of open innovation in genomics may be

[584] IPR Act (note 213 above).

[585] Section II (a).

unrealistic. However, the policy could better address innovation in healthcare, which has been cursorily mentioned in its objectives. The MRC is in a prime position to address the specific topic of open innovation in genomic medicine, as it as a national body that coordinates research and governs key players in the field. If the MRC is to adopt a firm stance promoting openness in innovation, it would need to first ascertain the amenability of the domestic and international industries to adopting open collaborative approaches. It is found that the biotechnology and pharmaceutical industries are accelerating in their willingness to adopt openness. Pursuant to this, the MRC should base its policy on existing best practices that are evidently viable in the industry. As it has already laid a reasonable foundation in its IP policy for openness in innovation, as discussed above, the MRC has the potential to drive open collaborative innovation in genomic medicine.

Chapter Five: Conclusion

Open collaborative innovation, evolved from Chesbrough's firm-centric open innovation model, is based on the flow of knowledge between collaborators.[586] Juxtaposed to the traditional closed innovation model, open collaboration uses both the public domain and knowledge commons, as well as IPRs to facilitate the transfer of knowledge. This open model has established itself in the software industry, and is budding in the biotechnology industry as players address declining R&D and increasing costs and complexity of technologies. Players recognise that a model promoting rapid breakthrough innovation is needed to satisfy: public interests to advanced health technologies; private interests to improved profits; and private-public interests in sustaining future innovation. As seen in the examples of CAMBIA's BIOS Initiative[587] and the 100KGP[588], although the research goals of collaborators may not be aligned, there is a common vision under the initiatives to create open access to knowledge and sustainable innovation to meet public healthcare needs.

Healthcare is also evolving to adopt a more personalised approach to medical decisions. This personalised medicine can be based on a number of individual characteristics, and herein genomic medicine is discussed, where medical decisions are based on a patient's unique genomic constitution. These decisions involve the use of diagnostic and therapeutic technologies that are highly complex and developed from extensive genomic knowledge. As a relatively nascent field, significant R&D is required to rapidly generate a rich source of genomic knowledge and research tools for these technologies to emerge, and innovation has to be optimised to apply these technologies effectively to address the needs of public health. Genomic databases and biobanks are critical infrastructures in the generation of genomic knowledge, as discussed in Chapter Two, and under a suitable model can foster downstream innovation by coordinating knowledge and making this available to researchers. In this dissertation, it is proposed that open collaborative innovation is a fitting model, as various examples of initiatives that employ this model in a private-public sphere, such as BIOS[589] and 100KGP[590], are used. The policies of these initiatives dictate how open collaboration may be achieved, and particularly focus is on their IP policies to examine the role of IP in engendering open innovation. These policies are dictated by international, national and regional IP law, which have been discussed in Chapter Three.

Open collaborative innovation is a model that does not only incorporate the public domain and knowledge commons; it is also steeped in Chesbrough's model of open innovation that relies on

[586] Shuman & Twombly (note 380 above; 12).

[587] CAMBIA (note 57 above).
[588] Genomics England (note 405 above).
[589] CAMBIA (note 57 above).
[590] Genomics England (note 405 above).

active IP strategy to achieve knowledge flows. Though there is a paucity of conclusive evidence on the impact of IPRs on innovation in genomic medicine under a closed innovation model, it is found that IPRs are important in the structure of open collaborative innovation, enabling licensing and stimulating participation of profit-seeking entities in open initiatives. For such a model to function optimally in genomic medicine, patent law and policy needs to be clarified. It is concurred with prior commentary that although there is an attempt to harmonise IP law through the international framework of the TRIPS Agreement, there is divergence amongst member states when it comes to the particulars of genomics.[591] TRIPS does not elaborate on the issues of genomic patenting; rather, its open-ended provisions underpin the needs to transfer technology, protect inventors and satisfy public health goals. And as yet, there is no legal international consensus on the patenting of the human genomic knowledge and downstream technologies. Landmark cases, such as *Myriad*,[592] have led to a review of legislation on patenting regarding biological material in certain jurisdictions, such as the US, but relying on litigation to ignite a response to genome patenting may not be the most effective and expeditious solution to providing clarification to support innovation. This is a challenge that South Africa faces in light of its depository system of patent application, where the criteria for inventiveness are not examined, and the patent is only challenged in litigation. As litigation is costly and time-consuming, patents may be left unchallenged despite their weak grounds for inventiveness and their impact on further innovation. South Africa's Draft IP Policy[593] intends to reform the depository system to that of a search-and-examination (SSE) system, but this will require significantly greater human resources. The suggestion that the SSE system should be first adopted by priority areas is agreeable. Considering the Draft Policy's attention to public health, and the potential of genomic medicine to address public health needs, it is recommended that development and adoption of patent law and policy on genomics be prioritised. As this national IP policy is still in its draft phase, there may be ample opportunity to amend its provisions, and once this is achieved, other bodies, such as the MRC, may have greater clarity in building a foundation geared towards open innovation in genomic medicine.

Once the field of genomics is prioritised, the next task is to determine what constitutes a patentable invention. Though TRIPS[594] and national legislature include the criteria of inventiveness, novelty and utility in their provisions, without clear guidance, there is significant room for interpretation. The USPTO guidelines[595] and the EU Directive[596] are examples of provisions that are

[591] Strandburg (note 42 above).

[592] *Myriad* (note 24 above).

[593] Draft IP Policy (note 81 above).
[594] TRIPS Agreement (note 15 above).
[595] USPTO (note 288 above).
[596] EU Directive (note 44 above).

more specific in how elements of genomic medicine may be treated, although countries such as SA lag behind in providing clear guidance. Moreover, even although these guidelines provide clarity, they are divergent, and in a globalised economy of international players, initiatives in genomics that rely on crossing borders need aligned provisions. To address this it is firstly suggest that genomics is divided into a) genomic knowledge that is essential as research tools, and b) downstream applications of that knowledge, and that these divisions are subjected to tailored provisions, as proposed by BIOS.[597] Drawing on *Myriad*[598], it is then recommended that isolated DNA should be non-patentable, and a review of the decision on cDNA, which is also a critical research tool found to be a product of an obvious step found in nature, is advocated. Then, following the examples of the SNP Consortium, the HapMap Project, BIOS[599] and 100KGP,[600] it is suggested that such basic genomic knowledge is placed in a knowledge commons that can be freely accessed, but is protected by creative licensing clauses, such as click-wrap licensing or copyleft licensing, to enable sustainable open innovation practices. Downstream technologies should also be licensed according to open practices to maintain knowledge flow, which includes non-exclusive licensing and reduced licensing costs, which can be facilitated by patent pools and clearinghouses.

To optimise the potential of genomic medicine in public health, public-based infrastructures such as genomic biobanks and databases are critical. The South African Medical Research Council (MRC) is a foremost organisation of research in the country, and as such, has a vital role in directing the course of innovation in genomic medicine. The MRC, like other public-based initiatives in other countries such as the 100KGP[601], can encourage the generation of vast amounts of genomic knowledge on sequences and their relation to disease through establishing or overseeing public biobanks used for research, and can coordinate this knowledge in public databases. This knowledge can then be used by developers in the private or public sector in downstream innovation. However, before fuelling the engine of genomics medicine, the MRC will need a comprehensive IP policy on what may be patented and what remains in the public domain, how access to resources will be governed, and on the particulars of licensing and the engagement of private and public actors. This is largely determined by the national patent laws and policies, but as these are vague on the matter of genomics, it is recommended that the MRC follows the emerging trend in healthcare of open collaborative innovation, and a comprehensive policy framework built on the IP policies on various open initiatives has been provided. With the initiation of the South African Human Genome

[597] CAMBIA (note 57 above).
[598] *Myriad* (note 24 above).
[599] CAMBIA (note 57 above).
[600] Genomics England (note 405 above).
[601] Genomics England (note 405 above).

Programme by the Department of Science and Technology,[602] the role of the MRC and public policy will be more prominent in guiding how the data of this project is governed to allow future innovation.

Although there is a focus on the transfer of resources as knowledge and technology through IP policy and law, the foundation of IP resides within the human resources of an entity, and for open collaborative innovation to be optimised, there needs to be a development of a community of collaboration, rather than just policy on licensing practices and how IPRs are allocated. This is based on Aubrey and Al-Laham's findings that alliances based solely on licensing patents was not sustainable or useful,[603] and that together with the knowledge-based transfer of licensing patents, it was also necessary to transfer relational components, such as expertise and skills of researchers.[604] The Human Genome Project is such an example, where a global community of researchers contributed to a common goal. However, collaboration does not necessarily necessitate a common goal, but rather, in the case of open collaborative innovation, a dedication to creating openness. Future research should explore how meaningful communities of collaborators are created and sustained, examining the all relevant policies, not only those limited to IP, that bear on innovation.

An additional point on the extensive R&D that is required in genomic medicine to understand and treat genome–linked diseases is that the genome is now recognised as only one aspect of disease aetiology from the working of the cell; a second aspect, called epigenomics, has also been identified. Epigenomics relates to mechanisms apart from DNA sequences that cause changes in genome expression.[605] These mechanisms incorporate environmental influences on genome expression, which may even include childhood care or the lifestyle of ancestors,[606] and as such, requires extensive data collection. Cancer is one disease in which the study epigenomics is established — scientists find that a certain mechanism called DNA methylation of genes is much higher in cancerous cells than in normal cells.[607] The understanding of these mechanisms, and the technologies developed thereafter have led to patents, much like in genetics and genomics. Similarly, important research tools or diagnostic methods may be patented,[608] and the field of epigenomics may be stagnated by a closed model of innovation, as discussed in genomics. As genomics and epigenomics operate together in the workings of the cell, these should be studied concurrently. Thus, when developing the IP policies for

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[602] M S Pepper 'Launch of the South African Human Genome Programme' (2011) 101(5) *SAMJ* 287.

[603] Clarke & Turner (note 194 above; 90-91).

[604] Ibid.

[605] W Noonan, A D Dismuke & M S Turker 'Epigenetic patents: a stressful environment for an emerging science' (2013) 32(5) *Biotechnology Law Report* 303.

[606] Ibid 302.

[607] Ibid 304.

[608] Ibid 305-310.

an open collaboration innovation model in genomics, these policies must also consider the role of IP in epigenomics.

Lastly, whilst open collaborative innovation, based on the current trends of transition in innovation models in the biotechnology industry, is advocated, the model must be analysed to produce conclusive evidence that it is indeed a beneficial model to adopt in genomic medicine. In the long-run, the licensing practices, knowledge sharing, and networking effects and strategic alliances[609] of open collaborative initiatives needs to be evaluated in terms of their impact on innovation, the economy and access to healthcare.

[609] Clarke & Turner (note 194 above; 95).

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UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

29 June 2017

Ms Siddharthiya Pillay (211505906)
School of Law
Howard College Campus

Dear Ms Pillay,

Protocol reference number: HSS/0930/017M
Project title: Examining the role of intellectual property law, policy and management in open innovation models that facilitate innovation in and access to personalised medicine

Approval Notification – No Risk / Exempt Application

In response to your application received on 27 June 2017, the Humanities & Social Sciences Research Ethics Committee has considered the abovementioned application and the protocol has been granted **FULL APPROVAL.**

Any alteration/s to the approved research protocol i.e. Questionnaire/Interview Schedule, Informed Consent Form, Title of the Project, Location of the Study, Research Approach and Methods must be reviewed and approved through the amendment/modification prior to its implementation. In case you have further queries, please quote the above reference number.

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

The ethical clearance certificate is only valid for a period of 3 years from the date of issue. Thereafter Recertification must be applied for on an annual basis.

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

Yours faithfully

.....
Dr Shamila Naidoo (Deputy Chair)

/ms

Cc Supervisor: Dr Donrich Jordaan
Cc Academic Leader Research: Dr Shannon Bosch
Cc School Administrator: Mr Pradeep Ramsewak

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HUMANITIES AND SOCIAL SCIENCES RESEARCH ETHICS COMMITTEE ETHICAL CLEARANCE CHANGE OF DISSERTATION TITLE FORM	
School	Law
Student Name	Siddharthiya Pillay
Student Number	211505906
Supervisor	Dr D W Thaldar (formerly known as D W Jordaan)
Co-supervisor	N/A
Old Title	Examining role of IP law, policy and management in open innovation models that facilitate innovation in and access to personalised medicine.
New Title	Examining role of IP law, policy and management in open innovation models that facilitate innovation in and access to genomic medicine.
Reason for Change	The reference to *genomic* medicine is more accurate than the overarching term of *personalised* medicine.
Signatures	
Student:	
Supervisor:	
Co-supervisor:	N/A
ALR:	
HSSREC:	

*Reference number: **HSS/0930/017M**

****This request was submitted to the College Office upon submission of the mini-dissertation in February 2018.**