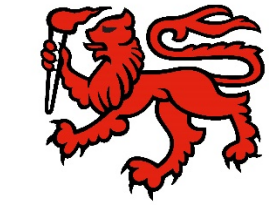

Patenting Bioprinting: An Ethical Dilemma in the Provision of Accessible Health Technologies

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May 2021

In memory of the ones lost on this journey

Oludolapo Bryan Oduniyi (1983 – 2019)

Henry Kehinde Aderibigbe (1930 – 2021)

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Abstract

For decades, researchers in the tissue engineering and regenerative medicine sphere have continuously worked to replicate naturally occurring tissues and organs for research and transplantation purposes. Whilst this has been met with a certain degree of success, it would appear that many engineered tissue products lack the structural and functional complexity found in their naturally occurring counterparts. To this end, the emergence of bioprinting with its promises to reproduce the complexity and intricacy of native tissues through precise placement of cells marks an important milestone not only in the advancement of tissue engineering, but also for the future of healthcare.

In simple terms, bioprinting involves the use of a combination of living biological cells, and other living and non-living materials to print three-dimensional functional living tissue constructs such as breast, liver, kidney and skin tissue. It is anticipated that such bioprinted constructs[1] will be used in the areas of disease modelling and research; drug discovery and animal testing; as well as treatment of chronic diseases and tissue/organ transplantation. Given these potential applications of bioprinting, it is pertinent that ethical,[2] legal and socio-economic concerns regarding the technology are fully explored as the technology advances. This is especially so in light of the developing patent landscape for bioprinted constructs which are generally designed to replicate their naturally occurring counterparts - the latter being unpatentable subject matter.

Accordingly, this thesis examines the law on patentability of bioprinted constructs (which are combinations of living and non-living materials) and questions whether they ought to be patentable given the implications of monopolising body parts. In particular, this thesis focuses on three jurisdictions with disparate approaches to patentability – Australia, Europe (under the *European Patent Convention*) and the United States of America. It considers whether the disparate approaches to patentable subject matter and morality of patenting yield similar or different results.

[1] This is the collective term adopted in this thesis to describe all the various kinds of living tissues and organs fabricated via bioprinting.

[2] The term ethics/ethical is used throughout this thesis in its general sense to encompass questions about justice, morality, right and wrong.

Noting that the differences in legislative provisions appear to have limited impact on patentability, this thesis also considers the parameters of access to patented bioprinted constructs. It examines matters pertaining to access to bioprinted constructs in themselves, as well as access to the technology. In this regard, this thesis concludes that patent flexibilities in their current form are not particularly suited to the nature of bioprinted constructs. Accordingly, ensuring technological access is especially important in order to ameliorate the effects of a patent grant and ensure equitable access for all.

Chapter 1

1 Introduction to Thesis

1.1 Introduction

Patents have generally been considered a means of incentivising innovation in all fields of technology. This is premised on the exclusive rights granted to right holders in exchange for public disclosure. Nonetheless, the emergence of new technologies particularly in the biotechnology space has continuously challenged existing notions about the suitability of patents for all fields of technology. This is especially in light of ethical concerns about access to such technologies and the implications of patenting of life forms.[1]

This thesis is concerned with one such emerging technology – bioprinting. Bioprinting is one of the most innovative health technologies to have emerged in the past decade.[2] Originally, it was defined as 'the use of material transfer processes for patterning and assembling biologically relevant materials, molecules, cells, tissues, and biodegradable biomaterials with a prescribed organization to accomplish one or more biological functions'.[3] However, this definition has since been enlarged to

> the use of computer-aided transfer processes for patterning and assembling living and non-living materials with a prescribed 2D or 3D organization in order to produce bio-

[1] See generally Robert P Merges, 'Intellectual Property in Higher Life Forms: The Patent System and Controversial Technologies' (1988) 47 *Maryland Law Review* 1051; Timothy Caulfield and Roger Brownsword, 'Human Dignity: A Guide to Policy Making in the Biotechnology Era?' (2006) 7(1) *Nature Reviews Genetics* 72; Timothy Caulfield and Audrey Chapman, 'Human Dignity as a Criterion for Science Policy' (2005) 2(8) *PLoS Med* e244; Abraham Drassinower, 'Property, Patents and Ethics: A Comment on Wendy Adams' '"The Myth of Ethical Neutrality"' (2003) 39(2) (2003) *Canadian Business Law Journal* 214; L Bently and B Sherman, 'The Ethics of Patenting: Towards A Transgenic Patent System' (1995) 3(3) *Med Law Rev* 275; Belinda Huang, 'Biotech Patents in Australia: Raising the Bar on the Generally Inconvenient Exception' (2013) 24 *Australian Intellectual Property Journal* 40; David B Resnik, 'DNA Patents and Human Dignity' (2001) 29(2) *The Journal of Law, Medicine & Ethics* 152; Australian Law Reform Commission, *Genes and Ingenuity: Gene Patenting and Human Health* (Report 99, 29 June 2004) <http://www.alrc.gov.au/publications/report-99>; Michael A Heller and Rebecca S Eisenberg, 'Can Patents Deter Innovation? The Anticommons in Biomedical Research' (1998) 280 *Science* 698; Andrea Boggio and Calvin W. L. Ho, 'The Human Right to Science and Foundational Technologies' (2018) 18(12) *The American Journal of Bioethics* 69; Nuffield Council on Bioethics, *Emerging Biotechnologies: Technology, Choice and the Public Good* (Nuffield Council on Bioethics, 2012).

[2] 'Top 10 Medical Innovations in the Last Decade', *Firstpost* (Web Page, 30 December 2019) <https://www.firstpost.com/india/india-reports-highest-single-day-spike-of-over-1-15-lakh-new-covid-19-cases-tally-reaches-12801785-9504591.html>; Sergey Young, 'Five Tech Innovations That Could Change Healthcare This Decade', *Forbes* (Web Page, 2 September 2020) <https://www.forbes.com/sites/forbestechcouncil/2020/09/02/five-tech-innovations-that-could-change-healthcare-this-decade/?sh=714088252145>.

[3] This definition was formulated at the First International Workshop on Bioprinting and Biopatterning held at the University of Manchester (United Kingdom) in September 2004: Fabien Guillemot, Vladimir Mironov and Makoto Nakamura, 'Bioprinting is Coming of Age: Report from the International Conference on Bioprinting and Biofabrication in Bordeaux (3B'09)' (2010) 2(1) *Biofabrication* 010201, 2.

engineered structures serving in regenerative medicine, pharmacokinetic and basic cell biology studies.[4]

Simply put, bioprinting involves the use of a combination of living biological cells and non-living material to print functional living tissues/organs such as breast, liver, kidney and skin tissue in three-dimensional ('3D') form. By virtue of the fact that such tissues/organs are bioprinted, they have generally been described as 'bioprinted constructs' in existing literature.[5] As such, this is the term adopted throughout this thesis in describing tissues/organs fabricated via bioprinting.

Whilst bioprinting in itself is a relatively recent development, its core features are rooted in the concept of 3D printing (otherwise known as additive manufacturing), which is often traced back to an article published by David Jones on 3 October 1974 in the New Scientist.[6] It is useful, however, to note that earlier in 1971, Wyn Kelly Swain had filed a patent for an idea similar to what Jones had described in his article, but was not granted said patent until 1977.[7] Thereafter, in 1983, Charles (Chuck) Hull created the first-ever 3D printed part, and is thus regarded as the inventor of Stereolithography (a form of 3D printing).[8] Between 1984 and 1986, he filed and received a patent for his Stereolithography Apparatus ('SLA') - the world's first 3D printer, which was commercialised in 1987.[9]

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[4] Ibid: This new definition was proposed at the International Conference on Bioprinting and Biofabrication held in Bordeaux (France) in July 2009.

[5] See, eg, Nitin Charbe, Paul A McCarron and Murtaza M Tambuwala, 'Three-Dimensional Bio-Printing: A New Frontier in Oncology Research' (2017) 8(1) *World Journal of Clinical Oncology* 21; Sean V Murphy and Anthony Atala, '3D Bioprinting of Tissues and Organs' (2014) 32 *Nature Biotechnology* 773; Hemanth Gudapati, Madhuri Dey and Ibrahim Ozbolat, 'A Comprehensive Review on Droplet-based Bioprinting: Past, Present and Future' (2016) 102 (September) *Biomaterials* 20; Zeming Gu et al, 'Development of 3D Bioprinting: From Printing Methods to Biomedical Applications' (2019) *Asian Journal of Pharmaceutical Sciences*.

[6] Shane Hickey, 'Chuck Hull: The Father of 3D Printing who Shaped Technology', *The Guardian* (online, 22 June 2014) <https://www.theguardian.com/business/2014/jun/22/chuck-hull-father-3d-printing-shaped-technology>; David Jones, 'Ariadne', (3 October 1974), *New Scientist* 80; Matthew Ponsford and Nick Glass, 'The Night I Invented 3D Printing', *CNN* (Web Page, 14 February 2014) <http://edition.cnn.com/2014/02/13/tech/innovation/the-night-i-invented-3d-printing-chuck-hall/index.html>; Simon Bradshaw, Adrian Bowyer and Patrick Haufe, 'The Intellectual Property Implications of Low-Cost 3D Printing' (2010) 7(1) *SCRIPTed* 5; Dinusha Mendis, '"Clone Wars": Episode II - The Next Generation: The Copyright Implications relating to 3D Printing and Computer-Aided Design (CAD) Files' (2014) 2 *Law, Innovation and Technology* 265; 'Our Story', *3D Systems* (Web Page, 2017) <https://www.3dsystems.com/our-story>.

[7] Hickey (n 6); Jones (n 6); Ponsford and Glass (n 6); Bradshaw, Bowyer and Haufe (n 6); Mendis (n 6); 3D Systems (n 6).

[8] Hickey (n 6); Jones (n 6); Ponsford and Glass (n 6); Bradshaw, Bowyer and Haufe (n 6); Mendis (n 6); 3D Systems (n 6).

[9] Hickey (n 6); Jones (n 6); Ponsford and Glass (n 6); Bradshaw, Bowyer and Haufe (n 6); Mendis (n 6); 3D Systems (n 6).

It was, however, Thomas Boland who pioneered bioprinting when he modified an inkjet printer using the principles of 3D printing to accommodate and dispense living cells in scaffolds.[10] Since then, bioprinting has progressively evolved with projections that the United States Food and Drug Administration should receive an Investigational New Drug[11] application for therapeutic 3D bioprinted human liver tissue in 2021.[12]

Further to the above explanation of bioprinting and 3D printing, it is useful at this juncture to distinguish bioprinting from other applications of 3D printing in medicine. Whereas 3D printing in medicine generally encompasses bioprinting, it would appear from the definition of bioprinting that the use of living cells distinguishes bioprinting from other applications of 3D printing in medicine. Thus, these other applications of 3D printing in medicine typically involve the use of materials such as ceramics, metals and plastics to the exclusion of living cells in the production of surgical tools,[13] dental implants,[14] orthotics,[15] jaws,[16] heel bone,[17] titanium sternum and rib cage,[18] and pre-surgical models.[19] It is important to make this distinction as the embodiment of living cells in bioprinted constructs presents separate ethical and legal considerations, in addition to those presented

[10] Gu et al (n 5).
[11] An investigational new drug application refers to the means by which drug sponsors (usually the manufacturer or potential marketer) obtain exemption from the FDA in order to transport experimental drugs to clinical investigators aross state lines before marketing application for the drug has been approved. This is because Federal law requires an approved marketing application before drugs can be transported or distributed across state lines: 'Investigational New Drug (IND) Application', *United States Food and Drug Administration* (Web Page, 12 May 2020) United States Food and Drug Administration <https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application>.
[12] 'Organovo Updates Key Clinical Development Goals; Company Reports Preliminary Fiscal Fourth-Quarter 2019 Results', *Organovo* (Web Page, 22 May 2019) <https://ir.organovo.com/news-releases/news-release-details/organovo-updates-key-clinical-development-goals-company-reports>.
[13] Nick Parkin, 'Doctors turn to 3D Printing to source Medical Supplies in Earthquake-Recovering Nepal', *ABC News* (Web Page, 5 March 2017) <http://www.abc.net.au/news/2017-03-05/3d-printers-help-remote-health-clinics-after-nepal-earthquake/8317502>.
[14] Dudley, Amos, 'Orthoprint, or How I Open-Sourced My Face', *Amos Dudley* (Web Page, 10 March 2016) <http://amosdudley.com/weblog/Ortho>.
[15] Amy Fallon, How 3D Printing can Revolutionise the Medical Profession', *The Guardian* (online, 2 September 2016) <https://www.theguardian.com/media-network/2016/sep/29/3d-printing-revolutionise-medical-profession>.
[16] Stephanie Ferrier, 'Titanium, 3D-Printed Prosthetic Jaw Implanted in Melbourne Man in Australian First Surgery', *ABC News* (Web Page, 22 June 2015) <http://www.abc.net.au/news/2015-06-20/melbourne-man-receives-titanium-3d-printed-prosthetic-jaw/6536788>.
[17] 'World-First Surgery Saves Cancer Patient's Leg', *CSIRO* (Web Page, 6 December 2016) <https://www.csiro.au/en/Research/MF/Areas/Metals/Lab22/Titanium-Heel>.
[18] 'Cancer Patient Receives 3D Printed Rib Cage', *CSIRO* (Web Page, 6 December 2016) <https://www.csiro.au/en/Research/MF/Areas/Metals/Lab22/Sternum-and-ribs>.
[19] Carrie Wyman, 'Customized 3D Printed Medical Models Enhance Surgical Training at CBMTI', *Stratasys* (Web Page, 6 July 2016) <http://blog.stratasys.com/2016/07/06/3d-printed-surgical-training-models-video/>.

by the use of 3D printing generally, which have already been discussed extensively in existing literature.[20]

So far, constructs ranging from liver tissue to heart valves have been printed for use in pre-clinical testing in animals.[21] Even more recently, scientists have been able to print a mini beating human heart using stem cells, albeit not as complex as a fully developed human heart.[22] Ultimately, the goal is to produce functional tissue and organs suitable for clinical implantation in humans.[23] This is in addition to applying bioprinting in clinical research, drug discovery and toxicology. If the goal of printing implantable tissues/organs is achieved, it is possible that existing issues such as organ shortage, lifelong immunosuppression therapy and animal testing will cease to exist.

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[20] See, eg, Olasupo Owoeye and Modupe Adewale, '3D Printing and Patent Law: A Balance of Rights and Obligations' (2016) 38 *European Intellectual Property Review* 697; Geertrui Van Overwalle and Reinout Leys, '3D Printing and Patent Law: A Disruptive Technology Disrupting Patent Law?' (2017) 48 *International Review of Intellectual Property and Competition Law* 504; Shlomit Yanisky-Ravid and Kenneth S Kwan, '3D Printing the Road Ahead: The Digitization of Products when Public Safety Meets Intellectual Property Rights - A New Model' (2017) 38 *Cardozo Law Review* 921; Stefan Bechtold, '3D Printing, Intellectual Property and Innovation Policy' (2016) 47 *International Review of Intellectual Property and Competition Law* 517; Tabrez Y Ebrahim, '3D Printing: Digital Infringement and Digital Regulation' (2016) 14 *Northwestern Journal of Technology and Intellectual Property* 37; Bibi van den Berg, Simone van der Hof and Eleni Kosta, *3D Printing: Legal, Philosophical and Economic Dimensions,* Information Technology and Law Series (Springer, 2016); Tom Schneider et al, '3D Printing: Perception, Risks and Opportunity' (4 November 2014) <https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2533681>; Timothy R Holbrook and Lucas Osborn, 'Digital Patent Infringement in an Era of 3D Printing' (2015) 48 *UC Davis Law Review* 1319; Nicole A Syzdek, 'Five Stages of Patent Grief to Achieve 3D Printing Acceptance' (2015) 49 *University of San Francisco Law Review* 335; Amanda Scardamaglia, 'Flashpoints in 3D Printing and Trade Mark Law' (2015) 23 *Journal of Law, Information and Science*; Bradshaw, Bowyer and Haufe (n 5); Matthew Rimmer, 'Inventing the Future: Intellectual Property and 3D Printing', *Elgarblog* (Blog Post, 18 October 2012) <https://elgar.blog/2012/10/18/inventing-the-future-intellectual-property-and-3d-printing-by-matthew-rimmer/>; Jasper Tran, 'The Law and 3D Printing' (2015) 31 *John Marshall Journal of Information Technology & Privacy Law* 505; Dinusha Mendis, Davide Secchi and Phil Reeves, 'A Legal and Empirical Study into the Intellectual Property Implications of 3D Printing - Executive Summary' (2015/41, Intellectual Property Office, 29 April 2015) <https://www.gov.uk/government/publications/3d-printing-research-reports>; Len Mancini and Andy Mukherji, 'The Legal Implications of 3D Printing: An Australian Perspective', *Cullens Patent and Trade Mark Attorneys* (Web Page, 2016) <http://www.cullens.com.au/wp-content/uploads/2016/08/Cullens-3D-Printing.pdf>; Deven R Desai and Gerard N Magliocca, 'Patents, Meet Napster: 3D Printing and the Digitization of Things' (2014) 102 *Georgetown Law Journal* 1691; Angela Daly, *Socio-Legal Aspects of the 3D Printing Revolution* (Palgrave Macmillan, 2016).

[21] David B Kolesky et al, '3D Bioprinting of Vascularized, Heterogeneous Cell-Laden Tissue Constructs' (2014) 26 *Advanced Materials* 3124; Hyun-Wook Kang et al, 'A 3D bioprinting System to Produce Human-Scale Tissue Constructs with Structural Integrity' (2016) 34 *Nature Biotechnology* 312; David A Zopf et al, 'Bioresorbable Airway Splint Created with a Three-Dimensional Printer' (2013) 368 *New England Journal of Medicine* 2043; Faulkner-Jones Alan et al, 'Development of A Valve-Based Cell Printer for the Formation of Human Embryonic Stem Cell Spheroid Aggregates' (2013) 5(1) *Biofabrication* 015013; Wei Zhu et al, 'Direct 3D Bioprinting of Prevascularized Tissue Constructs with Complex Microarchitecture' (2017) 124 *Biomaterials* 106; Hirofumi Yurie et al, 'The Efficacy of a Scaffold-Free Bio 3D Conduit Developed from Human Fibroblasts on Peripheral Nerve Regeneration in a Rat Sciatic Nerve Model' (2017) 12(2) *PLoS ONE* e0171448.

[22] Molly E Kupfer et al, 'In Situ Expansion, Differentiation, and Electromechanical Coupling of Human Cardiac Muscle in a 3D Bioprinted, Chambered Organoid' (2020) 127(2) *Circulation Research* 207; Jay Stone, 'A 3D Bioprinter Produces a Beating Human Heart Using Stem Cells', *BioNews* (Web Page, 27 July 2020) <https://www.bionews.org.uk/page_151016>.

[23] Murphy and Atala (n 5).

Nonetheless, beneficial as bioprinting might appear, there are ethical concerns about the technology and its application, particularly in relation to patentability.[24] For an invention to be patentable, it must meet the threshold for patentable subject matter.[25] Additionally, it must be novel, inventive (non-obvious) and capable of industrial application (useful).[26] Even where these criteria are met, an invention may still be excluded from patentability if it falls under any of the exceptions contained in patent legislations. This includes where the commercial exploitation of an invention is contrary to *ordre public* or morality.[27] Accordingly, the question of whether exclusions from patentability address all of the ethical concerns associated with patentability of bioprinting inventions is one of the key issues to be considered in this thesis.

As noted earlier, patents exist to incentivise innovation by vesting right holders with exclusive rights over claimed inventions. For a capital-intensive technology such as bioprinting,[28] this feature of the patent system is undoubtedly attractive for the opportunity

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[24] See, eg, Mathew Varkey and Anthony Atala, 'Organ Bioprinting - A Closer Look at Ethics and Policies' (2015) 5 *Wake Forest Journal of Law and Policy* 275; Jeremy Thomas Harbaugh, 'Do You Own Your 3D Bioprinted Body?' (2015) 41 *American Journal of Law and Medicine* 167; S Vijayavenkataraman, W F Lu and J Y H Fuh, '3D Bioprinting – An Ethical, Legal and Social Aspects (ELSA) Framework' (2016) 1-2 *Bioprinting* 11; Tabrez Y Ebrahim, '3D Bioprinting Patentable Subject Matter Boundaries' (2017) 41 *Seattle University Law Review* 1; Phoebe Li, '3D Bioprinting Technologies: Patents, Innovation and Access' (2015) 6 *Law, Innovation and Technology* 282.

[25] *Marrakesh Agreement Establishing the World Trade Organization*, opened for signature 15 April 1994, 1867 UNTS 3 (entered into force 1 January 1995) annex 1C art 27(1) ('*TRIPS Agreement*'). The *TRIPS Agreement* sets out minimum standards of protection for various forms of Intellectual Property rights to be provided by each member of the World Trade Organization (WTO).

[26] *TRIPS Agreement* (n 25) art 27(1).

[27] *TRIPS Agreement* (n 25) art 27(2).

[28] See, eg, 'NIH Grant Funds Center for Engineering Complex Tissues at Rice', *Rice University* (Web Page, 10 April 2017) <http://news.rice.edu/2017/04/10/nih-grant-funds-center-for-engineering-complex-tissues-at-rice-2/>; A'ndrea Elyse Messer, '$2.8M Grant to Fund Bioprinting for Reconstruction of Face, Mouth, Skull Tissues', *Pennsylvania State University* (Web Page, 10 February 2020), <https://news.psu.edu/story/607225/2020/02/07/research/28m-grant-fund-bioprinting-reconstruction-face-mouth-skull-tissues>; 'Industrial Transformation Training Centres - Selection Report for Funding Commencing in 2016', *Australian Research Council* (Web Page, 30 May 2017) <http://www.arc.gov.au/selection-report-industrial-transformation-training-centres-2016>; Rushabh Haria, '3D Printing in Education Boosted with Wollongong and Maryland Centres', *3D Printing Industry* (Web Page, 22 November 2017) <https://3dprintingindustry.com/news/3d-printing-education-boosted-wollongong-maryland-centres-124969/>; Ben Long, 'UOW Researchers Awarded $8.7m in ARC Funding', *University of Wollongong* (Web Page, 10 November 2017) <https://media.uow.edu.au/releases/UOW240204.html>; Lisa Hutton, 'Funding Boost for University of Wollongong Bioprint Facility', *University of Wollongong* (Web Page, 26 October 2017) <https://media.uow.edu.au/releases/UOW239659.html>; 'Australia-first Biofabrication Institute Announced', *Queensland University of Technology* (Web Page, 21 November 2016) <https://www.qut.edu.au/about/news/news?news-id=111977>; Amy Mitchell-Whittington, 'Biofabrication Institute Announced for Herston Health Precinct', *Brisbane Times* (Web Page, 21 November 2016) <https://www.brisbanetimes.com.au/national/queensland/biofabrication-institute-announced-for-herston-health-precinct-20161121-gstwux.html>; '£4m Dedicated to Advancing the Development and Application of Non-Animal Technologies, such as Bioprinting Human Tissue', *National Centre for the Replacement, Refinement and Reduction of Animals in Research* (Web Page, 8 July 2014) <https://www.nc3rs.org.uk/news/%C2%A34m-dedicated-advancing-development-and-application-non-animal-technologies-such-bioprinting>.

it provides to recoup research and development costs.[29] As of June 2016, almost 950 bioprinting-related patents and pending applications had been filed worldwide, with majority of the inventors resident in the United States of America ('USA'), China, Japan, and South Korea.[30] These patents/applications cover processes and products including bioprinted constructs. While it may appear that the patented bioprinting-related inventions have successfully crossed the patentable subject matter hurdle, their validity remains presumed only until challenged in the courts. Existing literature suggests that this is inevitable.[31] This is particularly so in respect of claimed inventions such as bioprinted constructs which embody natural phenomena.[32] Already, some commentators have identified the use of human embryonic stem cells in bioprinting as posing ethical concerns in the context of patentability.[33] As it stands, the patenting of inventions embodying natural phenomena remains contentious and there have been numerous judicial pronouncements in that regard in recent times,[34] which will be considered extensively in this thesis.

Furthermore, apart from generating debates about whether bioprinted constructs qualify as patentable subject matter, the act of patenting of bioprinted constructs in itself would appear to raise significant ethical concerns particularly in the context of access.[35] This includes considerations about access to bioprinted constructs by patients and research

[29] Section 1.2.1 further explores some of the anticipated benefits of patenting bioprinting-related inventions to patent holders, third-party users and the public.

[30] The search only includes issued patents and published applications. As such, the authors suggest that this number may not tell the whole story as there could be numerous unpublished applications that will increase the overall number: John F Hornick and Kai Rajan, 'The 3D Bioprinting Patent Landscape Takes Shape as IP Leaders Emerge', *3D Printing Industry* (Web Page, 7 July 2016) <https://3dprintingindustry.com/news/3d-bioprinting-patent-landscape-takes-shape-ip-leaders-emerge-84541/>.

[31] Jasper L Tran, 'Patenting Bioprinting' (2015) 29 *Harvard Journal of Law and Technology Digest*; Timo Minssen and Marc Mimler, 'Patenting Bioprinting-Technologies in the US and Europe – The 5th Element in the 3rd Dimension' in Rosa Maria Ballardini, Marcus Norrgård and Jouni Partanen (eds), *3D printing, Intellectual Property and Innovation – Insights from Law and Technology* (Wolters Kluwer, 2017).

[32] 'Natural phenomena' refers to observable processes seen to occur or exit in nature such as biological processes. 'Scientific Explanation of Natural Phenomena', *CORDIS* (Web Page, 3 March 2016) <https://cordis.europa.eu/article/id/175232-scientific-explanation-of-natural-phenomena>; Kate Latham, 'Natural Science', *Biology Dictionary* (Web Page, 22 January 2021) <https://biologydictionary.net/natural-science/>.

[33] Li (n 24); Minssen and Mimler (n 31).

[34] See, eg, *Association for Molecular Pathology v Myriad Genetics Inc,* 569 US 576 (2013); *D'Arcy v Myriad Genetics Inc* (2015) 258 CLR 334; *International Stem Cell Corporation v Comptroller General of Patents* (C-364/13) [2015] OJ C 65/7; *Re International Stem Cell Corp* (2016) 123 IPR 142.

[35] 'Access', in the context of healthcare, has been described as 'a general concept that summarizes a set of more specific dimensions describing the fit between the patient and the healthcare system'. These dimensions include availability, accessibility, accommodation, affordability and acceptability. Roy Penchansky and J William Thomas, 'The Concept of Access: Definition and Relationship to Consumer Satisfaction' (1981) 19 *Medical Care* 127, 128-9.

access to the technology, which are considered in this thesis.[36] That is not to say that the patenting of other bioprinting-related inventions does not also raise concerns about access. However, given bioprinted constructs are intended to be utilised in addressing issues such as organ shortage, lifelong immunosuppression therapy and animal testing, it is questionable whether any person or institution ought to receive exclusive rights over such products even if the requirements for patentability are met.

1.2 The Choice of Patent Protection for Bioprinting-Related Inventions

According to the World Trade Organisation,[37] 'intellectual property rights are the rights given to persons over the creations of their minds'. These rights exist for a specified period and are exclusive to the holder, subject to certain conditions and exceptions stipulated by law. Modern intellectual property rights fall into two main categories: Copyright (and related rights); and Industrial Property (Trademarks, Geographical Indications, Patents, Industrial Design and Trade Secrets).[38] It is important to emphasise that all forms of intellectual property rights are territorial in nature and, as such, protection is limited to the country of publication, registration or grant. Nevertheless, creators/inventors may seek protection in as many countries of their choosing subject to cost and patent strategies. Generally, the protection afforded by these rights is supposed to serve as an incentive to innovate.[39]

With patents ostensibly being the most suitable form of intellectual property to protect most bioprinting-related inventions,[40] it is pertinent to consider what patent protection

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[36] See chapter seven for further discussions about access to bioprinting-related inventions.

[37] 'What are Intellectual Property Rights?', *World Trade Organization* (Web Page, 2017) <https://www.wto.org/english/tratop_e/trips_e/intel1_e.htm> ('*What are Intellectual Property Rights?*').

[38] 'Types of IP', *IP Australia* (Web Page) <https://www.ipaustralia.gov.au/understanding-ip/getting-started-with-ip/types-of-ip>; *What are Intellectual Property Rights?* (n 37); 'What is Intellectual Property?', *World Intellectual Property Organisation* (Web Page) <http://www.wipo.int/about-ip/en/>.

[39] There have been arguments about the role of Intellectual Property in stimulating innovation. While some argue that Intellectual Property stimulates innovation, others argue that it threatens innovation. This argument is, however, beyond the scope of this research. See generally Michele Boldrin and David K Levine, *Against Intellectual Monopoly* (Cambridge University Press, 2008); Stuart J H Graham et al, 'High Technology Entrepreneurs and the Patent System: Results of the 2008 Berkeley Patent Survey' (2009) 24 *Berkeley Technology Law Journal* 255; Richard Gilbert, 'A World Without Intellectual Property? Boldrin and Levine, Against Intellectual Monopoly' (2011) 49 *Journal of Economic Literature* 421; Daniel J Gifford, 'How Do the Social Benefits and Costs of the Patent System Stack Up in Pharmaceuticals?' (2004) 12 *Journal of Intellectual Property Law & Practice* 75; Hazel V J Moir, 'What are the Costs and Benefits of Patent Systems?' in William van Caenegem and Christopher Arup (eds), *Intellectual Property Policy Reform: Fostering Innovation and Development* (Edward Elgar, 2009) 29.

[40] It should be noted that other forms of intellectual property rights such as copyright, trademarks and designs are equally relevant to bioprinting-related inventions. See, eg, Dinusha Mendis, '"Clone Wars": Episode II - The Next Generation: The Copyright Implications relating to 3D Printing and Computer-Aided Design (CAD) Files' (2014) 2 *Law, Innovation and Technology* 265; John Liddicoat, Jane Nielsen and Dianne Nicol, 'Three Dimensions of Patent

entails. A patent is an exclusive right available for any invention (product or process) in all fields of technology usually for a period of 20 years from the filing date.[41] As negative rights, patents do not grant the holder a right to exploit his/her invention per se.[42] Rather, patents confer on the holder exclusive rights to make, use, offer for sale, sell or import the invention to the exclusion of third parties.[43] Patent holders may nevertheless choose to assign, transfer or license their inventions.[44]

1.2.1 Benefits of Patenting Bioprinting-Related Inventions

By design, the patent system is intended to benefit both patent holders and the public. While the term 'benefit' has multiple meanings under patent and health law, it is used in its ordinary sense in this section. Thus, for patent holders, benefit occurs in form of the exclusive rights previously mentioned.[45] For third-party users and the public, the benefit is in the hastening scientific progress, which theoretically occurs as a result of patent disclosures.[46] This is aside benefiting from the invention itself. Some literature, however, suggest that the postulated public benefits are mere theoretical assumptions that have no bearing in practice.[47]

Nonetheless, this section provides an overview of some of the anticipated benefits of patenting bioprinting-related inventions to patent holders, third-party users and the public. Overall, it should be noted that the anticipated benefits are fundamentally similar to the overarching benefits most patent holders would derive from patenting inventions in general. In other words, the anticipated benefits discussed below are inextricably linked to fundamental justifications of the patent system.

a) *The Patent Holder*

Infringement: Liability for Creation and Distribution of CAD Files' (2016) 26 *Australian Intellectual Property Journal* 165, 166.

[41] T*RIPS Agreement* (n 25) art 33; *Patents Act 1990* (Cth) s 67 ('*Patents Act*'); *Convention on the Grant of European Patents*, signed 5 October 1973, 1065 UNTS 255 (entered into force 7 October 1977) art 63('*EPC*'); 35 USC § 154 (2018).

[42] Adam Mossoff, 'Exclusion and Exclusive Use in Patent Law' (2009) 22(2) *Harvard Journal of Law & Technology* 321

[43] *TRIPS Agreement* (n 25) art 28(1); *Patents Act* (n 41) s 13; *EPC* (n 41) art 64, 67; 35 USC § 271 (2018).

[44] *TRIPS Agreement* (n 25 art 28(2); *Patents Act* (n 41) s 14; *EPC* (n 41) art 71-74; 35 USC § 261 (2018).

[45] Richard C Levin et al, 'Appropriating the Returns from Industrial Research and Development' (1987) 3 *Brookings Papers on Economic Activity* 783, 783.

[46] Ibid 783-4.

[47] Boldrin and Levine (n 39); Jeanne C Fromer, 'Patent Disclosure' (2009) 94 *Iowa Law Review* 539; Gifford (n 39); Richard Gilbert (n 39); Moir (n 39); Lisa Larrimore Ouellette, 'Do Patents Disclose Useful Information?' (2012) 25 *Harvard Journal of Law and Technology* 545, Levin et al (n 45) 784.

In relation to the overarching aim of intellectual property rights to incentivise innovation, patents provide holders with an exclusive period within which to work their inventions in exchange for public disclosure of their invention.[48] Given the costs, risks and delays involved in clinically translating bioprinting, this exclusive period will undoubtedly be attractive to patent holders seeking to profit from their investments and raise additional capital from other sources.[49] In addition, the exclusivity period afforded by the grant of patents also gives patent holders a market advantage over their competitors in the development of market-ready products/services. This is aside the opportunity to profit from licensing said products/services to interested third parties, as the pioneer bioprinting company, Organovo is currently doing with its 3D bioprinted tissue models.[50] Indeed, these anticipated benefits are similar to those mentioned when justifying the grant of patents for biopharmaceutical innovation.[51]

Another benefit of patent protection is that patents appear to offer the most secure form of protection in comparison to other alternatives. For instance, although trade secrecy protection is easier to establish, protection exists only as long as the technical information remains confidential, reverse engineering is unsuccessful and independent discovery does not occur.[52] The moment any of this occurs, the trade secret holder loses their advantage in the market and may be unable to recoup their investments if the competitor's products are better. This is not so with patents, which provide protection in the face of public disclosure. Even though technical information is disclosed to the public as a pre-condition for the grant of patent, the inventor retains exclusive rights over the claimed invention even if temporarily.[53] This means that patent holders do not have to worry about the

[48] *TRIPS Agreement* (n 25) art 29 requires that applicants disclose their invention in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art. See also *Patents Act* (n 41) s 40; *EPC* (n 41) art 83; 35 USC § 112 (2018).

[49] Lila Feisee and Brian Stanton, 'Are Biotechnology Patents Important', *PTO Pulse* (Web Page, March 2000) <http://www.consultstanton.com/wp-content/uploads/2015/02/Stanton-Feisee-PTO-Pulse-2000.pdf>; Edison Bicudo, Alex Faulkner and Phoebe Li, 'Patents and the Experimental Space: Social, Legal and Geographical Dimensions of 3D Bioprinting' (2021) 35(1) *International Review of Law, Computers & Technology* 2, 8; Richard Gilbert (n 39); Graham et al (n 39).

[50] 'ExVive™ Human Tissue Models & Services for Research', *Organovo* (Web Page, 2017) <http://organovo.com/tissues-services/exvive3d-human-tissue-models-services-research/>; 'History', *Organovo* (Web Page, 2017) <http://organovo.com/about/history/> ('*History*').

[51] Henry G Grabowski, Joseph A DiMasi and Genia Long, 'The Roles of Patents and Research and Development Incentives in Biopharmaceutical Innovation' (2015) 34(2) *Health Affairs* 302

[52] Lijie Grace Zhang, John P Fisher and Kam W Leong, *3D Bioprinting and Nanotechnology in Tissue Engineering and Regenerative Medicine* (Academic Press, 2015).

[53] There are limitations to this monopoly, for example, the experimental use exception. See *TRIPS Agreement* (n 25) art 30; *Patents Act* (n 41) s 97; 35 USC § 271(e)(1) (2018).

possibility of having technical information leaked, the process being reverse-engineered or independently discovered. Other researchers have to wait for the patent term to expire before they can launch their own similar inventions, no matter how improved. As will be explained shortly, this waiting period may not necessarily be beneficial to the public. Nonetheless, for the inventor, this is certainly a good reason to seek patent protection.

It should be emphasised that while trade secrecy may not always offer a reliable form of protection, patent holders can utilise it to complement patent protection, particularly through the protection of confidential information (especially know-how), which may fall outside the scope of patent protection. Patent holders may also rely on trade secrets to protect inventions which do not meet the patentability criteria or process technologies, which they are unwilling to disclose.[54]

The benefits notwithstanding, securing a patent can be a long, arduous and expensive process, more so when defending infringement suits.[55] Nevertheless, if patent holders are able to maximise the exclusive period effectively, the benefits of patenting should outweigh the costs, making patent protection a desirable choice.

b) *Third-Party Users*

Patent holders are not the only group who stand to benefit from patenting bioprinting-related inventions. In exchange for exclusive rights, the patent holder makes a public disclosure on how to work the invention and, upon the expiration of the patent term, the invention becomes freely available for commercial exploitation by others. On the face of

[54] In a survey of more than one hundred manufacturing industries, Levin et al found that trade secrecy was considered more effective for protecting processes in comparison to products. This was attributed to 'the greater ease and desirability of maintaining secrecy about process technology'. Levin et al (n 45) 795. See also Dan L Burk, 'Patent Silences' (2016) 69(6) *Vanderbilt Law Review* 1603, 1611-2.

[55] See, eg, Daisuke Wakabayashi, 'Apple Legal Fees in Samsung Patent Case Topped $60 Million', *The Wall Street Journal* (online, 6 December 2013) <https://www.wsj.com/articles/apple-legal-fees-in-samsung-patent-case-topped-60-million-1386360450>; Dan Levine, *'Apple Spent Over $60 million on U.S. Lawyers Against Samsung', Reuters (Web Page, 7 December 2013)* <http://www.reuters.com/article/us-apple-samsung-fees-idUSBRE9B50QC20131206>; Chris Neumeyer, 'Managing Costs of Patent Litigation', *IPWatchdog* (Web Page, 5 February 2013) <http://www.ipwatchdog.com/2013/02/05/managing-costs-of-patent-litigation/id=34808/>; American Intellectual Property Law Association, *Report of the Economic Survey 2015* (2015); IP Australia, 'Time and Costs', *IP Australia* (Web Page, 10 October 2016) <https://www.ipaustralia.gov.au/patents/understanding-patents/time-and-costs>; Gene Quinn, 'The Cost of Obtaining a Patent in the US', *IPWatchdog* (Web Page, 4 April 2015) <http://www.ipwatchdog.com/2015/04/04/the-cost-of-obtaining-a-patent-in-the-us/id=56485/>; Bicudo, Faulkner and Li (n 49).

it, this arrangement appears to be a win-win for all, but as will be explained subsequently, this may not necessarily be the case especially as far as access is concerned.

The disclosure of technical information in patent claims allows for the dissemination of potentially valuable scientific information, which can be used by third-party users to produce improved alternatives or even new inventions during the patent term or after its expiration.[56] This is especially important when one considers the fact that new inventions build on prior discoveries.[57] With access to potentially valuable scientific information, it is anticipated that third-party users in the field of bioprinting are able to minimise research and development costs by focusing on proven methods. In addition, it is also possible that third-party users reading patent claims could identify potentially new areas of research interest that are yet to be explored. Given the capital-intensive nature of bioprinting as previously noted, this is especially beneficial. More so as patent documents function as a useful source of information for ascertaining the state of the art of bioprinting.

Indeed, the disclosure theory is one of the justifications of modern patent systems.[58] Under this theory, patents not only disclose the existence of an invention but also facilitate non-infringing uses and licensing of what would otherwise be infringing uses, which enables technology sharing.[59] It is believed that disclosure hastens scientific progress, as different third-party users are able to combine their individual expertise in improving a technology.[60] This is as opposed to the development of a technology being dictated solely by an individual/institution whose expertise is limited to their perspective. As noted in subsequent parts of this thesis, the realisation of bioprinting's full potential will depend largely on co-operation across multiple disciplines given the complexity of the issues involved. Patent disclosure thus offers a useful means for facilitating such collaboration.

c) *The Public*

[56] Feisee and Stanton (n 49); Fromer (n 47). The ability of third-party users to produce improved alternatives or even new inventions during the patent term is generally protected by the experimental use exception, which is discussed further in chapter seven.
[57] Boldrin and Levine (n 39); See also Richard Gilbert (n 39); Feisee and Stanton (n 49); Fromer (n 47)
[58] Ouellette (n 47); National Research Council, *Intellectual Property Rights and the Dissemination of Research Tools in Molecular Biology* (National Academies Press, 1997) ('*Intellectual Property Rights and the Dissemination of Research Tools in Molecular Biology*'); Fromer (n 47).
[59] *Intellectual Property Rights and the Dissemination of Research Tools in Molecular Biology* (n 58).
[60] Fromer (n 47).

In the context of bioprinting, technology sharing and licensing that arise from disclosure of patented bioprinting-related inventions could fast track the advancement of the technology such that researchers are able to print viable living constructs suitable for clinical implantation and research. With more researchers working in concert to achieve this common goal, the chances of attaining the goal are significantly increased. Invariably, once the goal is attained, the public benefits from the availability of new and improved medical technologies that improve community health. An improvement in community health means a reduction in healthcare costs.

In addition, the additional research stimulated by public disclosure has the capacity to result in the expansion of existing industries, the establishment of new industries, technology transfer and consequently, increased job opportunities.[61]

1.2.2 Socio-Economic Costs of Patenting Bioprinting-Related Inventions

Whilst multiple patents have been granted for bioprinting-related inventions worldwide with many more still pending, it is not immediately apparent how such patents will be exploited. This is notwithstanding reported instances of collaboration amongst key players in the bioprinting industry.[62] While these collaborative research agreements might suggest the use of patents in an ethical manner, it does not necessarily displace concerns about the general impact of patenting life-saving technologies.

As such, it is useful to consider the potential socio-economic costs of patenting bioprinting-related inventions. It should be noted that as with the benefits highlighted above, it is highly probable that the socio-economic costs of patenting bioprinting-related inventions will be similar to general concerns about patenting inventions in any field of technology. Thus, the socio-economic costs identified in this section are fundamentally similar to those emanating from patenting inventions in general.

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[61] Feisee and Stanton (n 49).

[62] Aspect Biosystems, *Collaboration with Johnson & Johnson Innovation* (5 January 2017) <https://www.aspectbiosystems.com/news-resources/collaboration-with-johnson-johnson-innovation>; 3D Printing Media Network, *Aspect Biosystems Partners with Fraunhofer and InSCREENeX on 3DBioRing Bioprinted Muscle Tissue* (18 September 2017) <https://www.3dprintingmedia.network/aspect-biosystems-partners-fraunhofer-inscreenex-3dbioring-bioprinted-muscle-tissue/>; CELLINK, *CELLINK and the Adult Stem Cell Research Center at Seoul National University Announce New Agreement for Bioprinting Research* (22 March 2019) <https://cellink.com/cellink-and-the-adult-stem-cell-research-center-at-seoul-national-university-announce-new-agreement-for-bioprinting-research/>.

First, patents offer protection to the first to file not necessarily first to invent. As such, in a situation where different independent researchers make simultaneous discoveries, only the first to file benefits from patent protection to the exclusion of others.[63] Consequently, other independent researchers are unable to commercialise their similar inventions during the period of exclusivity, as independent discovery is not a defence to patent infringement.[64] For some, this might be considered a waste of time and resources if they are unable to recoup their research and development costs during an exclusive period. In addition, patentees seeking to stake their claim may end up filing overly broad claims including unanticipated inventions, which if granted could affect the development and patenting of future innovations in the field.[65]

Furthermore, as earlier mentioned, patentees may license their inventions to third parties. In exchange for the grant of a licence, licensees may be required to make up front royalty payments to the licensor. Where multiple licenses are required from multiple licensors in order to commercialise a product, multiple royalties have to be paid by the licensee, which results in what is known as 'royalty-stacking'.[66] The multiplicity of licences required implies the existence of a patent thicket, which is unfavourable to research and product development. In addition, multiple royalties and the cost of undertaking negotiations for a licence further drive up research and development costs, which is ultimately passed on to consumers, who may be unable to afford the price of bioprinting treatments as a result. The complexities and cost of negotiating a licence may also impede further research in the field because researchers are either unable to afford licence fees or unable to navigate the process.[67] This is aside the risk of licensors refusing to license their patented inventions to third parties.

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[63] Boldrin and Levine (n 39); Richard Gilbert (n 39).

[64] Richard Gilbert (n 39); Christopher Anthony Cotropia and Mark A Lemley, 'Copying in Patent Law' (2009) 87 *North Carolina Law Review* 1421; Zhang, Fisher and Leong (n 52).

[65] Richard Gilbert (n 39); James Bessen and Michael J Meurer, *Patent Failure: How Judges, Bureaucrats, and Lawyers Put Innovators at Risk* (Princeton University Press, 2008); *Association for Molecular Pathology v Myriad Genetics Inc,* 569 US 576 (2013); *D'Arcy v Myriad Genetics Inc* (2015) 258 CLR 334.

[66] Jane Nielsen, Dianne Nicol and John Liddicoat, 'Sharing the Burden in Australian Drug Discovery and Development: Collaborative Trends in Translational Research' (2014) 3 *Intellectual Property Quarterly* 181; Janet Hope, *BioBazaar: The Open Source Revolution and Biotechnology* (Harvard University Press, 2008).

[67] Richard Gilbert (n 39); Greenpeace, 'The True Costs of Gene Patents: The Economic and Social Consequences of Patenting Genes and Living Organisms' (Greenpeace, 15 June 2004); Heller and Eisenberg (n 1); *Intellectual Property Rights and the Dissemination of Research Tools in Molecular Biology* (n 58); Levin et al (n 45) 795.

With regard to the benefits of patent disclosures for follow on inventions articulated above, some literature suggest that these are merely theoretical assumptions. In summary, the authors argue that:

i. some researchers deliberately refrain from reading claims in order to avoid being caught by the rule of wilful infringement;[68]
ii. some researchers who read patent claims actually do so to determine whether their inventions will be considered an infringement of a patented invention rather than for technical information to inspire their research;[69] and
iii. technical information disclosed in patent claims is often inadequate and unclear for stimulating further invention.[70]

Some authors further argue that rather than promote scientific progress, patents actually stall scientific progress since others are precluded from working patented inventions for a period of at least 20 years.[71] For instance, Boldrin and Levine argue that most technologies did not advance until key patents elapsed and as such, 'intellectual monopoly' stifles innovation.[72] As far as general 3D printing is concerned, some authors are of the opinion that amongst other factors, the industry only began to witness significant growth upon the expiration of key patents between 2013-2015.[73] While this may be true, reliance on the alternative of trade secret protection does not necessarily bode well for inventions either. If reverse engineering is unsuccessful, and inventors are able to protect their trade secrets as effectively as Coca-Cola and Kentucky Fried Chicken have over the years, other third-party users may lose out on the knowledge that could otherwise have been gained through public disclosure from patent claims.[74] This is assuming the patent disclosure function performs adequately.[75]

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[68] Fromer (n 47); Ouellette (n 47).
[69] Fromer (n 47); Gifford (n 39); Moir (n 39).
[70] Fromer (n 47); Boldrin and Levine (n 39); Richard Gilbert (n 39); Ouellette (n 47); Gifford (n 39); Moir (n 39), Burk (n 54).
[71] Levin et al (n 45) 788.
[72] Boldrin and Levine (n 39). Similarly, Levin et al contends that the rapid progress of the semiconductor industry between 1950 and 1960 would have been impossible under a regime with strong intellectual property rights. Levin et al (n 45) 788.
[73] Terry Wohlers and Tim Caffre, *Wohlers Report 2014* (Wohlers Associates, 2014); Bechtold (n 20).
[74] Boldrin and Levine counter argue that patent disclosures are often inadequate anyway and as such relying on trade secrets makes no difference. On the other hand, Gilbert admits that while this may be true for some industries, for others, innovation would likely suffer if a lack of patent protection forced firms to rely on trade secrets: Boldrin and Levine (n 39); Richard Gilbert (n 39).
[75] See generally Burk (n 54) for extensive discussion about the sufficiency of patent disclosure.

At the same time, however, it is important to note that irrespective of how adequate or inadequate patent disclosures are, there are additional factors which can contribute to delays in the developments of technologies such as bioprinting. These generally include the feasibility of translating technologies into clinical applications. As will be explained in chapter two, there are currently many challenges facing the bioprinting industry. These include issues with sourcing cells of the right quality and quantity, ensuring cell survival and viability during the printing process, and limited understanding of the biology and biophysics underlying regenerative processes *in vivo*. In light of this, it may very well be that the grant of patents for bioprinted-related inventions are not ultimately the most significant impediment to the development of bioprinting.

Nonetheless, given the exclusive rights afforded by patent grants is a contributing factor to possible delays in the diffusion of a technology, it is pertinent to consider how those ethical concerns stemming from the grant of patent monopolies can be resolved within the patent system, if at all.

1.3 Ethics of Bioprinting and Ethics of Patenting Bioprinting

As a technology, bioprinting generates a number of ethical concerns, namely: the ethics and safety of using xenogeneic and human embryonic stem cells; safety and efficacy of bioprinted constructs; access and social justice; and possible use of bioprinted constructs for human enhancement. While some of these issues overlap with ethical concerns about patenting bioprinting, it is important to note that there is a distinction between both ethical concerns.

Whereas the ethical concerns about bioprinting are all-encompassing, ethical concerns about patenting bioprinting are primarily concerned with the appropriateness and impact of patenting. Accordingly, there are two key questions that must be addressed when examining the ethics of patenting bioprinting, namely:

i. What are the broader implications of patenting bioprinting?
ii. Should bioprinting be patentable in light of these implications?

In order to address these questions, it is important to identify the relevant elements of bioprinting that are potentially eligible for patenting. These have been categorised as follows:[76]

i. **Hardware**: This includes 3D scanners, bioprinters (including biopens) and bioreactors, as well as their components.

ii. **Software:**[77] Software incorporates the computer programs that instruct 3D printers to perform their functions.

iii. **Computer-Aided Design files:** It is important to clarify the difference between computer-aided design ('CAD') files and software (such as CAD programs) at this juncture.[78] Whereas CAD files consist of scanned or digitally designed images, software refers to programs and other operating information, which may be used to create or design CAD files,[79] scan existing objects or print.[80]

iv. **Processes/Methods**: This covers methods of treatment and biological processes (such as the isolation and culturing of cells, as well as maturation of bioprinted constructs in a bioreactor).[81]

v. **Cells, Materials and Bioprinted Constructs:** These include stem cells, naturally derived polymers, decellularised extracellular matrix isolated from its inhabiting cells, bioinks and bioprinted constructs.

The patenting of the above elements presents different considerations. While hardware is generally non-contentious as far as patenting is concerned, the patentability of software,

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[76] See generally Seung-Schik Yoo, '3D-Printed Biological Organs: Medical Potential and Patenting Opportunity' (2015) 25 *Expert Opinion on Therapeutic Patents* 507.

[77] Curiously, Tran asserts that 3D printing and bioprinting do not fundamentally depend on software, but print using an electronic blueprint, that is, computer-aided design (CAD) files. Minssen and Mimler appear to agree with this assertion. This position appears to be a misunderstanding of the nature of bioprinting as both software and CAD files are indeed used in 3D printing and bioprinting: Tran, 'Patenting Bioprinting' (n 31); Minssen and Mimler (n 31).

[78] There appears to be some uncertainty over the classification of CAD files as software. See generally Brian Rideout, 'Printing the Impossible Triangle: The Copyright Implications of Three-Dimensional Printing' (2011) 5 *Journal of Business, Entrepreneurship & the Law* 161; Mendis (n 6); Rosa Maria Ballardini, Marcus Norrgård and Timo Minssen, 'Enforcing Patents in the Era of 3D Printing' (2015) 10 *Journal of Intellectual Property Law & Practice* 850; Dinusha Mendis et al, 'The Co-Existence of Copyright and Patent Laws to Protect Innovation: A Case Study of 3D Printing in UK and Australian Law' in Roger Brownsword, Eloise Scotford and Karen Yeung (eds), *The Oxford Handbook of Law, Regulation and Technology* (Oxford University Press, 2017).

[79] In 2011, Organovo entered into a partnership with Autodesk Research to develop design software for designing and printing living tissue: *History* (n 50).

[80] van den Berg, van der Hof and Kosta (n 20); Van Overwalle and Leys (n 20); Ebrahim, '3D Printing: Digital Infringement and Digital Regulation' (n 20); Yanisky-Ravid and Kwan (n 20).

[81] Owing to the complex nature of engineering tissues/organs, which makes reverse engineering almost impossible, inventors, may prefer to protect some of their methods as trade secrets as opposed to patenting them: Zhang, Fisher and Leong (n 52).

on the other hand, remains contentious given some claims have been found to merely recite abstract ideas, schemes or information, which are otherwise not patent eligible subject matter.[82] However, these issues are not such as to generate significant ethical concerns about their patenting. Neither are issues relating to the eligibility of CAD files as patentable subject matter.[83]

On the other hand, however, the patenting of cells, materials, bioprinted constructs, and bioprinting processes/methods by extension, raises significant ethical issues given their embodiment of natural phenomena, especially living cells as noted earlier. Indeed, the patenting of life forms and human cloning technologies in general have long generated significant ethical concerns about the appropriateness of commoditising and monopolising such products, as well as the implications of patents on access. Whilst many of these concerns have been examined extensively in other literature,[84] emerging healthcare technologies such as bioprinting continue to further aggravate such concerns thus making them a topical issue. Accordingly, this thesis aims to explore the tripartite relationship between patents, ethics and access in the context of bioprinting.

1.4 Original Contribution to Existing Knowledge

As bioprinting is still in its infancy, it is unsurprising that there has been limited empirical or doctrinal analysis on the ethical and access issues surrounding patenting bioprinting,

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[82] See generally *CCOM Pty Ltd v Jiejing Pty Ltd* (1994) 51 FCR 260; *Commissioner of Patents v RPL Central Pty Ltd* (2015) 238 FCR 27; *International Business Machines Corporation v Commissioner of Patents* (1991) 33 FCR 218; *Research Affiliates LLC v Commissioner of Patents* (2014) 227 FCR 378; Australian Patent Office, '2.9.2.7 Computer Implemented Inventions - Schemes and Business Methods', *Patent Manual of Practice & Procedure* (Web Page, 5 February 2020) <http://manuals.ipaustralia.gov.au/patents/national/patentable/2.9.2.7_Computer_Implemented_Inventions_-_Schemes_and_Business_Methods.htm>; *Encompass Corp Pty Ltd v InfoTrack Pty Ltd* (2019) 372 ALR 646; *Alice Corporation Pty Ltd v CLS Bank International*, 573 US 208 (2014); *Aristocrat Technologies Australia Pty Ltd* (2016) 123 IPR 341; *Association for Molecular Pathology v Myriad Genetics Inc,* 569 US 576 (2013); *Circuit simulation I/Infineon Technologies* [2006] T 1227/05; *Computer program product/IBM* [1998] T 1173/97; *Grant v Commissioner of Patents* (2006) 154 FCR 62; *Intellectual Ventures I LLC v Capital One Bank (USA)*, 838 F 3d 1307, 1323-1325 (Fed Cir 2016); *Mayo Collaborative Services v Prometheus Laboratories Inc*, 566 US 66 (2012); *Programs for computers* [2009] G 0003/08); *Research Affiliates LLC v Commissioner of Patents* (2014) 227 FCR 378; *Two identities/Comvik* [2002] T 0641/00.

[83] See generally Bradshaw, Bowyer and Haufe (n 6); Desai and Magliocca (n 20); Yanisky-Ravid and Kwan (n 20); Bechtold (n 20); Ballardini, Norrgård and Minssen (n 78); Iona Silverman, 'Optimising Protection: IP Rights in 3D Printing' (2016) 38 *European Intellectual Property Review* 5; Mendis et al (n 78); Mendis (n 6); Ebrahim, '3D Printing: Digital Infringement and Digital Regulation' (n 20); Holbrook and Osborn (n 20); Owoeye and Adewale (n 20); Syzdek (n 20).

[84] See, eg, I A Wilson and K R Wilson, 'Patenting New Life Forms: A Dilemma in Bioethics and the Law' (1987) 3 *Queensland Institute of Technology Law Journal* 99; Deryck Beyleveld and Roger Brownsword, *Mice, Morality and Patents* (Common Law Institute of Intellectual Property, 1993); Margo A Bagley, 'Patent First Ask Questions Later: Morality and Biotechnology in Patent Law' (2003) 45 *William & Mary Law Review* 469; R Stephen Crespi, 'Patenting and Ethics - A Dubious Connection' (2003) 85 *Journal of the Patent and Trademark Office Society* 31; Cynthia M Ho, 'Splicing Morality and Patent Law: Issues Arising from Mixing Mice and Men' (2000) 2 *Washington University Journal of Law and Policy* 247.

either in Australia or on a global scale.[85] Given the prospects of bioprinting and current awareness about associated ethical concerns, it is important for holistic research to be undertaken at this stage of its development.

Thus, this thesis intends to evaluate ethical concerns arising from patenting bioprinting and propose measures for the protection of bioprinting-related inventions which balance the interests of inventors and the public. In particular, this analysis focuses predominantly on bioprinted constructs and to a lesser extent, bioprinting processes. This is further to earlier explanations that their embodiment of living cells and their inherent nature as replacement tissues/organs raises significant debates in the context of patent subject matter eligibility and access.

As such, one of the main contributions of this thesis is the assessment of bioprinted constructs and related bioprinting processes as patent eligible subject matter in three jurisdictions selected for their divergent approaches to the question of patentability. These are Australia, Europe (under the *European Patent Convention* ('*EPC*')) and the USA.[86] In this regard, this thesis draws from legislative provisions and their subsequent interpretation by the courts to consider the extent to which variations in legislative provisions across the three jurisdictions might affect patentability. This is in addition to a review of the usefulness of ethically informed exclusions in addressing ethical concerns about patenting bioprinted constructs.

It should be emphasised that many bioprinting processes derive from existing practices in tissue engineering, regenerative medicine and 3D printing. Accordingly, issues surrounding their eligibility as patentable subject matter are not necessarily unique to bioprinting. However, to the extent that there are suggestions that bioprinting patents should be limited to the process/method of manufacture to the exclusion of bioprinted constructs,[87] it was considered useful to examine their patentability in this thesis.

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[85] Frederic Gilbert et al, 'Enthusiastic Portrayal of 3D Bioprinting In The Media: Ethical Side Effects' (2018) 32 *Bioethics* 94, 99.

[86] It should be noted that Australia, the United States of America and nearly all the contracting states of the *EPC* are members of the WTO, and are thus signatories to the *TRIPS Agreement*.

[87] Jasper L Tran, 'Patenting Bioprinting' (2015) 29 *Harvard Journal of Law and Technology Digest* <https://jolt.law.harvard.edu/digest/patenting-bioprinting>. See also chapter eight for a consideration of this suggestion.

Furthermore, this thesis also intends to fill an identified gap in existing literature - the absence of a specialised patent landscape report focused exclusively on bioprinted constructs. Up until now, there does not appear to have been any reported patent landscaping of bioprinted constructs in any jurisdiction across the world. Rather, the patent landscape reports in the field of bioprinting have been more general in coverage as opposed to specialised reports focused on specific types of bioprinting-related inventions.[88] Whilst it is possible to consider the ethical, legal and social implications of patenting bioprinted constructs as it would appear from the growing body of literature in this field, much of the current discourse lacks the nuance that can only be achieved from a review of evidentiary data.

Accordingly, it is anticipated that the information contained in the landscape report will serve as a useful resource in further deliberations about the issues arising from patenting bioprinted constructs. This is especially important given growing attempts at regulating 3D printing and potentially bioprinting.[89]

1.5 Research Methodology and Outline

The overall objective of this thesis is to assess whether patenting bioprinting is an appropriate form of protection for the technology especially in light of ethical concerns associated with patenting bioprinted constructs.

In particular, this thesis intends to address the following questions:

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[88] See, eg, Robert W Esmond and Deborah Sterling, 'Bioprinting: The Intellectual Property Landscape' in Aleksandr Ovsianikov, James Yoo and Vladimir Mironov (eds), *3D Printing and Biofabrication* (Springer International Publishing, 2016) 1; Hornick and Rajan (n 30); Marisela Rodríguez-Salvador, Rosa María Rio-Belver and Gaizka Garechana-Anacabe, 'Scientometric and Patentometric Analyses to Determine the Knowledge Landscape in Innovative Technologies: The Case of 3D Bioprinting' (2017) 12(6) *PLoS ONE* <https://doi.org/10.1371/journal.pone.0180375>; Timothy Sheehan et al, 'Recent Patents and Trends in Bioprinting' (2011) 4 *Recent Patents on Biomedical Engineering* 26; Amy J C Trappey, Charles V Trappey and Kurt L C Lee, 'Tracing the Evolution of Biomedical 3D Printing Technology Using Ontology-Based Patent Concept Analysis' (2017) 29 *Technology Analysis & Strategic Management* 339.

[89] Frederic Gilbert et al, 'Print Me an Organ? Ethical and Regulatory Issues Emerging from 3D Bioprinting in Medicine' (2017) *Science and Engineering Ethics* 1 <http://link.springer.com/article/10; Frederic Gilbert et al, 'Enthusiastic Portrayal of 3D Bioprinting In The Media: Ethical Side Effects' (n 85) 99; 'FDA's Role in 3D Printing', *United States Food and Drug Administration* (Web Page, 4 December 2017) <https://www.fda.gov/medical-devices/3d-printing-medical-devices/fdas-role-3d-printing>; 'Consultation: Proposed Regulatory Scheme for Personalised Medical Devices, Including 3D-Printed Devices', *Therapeutic Goods Administration* (Web Page, 13 February 2019) <https://www.tga.gov.au/consultation/consultation-proposed-regulatory-scheme-personalised-medical-devices-including-3d-printed-devices>.

i. Are bioprinted constructs and related bioprinting processes patent eligible subject matter?
ii. Are there any ethical considerations that might preclude bioprinted constructs in particular from patentability?
iii. Have patents been granted for bioprinted constructs and if yes, to what extent?
iv. Should patents even be granted for bioprinted constructs?
v. If yes, are there any measures within the patent system that can be deployed to minimise the impact of patenting bioprinted constructs particularly in the context of improving access?

Whilst the *Agreement on Trade-related Aspects of Intellectual Property Rights* ('*TRIPS Agreement*') provides an overarching framework for discussions about patentability and access in this thesis, it should be noted that the rules on patentability differ across jurisdictions. Thus, as noted earlier, it was decided to examine the rules on patentability in Australia, Europe (under the *EPC*) and the USA in order to address questions (i) and (ii) in particular. These jurisdictions were carefully selected on the basis that judicial decisions taken in each of them appear to inform the application of patent laws to emerging technologies globally. Their disparate approaches to the matter of patentability are also broadly representative of existing rules on patentability globally. To this end, this thesis also considers whether the disparate approaches to patentable subject matter and the role of morality in patenting yield similar or different results.

It should be noted that this thesis is primarily a doctrinal analysis of existing primary and secondary sources in both legal and science databases. In addition to the fact that the doctrinal research methodology is recognised as the core legal research method,[90] the doctrinal research methodology has been adopted as the primary methodology for this research because its aims are best suited to the research questions identified above. It has been noted by some authors that the doctrinal research methodology (otherwise known as the black-letter law approach) aims to 'systematise, rectify and clarify the law on any

[90] Terry Hutchinson and Nigel Duncan, 'Defining and Describing What We Do: Doctrinal Legal Research' (2012) 17 *Deakin Law Review* 83, 85.

particular topic by a distinctive mode of analysis of authoritative texts that consist of primary and secondary sources'.[91]

Furthermore, the doctrinal research methodology 'provides a systematic exposition of the rules governing a particular legal category, analyses the relationship between rules, explains areas of difficulty and, perhaps, predicts future developments'.[92] In itself, the doctrinal research methodology comprises of a two-part process which begins with locating the sources of the law,[93] which include not just secondary information, but also primary sources - legislation and case law. [94]

After the sources have been located, the next step is to interpret and analyse the text. This analytical aspect contains a qualitative methodology element, and can be performed using a number of techniques such as deductive logic, inductive reasoning and analogy.[95] As bioprinting is an emerging technology with limited sources of both primary and secondary information, this thesis relies heavily on the use of analogy particularly in chapters three, four and five. As noted by Hutchinson and Duncan, analogy involves 'locating similar situations arising, for example, in common law cases, and then arguing that similar cases should be governed by the same principle and have similar outcomes'.[96]

For reasons explained earlier in this section and the preceding section regarding the choice of jurisdictions, this thesis also adopts the use of international and comparative legal research methodology. This type of research methodology is generally aimed at facilitating the 'understanding of the operation of international law and legal systems and its impact on the formulation of public policy in an era of global interdependence'.[97]

To this end, this thesis encompasses an analytical, comparative and evaluative appraisal of official texts of international conventions and instruments, national and regional legislations, statutory instruments, decided court and patent office cases, policy papers as

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[91] Mike McConville and Wing Hong Chui, 'Introduction and Overview' in Mike McConville and Wing Hong Chui (ed), *Research Methods for Law* (Edinburgh University Press, 2nd ed, 2017) 1, 4.
[92] Dennis Pearce, Enid Campbell and Don Harding, *Australian Law Schools: A Discipline Assessment for the Commonwealth Tertiary Education Commission* (Australian Government Publishing Service, 1987) cited in Hutchinson and Duncan (n 89) 101.
[93] Hutchinson and Duncan (n 90) 110.
[94] Hutchinson and Duncan (n 90) 113.
[95] Hutchinson and Duncan (n 90) 111, 116.
[96] Hutchinson and Duncan (n 90) 111.
[97] McConville and Chui (n 91) 7.

well as publications of renowned experts in bioprinting and patent law. Given limited publications in the area of focus this thesis, much of the analysis draws from an extrapolation of existing analysis on related issues in similar biotechnology fields.

In addition, given that this thesis includes a patent landscape report, some empirical analysis was also conducted. Whilst a more detailed methodology is contained in the relevant chapter,[98] it suffices to state at this juncture that the patent search was conducted in the patent databases of the aforementioned jurisdictions. This is because the patent landscaping sought primarily to confirm prior analysis about the state of the law on patentability of bioprinted constructs and related bioprinting processes in those jurisdictions.

This thesis is divided into seven chapters. The **first chapter**, being this chapter, provides a general introduction to this thesis.

Chapter two provides a broad overview of the state of the art of bioprinting. It examines each stage of the bioprinting process from the creation of a digital blueprint design of the required construct up until the construct is printed and ready for use. Furthermore, it explores the potential applications of bioprinting whilst highlighting current challenges which could potentially inhibit the realization of the full potential of the technology. Thereafter, ethical, legal and socio-economic concerns about bioprinting as a technology are considered with the aim of subsequently distinguishing such concerns from those issues which are within the purview of the patent system.

Chapters three, four and five examine the state of the law on patentability of bioprinted constructs and the processes involved in their production in Australia, *EPC* member countries, and the USA. Whereas chapter three examines the Australian position, the *EPC* and American positions are considered in chapters four and five, respectively. In particular, these chapters examine two key aspects of patentability – eligible subject matter and exceptions from patentability. Overall, this thesis concludes that whilst there are ethical concerns associated with patentability, these are unlikely to have any significant impact on patentability. Additionally, this thesis also concludes that bioprinted constructs and related

[98] See chapter six.

processes appear generally patentable in each of these jurisdictions subject to certain exceptions.

Chapter six aims to test the conclusions drawn from the preceding chapters about the patentability of bioprinted constructs since these are considered to be the most contentious aspect of patenting bioprinting. Thus, the patent databases for each of the aforementioned jurisdictions are reviewed for patents and pending applications relating to bioprinted constructs. The results obtained confirm that indeed patents are being granted for bioprinted constructs, in accordance with the legal analysis presented in chapters three, four and five.

Chapter seven examines ethical concerns about the impact of patenting bioprinting as a whole and considers whether these are sufficient to warrant a reconsideration of the grant of patents for bioprinting-related inventions, especially bioprinted constructs. These include concerns about the impact of patenting on the patentability of future biotechnological innovations, commodification of life and the human body, and access. This thesis argues that whilst the first two concerns are valid, they are neither peculiar to bioprinting nor are they necessarily caused by the act of patenting in itself. Thus, withholding patents is unlikely to resolve these concerns.

On the other hand, this thesis notes that access, especially research access, is likely to be a prominent issue at this stage of the technology's development. Whilst the grant of patents does create access concerns by virtue of the ensuing monopoly, this thesis argues that the grant of patents is equally beneficial to the growth of the technology. Thus, rather than withhold patents because of access concerns, this thesis argues that it is in the interest of stakeholders to consider an approach which aims at striking a balance between incentivising innovation and rewarding innovators on the one hand, and ensuring access to these innovations on the other hand. In light of this, the patent flexibilities contained in the *TRIPS Agreement* are considered.

Overall, this thesis concludes that whilst flexibilities such as the experimental use exception and compulsory licensing are of particular significance in improving access, other measures, such as limiting the scope of patents and industry-driven initiatives (with emphasis on

non-exclusive licensing), are equally crucial to promoting access and consequently, the development of the technology.

1.6 Publications from the Thesis

The following article was extracted from this thesis and has been peer-reviewed and published

- O O Adesanya, 'Patenting Bioprinted Structures in a Clime of Moral Uncertainty: Time to Amend the Patents Act?' (2019) **29** (4) *Australian Intellectual Property Journal* 222-238 (ABDC Rank C, Journal listed in ERA 2018 Journal List)

Chapter 2

2 Bioprinting: A New Frontier in Healthcare

2.1 Introduction

Amidst global health concerns about increasing mortality rate from chronic diseases as well as a global shift towards ethical and reliable alternatives to animal research, the emergence of bioprinting marks an important milestone for global health given its potential to significantly transform healthcare delivery. Nevertheless, there are emerging ethical, legal and socio-economic concerns about the technology, which ought to be addressed as the technology advances.

Prior to examining these concerns, however, it is important to understand what bioprinting as a technology entails. Accordingly, this chapter begins by tracing the origins of bioprinting in regenerative medicine and tissue engineering. Thereafter, it examines the bioprinting process and potential applications of the technology in the areas of disease modelling and research; drug discovery and animal testing; and chronic diseases and tissue/organ transplantation. It should be emphasised that this chapter does not purport to provide a comprehensive overview of the bioprinting process. Rather, it is intended to provide a basic understanding of bioprinting and highlight aspects relevant to further discourse about the ethical issues pertaining to patenting bioprinting-related inventions.

Subsequently, this chapter considers the state of the art and highlights notable achievements in this regard. In the same vein, this chapter also accentuates some of the many challenges encountered in the development of bioprinting. In particular, it is noted that there are opposing views regarding the viability of bioprinting complex implantable constructs such as kidneys in the long term.

Finally, this chapter concludes with an examination of ethical, legal and socio-economic concerns about bioprinting that could potentially affect how the technology is developed and the benefits enjoyed. These include questions about the ethics and safety of using xenogeneic and human embryonic stem cells, safety and efficacy of bioprinted constructs, access and social justice, and possible use of bioprinted constructs for human enhancement.

2.2 Bioprinting and its Origins in Regenerative Medicine and Tissue Engineering

Bioprinting stems from prior activities of researchers within the regenerative medicine and tissue engineering sphere. For a long time now, researchers have conducted multiple comparative studies on regeneration in humans and animals.[1] They note that unlike the salamander, which for instance is capable of growing a new limb to replace a damaged one, most tissues/organs in the human body save for the liver and skin are incapable of regeneration.[2] This limited capacity for regeneration in humans is a huge concern because injury or damage to tissues/organs often results in impaired capacity and consequently, a diminished quality of life.

In order to make up for this 'evolutionary deficiency', medical therapies such as surgery, surgical implants, organ and bone marrow transplant have been developed to assist the human body with regeneration.[3] While many of these therapies aid in alleviating diseases and improving quality as well as length of life, others such as organ transplantation remain largely palliative, with associated risks ranging from surgical complications such as shock, haemorrhaging and infection, to transplant rejection as well as side effects arising from using post-surgery medications. As such, there is a pressing demand for lasting solutions with minimal side effects. Most promising at this stage is regenerative medicine, which 'aims to replace or regenerate human cells, tissues, or organs in order to restore or establish normal function',[4] thereby providing as close a remedy as possible for previously untreatable diseases and injuries.

Regenerative medicine is a broad field which encompasses research on cell regeneration and the self-healing capability of the human body.[5] The overarching emphasis in cell regeneration is premised on the fact that cells, which make up tissues and consequently

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[1] 'Regeneration: What Does it Mean and How Does it Work?', EuroStemCell (Web Page, 25 November 2015) <http://www.eurostemcell.org/regeneration-what-does-it-mean-and-how-does-it-work> 24 ('*Regeneration: What Does it Mean and How Does it Work?*'); Patima Sdek et al, 'Rb and p130 Control Cell Cycle Gene Silencing to Maintain the Postmitotic Phenotype in Cardiac Myocytes' (2011) 194 *Journal of Cell Biology* 407.

[2] Kevin Xu, 'Humans' Ability to Regenerate Damaged Organs is at Our Fingertips', *Business Insider* (Web Page, 19 July 2013) <http://www.businessinsider.com/how-regeneration-works-2013-7/?r=AU&IR=T>; *Regeneration: What Does it Mean and How Does it Work?* (n 1).

[3] Chris Mason and Peter Dunnill, 'A Brief Definition of Regenerative Medicine' (2008) 3 *Regenerative Medicine* 1.

[4] Massimo Conese, 'Bioprinting: A Further Step to Effective Regenerative Medicine and Tissue Engineering' (2014) 2(3) *Advancements in Genetic Engineering* e112.

[5] 'Tissue Engineering and Regenerative Medicine', *National Institute of Biomedical Imaging and Bioengineering, U S Department of Health & Human Services* (Web Page) <https://www.nibib.nih.gov/science-education/science-topics/tissue-engineering-and-regenerative-medicine> ('*Tissue Engineering and Regenerative Medicine*').

organs, are considered the basic unit of life.[6] The development of any holistic remedy for diseased or injured tissues/organs therefore requires that problems or changes at the cellular level are addressed.

Regenerative medicine entails recreating cells and rebuilding tissues/organs using stem cells (such as embryonic, adult or induced pluripotent stem cells), natural or synthetic cell-supporting scaffold materials, bioactive molecules, genetic manipulation, or combinations thereof.[7] It is useful to note that the preference for stem cells in regenerative medicine is as a result of their self-renewing abilities and their unspecialised nature, which allows for their differentiation into various types of specialised cells (such as muscle or nerve cells) required to develop tissues and organs.[8] This is as opposed to using specialised cells which are already differentiated with tissue-specific characteristics and generally unable to replicate.[9]

Furthermore, regenerative medicine also encompasses the subfield of tissue engineering,[10] which in itself has been described as an interdisciplinary field that involves

> the application of the principles and methods of engineering and life sciences toward the fundamental understanding of structure-function relationships in normal and pathologic mammalian tissue and the development of biological substitutes to restore, maintain, or improve function.[11]

Overall, tissue engineering involves combining scaffolds, cells and biologically active molecules into functional tissue constructs that restore, maintain, or improve damaged

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[6] 'Connecting Human Biology and Health Choices', *California Society for Biomedical Research* (Web Page, 2014) <http://www.ca-biomed.org/csbr/pdf/connect.pdf>, 331; *Tissue Engineering and Regenerative Medicine* (n 5); Rouchi A Heidary, 'Regenerative Medicine in Organ and Tissue Transplantation: Shortly and Practically Achievable?' (2015) 6 *International Journal of Organ Transplantation Medicine* 93, 94; Qi Gu et al, 'Three-Dimensional Bioprinting Speeds up Smart Regenerative Medicine' (2016) 3 *National Science Review* 331.

[7] *Tissue Engineering and Regenerative Medicine* (n 5); Conese (n 4).

[8] 'Stem Cell Information', *National Institutes of Health, U S Department of Health and Human Services* (Web Page, 2016) <https://stemcells.nih.gov/info/basics.htm> ('*Stem Cell Information*'); Heidary (n 6); Gu et al, 'Three-Dimensional Bioprinting Speeds up Smart Regenerative Medicine' (n 6).

[9] *Stem Cell Information* (n 8).

[10] *Tissue Engineering and Regenerative Medicine* (n 5).

[11] Chee Kai Chua and Wai Yee Yeong, *Bioprinting: Principles and Applications* (World Scientific, 2015), 5; Ulrich Meyer, 'The History of Tissue Engineering and Regenerative Medicine in Perspective' in Ulrich Meyer et al (eds), *Fundamentals of Tissue Engineering and Regenerative Medicine* (Springer Berlin Heidelberg, 2009) 5, 9.

tissues or whole organs.[12] Notable examples of engineered tissue which have been implanted in human subjects include bladder, cartilage and artificial skin.[13]

Notwithstanding recorded successes in the tissue engineering and regenerative medicine field, a number of challenges still exist with large-scale production of functional tissue constructs equally suitable for implantation. These include reliance on manual manipulation which limits the scale of production, lack of ordered tissue microstructure, difficulties supporting growth of cells in three-dimensional ('3D') form, difficulties depositing different cell types at specified locations, and limitation to the production of two-dimensional ('2D') simple tissues as opposed to 3D complex organs.[14] Given its capacity to fabricate tissues/organs in 2D and 3D, bioprinting has the potential to remedy the shortcomings of traditional regenerative medicine approaches whilst still embodying the basic principles of regenerative medicine.

Specifically, bioprinting offers the ability to not only build 3D constructs, but also reproduce the complexity and intricacy of native tissues through precise placements of cells.[15] This is in addition to the possibility of printing new organs as opposed to simply repairing tissue defects.[16] Indeed, the ultimate goal is to produce functional vascularised living constructs suitable for clinical implantation without the shortcomings associated with donor-based organ transplantation therapies such as immune rejection and organ shortage.[17] It should, however, be noted that opinions are divided on the feasibility of this goal, given current challenges which will be considered later on in this chapter.[18]

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[12] *Tissue Engineering and Regenerative Medicine* (n 5); Chua and Yeong (n 11) 7-8; Cristina Castells-Sala et al, 'Current Applications of Tissue Engineering in Biomedicine' (2013) S2 *Journal of Biochips & Tissue Chips*.

[13] Anthony Atala, 'Tissue Engineering of Human Bladder' (2011) 97 *British Medical Bulletin* 81; *Tissue Engineering and Regenerative Medicine* (n 5); Anthony Atala et al, 'Tissue-Engineered Autologous Bladders for Patients Needing Cystoplasty' (2006) 367 *Lancet* 1241; Sara Llames et al, 'Clinical Results of an Autologous Engineered Skin' (2006) 7 *Cell and Tissue Banking* 47.

[14] Conese (n 4); Chua and Yeong (n 11) 11-12; Dhakshinamoorthy Sundaramurthi, Sakandar Rauf and Charlotte A E Hauser, '3D Bioprinting Technology for Regenerative Medicine Applications' (2016) 2(2) *International Journal of Bioprinting* 9.

[15] Sundaramurthi, Rauf and Hauser (n 14); Conese (n 4).

[16] Sundaramurthi, Rauf and Hauser (n 14).

[17] Chua and Yeong (n 11) 11-12.

[18] See generally Sundaramurthi, Rauf and Hauser (n 14); Sean V Murphy and Anthony Atala, '3D Bioprinting of Tissues and Organs' (2014) 32 *Nature Biotechnology* 773; Conese (n 4); Heidi Ledford, 'Printed Body Parts Come Alive' (2015) 520 *Nature* 273; Wei Long Ng, Chee Kai Chua and Yu-Fang Shen, 'Print Me An Organ! Why We Are Not There Yet' (2019) 97 *Progress in Polymer Science* 101145; Neil Savage, 'The Promise of Printing' (2016) 540 *Nature* S56; Gu et al, 'Three-Dimensional Bioprinting Speeds up Smart Regenerative Medicine' (n 6); Ahu Arslan-Yildiz et al, 'Towards Artificial Tissue Models: Past, Present and Future of 3D Bioprinting' (2016) 8(1) *Biofabrication* 014103; Stuart

Other advantages of bioprinting over traditional regenerative medicine approaches include *in situ* (otherwise known as *in vivo*) printing as well as digitised production which enables precise positioning of multiple cell types and large-scale production. To this end, it is useful to now consider what the bioprinting process entails.

2.3 The Bioprinting Process

In order to wholly appreciate the potential legal and ethical issues associated with bioprinting, which forms the substratum of this thesis, it is instructive to not only explain the concept of bioprinting as has been done in the previous section, but to also explore the workings of the technology. By so doing, it becomes apparent why these issues are topical and deserving of deliberate consideration at this stage of the technology's development.

Generally, the bioprinting process begins with a digital blueprint design of the required construct. Living cells are isolated from a donor, cultured and combined with other non-living material to produce what is known as bioink - the equivalent of traditional printing ink. Guided by the blueprint, the bioink is deposited layer by layer on a receiving substrate[19] until the required construct is fully built. Thereafter, the construct is left to mature in a bioreactor before it can be used in *in vivo* or *in vitro* applications. This approach is known as *in vitro* bioprinting.

A more recent approach also in development is *in situ* bioprinting, which has so far been tested in bone, cartilage and skin fabrication studies.[20] This approach involves printing the construct directly on the intended anatomical location in the living body with the aid of a robotic arm or a handheld device, using the body as a bioreactor.[21] While there are benefits and limitations of each approach over the other,[22] further consideration of these matters is of limited significance to the overall arguments in this thesis.

Kyl and Iain S Whitaker, 'To Print or Not to Print, That is the Question: How Close Are We to Clinical Translation of Contemporary Bioinks?' (2018) 2 *Journal of 3D Printing in Medicine* 1; Chua and Yeong (n 11).

[19] The receiving substrate refers to the base material onto which bioprinted constructs are built. This can be solid (for example, culture dish), liquid (for example, growth medium) or gel derived materials: Zeming Gu et al, 'Development of 3D Bioprinting: From Printing Methods to Biomedical Applications' (2019) *Asian Journal of Pharmaceutical Sciences*.

[20] Satnam Singh et al, '*In Situ* Bioprinting – Bioprinting from Benchside to Bedside?' (2020) 101 *Acta Biomaterialia* 14; Murphy and Atala (n 18).

[21] Singh et al (n 20); D. O'Connell Cathal et al, 'Development of the Biopen: A Handheld Device for Surgical Printing of Adipose Stem Cells at a Chondral Wound Site' (2016) 8(1) *Biofabrication* 015019.

[22] See generally Singh et al (n 20); Dino J Ravnic et al, 'Transplantation of Bioprinted Tissues and Organs: Technical and Clinical Challenges and Future Perspectives' (2017) 266 *Annals of Surgery* 48.

As *in vitro* bioprinting is the most common approach, this section provides a general overview of the typical *in vitro* bioprinting process without delving into much of the technicalities except where considered relevant to the overall thesis. The process, represented by the diagram below, is discussed under three main headings: pre-printing, printing and post-printing.

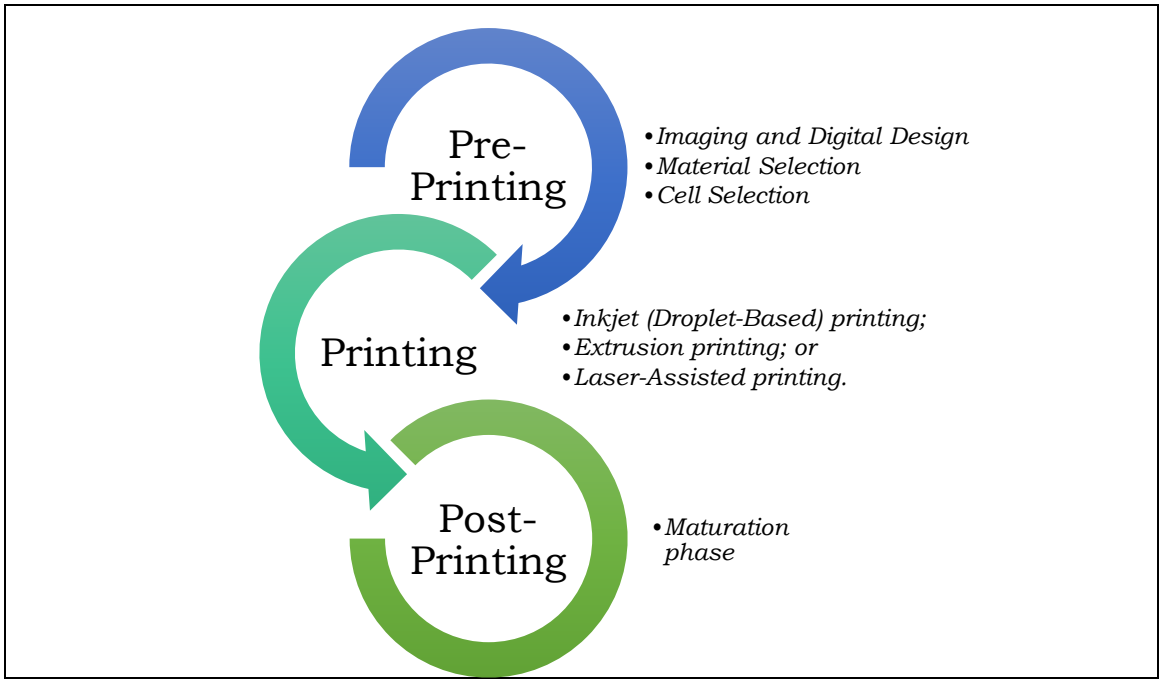

Figure 2.1: Typical bioprinting process

2.3.1 Pre-Printing

The pre-printing process consists of three steps: imaging and digital design, material selection, and cell selection which are explained below. While decisions made at this stage are important to the overall structural integrity and viability of the printed construct, it is pertinent to note that issues pertaining to the patentability of bioprinted constructs also arise at this stage. This is in relation to the replication of naturally occurring tissues/organs and use of human cells which are discussed extensively in chapters three, four and five.

2.3.1.1 Imaging and Digital Design

Often, with bioprinting, the goal is to create an exact replica of a naturally occurring tissue/organ as substitute for the original. While there might be attempts in the future to design constructs that function similarly to naturally occurring tissues/organs but differ

structurally,[23] analysis in this thesis is premised on the notion that bioprinted constructs are replicas of existing constructs, both structurally and functionally, with minimal creative input, if any.

In order to ensure accurate reproduction of the required construct, scans are taken of the original construct using medical imaging techniques such as optical microscopy, X-rays, computed tomography or magnetic resonance imaging.[24] With the aid of computer-aided design/manufacturing tools and mathematical modelling, the scanned images are then converted into 3D models which serve as the digital blueprint design of the replacement constructs.[25]

2.3.1.2 Material Selection

For decades, biomaterials derived from ceramic, metals and polymers have been used in therapeutic and diagnostic systems with the purpose of replacing biological materials.[26] A biomaterial generally refers to 'a substance that has been engineered to take a form which, alone or as part of a complex system, is used to direct, by control of interactions with components of living systems, the course of any therapeutic or diagnostic procedure, in human or veterinary medicine'.[27] In the context of bioprinting, biomaterials are used to provide structural and biochemical support to cells pending the production of natural extracellular matrix (ECM)[28] proteins by the cells required to bind them together.[29]

As biomaterials serve as artificial ECM for the cells, it is essential that they are biocompatible, biodegradable and non-immunogenic.[30] This is to prevent the release of

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[23] 'Bioprinters: Printing a Bit of Me', *Technology Quarterly, The Economist* (online, 8 March 2014) <http://www.economist.com/news/technology-quarterly/21598322-bioprinting-building-living-tissue-3d-printer-becoming-new-business>.

[24] Murphy and Atala (n 18); Chua and Yeong (n 11); S Vijayavenkataraman, W F Lu and J Y Fuh, '3D Bioprinting of Skin: A State-of-the-Art Review on Modelling, Materials and Processes' (2016) 8(3) *Biofabrication* 032001.

[25] Murphy and Atala (n 18); Chua and Yeong (n 11).

[26] Chua and Yeong (n 11); David F Williams, 'On the Nature of Biomaterials' (2009) 30 *Biomaterials* 5897.

[27] Williams (n 26).

[28] Extracellular matrix (ECM) refers to the non-cellular component of tissues and organs comprised of collagens and several other glycoproteins, which provide essential physical scaffolding for the cellular constituents. In addition, ECM also initiate crucial biochemical and biomechanical cues required for tissue morphogenesis, differentiation and homeostasis: Christian Frantz, Kathleen M Stewart and Valerie M Weaver, 'The Extracellular Matrix at a Glance' (2010) 123 *Journal of Cell Science* 4195; Achilleas D Theocharis et al, 'Extracellular Matrix Structure' (2016) 97 *Advanced Drug Delivery Reviews* 4.

[29] Lijie Grace Zhang, John P Fisher and Kam W Leong, *3D Bioprinting and Nanotechnology in Tissue Engineering and Regenerative Medicine* (Academic Press, 2015); Chua and Yeong (n 11).

[30] Murphy and Atala (n 18); Chua and Yeong (n 11); Vijayavenkataraman, Lu and Fuh, '3D Bioprinting of Skin: A State-of-the-Art Review on Modelling, Materials and Processes' (n 24).

toxic by-products from degradation, which could be detrimental to cell viability and function on the one hand, and to minimise the likelihood of rejection by the patient's immune system on the other hand.[31] In addition, it is equally important that selected materials are compatible with the printing process and are capable of providing the desired mechanical and functional properties for tissue constructs.[32]

Biomaterials generally used in regenerative medicine, which are equally available for use in bioprinting include naturally derived polymers (such as alginate, gelatin, collagen, chitosan, fibrin and hyaluronic acid which are often isolated from human or animal tissues), synthetic polymers (such as polyethylene glycol, polylactic acid and polyglycolic acid), and decellularised ECM isolated from its inhabiting cells.[33]

2.3.1.3 Cell Selection

As with material selection, cells selected for use in bioprinting must possess certain important characteristics in order to ensure correct functioning of the fabricated construct. These include the ability to expand and differentiate into required cell types as well as the capacity to survive the bioprinting process and withstand physiological stresses once transplanted.[34] Most importantly, where the construct is intended for implantation, selected cells must be immunocompatible with the intended recipient.

Cells used in bioprinting can be categorised based on the following:

a) *Cell Sources*

Cell sources may be autologous (from the patient), allogeneic (donor-based from the same species) or xenogeneic (from a different species).[35] Of the three sources, autologous cells are preferred where the bioprinted construct is intended for human implantation. This is because of the reduced risk of immune rejection and disease transmission since the cells are sourced from the intended recipient.[36] Nevertheless, notwithstanding the increased risk of immune rejection, allogeneic and xenogeneic cells remain useful sources particularly in circumstances where it is impossible to obtain cells from the patient owing to either illness

[31] Murphy and Atala (n 18).
[32] Ibid; Chua and Yeong (n 11).
[33] Zhang, Fisher and Leong (n 29); Murphy and Atala (n 18); Chua and Yeong (n 11).
[34] Murphy and Atala (n 18); Chua and Yeong (n 11).
[35] Murphy and Atala (n 18); Chua and Yeong (n 11).
[36] Chua and Yeong (n 11).

or genetic disorders.[37] Compared to allogeneic sources, however, the risk of immune rejection is much higher with xenogeneic sources, which also carry an added risk of introducing pathogenic agents (such as bacteria, viruses, and other infectious agents) common to that species into humans.[38] This, in addition to ethical concerns about using cells of animal origin, make xenogeneic sources the least favoured option.[39]

b) *Potential for Expansion and Differentiation*

As explained earlier, stem cells, in comparison to specialised cells are adjudged the best type of cells for use in regenerative medicine applications such as bioprinting because of their unspecialised nature, and their ability to self-renew and differentiate into specialised cells performing specific functions in the body.[40] These unique properties mean that stem cells can be cultured almost indefinitely in the laboratory and adapted for use in printing different types of tissues/organs. The various types of stem cells often used in bioprinting include human embryonic stem cells (hESCs), adult/somatic stem cells and induced pluripotent stem cells (iPSCs).

Whereas hESCs and iPSCs have demonstrated longevity and are capable of indefinite self-renewal, adult stem cells have been found to have a more restricted differentiation capacity.[41] This is notwithstanding that iPSCs are actually adult cells, which have been reprogrammed back to form pluripotent stem cells.[42] Ultimately, the similarities between both cell types in terms of their capacity for pluripotency and self-renewal makes hESCs and iPSCs more viable options for bioprinting.

Nevertheless, iPSCs appear more advantageous in certain respects. First, the production of iPSCs does not involve the destruction of pre-implantation human embryos, which has

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[37] Murphy and Atala (n 18); Vijayavenkataraman, Lu and Fuh, '3D Bioprinting of Skin: A State-of-the-Art Review on Modelling, Materials and Processes' (n 24).

[38] Mathew Varkey and Anthony Atala, 'Organ Bioprinting - A Closer Look at Ethics and Policies' (2015) 5 *Wake Forest Journal of Law and Policy* 275; Marc R Hammerman and Raffaello Cortesini, 'Organogenesis and Tissue Engineering' (2004) 12 *Transplant immunology* 191.

[39] Varkey and Atala (n 38); Hammerman and Cortesini (n 38).

[40] Murphy and Atala (n 18); Chua and Yeong (n 11); Vijayavenkataraman, Lu and Fuh, '3D Bioprinting of Skin: A State-of-the-Art Review on Modelling, Materials and Processes' (n 24).

[41] Murphy and Atala (n 18); Chua and Yeong (n 11).

[42] Chua and Yeong (n 11); Kazutoshi Takahashi et al, 'Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors' (2007) 131 *Cell* 861; Junying Yu et al, 'Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells' (2007) 318 *Science* 1917.

generated significant ethical concerns in the use of hESCs in regenerative medicine.[43] Furthermore, because iPSCs can be produced in a patient-specific manner, given they are artificially generated from adult cells, their use largely eliminates immunological rejection upon implantation in comparison to hESCs, which are derived solely from allogeneic sources.[44]

Given iPSCs are a recent development in regenerative medicine, however, there are still a number of challenges which must be overcome before they can be effectively used in clinical applications as hESCs replacements. This include concerns about chromosomal abnormalities as well as the risk of tumour production and possible mutations.[45] Thus, at this stage, hESCs have not been effectively replaced by iPSCs and accordingly remain a predominant cell source in regenerative medicine. This is notwithstanding ethical concerns about their use which will be examined later in this chapter.[46]

After a decision has been made on the source and type of cells to be used, the required cells are isolated from tissue samples obtained from the donor. These isolated cells are then cultured in the laboratory to obtain a number sufficient for printing the required construct. Together with the selected materials, these form the bioink used for printing the required construct.[47]

2.3.2 Printing

There are a variety of printing techniques that can be used depending on the material delivery method. These include contact techniques such as the extrusion method which involves contact between the delivery apparatus and the receiving substrate, and non-contact methods such as inkjet (droplet-based) and laser-assisted techniques in which the delivery apparatus and the receiving substrate are located closely but do not touch.[48]

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[43] Takahashi et al (n 42); Yu et al (n 42); Michael Xavier Doss and Agapios Sachinidis, 'Current Challenges of iPSC-Based Disease Modeling and Therapeutic Implications' (2019) 8 *Cells* 403; S P Medvedev, A I Shevchenko and S M Zakian, 'Induced Pluripotent Stem Cells: Problems and Advantages when Applying them in Regenerative Medicine' (2010) 2(2) *Acta Naturae* 18.

[44] Yu et al (n 42); Sharif Moradi et al, 'Research and Therapy with Induced Pluripotent Stem Cells (iPSCs): Social, Legal, And Ethical Considerations' (2019) 10 *Stem Cell Research & Therapy* 341; Doss and Sachinidis (n 43); Medvedev, Shevchenko and Zakian (n 43).

[45] Yu et al (n 42); Doss and Sachinidis (n 43); Medvedev, Shevchenko and Zakian (n 43); Wei Sun et al, 'The Bioprinting Roadmap' (2020) 12(2) (2020/02/06) *Biofabrication* 022002.

[46] See below section 2.6.1.

[47] Sun et al (n 45); Ravnic et al (n 22).

[48] Murphy and Atala (n 18); Chua and Yeong (n 11); Zhang, Fisher and Leong (n 29).

While each of these techniques have their individual limitations in terms of scalability, process resolution and compatibility with bioinks, factors such as the complexity of the required constructs, costs, cell type, cell viability, available time and expertise will often influence the choice of techniques.[49] Thus, for instance, the inkjet technique, which has its origins in traditional inkjet printing, has been noted as the preferred choice 'for medium/high resolution and high-throughput applications, such as tissue models for drug screening and disease modelling',[50] while laser-assisted techniques appear to be 'mainly used in applications requiring high-precision patterning of cells, or high-resolution fabrication of tissue constructs'.[51] The extrusion method, on the other hand, is described as simple, easy and quick to use in generating scalable and structurally stable constructs in a relatively short time, making it the most commonly used technique in the bioprinting community.[52]

Nevertheless, it should be noted that these techniques are in a constant state of development, just as is the general field of bioprinting. In particular, it has been estimated that it is likely future technologies will encompass and utilize multiple techniques into single platforms along with the integration of novel processes especially as advances in each technique appears to complement the shortcomings of other techniques.[53]

2.3.3 Post-Printing

After printing, the resulting bioprinted construct may be used in *in vitro* applications or implanted in a prospective recipient after a period of maturation.[54] The maturation process typically takes place under controlled conditions in a bioreactor designed to facilitate cell growth, maturation, organ remodelling, proliferation, tissue fusion and vascularization.[55] Much of the maturation process relies on the intrinsic ability of cells to fuse together and proliferate.[56] During this process, the cells produce natural ECM proteins which provide

[49] Sun et al (n 45); Anh-Vu Do et al, '3D Printing of Scaffolds for Tissue Regeneration Applications' (2015) 4 *Advanced Health Care Materials* 1742.
[50] Sun et al (n 45).
[51] Ibid 28.
[52] Ibid 28.
[53] Ibid 29-30.
[54] Murphy and Atala (n 18); Ravnic et al (n 22); Gu et al, 'Three-Dimensional Bioprinting Speeds up Smart Regenerative Medicine' (n 6).
[55] Ravnic et al (n 22); Chua and Yeong (n 11); Gu et al, 'Three-Dimensional Bioprinting Speeds up Smart Regenerative Medicine' (n 6).
[56] Murphy and Atala (n 18); Ravnic et al (n 22).

structural and functional support to the bioprinted construct.[57] These ECM proteins, as explained earlier, replace the biomaterials used during the printing process to construct material scaffolds.

The maturation process is particularly important because the construct, immediately after printing, is often in a fluid-like state and not sufficiently structurally coherent or integrated for implantation.[58] Maturation ensures the bioprinted construct is functional, innervated, mechanically stable and solid.[59] Depending on the construct printed, the materials used and the printing strategy, the maturation process may take several months before a native-like state is achieved.[60] It is only when this occurs, and the construct is sufficiently tested that the bioprinted construct can be implanted in patients if so required.[61]

Overall, it is important for the entire bioprinting process to be conducted in sterile conditions to limit contamination of raw materials and the final construct, which if not avoided could potentially lead to infections in patients.[62]

2.4 Potential Applications of Bioprinting

This section examines the areas of medical research considered most likely to benefit from the bioprinting revolution. These areas as identified in existing literature have been categorised under three distinct headings, namely: disease modelling and research; drug discovery and animal testing; and chronic diseases and tissue/organ transplantation.[63]

2.4.1 Disease Modelling and Research

Up until now, most disease studies have been carried out using animals, 2D cell culture and engineered 3D tissue models, which do not adequately mimic the physiological structure

[57] Murphy and Atala (n 18); Ravnic et al (n 22).
[58] Ravnic et al (n 22).
[59] Ibid.
[60] Ibid.
[61] Ibid.
[62] Ibid; Zhang, Fisher and Leong (n 29).
[63] Murphy and Atala (n 18); Sundaramurthi, Rauf and Hauser (n 14); David B Kolesky et al, '3D Bioprinting of Vascularized, Heterogeneous Cell-Laden Tissue Constructs' (2014) 26 *Advanced Materials* 3124; Ibrahim T Ozbolat, Weijie Peng and Veli Ozbolat, 'Application Areas of 3D Bioprinting' (2016) 21 *Drug Discovery Today* 1257; Do et al (n 49); Stephanie Knowlton et al, 'Bioprinting For Cancer Research' (2015) 33 *Trends in Biotechnology* 504; Deborah G Nguyen and Stephen L Pentoney, 'Bioprinted Three Dimensional Human Tissues for Toxicology and Disease Modeling' (2017) 23(Supplement C) *Drug Discovery Today: Technologies* 37; Vladimir Mironov et al, 'Organ Printing: Promises and Challenges' (2008) 3 *Regenerative Medicine* 93; Ng, Chua and Shen (n 18); Ishita Matai et al, 'Progress in 3D Bioprinting Technology for Tissue/Organ Regenerative Engineering' (2020) 226 *Biomaterials* 119536; Guohao Dai and Vivian Lee, 'Three-Dimensional Bioprinting and Tissue Fabrication: Prospects for Drug Discovery and Regenerative Medicine' (2015) 1 *Advanced Health Care Technologies* 23; Chua and Yeong (n 11).

and functions of living human tissue.[64] While this has not inhibited the development of clinically successful therapeutic treatments, it has been noted that the differences in physiological structure and function is a contributory factor in the failure of some therapeutic treatments to translate into clinical success.[65] Given the possibility of engineering complex tissue models that mimic the *in vivo* microenvironment inside the human body, bioprinting thus appears to offer researchers a complementary and perhaps more advantageous method for disease modelling and research.[66]

Bioprinted tissue models are anticipated to assist with understanding internal biological processes involved in disease progression.[67] In addition, studies carried out on bioprinted tissue models are expected to produce more reliable and accurate results that can be translated into successful clinical trials.[68] This would in turn allow for the development of more effective therapeutic strategies including the production of personalised medicine.[69] Results from such studies could also potentially reduce the risks, costs and time associated with drug and therapeutic development.[70]

A noteworthy development in this area is the development of a 3D-printed heart-on-a-chip, which mimics the structure and functions of living human organs making it useful for drug screening and disease modelling.[71]

2.4.2 Drug Discovery and Animal Testing

Closely linked to bioprinting's application in disease modelling is its application to drug testing through the use of bioprinted tissue models as a potential alternative to animal

[64] Nitin Charbe, Paul A McCarron and Murtaza M Tambuwala, 'Three-Dimensional Bio-Printing: A New Frontier in Oncology Research' (2017) 8(1) *World Journal of Clinical Oncology* 21; Adnan Memic et al, 'Bioprinting Technologies for Disease Modeling' (2017) 39 *Biotechnology Letters* 1279; Ozbolat, Peng and Ozbolat (n 63).
[65] Charbe, McCarron and Tambuwala (n 64) 22.
[66] Nguyen and Pentoney (n 63); Memic et al (n 64); Knowlton et al (n 63).
[67] Memic et al (n 64).
[68] Charbe, McCarron and Tambuwala (n 64); Arslan-Yildiz et al (n 18); Ozbolat, Peng and Ozbolat (n 63); Knowlton et al (n 63).
[69] Memic et al (n 64).
[70] Charbe, McCarron and Tambuwala (n 64); Arslan-Yildiz et al (n 18).
[71] Leah Burrows, 'First Entirely 3D-Printed Organ-on-a-Chip with Integrated Sensors', *Wyss Institute* (Web Page, 24 October 2016) <https://wyss.harvard.edu/first-entirely-3d-printed-organ-on-a-chip-with-integrated-sensors/>; Ozbolat, Peng and Ozbolat (n 63).

subjects. Indeed, the reduction in and possible elimination of animal testing is considered one of the most feasible benefits of bioprinting.[72]

For years, animal testing has played a key role in biomedical research as well as in the development of new pharmaceutical and cosmetic products.[73] This is so as to evaluate the safety of such products before it is tested in humans. In recent years, however, there has been an increasing shift towards alternative forms of experimentation in part due to ethical controversies surrounding animal experimentation.

Opponents of animal testing argue that animals used are isolated from their natural habitat, and subjected to cruel and inhumane treatments in the form of tests carried out.[74] They further argue that evidence from clinical trials has proven that animal testing is unreliable for determining the safety of chemicals or drugs in humans owing to physiological differences between the two species.[75] For example, the sedative Thalidomide, considered safe after pre-clinical testing in animals, led to severe birth defects - mostly limb deformities in thousands of children born to women who had taken the drug during pregnancy between the 1950s and 1960s.[76] The drug is, however, still being used under strict conditions for the treatment of cancer and leprosy.[77] Similarly, TGN1412, an experimental therapy for rheumatoid arthritis and multiple sclerosis, previously tested in animals without

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[72] Clare Scott, 'Why Drug Testing May Be the Most Important Application of 3D Bioprinting', *3DR Holdings* (Web Page, 31 July 2017) <https://3dprint.com/182475/drug-testing-3d-bioprinting/>; Knowlton et al (n 63).

[73] Nuno Henrique Franco, 'Animal Experiments in Biomedical Research: A Historical Perspective' (2013) 3(1) *Animals* 238; Rachel Hajar, 'Animal Testing and Medicine' (2011) 12(1) *Heart Views* 42.

[74] 'Animal Testing 101', *People for the Ethical Treatment of Animals* (Web Page, 2017) <https://www.peta.org/issues/animals-used-for-experimentation/animal-testing-101/> ('*Animal Testing 101*'); 'What is Animal Testing?', *Cruelty Free International* (Web Page) <https://www.crueltyfreeinternational.org/why-we-do-it/what-animal-testing> ('*What is Animal Testing?*').

[75] Scott (n 72); *What is Animal Testing?* (n 74); Richard Harris, 'Drugs That Work in Mice Often Fail When Tried in People', *National Public Radio* (Web Page, 10 August 2017) <https://www.npr.org/sections/health-shots/2017/04/10/522775456/drugs-that-work-in-mice-often-fail-when-tried-in-people?utm_campaign=storyshare&utm_source=twitter.com&utm_medium=social>; Niall Shanks, Ray Greek and Jean Greek, 'Are Animal Models Predictive for Humans?' (2009) 4(1) *Philosophy, Ethics, and Humanities in Medicine* 2; Knowlton et a (n 63).

[76] 'Fifty Years of Independent Expert Advice on Prescription Medicines', *Therapeutic Goods Administration* (Web Page, 12 February 2014) <https://www.tga.gov.au/book/fifty-years-independent-expert-advice-prescription-medicines-02> ('*Fifty Years of Independent Expert Advice on Prescription Medicines*'); Frederick Dove, *'What's Happened to Thalidomide Babies?', BBC (Web Page, 3 November 2011)* <http://www.bbc.com/news/magazine-15536544>; C G H Newman, 'The Thalidomide Syndrome: Risks of Exposure and Spectrum of Malformations' (1986) 13 *Clinics in Perinatology* 555; T Kajii, M Kida and K Takahashi, 'The Effect of Thalidomide Intake During 113 Human Pregnancies' (1973) 8 *Teratology* 163; Shanks, Greek and Greek (n 75).

[77] *Fifty Years of Independent Expert Advice on Prescription Medicines* (n 76); Pui-Kai Li et al, 'A Thalidomide Analogue with *in vitro* Antiproliferative, Antimitotic and Microtubule-Stabilizing Activities' (2006) 5 *Molecular Cancer Therapeutics* 450; Benjamin Chuah et al, 'Multi-Centre Phase II Trial of Thalidomide in the Treatment of Unresectable Hepatocellular Carcinoma' (2007) 46 *Acta Oncologica* 234.

reports of side effects, was found to have caused organ failure in human subjects during a clinical trial in March 2006.[78] Conversely, penicillin and products such as Tamoxifen, which are safe in humans, have been found to have adverse effects in animals.[79]

These concerns led to emergence of the 3Rs campaign, which advocates the search for *Replacement* of animals with non-living models; *Reduction* in the use of animals; and *Refinement* of animal use practices.[80] Some countries have also imposed strict regulations on animal testing and in some cases, such as for cosmetic purposes, an outright ban.[81] All these factors have spurred research into alternative forms of testing that are less controversial, cost-effective, faster and supposedly more reliable. Some of the alternatives currently under development include *in vitro* testing on isolated human cells, organ slices and engineered tissue models; patient simulators; *in silico* computer simulation; and even human volunteers.[82]

Bioprinting presents an equally attractive alternative to animal testing as it offers the added benefit of engineering 3D tissue models to varying degrees of complexity that mimic native-like tissue. Testing on such bioprinted tissue models has the potential to improve the ability to predict efficacy and toxicity of drug candidates.[83] Already, a number of companies are in the process of using bioprinted skin for drugs and cosmetic testing.[84] This includes L'Oréal in partnership with bioprinting company Organovo, as well as Procter & Gamble.[85] Organovo has also begun offering its proprietary exVi-ve3D™ liver

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[78] Arthur Allen, 'Of Mice or Men: The Problems with Animal Testing', *Slate* (Web Page, 1 June 2006) <http://www.slate.com/articles/health_and_science/medical_examiner/2006/06/of_mice_or_men.html>.

[79] Aysha Akhtar, 'The Flaws and Human Harms of Animal Experimentation' (2015) 24 *Cambridge Quarterly of Healthcare Ethics* 407; 'Follow the Yellow Brick Road' (2003) 2 *Nature Reviews Drug Discovery* 167.

[80] Hajar (n 73).

[81] 'Ban on Animal Testing', *European Commission* (Web Page, 7 December 2017) <https://ec.europa.eu/growth/sectors/cosmetics/animal-testing_en>; *Animal Testing 101* (n 74).

[82] 'Animal Experimentation', *Animals Australia* (Web Page) <http://www.animalsaustralia.org/issues/animal_experimentation.php>;'CAE iStan Male Patient Simulator', *CAE Healthcare* (Web Page, 2017) <https://caehealthcare.com/patient-simulation//istan>; 'Replacing Animal Testing with Accurate in vitro Innovations', *European Commission* (Web Page, 30 September 2013) <http://cordis.europa.eu/news/rcn/36113_en.html>; 'Reconstructed Human Tissues Models: From Laboratory to Industrialized Evaluation Models', *L'Oréal* (Web Page) <http://www.lorealpredictive.com/en/evaluation-center/reconstructed-tissues>.

[83] Ozbolat, Peng and Ozbolat (n 63); Arslan-Yildiz et al (n 18).

[84] S Vijayavenkataraman, '3D Bioprinted Skin: The First 'To-Be' Successful Printed Organ?' (2017) 1 *Journal of 3D Printing in Medicine* 143; Vijayavenkataraman, Lu and Fuh, '3D Bioprinting of Skin: A State-of-the-Art Review on Modelling, Materials and Processes' (n 24); Cristina Velasquillo et al, 'Skin 3D Bioprinting: Applications in Cosmetology' (2013) 3 *Journal of Cosmetics, Dermatological Sciences and Applications* 85

[85] Vijayavenkataraman, Lu and Fuh, '3D Bioprinting of Skin: A State-of-the-Art Review on Modelling, Materials and Processes' (n 24).

tissue models to screen drugs for liver toxicity.[86] This is in addition to other bioprinting companies such as Aspect Biosystems and Nano3D Biosciences working towards the development of bioprinted tissue models for drug testing.[87]

To this end, some have predicted that drug testing will likely be the first promising commercial application of bioprinting.[88] Ironically, however, with bioprinting currently in its experimental stages, most of the experiments are being carried out on animals. Although some organisations are committed to avoiding live animal testing in their bioprinting research,[89] the fact that animal testing plays some role in the development of bioprinting raises questions as to how much of an alternative it is to animal testing. As some authors have pointed out, most of the alternative forms of testing currently available rely on initial animal testing.[90] Accordingly, it would appear that perhaps, 'complimentary' would be a more appropriate adjective to describe the role of bioprinting in relation to animal testing. This is especially with additional concerns about the viability of bioprinting, which will be discussed shortly.

2.4.3 Chronic Diseases and Tissue/Organ Transplantation

On-demand availability of tissues/organs is the most touted benefit of bioprinting. At the same time, it is the most uncertain given the myriad of challenges yet to be overcome. Anthony Atala and Sean Murphy, leading experts in the field, categorise bioprinted constructs into four main types according to their complexity. The first type consists of simple 2D tissues/organs such as skin, followed by hollow tubes such as blood vessels, tracheas and urethras.[91] The third type identified by Atala and Murphy are hollow non-tubular organs such as the bladder, and finally, solid organs such as the kidney, which are considered the most complex.[92]

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[86] Ozbolat, Peng and Ozbola (n 63); Ledford (n 18); Chua and Yeong (n 11).
[87] Ozbolat, Peng and Ozbolat (n 63); Nguyen and Pentoney (n 63).
[88] Chua and Yeong (n 11).
[89] 'Aether Enters into Enormous Array of 3D Bioprinting Collaboration Agreements with World's Top Universities and Government Institutions', *Cision PRWeb* (Web Page, 14 September 2016) <http://www.prweb.com/releases/2016/09/prweb13682861.htm>
[90] Silvio Garattini and Giuliano Grignaschi, 'Animal Testing is Still the Best Way to Find New Treatments for Patients' (2017) 39(Supplement C) *European Journal of Internal Medicine* 32.
[91] Murphy and Atala (n 18); See also Gu et al, 'Three-Dimensional Bioprinting Speeds up Smart Regenerative Medicine' (n 6).
[92] Murphy and Atala (n 18); See also Gu et al, 'Three-Dimensional Bioprinting Speeds up Smart Regenerative Medicine' (n 6).

According to them, simple 2D tissues/organs such as skin and cartilage, which have currently been fabricated and tested, are likely the first to be transplanted in patients closely followed by hollow tubes which are also currently in development.[93] Hollow non-tubular organs which are more complex may take longer to produce, while the production of solid organs, which are the most complex is considered a long-term goal given challenges in achieving innervation and vascularization.[94]

That is not to say there are no challenges with printing functional 2D tissues/organs with sufficient innervation and vascularization. However, simple 2D tissues/organs such as the skin have a flat-layered structure making it easier to print in comparison to complex organs.[95] In addition, there is a great demand for artificial skin in the cosmetics industry as an alternative to animal testing, aside from its use in regenerative medicine and organ transplantation.[96] Furthermore, skin grafting appears to be one of the most popular forms of treatment for wound healing and skin regeneration particularly in burns victims.[97] With the availability of skin substitutes such as Apligraf® and Integra® commercially, it has been noted that the regulatory approval of bioprinted skin would likely be easier to obtain in comparison to complex organs.[98]

Notwithstanding which category of tissues/organs becomes commercially available first, it is useful to explain at this juncture why the prospect of on-demand availability of tissues/organs remains a highly anticipated application of bioprinting. Through the years, increased life expectancy and continuous improvements in medical technologies have led to an increase in the prevalence of chronic diseases and, ultimately, demand for organs.[99] Chronic diseases, also known as non-communicable diseases ('NCDs'),[100] are the result of

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[93] Murphy and Atala (n 18); Similar sentiments are shared in Vijayavenkataraman (n 84); Ozbolat, Peng and Ozbolat (n 63).

[94] This refers to the process of creating vascular and nerve systems within printed constructs to ensure proper functioning and long-term viability: Murphy and Atala (n 18); See also Ozbolat, Peng and Ozbolat (n 63).

[95] Vijayavenkataraman (n 84).

[96] Ibid

[97] Vijayavenkataraman, Lu and Fuh, '3D Bioprinting of Skin: A State-of-the-Art Review on Modelling, Materials and Processes' (n 24); Chua and Yeong (n 11).

[98] Vijayavenkataraman (n 84).

[99] Francesco Marincola and Sten Lindahl, 'Translational Medicine', *Encyclopaedia Britannica, Inc* (Web Page, 23 November 2016) <https://www.britannica.com/topic/translational-medicine>; World Health Organization, *WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation,* endorsed by WHA Res 63.22, 63rd World Health Assembly, 8th plen mtg, Agenda item 11.21, WHO Doc A63/VR/8 (21 May 2010) ('*WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation*').

[100] 'Fact Sheet: Noncommunicable Diseases', *World Health Organization* (Web Page, April 2017) <http://www.who.int/mediacentre/factsheets/fs355/en/>.

a combination of genetic, physiological, environmental and behavioural factors.[101] The four main types are cardiovascular diseases, cancer, respiratory diseases and diabetes.[102] Generally, NCDs tend to progress slowly and last for a lifetime.[103] As a result, NCDs carry an increased likelihood of associated organ damage.[104] Diabetes, for instance, has been linked to damage to the pancreas, heart, kidneys, eyes and nerve endings in the limbs.[105]

As NCDs are largely incurable, the available treatments are in form of long-term management plans, which are at best palliative. This includes organ transplantation in the case of end-stage organ failure arising from damage to the organs. While organ transplantation is currently the best possible treatment for end-stage organ failure,[106] it is fraught with shortcomings such as organ shortages and compatibility issues. Additionally, organ transplantation does not resolve the underlying NCDs.

At the end of 2015, over 120,000 persons were on the waiting list to receive organs in the United States of America ('USA').[107] Of that number, only 30,975 transplants occurred in 2016, with organs donated by 15,068 persons.[108] In Australia, the donor rate as of 2016 was 20.9 donors per million with 1,500 people on the transplant waiting list at any one time.[109] These figures are representative of the disparity that exists between organ demand and supply globally, despite increasing reliance on donations from living persons to supplement donations from deceased persons.[110]

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[101] Ibid 3.

[102] Ibid 2; World Health Organization, 'Global Action Plan for the Prevention and Control of NCDs 2013-2020' (World Health Organization, 2013) 3; 'Infographic: Global NCD Action Plan', *World Health Organization* (Web Page, July 2014) <http://www.who.int/nmh/publications/ncd-infographic-2014.pdf?ua=1>.

[103] 'Conditions and Diseases: Chronic Disease', *Australian Government Department of Health* (Web Page, 15 November 2015) <http://www.health.gov.au/internet/main/publishing.nsf/content/chronic-disease>.

[104] National Institutes of Health, *Report of the Director, National Institutes of Health: Fiscal Years 2012 & 2013* (Report, 2014) <https://report.nih.gov/biennialreport1213/>.

[105] Ibid.

[106] Roxana Moscalu, Anne Marie Smith and Harbans L Sharma, 'Diseases that can be Cured Only by Organ Donations' (2015) 2(4) *Archive of Clinical Cases* 182.

[107] It is unclear whether the number of donors include both living and deceased donors: 'Need Continues to Grow', *Organ Procurement and Transplantation Network* (Web Page) <https://optn.transplant.hrsa.gov/need-continues-to-grow/>.

[108] 'National Data', *Organ Procurement and Transplantation Network* (Web Page, 15 May 2017) <https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/#>.

[109] It is unclear whether the number of donors include both living and deceased donors: 'ANZOD 2016 Summary of Organ Donation', *Australia and New Zealand Organ Donation Registry* (Web Page, 2016) <http://www.anzdata.org.au/anzod/updates/ANZOD2016summary.pdf>.

[110] 'Home', *Organ Procurement and Transplantation Network* (Web Page) <https://optn.transplant.hrsa.gov/> ('*Home*'); Yosuke Shimazono, 'The State of the International Organ Trade: A Provisional Picture Based on Integration of Available Information' (2007) 85 *Bulletin of the World Health Organization* 955; *WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation*, WHO Doc A63/VR/8 (n 99).

Even when organs are available for transplant, there is the risk of transplant rejection in which the recipient's immune system attacks the transplanted organ or tissue because it recognizes the antigens on the cells of the organ as foreign.[111] To minimise the occurrence of transplant rejection, doctors try to match recipients with donors having similar antigens and blood type.[112] Nevertheless, achieving perfect matching is not always possible except in the case of identical twins who have identical antigens.[113]

In addition to matching, transplant recipients often receive lifelong treatments of immunosuppressants to suppress the body's natural immune response, thereby minimising the occurrence of transplant rejection later on.[114] Even with consistent use of immunosuppressants, which are often costly, patients are still at risk of transplant rejection and may consequently require another transplant.[115] Transplant rejection aside, there are also long-term risks associated with the use of immunosuppressants such as the development of infections, cancer, and metabolic complications.[116]

In essence, the relationship between chronic diseases and organ failure is an unending cycle in need of a permanent solution, such as that offered by bioprinting. With bioprinting, it is anticipated that not only will organs be available on demand, but more importantly, that the organs will be compatible with the recipient's immune system given the use of autologous cells from the recipient. The reality, however, is that using autologous cells may not always be possible for reasons explained earlier. As such, the use of donor cells in such

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111 'Transplant Rejection', *MedlinePlus* (Web Page, 25 February 2020) <https://medlineplus.gov/ency/article/000815.htm> ('*Transplant Rejection*'); Prashant Malhotra, Shruti Malu and Sandip Kapur, 'Immunology of Transplant Rejection', Medscape (Web Page, 30 December 2015) <http://emedicine.medscape.com/article/432209-overview>.

112 *Transplant Rejection* (n 111); Malhotra, Malu and Kapur (n 111).

113 Antigens refer to any substance that causes the immune system to produce antibodies against it. *Transplant Rejection* (n 111); Malhotra, Malu and Kapur (n 111).

114 Malhotra, Malu and Kapur (n 111); *Transplant Rejection* (n 111); 'Organ Rejection after Renal Transplant', *Columbia University Department of Surgery* (Web Page, 2017) <http://columbiasurgery.org/kidney-transplant/organ-rejection-after-renal-transplant> ('*Organ Rejection after Renal Transplant*'); 'Immunosuppression and Organ Rejection', *Columbia University Department of Surgery* (Web Page, 2017) <http://columbiasurgery.org/lung-transplant/immunosuppression-and-organ-rejection> ('*Immunosuppression and Organ Rejection*').

115 *Organ Rejection after Renal Transplant* (n 114); *Immunosuppression and Organ Rejection* (n 114); *Transplant Rejection* (n 111).

116 Malhotra, Malu and Kapur (n 111); 'Infections After Lung Transplant Surgery', *Columbia University Department of Surgery* (Web Page, 2017) <http://columbiasurgery.org/lung-transplant/infections-after-lung-transplant-surgery>; *Transplant Rejection* (n 111); Elizabeth Ingulli, 'Mechanism of Cellular Rejection in Transplantation' (2010) 25 *Pediatric Nephrology* 61; Giuseppe Orlando et al, 'Will Regenerative Medicine replace Transplantation?' (2013) 3(8) *Cold Spring Harbor Perspectives in Medicine* .

situations may pose the same immunocompatibility problems associated with using traditional donor organs.

Nevertheless, there will still be an increase in the supply of organs, which will augment current donation levels, thereby improving the chances of survival for people in need of organ transplants. Currently, it is estimated that 22 people die each day whilst waiting for a transplant.[117] The availability of organs on demand should thus translate into reduced wait times and, ultimately, fewer deaths. This should also minimise the impact of families refusing to honour their loved one's request to donate their organs after death. Potential living donors also stand to benefit from bioprinting, as donating exposes them to medical, financial and psychological risks, which they would not otherwise have been exposed to.[118]

In addition, the increased availability of organs through bioprinting may also serve to reduce incidences of organ trafficking and transplant tourism, which are a source of global concern.[119] The limited availability of organs coupled with variations in the cost of treatment and level of technical expertise across different countries often limit access to organs and organ transplantation.[120] As a result, a black market of sorts for the illicit trading of organs has emerged, facilitated by the relative ease of international communication and travel.[121] Often, the organs traded are sourced from persons wishing to sell their organs in return for monetary compensation, or from persons who are coerced into giving up their

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[117] *Home* (n 110); Shimazono (n 110); *WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation*, WHO Doc A63/VR/8 (n 99).

[118] Laura Meckler, 'Living Organ Donors Often Oblivious to Risks They Run', *Los Angeles Times* (online, 10 August 2003) <http://articles.latimes.com/2003/aug/10/news/adna-donors10>.

[119] Shimazono (n 110); 'Trafficking for Organ Trade', *United Nations Global Initiative to Fight Human Trafficking* (Web Page, 2017) <http://www.ungift.org/knowledgehub/en/about/trafficking-for-organ-trade.html> ('*Trafficking for Organ Trade*'); Dominique Martin, 'Action to Stop Thriving Global Organ Trade Must Start at Home', *The Conversation* (Web Page, 1 June 2012) <http://theconversation.com/action-to-stop-thriving-global-organ-trade-must-start-at-home-7333>; Stephanie Kirchgaessner, 'China may still be using Executed Prisoner's Organs, Official Admits', *The Guardian* (online, 8 February 2017) <https://www.theguardian.com/world/2017/feb/07/china-still-using-executed-prisoners-organs-transplants-vatican>; Nicola Davison, 'In China, Criminals Fill the Kidney Donor Deficit', *The Guardian* (online, 28 May 2012) <https://www.theguardian.com/world/2012/may/27/china-kidney-donor-shortage-crime?intcmp=239>; Asif Efrat, 'Organ Traffickers Lock up People to Harvest Their Kidneys. Here are the Politics Behind the Organ Trade', *The Washington Post* (online, 7 December 2016) <https://www.washingtonpost.com/news/monkey-cage/wp/2016/12/07/organ-traffickers-lock-up-people-to-harvest-their-kidneys-here-are-the-politics-behind-the-organ-trade/?utm_term=.9ac0a380dbbd>; James Griffiths, 'Report: China still Harvesting Organs from Prisoners at a Massive Scale', *CNN* (Web Page, 25 June 2016) <http://edition.cnn.com/2016/06/23/asia/china-organ-harvesting/>; David Kilgour, Ethan Gutmann and David Matas, 'Bloody Harvest/The Slaughter: An Update', *The International Coalition to End Organ Pillaging* (Web Page, 30 April 2017) <http://endorganpillaging.org/an-update/#toc>.

[120] Shimazono (n 110).

[121] *WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation*, WHO Doc A63/VR/8 (n 99).

organs as opposed to voluntary donation.[122] In extreme cases, medical practitioners acting in connivance with traffickers remove organs from victims under the guise of medical treatment or harvest organs from prisoners without their knowledge.[123]

While there are concerted efforts within the international community to address these concerns,[124] these do not address the limited supply of organs nor the inequality in accessing available organs. Boosting the supply of organs through bioprinting should increase access thereby eliminating incidences of illegal harvesting of organs. It should also reduce illegal activities associated with organ harvesting such as kidnapping, drugging and killing of victims. Surgical complications arising from illegal transplant operations carried out in violation of accepted medical conventions should also be minimised. The problem of inequality may, however, not be fully resolved by bioprinting for reasons that will be discussed in chapter seven dealing with access.

2.5 Prospects and Challenges of Bioprinting

Having examined the bioprinting process and its potential applications, it is pertinent at this juncture to consider the state of the art of bioprinting as well as challenges facing the industry. This is especially important given the global bioprinting industry has attracted significant investments from both public and private investors with some bioprinting companies listed on the stock exchange.[125] With estimations that the global bioprinting industry is set to be a multimillion-dollar industry in the next couple of years,[126] it is apparent that there are great expectations of translation of the technology into clinical applications.

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[122] *Trafficking for Organ Trade* (n 119); Efrat (n 119).
[123] *Trafficking for Organ Trade* (n 119); Martin (n 119); Kirchgaessner (n 119); Davison (n 119); Efrat (n 119); Griffiths (n 119); Kilgour, Gutmann and Matas (n 119).
[124] *WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation*, WHO Doc A63/VR/8 (n 99).
[125] 'History', *Organovo* (Web Page, 2017) <http://organovo.com/about/history/> ('*History*'); '3D Systems Moving to the New York Stock Exchange', *3D Systems* (Web Page, 13 May 2011) <https://www.3dsystems.com/press-releases/3d-systems-moving-new-york-stock-exchange>; '3D Systems Commences Trading On New York Stock Exchange', *3D Systems* (Web Page, 26 May 2011) <https://au.3dsystems.com/press-releases/3d-systems-commences-trading-new-york-stock-exchange>.
[126] '3D Bioprinting Market Size to be Worth $1.82 Billion by 2022', *Grand View Research* (Web Page, April 2016) <https://www.grandviewresearch.com/press-release/global-3d-bioprinting-market>; '3D Bioprinting Market by Technology (Microextrusion, Inkjet, Laser, Magnetic), Material (Cells, Hydrogels, Extracellular Matrices, Biomaterials), Application (Clinical (Bone, Cartilage, Skin) & Research (Regenerative Medicine)) - Global Forecasts to 2021', *MarketsandMarkets Research* (Web Page, January 2017) <https://www.marketsandmarkets.com/Market-Reports/3d-bioprinting-market-170201787.html>;'Global 3D Bioprinting Market Analysis & Forecast 2016-2022', *Research N Reports* (Web Page, 2016) <https://www.researchnreports.com/pharma-healthcare/Global-3D-Bioprinting-Market-Analysis---Forecast-2016-2022-54101?utm_source=NY_MD_BIS>.

Thus, the following sub-sections provide a broad overview of the state of the art of bioprinting and challenges currently facing the industry.

2.5.1 State of the Art

Generally, before human therapeutics can be marketed, such therapeutics have to be approved by regulatory agencies such as the European Medicines Agency ('EMA'), the United States Food and Drug Administration ('FDA') and the Australian Therapeutic Goods Administration ('TGA').[127] The approval process typically commences with the initial research and development phase followed by preclinical testing in the laboratory, which may involve animal testing. Thereafter, subject to approval from the relevant regulatory agency, promising therapeutics may be tested on human volunteers in clinical trials to evaluate their benefits and side effects. The results of these tests and other documentation as prescribed are then submitted for evaluation to the regulatory agencies who will only approve a therapeutic if it is determined to be effective, safe and of good quality. Depending on the therapeutic, the entire process may take from several months to years with only a fraction ever reaching the approval stage.

So far, most of the activities recorded in the bioprinting sphere within the last decade have been limited to preclinical testing of bioprinted constructs in animals, and use for other research such as drugs and cosmetic testing as well as disease modelling.[128] The tested

[127] It is useful to note that regulatory data exclusivity is fast becoming an important tool for pharmaceutical entities. See generally Gargi Chakrabarti, 'Need of Data Exclusivity: Impact on Access to Medicine' (2014) 19 *Journal of Intellectual Property Rights* 325; Lisa Diependaele, Julian Cockbain, and Sigrid Sterckx, 'Raising the Barriers to Access to Medicines in the Developing World - The Relentless Push for Data Exclusivity' (2017) 17(1) *Developing World Bioethics* 11; Srividhya Ragavan, 'Data Exclusivity: A Tool to Sustain Market Monopoly' (2017) 8 *Jindal Global Law Review* 241.

[128] Hyun-Wook Kang et al, 'A 3D bioprinting System to Produce Human-Scale Tissue Constructs with Structural Integrity' (2016) 34 *Nature Biotechnology* 312; Hirofumi Yurie et al, 'The Efficacy of a Scaffold-Free Bio 3D Conduit Developed from Human Fibroblasts on Peripheral Nerve Regeneration in a Rat Sciatic Nerve Model' (2017) 12(2) *PLoS ONE* e0171448; 'ExVive™ Human Tissue Models & Services for Research', *Organovo* (Web Page, 2017) <http://organovo.com/tissues-services/exvive3d-human-tissue-models-services-research/>; Beau Jackson, 'China Advances with "Unprecedented" 3D Printed Blood Vessel Research', *3D Printing Industry* (Web Page, 19 December 2016) <https://3dprintingindustry.com/news/china-advances-unprecedented-3d-printed-blood-vessel-research-101339/>.

constructs include liver tissue,[129] kidney tissue,[130] tracheal splint,[131] bone and muscle structures,[132] blood vessels,[133] heart valves,[134] and nerve tissue.[135]

It would appear that the results from some of this preclinical testing are promising to the extent that Organovo, the world's first publicly traded 3D bioprinting company and a pioneer in this field, estimates it will submit an investigational new drug ('IND')[136] application to the FDA for its therapeutic 3D bioprinted human liver tissue in 2021.[137] This is further to an earlier orphan drug designation grant by the FDA for Organovo's treatment of alpha-1 antitrypsin deficiency with its 3D bioprinted liver therapeutic tissue.[138] If the IND application is successful, Organovo estimates it will begin clinical testing in humans with end-stage liver disease by 2021.[139] Already, preclinical data of the bioprinted human liver tissue patches implanted onto the livers of mice has shown 'rapid vascularization and tissue engraftment, and evidence of function and durability … over several weeks'.[140] According to Organovo, its therapeutic liver tissue patch has the potential to treat a broad range of liver disease indications.

Another company that has indicated the likelihood of commencing a first-in-human clinical trial in 2021 is Precise Bio co-founded by Anthony Atala in the USA. This is for its 3D-printed cornea graft which has been preclinically tested in mice and rabbits.[141] According

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[129] *History* (n 125).
[130] Ibid.
[131] David A Zopf et al, 'Bioresorbable Airway Splint Created with a Three-Dimensional Printer' (2013) 368 *New England Journal of Medicine* 2043.
[132] Kang et al (n 128).
[133] Kolesky et al (n 63); Wei Zhu et al, 'Direct 3D Bioprinting of Prevascularized Tissue Constructs with Complex Microarchitecture' (2017) 124 *Biomaterials* 106.
[134] Bin Duan et al, '3D Bioprinting of Heterogeneous Aortic Valve Conduits with Alginate/Gelatin Hydrogels' (2013) 101 *Journal of Biomedical Materials Research Part A* 1255.
[135] Yurie et al (n 128).
[136] See chapter one (section 1.1)
[137] 'Organovo Presents First Preclinical Data on 3D Bioprinted Human Liver Tissues at TERMIS-Americas Meeting', *Organovo* (Web Page, 13 December 2016) <http://ir.organovo.com/phoenix.zhtml?c=254194&p=irol-newsArticle&ID=2229241> ('*Organovo Presents First Preclinical Data on 3D Bioprinted Human Liver Tissues at TERMIS-Americas Meeting*'); 'Organovo Updates Key Clinical Development Goals; Company Reports Preliminary Fiscal Fourth-Quarter 2019 Results', *Organovo* (Web Page, 22 May 2019) <https://ir.organovo.com/news-releases/news-release-details/organovo-updates-key-clinical-development-goals-company-reports> ('*Organovo Updates Key Clinical Development Goals; Company Reports Preliminary Fiscal Fourth-Quarter 2019 Results*').
[138] 'Organovo Receives Orphan Designation from U.S. FDA for 3D Bioprinted Therapeutic Liver Tissue Treatment of Alpha-1 Antitrypsin Deficiency', *Organovo* (Web Page, 26 December 2017) <https://ir.organovo.com/news-releases/news-release-details/organovo-receives-orphan-designation-us-fda-3d-bioprinted>.
[139] *Organovo Updates Key Clinical Development Goals; Company Reports Preliminary Fiscal Fourth-Quarter 2019 Results* (n 137).
[140] *Organovo Presents First Preclinical Data on 3D Bioprinted Human Liver Tissues at TERMIS-Americas Meeting* (n 137).
[141] Barry Teater, 'Precise Bio Developing '4-D' Process for Biofabricating Tissues, Organs', *North Carolina Biotechnology Center* (Web Page, 30 April 2018) <https://www.ncbiotech.org/news/precise-bio-developing-4-d-process-biofabricating-tissues-organs>.

to the company, the layered structure of the cornea and its lack of blood vessels, nerves or immune system response makes corneas well suited for bioprinting and potentially the first mainstream application of bioprinting.[142]

It would thus appear that within the next couple of years, bioprinting companies and research institutes are likely to begin moving from the pre-clinical testing phase into clinical testing of bioprinted constructs in human volunteers.

2.5.2 Challenges

Generally, it would appear that the challenges encountered within the bioprinting industry are similar to those encountered within the regenerative medicine and tissue engineering space. These range from sourcing cells of the right quality and quantity to the limited understanding of the biology and biophysics underlying regenerative processes *in vivo,* which has a significant impact on the ability to ensure sufficient vascularisation and innervation of bioprinted constructs.[143]

Furthermore, as explained earlier, although autologous cells are the preferred cell source option, it may be impossible to obtain cells from the patient in certain instances either due to an existing illness or genetic disorders.[144] As a result, donor cells, which carry the risk of immune rejection and disease transmission, may be used. Accordingly, researchers are faced with the challenge of identifying alternative sources or developing techniques of isolating cells that do not carry the risk of immune rejection and disease transmission.

This is in addition to identifying readily available cell sources that are easy to expand in culture, nonimmunogenic and capable of replicating all the natural functions of the required construct.[145] There is also a pressing demand for new strategies that can accelerate cell cycle time which currently takes up to several weeks or months,[146] as well as strategies

[142] Eliza Strickland, 'Corneas Could Be the First Mainstream Application of Bioprinting', *IEEE Spectrum* (Web Page, 7 November 2018) <https://spectrum.ieee.org/the-human-os/biomedical/devices/human-corneas-could-be-the-first-mainstream-application-of-bioprinting>; Teater (n 141).
[143] Murphy and Atala (n 18).
[144] Vijayavenkataraman, Lu and Fuh, '3D Bioprinting of Skin: A State-of-the-Art Review on Modelling, Materials and Processes' (n 24); Charbe, McCarron and Tambuwala (n 64); Murphy and Atala (n 18).
[145] Murphy and Atala (n 18).
[146] Hemanth Gudapati, Madhuri Dey and Ibrahim Ozbolat, 'A Comprehensive Review on Droplet-based Bioprinting: Past, Present and Future' (2016) 102 (September) *Biomaterials* 20.

that can improve cell attachment, cell stimulation, cell viability and mechanical stability during the printing process.[147]

Closely related to this is the matter of compatibility between the bioprinting process and materials. Since bioinks generally need to maintain low viscosity in order to prevent clogging of the delivery nozzles, materials possessing low mechanical properties are often used to circumvent the issue of clogging.[148] The implication however, is that the ensuing printed construct is unable to maintain its shape and withstand external stress after implantation due to the low mechanical properties of the materials used.[149] Moreover, since the materials generally used were designed with traditional tissue engineering techniques in mind, they are not particularly suited to the bioprinting process.[150] While researchers have begun to develop new materials suitable for bioprinting, it has been noted that these materials are proprietary, expensive and generally limited in availability.[151] The challenge therefore is for researchers to develop materials that possess all the required mechanical and functional properties at an affordable price. In developing these materials, researchers also need to develop printing techniques that are compatible with the materials on one hand, and printers that can accommodate multiple materials required for the production of complex constructs on the other hand.[152]

In addition, there is the challenge of balancing the speed and length of printing times. Currently, the printing time is so long that it affects cell viability negatively. However, increasing the speed of printing causes shear stress, that is, frictional force between the inner surface of the nozzle and the cells, which induces cell damage. [153] Whilst shear stress may not occur in all printing techniques such as laser-based bioprinting because of the

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[147] Karen Dubbin, 'The Future of 3D Bioprinting', *3D Printing Industry* (Web Page, 28 June 2017) <https://3dprintingindustry.com/news/future-3d-bioprinting-karen-dubbin-aether-science-director-117149/>; Charbe, McCarron and Tambuwala (n 64); Vijayavenkataraman, Lu and Fuh, '3D Bioprinting of Skin: A State-of-the-Art Review on Modelling, Materials and Processes' (n 24).

[148] Young-Joon Seol et al, 'Bioprinting Technology and its Applications' (2014) 46 *European Journal of Cardio-Thoracic Surgery* 342; Gudapati, Dey and Ozbolat (n 146); Dai and Lee (n 63).

[149] Seol et al (n 148).

[150] Dai and Lee (n 63).

[151] Zhang, Fisher and Leong (n 29).

[152] Jeong Hun Park et al, 'Current Advances in Three-Dimensional Tissue/Organ Printing' (2016) 13 *Tissue Engineering and Regenerative Medicine* 612; Bobak Mosadegh et al, 'Current Progress in 3D Printing for Cardiovascular Tissue Engineering' (2015) 10(3) *Biomed Materials* 034002; Rod R Jose et al, 'Evolution of Bioinks and Additive Manufacturing Technologies for 3D Bioprinting' (2016) 2(10) *ACS Biomaterials Science & Engineering* 1662; Dai and Lee (n 63); Ibrahim T Ozbolat, Kazim K Moncal and Hemanth Gudapati, 'Evaluation of Bioprinter Technologies' (2017) 13 *Additive Manufacturing* 179.

[153] Park et al (n 152); Seol et al (n 148); Ozbolat, Moncal and Gudapati (n 152).

technique involved, researchers still need to find a balance between the speed and length of printing times for other reasons such as increased resolution, sterility and cell survival.[154] This is in addition to designing nozzles that minimise cell damage.

Furthermore, there is the need for an ideal bioprinting system that integrates the printing and post-printing processes such that it mimics *in vivo* culture and maturation of tissue constructs.[155] Other challenges identified by researchers include the high cost of bioprinting tools, limited motion capabilities of bioprinters, lack of full automation and low process resolution of the bioprinting process.[156]

With regard to addressing the aforementioned challenges, some authors have noted that resolution is best achieved through multidisciplinary research, given the complexity of the issues involved.[157] This is especially important in ensuring successful translation into clinical application and, ultimately, realising the full potential of bioprinting. Additionally, another factor essential to realising the full potential of bioprinting is addressing the ethical, legal and socio-economic concerns about bioprinting. The following section examines some of these concerns.

2.6 Ethical, Legal and Socio-Economic Concerns about Bioprinting

In 2014, analyst group Gartner Inc predicted that the rapid advancement of bioprinting was bound to spark a major ethical debate on its use by 2016.[158] Given the nature of the technology, discussions on ethical as well as legal and socio-economic concerns are certainly inevitable. Accordingly, there is a developing body of literature focused on these concerns, which are largely similar to concerns raised about regenerative medicine and tissue engineering in general. These include questions about the ethics and safety of using xenogeneic and human embryonic stem cells, safety and efficacy of bioprinted constructs, access and social justice, and possible use of bioprinted constructs for human enhancement.

The potential applications of bioprinting in humans warrants a special reconsideration of these concerns especially in view of the emerging patent landscape, which has the potential

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[154] Ozbolat, Moncal and Gudapati (n 152).
[155] Arslan-Yildiz et al (n 18); Ozbolat, Moncal and Gudapati (n 152); Dai and Lee (n 63).
[156] Ozbolat, Moncal and Gudapati (n 152).
[157] Vijayavenkataraman, Lu and Fuh, '3D Bioprinting of Skin: A State-of-the-Art Review on Modelling, Materials and Processes' (n 24); Murphy and Atala (n 18).
[158] 'Gartner Says Uses of 3D Printing Will Ignite Major Debate on Ethics and Regulation', *Gartner* (Web Page, 29 January 2014) <http://www.gartner.com/newsroom/id/2658315>.

to affect access to therapeutic treatments developed through bioprinting. Thus, this section provides a broad overview of existing ethical, legal and socio-economic concerns about bioprinting as a technology in itself. Subsequent parts of this thesis will focus specifically on the issues that have significant bearing on patenting of bioprinting-related inventions.

2.6.1 Ethics and Safety of Using Xenogeneic and Human Embryonic Stem Cells

Xenotransplantation – the process of transplanting cells, tissues or organs between species, has long been fraught with concerns about safety and ethics. Its application to bioprinting through the use of xenogeneic cells equally raises similar concerns. In particular, the use of xenogeneic cells in bioprinting as noted earlier, carries the risk of immune rejection and disease transmission.[159] Furthermore, there are religious and cultural concerns about introducing animal cells into the body: one example is Muslims who forbid the consumption of pigs.[160] Notwithstanding, the challenges with identifying readily available cell sources for use in bioprinting necessitate that all viable cell sources are considered even if they originate from another species. More so when there is evidence to suggest that immunosuppressive therapy can be used to minimise the risks of rejection.[161]

In the same vein, the use of hESCs in medical research has also been fraught with ethical concerns which have been extensively covered in other literature and as such need not be analysed in detail here.[162] Suffice to say, however, that the concerns are centred around the concept of life and when it begins. Opponents of embryonic stem cell research argue that embryos are living organisms and their destruction for obtaining stem cells is equivalent to killing an innocent person, which is morally unjustifiable. Proponents, however, argue otherwise. With the ethical debate surrounding the moral status of embryos yet to be settled,

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[159] Benjamin Samstein and J L Platt, 'Physiologic and Immunologic Hurdles to Xenotransplantation' (2001) 12 *Journal of the American Society of Nephrology* 182; David DeGrazia and Tom L Beauchamp, 'Guest Editorial: Reassessing Animal Research Ethics' (2015) 24 *Cambridge Quarterly of Healthcare Ethics* 385; S Vijayavenkataraman, W F Lu and J Y H Fuh, '3D Bioprinting – An Ethical, Legal and Social Aspects (ELSA) Framework' (2016) 1-2 *Bioprinting* 11.

[160] Samstein and L Platt (n 159); Khazal Paradis et al, 'Search for Cross-Species Transmission of Porcine Endogenous Retrovirus in Patients Treated with Living Pig Tissue' (1999) 285 *Science* 1236.

[161] L Bühler et al, 'Xenotransplantation - State of the Art - Update 1999' (1999) 4 *Frontiers in Bioscience* D416; Samstein and L Platt (n 159).

[162] See, eg, Bernard Lo and Lindsay Parham, 'Ethical Issues in Stem Cell Research' (2009) 30 *Endocrine Reviews* 204; Guido de Wert and Christine Mummery, 'Human Embryonic Stem Cells: Research, Ethics and Policy' (2003) 18 *Human Reproduction* 672.

strict regulations on embryonic stem cell research have been imposed in some countries and in some cases, banned.[163]

Despite ethical concerns about the use of xenogeneic stem cells and hESCs, the alternative of iPSCs, as noted earlier, is still beset with safety and efficiency concerns which remain to be addressed.[164] Accordingly, xenogeneic stem cells and hESCs remain viable cell sources for use in bioprinting research, which of course raises ethical concerns over bioprinting research incorporating such cells.

Overall, irrespective of the source or type of cells used, there are still ethical concerns about obtaining informed consent, privacy and confidentiality as well as ownership.[165] This relates to providing donors with clear information about how their harvested cells will be used and the likelihood of patenting the resulting use,[166] as well as potentially informing recipients of the origin of cells used in producing the bioprinted constructs particularly where there might be cultural or religious reservations. While the former might be easier to achieve, the latter poses serious difficulty as bioprinting becomes more commonplace and commercially produced bioinks containing cells are used. There is also a further need to ensure a donor's identity is preserved, notwithstanding any disclosure about the origin of cells.[167] This is especially important in light of the fact that donors may be reidentified through genomic testing notwithstanding anonymisation of samples, as proposed by some as a method of preserving privacy.[168]

With regard to the issue of ownership, this stems from the age-long question about whether the human body and consequently, body parts can be considered a form of property.[169] Whilst the ownership of bioprinted constructs will likely generate ethical concerns, a

[163] Niki Vermeulen et al, '3D Bioprint Me: A Socioethical View of Bioprinting Human Organs and Tissues' (2017) *Journal of Medical Ethics*.
[164] Kazutoshi Takahashi and Shinya Yamanaka, 'A Decade of Transcription Factor-Mediated Reprogramming to Pluripotency' (2016) 17 *Nature Reviews Molecular Cell Biology* 183; Ravnic et al (n 22).
[165] Wert and Mummery (n 162); Lo and Parham (n 162); Laura M Beskow, 'Lessons from HeLa Cells: The Ethics and Policy of Biospecimens' (2016) 17 *Annual Review of Genomics and Human Genetics* 395
[166] Vermeulen et al (n 163); Lo and Parham (n 162).
[167] Vermeulen et al (n 163).
[168] Ibid; Lo and Parham (n 162).
[169] See generally Jane Nielsen et al, *My Way or the MTA: The Use of Material Transfer Agreements in Publicly Funded Research in Australia,* Occasional Paper 10 (Centre for Law and Genetics, 2018), 181-6; Jane Kaye et al, 'Trends and Challenges in Biobanking' in Ian Freckleton and Kerry Peterson (eds), *Tensions and Traumas in Health Law* (The Federation Press, 2017) 415; Lori B Andrews, 'My Body, My Property' (1986) 16(5) *The Hastings Center Report* 28; Imogen Goold et al (eds), *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (Hart Publishing, 2014).

detailed analysis of this issue is beyond the scope of this thesis given its primary focus on patentability. It will, however, suffice to state at this juncture that it is settled law that body parts are capable of ownership as property provided there has been some application of work and skill.[170] This would seem to suggest that bioprinted constructs, which are artificial body parts could potentially constitute property capable of ownership given the significant application of work and skill required to transform isolated cells into bioprinted constructs. In which case, any ownership interest that may arise will likely vest in the person who has exercised work and skill. It is highly unlikely that ownership of bioprinted constructs will vest in the donor of cells, hence debates over ownership will not be resolved in favour of the donor.

Finally, there is also the moral argument against stem cell research (and, by extension, bioprinting), that interference with nature amounts to playing god.[171] As has been generally argued, however, many medical breakthroughs such as in vitro fertilisation and even transplantation can also be perceived as playing god. Thus, if such therapies are generally accepted, bioprinting ought to be accorded similar acceptance, particularly in light of its aforementioned potential applications.

2.6.2 Safety and Efficacy of Bioprinted Constructs

As aforementioned, bioprinting is still in its experimental phase with use limited to preclinical testing and drug discovery research. While results of most of the studies so far appear promising, there are some concerns about the risk of disease transmission from using allogeneic or xenogeneic cells,[172] and the possibility of teratoma or cancer occurring from the mutation of autologous cells derived from other parts of the body.[173] There is also evidence to suggest that viruses used to reprogram adult stem cells into iPSCs may cause cancer.[174]

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[170] *Doodeward v Spence* (1908) 8 CLR 406. See also *R v Kelly* [1999] 2 WLR 384; *AB and Others v Leeds Teaching Hospital NHS Trust* [2005] 2 WLR 358; *Roche v Douglas* [2000] WASC 146 (7 June 2000) (Master Sanderson); *Moore v Regents of the University of California*, 249 Cl Rptr 494 (Cal Ct App, 1988); *Greenberg v Miami Childrens' Hospital Research Institute Inc*, 264 F Supp2d 1064 (Fla, 2003).

[171] Peter Dabrock, 'Playing God? Synthetic Biology as a Theological and Ethical Challenge' (2009) 3 *Systems and Synthetic Biology* 47; Vijayavenkataraman, Lu and Fuh, '3D Bioprinting – An Ethical, Legal and Social Aspects (ELSA) Framework' (n 159).

[172] Varkey and Atala (n 38); Hammerman and Cortesini (n 38).

[173] Vermeulen et al (n 163).

[174] *Stem Cell Information* (n 8)

Moreover, the long-term effects of implanting bioprinted constructs including interaction with other parts of the body as well as other medical implants remain relatively unknown and will remain so for a long time even after clinical testing. In this regard, some authors have raised concerns about the possible dislodgement and migrations of implanted bioprinted constructs, which will undoubtedly affect normal functioning of the body.[175]

Unfortunately, the only reliable way to assess short- and long-term safety is through long-term studies in humans, which could be potentially fatal. Even then, the personalised nature of therapeutic regimens developed through bioprinting puts the reliability and translatability of such studies in doubt.[176] The implication of this is that developing a minimum standard of safety based on clinical studies may be difficult, since results might potentially differ with each study. It should, however, be noted that this risk is not unique to bioprinting but applies to all forms of personalised therapies. Nonetheless, in order to assuage concerns over safety, researchers and regulatory bodies must find a way to test and standardize bioprinting production pursuant to results from clinical trials.

2.6.3 Access and Social Justice

Equitable access to healthcare is arguably one of the most topical issues as far as global health is concerned. Although there are other elements of access such as acceptability, accommodation and accessibility, access in this instance is often defined in the context of affordability (and availability to a lesser extent).[177] Promising as most medical breakthroughs are, the reality is that they are more often than not simply unaffordable for the average person. This is in part due to contributing factors such as research and development costs, the time required to satisfy the safety and efficacy requirements for regulatory approvals, as well as the grant of patents. Given the level of investment in bioprinting through research and development costs as well as increasing demand for patent protection,[178] access is likely going to be a significant issue for bioprinting as well.

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[175] Vermeulen et al (n 163).
[176] Ibid.
[177] Roy Penchansky and J William Thomas, 'The Concept of Access: Definition and Relationship to Consumer Satisfaction' (1981) 19 *Medical Care* 127.
[178] Varkey and Atala (n 38); Ozbolat, Moncal and Gudapati (n 152); John F Hornick and Kai Rajan, 'The 3D Bioprinting Patent Landscape Takes Shape as IP Leaders Emerge', *3D Printing Industry* (Web Page, 7 July 2016) <https://3dprintingindustry.com/news/3d-bioprinting-patent-landscape-takes-shape-ip-leaders-emerge-84541/>; Robert W Esmond and Deborah Sterling, 'Bioprinting: The Intellectual Property Landscape' in Aleksandr Ovsianikov, James Yoo and Vladimir Mironov (eds), *3D Printing and Biofabrication* (Springer International Publishing, 2016) 1; Terry Wohlers and Tim Caffre, *Wohlers Report 2014* (Wohlers Associates, 2014).

Indeed, the matter of access forms a substantial part of this thesis and is accordingly examined extensively in chapter seven.

2.6.4 Use for Human Enhancement

In addition to the aforementioned concerns about bioprinting, there are concerns that beyond replacing damaged tissues/organs, bioprinting may be used to extend human lifespan, enhance appearance or even enhance performance in sports for instance thereby gaining an unfair advantage over others.[179] As valid as these concerns might appear, it is important to note that like many of the aforementioned concerns, they are not unique to bioprinting. Rather these concerns form part of a larger debate about the role of medical technologies in human enhancement. As such, any attempts to address these concerns would require a holistic approach to the regulation of human enhancement in general.

2.7 Conclusion

In light of the above, it is apparent that bioprinting is a unique technology with the potential to revolutionise healthcare. Nevertheless, as with any emerging technology, there are challenges to overcome before bioprinting can be successfully translated into clinical applications. This is especially important if the ultimate goal of producing functional implantable constructs is to be achieved.

From a realistic point of view, the immediate benefits of bioprinting will likely be realised in the areas of disease modelling and research as well as drug discovery and animal testing. Its long-term application to chronic diseases and tissue/organ transplantation, however, remains uncertain. Nonetheless, given researchers have consistently stated this as an objective, it is an application that ought not to be overlooked in any discourse about bioprinting. More so as some researchers have indicated the possibility of printing functional implantable simple organs in the short- and medium-term. Accordingly, this thesis examines the broader issue of ethical concerns as relates to patenting bioprinting-related inventions with this objective in mind.

[179] Varkey and Atala (n 38) 291; Jasper Tran, 'To Bioprint or Not to Bioprint' (2015) 17 *North Carolina Journal of Law & Technology* 123.

Chapter 3

3 State of the Law on Patentability – Australia

3.1 Introduction

As exciting as the prospects of bioprinting might appear, an important consideration for stakeholders in this field is the extent to which resulting inventions can be patented. Whereas inventors/applicants might be more focused on pushing the boundaries of patentability and exploiting existing gaps within the patent system to their advantage, patent examiners and judicial officers will have to grapple with applying existing patent laws which pre-date bioprinting to this new technology. At the same time, long-time opponents of patenting life forms will also be eagerly monitoring developments in this field with the intent of challenging any applications or patents which they deem unethical. This is especially in respect of bioprinted constructs, which as noted in chapter one, appear to be the most contentious element of bioprinting as far as ethical considerations surrounding patenting are concerned because of their proximity to life forms and human cloning. Even so, on the face of the analysis in the preceding chapter, it is arguable that bioprinted constructs ought to be patentable since they are artificially produced in comparison to their naturally occurring counterparts, and are the result of human ingenuity.

In light of this, this chapter and the ensuing two chapters examine the law on patentability as it relates to bioprinted constructs and the processes involved in their production. Although this thesis is primarily concerned with patenting bioprinted constructs, it was considered equally important to consider the patentability of bioprinting process claims in light of ethical issues that may arise from their patenting. By virtue of art 27(1) of the *Agreement on Trade-Related Aspects of Intellectual Property Rights* ('*TRIPS Agreement*' or '*Agreement')*,[1] patents are available for all inventions, whether products or processes, in all fields of technology subject to certain exclusions. However, beyond this, the *Agreement* does not provide further clarification on what amounts to an invention, nor what is required to satisfy the other patent criteria. This is left to the discretion of member states, which have

[1] *Marrakesh Agreement Establishing the World Trade Organization*, opened for signature 15 April 1994, 1867 UNTS 3 (entered into force 1 January 1995) annex 1C ('*TRIPS Agreement*'). The *TRIPS Agreement* sets out minimum standards of protection for various forms of Intellectual Property rights to be provided by each member of the World Trade Organization ('WTO').

established varying thresholds for each patent requirement as well as grounds for exclusions in their national patent laws.

To this end, three jurisdictions with divergent approaches to the question of patentability have been selected as case studies. These are Australia, Europe (under the *European Patent Convention* system)[2] and the United States of America ('USA').[3] Whereas this chapter examines the Australian position, the *EPC* and the USA positions are considered in the ensuing two chapters, respectively. It should be noted that while there are a number of other factors involved in assessing patentability such as novelty, inventiveness (non-obviousness) and industrial application (usefulness),[4] this chapter and the ensuing two chapters are only concerned with what amounts to patentable subject matter (that is, invention) and the grounds for exclusion. This is because questions about novelty, inventiveness and industrial application are fact-specific and not directly relevant to the ethical issues which form the substratum of this thesis.

As this is the first of three chapters examining the question of patentability, this chapter begins with an overview of the international patent regime, which serves as the framework for further discourse on patentability, and on access, in chapter seven. Subsequently, this chapter considers the patent eligibility of bioprinted constructs and bioprinting processes against the threshold for patentability in Australia.

This chapter concludes that while it would appear that bioprinted constructs and bioprinting processes might generally be considered patentable subject matter, there are a number of uncertainties desirous of judicial and parliamentary clarification.

3.2 The International Patent Regime

In 1883, the *Paris Convention for the Protection of Industrial Property* ('*Paris Convention*' or '*Convention*')[5] was adopted by 11 states to provide uniform protection of industrial property

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[2] *Convention on the Grant of European Patents*, signed 5 October 1973, 1065 UNTS 255 (entered into force 7 October 1977) ('*EPC*').

[3] It should be noted that Australia, the United States of America and nearly all the contracting states of the *EPC* are members of the WTO, and are thus signatories to the *TRIPS Agreement*.

[4] *TRIPS Agreement* (n 1) art 27(1).

[5] *Paris Convention for the Protection of Industrial Property,* opened for signature 20 March 1883*,* 828 UNTS 305 (entered into force 7 July 1884) ('*Paris Convention*'). The *Paris Convention*, concluded in 1883, was revised at Brussels in 1900, at Washington in 1911, at The Hague in 1925, at London in 1934, at Lisbon in 1958 and at Stockholm in 1967, and was amended in 1979. 'Summary of the Paris Convention for the Protection of Industrial Property (1883)', *World Intellectual Property Organisation* (Web Page) <http://www.wipo.int/treaties/en/ip/paris/summary_paris.html> ('*Summary of the Paris Convention for the Protection of Industrial Property (1883)*').

across contracting states.[6] The provisions of this *Convention*, which is regarded as the first multilateral agreement in the field of patents are sub-divided into the following categories: national treatment;[7] right of priority; common rules; and administrative framework for implementing the *Convention*.

In order to minimise the difficulties associated with filing several applications in several countries within the timeframe stipulated by the *Paris Convention,* the *Patent Cooperation Treaty* ('*PCT*')[8] was introduced to streamline the application process. Filing under the *PCT* in itself does not import the grant of an 'international patent'. Instead, the *PCT* facilitates the grant of national patents by providing a centralised application system under which a single application in one language is filed in a single patent office and formally examined before being passed on to designated national offices which determine whether to grant or refuse the application within that country.[9] The *PCT* also provides for international prior art search, international publication and an optional international preliminary examination.[10]

The most important agreement in the international patent regime, however, is the *TRIPS Agreement*, which sets the minimum standards for intellectual property protection.[11] The *TRIPS Agreement* is annexed to the *Marrakesh Agreement Establishing the World Trade Organization*,[12] which was a result of the Uruguay Round of multilateral trade negotiations.[13] It is regarded as the most comprehensive multilateral agreement on intellectual property and marked the first time intellectual property was negotiated as part of a multilateral trade agreement.[14] More importantly, the *TRIPS Agreement* made intellectual property subject to its dispute resolution mechanism with enforcement measures. The *Agreement* allows countries different periods of time to delay applying its provisions with least-developed

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[6] World Intellectual Property Organisation, *WIPO Intellectual Property Handbook* (WIPO, 2nd ed, 2004) ('*WIPO Intellectual Property Handbook*'); *Summary of the Paris Convention for the Protection of Industrial Property (1883)* (n 5).

[7] The principle of national treatment requires States signatory to the *Convention* to grant the same protection of industrial property to nationals of other member states as they would their own nationals. In addition, Nationals of non-Contracting States are also entitled to national treatment provided they are domiciled or have a real and effective industrial or commercial establishment in the territory of a Contracting State. *Paris Convention* (n 5) art 2-3.

[8] *Patent Cooperation Treaty,* opened for signature 19 June 1970, 1160 UNTS 231 (entered into force 24 January 1978) ('*PCT*'). The *PCT* was concluded in 1970, amended in 1979 and further modified in 1984.

[9] *WIPO Intellectual Property Handbook* (n 6).

[10] Ibid.

[11] Member states are thus allowed to provide for more extensive protection in their national laws.

[12] *Marrakesh Agreement Establishing the World Trade Organization*, opened for signature 15 April 1994, 1867 UNTS 3 (entered into force 1 January 1995)

[13] *WIPO Intellectual Property Handbook* (n 6).

[14] Ibid; 'Overview: The *TRIPS Agreement*, World Trade Organization', *World Trade Organization* (Web Page, 2017) <https://www.wto.org/english/tratop_e/trips_e/intel2_e.htm>.

countries having the longest transition period (initially 1 January 2006 with the possibility of an extension).[15]

The *TRIPS Agreement* embodies the principles contained in the *Paris Convention* and as such provides for national treatment as well as most-favoured-nation treatment.[16] It also contains provisions relating to exhaustion of rights and exception to rights conferred, which will be considered later on in relevant portions of this thesis. For the purpose of this chapter and the following two chapters, however, the relevant provisions are those relating to patentability. These provisions serve as the framework against which the provisions of the *EPC* and patent laws in Australia and the USA are examined.

3.3 Patentable Subject Matter under Australian Law

Under s 18(1) and (1A) of the *Patents Act 1990* (Cth) ('*Patents Act*'),[17] an invention is patentable if the invention is a manner of manufacture within the meaning of s 6 of the *Statute of Monopolies*.[18] The term 'manner of manufacture' is, however, not defined in either piece of legislation. Accordingly, in order to ascertain whether bioprinted constructs and bioprinting processes amount to a manner of manufacture, reference must be made to case law.

The starting point for this is the High Court's landmark decision in *National Research Development Corp v Commissioner of Patents* ('*NRDC*'),[19] which offers some useful guidance on what constitutes a manner of manufacture. In that case, the Court noted that:

> [t]he word 'manufacture' finds a place in the present Act, not as a word intended to reduce a question of patentability to a question of verbal interpretation, but simply as the general title found in the *Statute of Monopolies* for the whole category under which all grants of patents which may be made in accordance with the developed principles of patent law are to be subsumed. It is therefore a mistake, and a mistake likely to lead to an incorrect conclusion, to treat the question whether a given process or product is within the definition

[15] *TRIPS Agreement* (n 1) art 66(1). Least-developed countries will not have to protect pharmaceutical patents and test data until 1 January 2033.
[16] The most-favoured-nation treatment forbids discrimination amongst nationals of other members. *TRIPS Agreement* (n 1) art 2-4.
[17] *Patents Act 1990* (Cth) ('*Patents Act*').
[18] *Patents Act* (n 17) sch 1 defines an invention as any manner of new manufacture the subject of letters patent and grant of privilege within section 6 of the *Statute of Monopolies*, and includes an alleged invention. *Statute of Monopolies 1623,* 21 Jac 1, c 3.
[19] (1959) 102 CLR 252 ('*NRDC*').

> as if that question could be restated in the form: 'Is this a manner (or kind) of manufacture?' It is a mistake which tends to limit one's thinking by reference to the idea of making tangible goods by hand or by machine, because 'manufacture' as a word of everyday speech generally conveys that idea. The right question is: 'Is this a proper subject of letters patent according to the principles which have been developed for the application of s. 6 of the *Statute of Monopolies*?'[20]

The Court further reiterated that 'any attempt to state the ambit of s. 6 of the *Statute of Monopolies* by precisely defining "manufacture" is bound to fail'. This is because the purpose of s 6,

> was to allow the use of the prerogative to encourage national development in a field which already, in 1623, was seen to be excitingly unpredictable. To attempt to place upon the idea the fetters of an exact verbal formula could never have been sound. It would be unsound to the point of folly to attempt to do so now, when science has made such advances that the concrete applications of the notion which were familiar in 1623 can be seen to provide only the more obvious, not to say the more primitive, illustrations of the broad sweep of the concept.[21]

Thereafter, the Court examined the application of the guidelines proposed by Morton J in *Re Application by GEC*[22] in subsequent cases.[23] The proposition, was that

> a method or process is a manner of manufacture if it (a) results in the production of some vendible product or (b) improves or restores to its former condition a vendible product or (c) has the effect of preserving from deterioration some vendible product to which it is applied.[24]

Overall, the Court agreed that the underlying idea behind the Morton J's use of 'vendible product' was an emphasis on 'the trading or industrial character of the processes intended to be comprehended by the Acts'.[25] To this end, the Court noted that a process would satisfy the manner of manufacture requirement when:

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[20] Ibid 269.
[21] Ibid 271.
[22] (1942) 60 RPC 1. It should be noted that Morton J had disclaimed any intention for his proposition to be applied as a hard and fast rule.
[23] *NRDC* (n 19) 271-5.
[24] *Re Application by GEC* (n 22) 4.
[25] *NRDC* (n 19) 275.

i. an invention offers some advantage which is material;

ii. the invention belongs to a useful art as distinct from a fine art; and

iii. its value to the country is in the field of economic endeavour.[26]

With regard to the agricultural process under consideration in *NRDC*, the Court found that it was a 'product' because it consisted in an artificially created state of affairs, and it was also 'vendible' because it had economic significance.[27] This is now generally paraphrased as requiring the existence of an 'artificially created state of affairs with economic significance/utility', which involves some form of physical phenomenon or transformation. Accordingly, mere discoveries, ideas, schemes or plans, mathematical algorithms, scientific theories and laws of nature do not constitute patentable subject matter.[28]

Nevertheless, it has been noted that the above principles are not rigid rules of interepration, but rather a guide with which each case is to be assessed on its individual merits.[29] In *D'Arcy v Myriad Genetics Inc* ('*D'Arcy*'), the recent seminal decision of the High Court dealing with the patentability of isolated nucleic acid, the Court stated that any interpretation of the manner of manufacture requirement must take into account scientific discoveries made in the 20th and 21st centuries.[30] This includes discoveries which may fall on or outside the

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[26] Ibid 275.

[27] Ibid 277.

[28] Traditionally, this has been the case. See generally Australian Patent Office, '2.9 Annex A - History of Manner of Manufacture', *Patent Manual of Practice & Procedure* (Web Page, 1 August 2017) <http://manuals.ipaustralia.gov.au/patents/Patent_Examiners_Manual.htm#national/patentable/2.9.2.1_Introduction_Manner.htm>; *Commissioner of Patents v RPL Central Pty Ltd* (2015) 238 FCR 27 ('*RPL Central*'); *Grant v Commissioner of Patents* (2006) 154 FCR 62; *Hickton's Patent Syndicate v Patents & Machine Improvements Co Ltd* (1909) 26 RPC 339; *Lane Fox v Kensington & Knightsbridge Electric Lighting Co* (1892) 3 Ch 424; *Research Affiliates LLC v Commissioner of Patents* (2014) 227 FCR 378.

[29] *Anaesthetic Supplies Pty Ltd v Rescare Ltd* (1994) 50 FCR 1 ('*Rescare*'); *CCOM Pty Ltd v Jiejing Pty Ltd* (1994) 51 FCR 260; *Apotex Pty Ltd v Sanofi-Aventis Australia Pty Ltd* (2013) 304 ALR 1 ('*Apotex*').

[30] (2015) 258 CLR 334, 345 [18] ('*D'Arcy*'). Further to this decision and other cases, IP Australia has since set out the following general principles to be applied in assessing patent eligibility, namely: (i) construe the claim; (ii) identify the substance of the claim (what is the alleged or actual contribution?); (iii) ask whether the substance of the claim lies within established principles of what does not constitute a patentable invention (e.g. is it merely a scheme, plan, rules of gameplay, intellectual or genetic information?); and (iv) if not, consider whether the substance otherwise lies outside of existing concepts of manner of manufacture and is to be treated as a "new class" of subject matter (This leg of the approach will only be used in rare situations). Regarding the patentability of claims directed to nucleic acids or genetic information in particular, the relevant key principles are: (i) identifying the substance of the claim; and (ii) ascertaining whether the substance of the claim is "made". In line with this, it is noted that genomic DNA and cDNA are potentially ineligible for patenting given the substance of such claims are likely to be directed to genetic information as that in the genome of an organism. Australian Patent Office, '2.9.2.6 Nucleic Acids and Genetic Information', *Patent Manual of Practice & Procedure* (Web Page, 2 June 2020) <http://manuals.ipaustralia.gov.au/patents/national/patentable/2.9.2.6_Nucleic_acids_and_genetic_information.htm> ('*2.9.2.6 Nucleic Acids and Genetic Information*'); Australian Patent Office, '2.9.2.2 Principles for Examination', *Patent Manual of Practice & Procedure* (Web Page, 2 October 2018)

boundaries of patentability set by the case law that predated their emergence.[31] To this end, the Court identified a number of additional factors to be considered when assessing the patentability of such new discoveries. They include:

> 3. Whether patentability would be consistent with the purposes of the Act and, in particular:
>
> > 3.1. whether the invention as claimed, if patentable under s 18(1)(a), could give rise to a large new field of monopoly protection with potentially negative effects on innovation;
> >
> > 3.2. whether the invention as claimed, if patentable under s 18(1)(a), could, because of the content of the claims, have a chilling effect on activities beyond those formally the subject of the exclusive rights granted to the patentee;
> >
> > 3.3. whether to accord patentability to the invention as claimed would involve the court in assessing important and conflicting public and private interests and purposes.
>
> 4. Whether to accord patentability to the invention as claimed would enhance or detract from the coherence of the law relating to inherent patentability.
>
> 5. Relevantly to Australia's place in the international community of nations:
>
> > 5.1. Australia's obligations under international law;
> >
> > 5.2. the patent laws of other countries.
>
> 6. Whether to accord patentability to the class of invention as claimed would involve law-making of a kind which should be done by the legislature.[32]

The Court further emphasised that while factors 3, 4 and 6 are of primary importance, the factors are not mutually exclusive.[33] It went on to add that one or more of these factors could inform the 'generally inconvenient' limitation in s 6 of the *Statute of Monopolies*.[34] As the 'general inconvenience' proviso deals with exclusions from patentability, this will be considered separately.

<http://manuals.ipaustralia.gov.au/patents/adaptive_patents_manual/national/patentable/2.9.2.2_Principles_for_Examination.htm> ('*2.9.2.2 Principles for Examination*').

[31] *D'Arcy* (n 30) 345 [18].

[32] Ibid 351 [28].

[33] Ibid 351 [28].

[34] Ibid 351 [28].

Finally, the Court noted that the terminology 'artificially created state of affairs of economic significance' was not intended as a formula exhaustive of the concept of manner of manufacture, but rather to be understood within the context in which it was used in *NRDC.*[35]

Thus, having examined the threshold for patentability in Australia further to judicial interpretation of the scope of manner of manufacture, this section will now examine the patentability of bioprinted constructs and bioprinting processes/methods using the suggested principles as guidance.

3.3.1 Bioprinted Constructs

Further to the High Court's comments in *D'Arcy*,[36] a key consideration in determining the patent eligibility of bioprinted constructs would be to ascertain whether they belong to a new class of claim. If they do not, it would suffice to simply assess whether the claimed constructs are the result of an artificially created state of affairs, and whether they have economic utility. If, on the other hand, bioprinted constructs are assessed as belonging to a new class of claim, the aforementioned additional factors identified in *D'Arcy* have to be considered as well.

Thus, to the extent that bioprinting represents an improvement on traditional tissue engineering techniques, it is useful to begin an analysis of their patent eligibility by considering whether bioprinted constructs could potentially fall under a new class of claim. In order to do so, however, it is important to understand what is meant by a 'new class of claim'. According to the High Court in *D'Arcy*, a new class of claim is one which 'involves a significant new application or extension of the concept of "manner of manufacture"'.[37] In particular, the Patent Examiner's Manual provides that the relevant consideration in ascertaining whether a claim relates to a new class of claim, is 'whether the Courts have previously dealt with subject matter of that type and whether that subject matter has been excluded in the context of manner of manufacture'.[38]

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[35] Ibid 346 [20].
[36] Ibid 351 [28].
[37] Ibid 351 [28].
[38] Examples of technical subject matter which have previously been held to be patent-eligible by the courts include 'recombinant or isolated proteins, pharmaceuticals and other chemical substances, methods of treatment, methods of applying herbicides, and applications of computer technology': *2.9.2.2 Principles for Examination* (n 30).

3.3.1.1 Bioprinted Constructs - A New Class of Claim?

In light of this, the relevant question is whether the Courts have previously dealt with the types of subject matter that might be included in claims for bioprinted constructs and whether these have been excluded from patentability. As explained in chapter two, bioprinting has its origins in regenerative medicine and tissue engineering, which have been in existence for decades. Accordingly, while bioprinting offers an alternative method for fabricating functional tissue constructs, the production of engineered tissue (which bioprinted constructs effectively are) as a whole is not in itself a new phenomenon. Neither is consideration about the patent eligibility of engineered tissue products fabricated via traditional means.

A review of the Australian patent database (AusPat) reveals that patents have previously been granted for engineered tissue in Australia. An example is Australian patent 2013375655 (Preparation of extracellular matrix-modified tissue engineered nerve grafts for peripheral nerve injury repair), which includes a claim for a tissue engineered nerve graft. Other examples include Australian patent 2010244121 (Lung tissue model), which includes a claim for an engineered three-dimensional pulmonary model tissue culture; and Australian patent 2006223112 (Production of tissue engineered heart valves), which includes a claim for a preconditioned tissue engineered heart valve. In light of these grants, it would thus appear that there is precedent for granting patents over engineered tissue and by extension, bioprinted constructs.

In addition, there does not appear to be any evidence to suggest that engineered tissues have specifically been excluded from patentability by the courts or IP Australia. Accordingly, given the fact that bioprinted constructs effectively amount to engineered tissues, it is arguable that bioprinted constructs fall within an existing class of claim rather than a new class of claim. This is notwithstanding the fact that they are fabricated via a novel method different from traditional tissue engineering techniques.

As has been noted by IP Australia and other commentators, the question of whether a claimed invention belongs to a new class of claim is likely to occur only in the rarest of circumstances.[39] So far, in the cases decided after *D'Arcy* (some of which will be considered

[39] Ibid; Rochelle C Dreyfuss, Jane Nielsen and Dianne Nicol, 'Patenting Nature - A Comparative Perspective' (2018) 5 *Journal of Law and the Biosciences* 550, 573.

shortly), the courts have yet to determine that a disputed claim involved a new class of claim. In fact, it has been questioned whether the disputed claims in *D'Arcy* involved a new class of claim given the majority's finding that there was nothing 'made' as to satisfy the manner of manufacture requirement.[40] While this is arguably true, it is nonetheless useful to note the majority's conclusion that the subject matter of the claims in dispute lay at the boundaries of the concept of manufacture given its emphasis on genetic information and the possibility that if patented, it could be unknowingly infringed.[41]

Further to *D'Arcy,* the Federal Court of Australia has been given new opportunities to explore the parameters of the manner of manufacture requirement set forth by the High Court in the *D'Arcy* decision. This includes decisions by the Full Court of the Federal Court of Australia ('Full Court') on the patentability of subject matter relating to software and business methods.[42] In addition, there have also been two significant first instance decisions relating to methods of using nucleic acid information in *Meat & Livestock Australia Limited v Cargill, Inc* ('*MLA*')[43] and *Sequenom Inc v Ariosa Diagnostics Inc* ('*Sequenom*').[44] While both of these decisions were appealed to the Full Court, the grounds of appeal in *MLA* did not include the manner of manufacture question.[45] However, the decisions of the Full Court in respect of *Sequenom* remains pending at the time of writing.

Regarding the matter of whether a claimed invention involves a new class of claim, the respective courts in both *MLA* and *Commissioner of Patents v RPL Central Pty Ltd* ('*RPL Central*'),[46] concluded that the claims in dispute did not involve a new class of claim.[47] In *RPL Central*, the Full Court found that the claimed invention (a method and system for gathering evidence relevant to an assessment of an individual's competency relative to a recognised qualification standard) was to a scheme or a business method which was not properly the subject of letters patent.[48] In particular, the Court noted that it had relied on

[40] Charles Lawson, 'Patenting Nucleic Acid Sequences: More Ambiguity from the High Court?' (2018) 25 *Journal of Law and Medicine* 741, 749-50.
[41] *D'Arcy* (n 30) 372 [93].
[42] *RPL Central* (n 28); *Encompass Corp Pty Ltd v InfoTrack Pty Ltd* (2019) 372 ALR 646; *Watson v Commissioner of Patents* [2020] FCAFC 56; *Commissioner of Patents v Rokt Pte Ltd* (2020) 379 ALR 86.
[43] (2018) 354 ALR 95 ('*MLA*').
[44] [2019] FCA 1011 ('*Sequenom*').
[45] *Meat and Livestock Australia Ltd v Branhaven LLC* [2020] FCAFC 171.
[46] *RPL Central* (n 28).
[47] Ibid 53 [115]; *MLA* (n 43) 216 [486].
[48] *RPL Central* (n 28) 53 [113].

established principles as they relate to a computer-implemented business method in assessing the patent eligibility of the claimed invention.[49] Thus, having considered that the claimed invention belonged to an established class of claim (computer-implemented business method), the Court concluded that the claimed invention did not concern a new class of claim as propounded in *D'Arcy*.[50]

In *MLA* which was concerned with a claimed method for identifying a trait of a bovine subject from a nucleic acid sample of the bovine subject, Beach J at first instance held that Meat & Livestock Australia Ltd had failed to establish that the claims (apart from claim 13) were 'outside or at the margin of the established boundaries of what constitutes patentable subject matter'.[51] This was unsurprising as, according to Beach J, the claims of the patent application (other than claim 13) fell within the plain vanilla concept of manner of manufacture as outlined in *NRDC* and *D'Arcy*.[52]

In particular, Beach J noted that the claims were not 'directed purely to genetic information' but rather to 'methods and other embodiments involving the practical application of the identification of single nucleotide polymorphisms from a nucleic acid sample of the bovine subject and their association with a trait of interest'.[53] The claims went beyond the 'mere identification or discernment of a naturally occurring phenomenon' to involve the 'practical *application* of a naturally occurring phenomenon to a *particular use*'.[54] This involved the use of human interaction to create an artificially created state of affairs with economic utility.[55] With regard to claim 13, however, while it may have potentially belonged to a new class of claim, Beach J found that it was not a manner of manufacture because it did not disclose a patentable subject-matter.[56]

Thus, having argued that bioprinted constructs do not belong to a new class of claim but rather ought to be considered as engineered tissues which have been the subject of patent grants, the relevant factors in assessing their patent eligibility ought to be limited to the two

[49] Ibid 53 [115].
[50] Ibid 53-4 [113]-[119].
[51] *MLA* (n 43) 216 [486].
[52] Ibid 206 [428].
[53] Ibid 210 [453].
[54] Ibid 211 [455].
[55] Ibid 211 [455].
[56] Ibid 215-16 [477]–[482].

factors derived from the decision in *NRDC* – an artificially created state of affairs and economic utility. Accordingly, the next part of this section considers whether bioprinted constructs satisfy these factors.

3.3.1.2 Bioprinted Constructs as an Artificially Created State of Affairs and Possessing Economic Utility

The bioprinting process as explained in chapter two relies on a combination of human intervention and biological processes. The first step of imaging and digital design requires a considerable measure of human intervention in the scanning of the desired construct and their subsequent conversion into three-dimensional ('3D') models. Additionally, the selection of biomaterials and living cells also require some measure of human intervention. Whilst biomaterials derived from synthetic polymer are essentially artificial, biomaterials derived from natural polymers and living cells involve the isolation of such components from human or animal tissues by humans using specified techniques. In some instances, such as with induced pluripotent stem cells (iPSCs), this involves an additional step of reprogramming adult cells back to a pluripotent state. Thereafter, the cells are cultured in the laboratory under carefully controlled conditions in order to obtain a number sufficient for printing the required construct. Although the process of culturing cells relies on intrinsic biological processes in order for the cells to reproduce, human intervention is required to ensure appropriate growth rates since culturing occurs in an artificial environment outside of the host body from which the tissue samples were obtained. So also, human intervention is required in order to transform naturally derived polymers into suitable biomaterials.

Subsequently, the prepared biomaterials and cells are combined to create a bioink which is then dispensed to replicate the aforementioned 3D models. Again, the bioink created and the printing are results of human intervention and not mere discoveries of nature. Although the resulting construct relies on intrinsic biological processes for cell adhesion, growth and maturation with the cells producing natural extracellular matrix proteins in replacement of the biomaterials which are expected to degrade overtime, it should be recalled that these processes occur under controlled conditions supervised by humans. Without human intervention, a cell isolated from human or animal tissue samples will simply not grow into a tissue by itself.

Thus, notwithstanding that bioprinted constructs are generally modelled after their naturally occurring counterparts and rely on intrinsic biological processes to an extent, it cannot be disputed that in themselves, bioprinted constructs are equally the result of human actions, which ought to satisfy the requirement of an artificially created state of affairs.[57] More so as it has been noted that the 'artificiality of a product may be perceived in a number of factors, including the labour required to create it and the physical differences between it and the raw natural material from which it is derived'.[58] As evidenced by the printing process, bioprinting involves extensive human labour and the resulting construct is significantly different from the raw natural materials (living cells and materials) from which it was derived. This would appear to satisfy two out of the four different overlapping approaches used to determine patent eligibility.[59] The first is a labour-centred approach which focuses on 'the work of the inventor and whether they have exercised the requisite skill to individualise nature'.[60] The other is that 'a nature-based invention will only be patent-eligible if the invention is different from the raw material from which it is derived'.[61]

Furthermore, given their potential commercial applications in *in vitro* research and organ transplantation as noted in chapter two, it is indisputable that bioprinted constructs have an apparent economic utility. As has been noted by the courts, the economic utility requirement implies that an invention must have a commercial application - whether in the sense of commercial exploitation of the process or the resulting product.[62] In other words, for an invention to satisfy the 'economic utility', such an invention must be susceptible or capable of industrial application.[63] Arguably, this is a very low threshold which most biotechnological inventions including bioprinted constructs would ordinarily satisfy and as such requires no further consideration at this stage.

[57] *D'Arcy* (n 30) 340 [6].
[58] Ibid 382 [128].
[59] Brad Sherman, 'D'Arcy v Myriad Genetics Inc: Patenting Genes in Australia' (2015) 37 *Sydney Law Review* 135, 138.
[60] Ibid.
[61] Ibid.
[62] See generally *Apotex* (n 29) 44-6 [151]-[158] (Hayne J).
[63] Ibid 71 [278].

3.3.1.3 Bioprinted Constructs and the Factorial Approach in *D'Arcy*

Thus, having established that bioprinted constructs occur as a result of an artificially created state of affairs and possess economic utility, it would appear that they will ordinarily satisfy the criteria for patentability as a manner of manufacture. To the extent that this thesis argues that bioprinted constructs do not belong to a new class of claim, the additional factors articulated in *D'Arcy* need not be considered. Nevertheless, this thesis does not overlook the relevance of these factors to arguments against patenting bioprinting. Moreover, as observed by Beach J in *MLA*, it is possible that 'in some cases, reasonable minds might differ as to whether a case is within or without existing boundaries'.[64]

Even so, it is worthy to note that there have been concerns about the relationship between the additional factors and how these might be applied in practice.[65] While it would appear that evidence must be called to enliven the factors, it is not immediately apparent what would suffice to establish any of the factors.[66] According to Beach J in *MLA*,

> various issues concerning the priority ranking and weighting to be given to these factors remain to be explored. For example, how are factors 3.1 and 3.2 to be ranked and weighted with factor 3.3? And what is the scope of factor 3.3? How are factors 3, 4 and 6 ranked and weighted as between themselves? How is factor 5 to be weighted with the other factors, even if it is only of secondary significance? And am I obliged to consider each and all of the factors or only some of them?[67]

Thus, while it would appear that the High Court in *D'Arcy* provided 'clear guidance on the approach courts and patent examiners should take when determining whether new inventions in emerging fields of technology should be protected by a patent monopoly',[68] the available evidence seems to suggest otherwise. It has been suggested instead that 'the plurality's factorial approach is too wide and introduces a degree of uncertainty into the law'.[69] Yet, another school of thought argues that *D'Arcy* is in fact consistent with its

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[64] *MLA* (n 43) 198 [391].
[65] Jessica C Lai, 'D'Arcy v Myriad Genetics: A Demand for the "Made" or "Non-Information" and Clear Subject Matter' (2016) 47 *International Review of Intellectual Property and Competition Law* 537, 552; W Bartlett, '*D'Arcy v Myriad Genetics Inc* [2015] HCA 35: The Plurality's New Factorial Approach to Patentability Rearticulates the Question Asked in *NRDC*' (2015) 24 *Journal of Law, Information and Science* 120, 142-3.
[66] *RPL Central* (n 28) 54 [119]; *MLA* (n 43) 202 [407], 218-19 [495]-[498]
[67] *MLA* (n 43) 199 [391].
[68] Bartlett (n 65).
[69] Ibid; See also Lawson (n 40).

predecessor decisions given that it 'merely affirmed the correctness' of the *NRDC* 'approach to areas of technology within the established boundaries of patentability'.[70] This would seem to align with Beach J's position in *MLA* that the additional factors in *D'Arcy* unidirectionally pointed towards patentability in the circumstances of the case.[71]

Although Beach J was not required to apply the additional factors in *MLA*, he nevertheless explained how he might have applied it in the event his conclusion was wrong.[72] In particular, he noted that while assertions about breadth of claims may be relevant to factors 3.1 and 3.2, it ought to generally be assessed by reference to other technical grounds as opposed to the manner of manufacture rubric.[73] This is because the breadth of claims per se is not indicative of a lack of patentable subject matter, but instead arises under other grounds of invalidity such as lack of clarity or a failure to define the invention.[74]

In this regard, Beach J's comment is especially relevant to possible objections to patenting bioprinted constructs. Whilst it has been argued that bioprinted constructs do not belong to a new class of claim, it is nonetheless possible that if classified otherwise, opposition to their patenting will likely be predicated on the chilling effect patenting will have on research activities in that field (factor 3). It is unlikely that according patentability to bioprinted constructs will enhance or detract from the coherence of the law relating to inherent patentability (factor 4), or that it would involve law-making of a kind which should be done by the legislature (factor 6). This is especially because, as noted earlier, bioprinting stems from tissue engineering wherein patents have previously been issued for engineered tissue constructs.

The problem, however, with invoking factor 3 is that it is a difficult argument to substantiate especially in the early lifecycle of a patent. At the point of patenting any invention, it is difficult to state with certainty whether the act of patenting will have a chilling effect on further innovation. This is especially so with new fields of invention where early patents tend to be upstream and drafted more broadly. Even if the patent were nearing expiration and research in that field had stalled, it would still be difficult to prove

[70] Dreyfuss, Nielsen and Nicol (n 39) 574.
[71] *MLA* (n 43) 199 [391], 219 [501].
[72] See generally ibid 216-19 [485]-[501]; See also Dreyfuss, Nielsen and Nicol (n 39) 575-76.
[73] *MLA* (n 43) 219 [500].
[74] Ibid 219 [499].

that patenting was the sole or major contributing factor to the halt in progress. At best, any argument put forward will likely be circumstantial.

Nevertheless, it should be noted that, further to the *D'Arcy* decision, IP Australia has since suggested that, in deciding whether particular subject matter is patentable (with particular emphasis on nucleic acids, genetic information, micro-organisms and other life forms) examiners should determine:

i. The substance of the claim in light of the description of the claimed invention; and
ii. Whether that substance is 'made' or changed by human intervention. The state of affairs before the invention and as a result of the invention are to be compared to ascertain this.[75]

Thus, while this section concludes that bioprinted constructs appear to be generally patentable, their patentability will ultimately depend on the substance of the applicant's claims.

3.3.2 Bioprinting Process Claims

Further to the explanation of the bioprinting process in chapter two, it would appear that there are many processes involved in bioprinting. These can generally be categorised into two distinct stages – fabrication and usage. Whereas the latter encompasses methods of using bioprinted constructs in *in vitro* research and medical treatment of humans, the fabrication stage encompasses activities up to the point the bioprinted construct is ready for use. These include the isolation and cultivation of living cells, biological/cellular processes, preparation of materials, printing methods, and maturation of the finished construct.

As noted earlier, art 27(1) of the *TRIPS Agreement* provides that processes in all fields of technology are patentable. This was acknowledged in the *NRDC* case where the High Court observed that methods or processes are patentable in so far as they fulfil the manner of manufacture requirement earlier explained in this chapter.[76] Nevertheless, some

[75] Australian Patent Office, '2.9.2.14 Micro-Organisms and Other Life Forms', *Patent Manual of Practice & Procedure* (Web Page, 11 January 2016) <http://manuals.ipaustralia.gov.au/patents/Patent_Examiners_Manual.htm#national/patentable/2.9.2.1_Introduction_Manner.htm>; *2.9.2.6 Nucleic Acids and Genetic Information* (n 30).
[76] *NRDC* (n 19) 275.

processes such as biological processes for the generation of human beings are specifically excluded from patentability.[77] There has also been some debate in Australia as to whether or not methods of medical treatment are equally excluded from patentability for failure to satisfy the *NRDC* requirements. As these exceptions fall under exclusions from patentability, they will be considered separately under the relevant heading.

For the purpose of this section, however, it is useful to consider the remaining processes which do not fall within the aforementioned exclusions from patentability. These include the use of bioprinted constructs in *in vitro* research, isolation and cultivation of living cells, cellular/biological processes, preparation of materials, printing methods, and maturation of the finished construct.

On the whole, it would appear that many of the aforementioned bioprinting processes will likely satisfy the manner of manufacture requirement given they involve the creation of an artificially created state of affairs and the fact that they arguably possess economic utility. This is further to previous analysis of the bioprinting process in the preceding section and chapter. In the same vein, it is arguable that many of these processes belong to an existing class of claim and as such do not require a consideration of the additional factors propounded in *D'Arcy*. As noted by Beach J in *MLA*, the implication of *D'Arcy* seems to be that method claims 'on their face may *perhaps* be more readily seen as within the existing boundaries of "manner of manufacture"' barring any countervailing considerations.[78]

Thus, for instance, whilst bioprinting may differ from traditional printing in its use of bioinks and printing in 3D, printing and more recently additive manufacturing (including 3D printing) are recognised categories of inventions under both the International Patent Classification scheme (used by IP Australia) and the Cooperative Patent Classification scheme (used by the European Patent Office and the United States Patent and Trademark Office).[79] It is therefore likely that many bioprinting process claims especially as relates to the preparation of materials and printing methods will be assessed in relation to existing patents. At the same time, other bioprinting processes such as the use of bioprinted constructs in *in vitro* research, isolation and cultivation of living cells, cellular/biological

[77] *Patents Act* (n 17) s 18(2).
[78] *MLA* (n 43) 202 [409]; See also *D'Arcy* (n 30) 346 [20], 365 [71].
[79] See subclass B33Y and B41 – B44 of both the International Patent Classification (IPC) scheme and the Cooperative Patent Classification scheme.

processes, and maturation of the finished construct draw from similar traditional tissue engineering practices which have previously been dealt with by the patent offices and the courts.

To the extent, however, that processes such as the isolation and cultivation of living cells as well as cellular/biological processes involve naturally occurring phenomena, it is important to consider recent judicial pronouncements in that regard. In recent times, Australian courts have been confronted with questions about the patentability of naturally occurring phenomena and related processes.[80] This is in part due to ongoing discoveries about genetic matter and their inherent characteristics, which were hitherto unknown, but have been found to be of exceptional significance in diagnostic treatment. Whilst the claims in dispute in these cases are more concerned with genetic matter,[81] the principles derived are nevertheless relevant to other forms of naturally occurring phenomena such as the isolation and cultivation of living cells as well as cellular/biological processes.

In *D'Arcy*, Gageler and Nettle JJ observed that

> the application of naturally occurring phenomena to a particular use may be a manner of manufacture if it amounts to a new process or method of bringing about an artificially created state of affairs of economic significance. Even so, the inventor cannot claim to have invented the naturally occurring product as opposed to the process of application.[82]

Thus, while discovery of a naturally occurring phenomenon or a correlation between naturally occurring phenomena adds to the sum of human knowledge, they do not in themselves amount to a manner of manufacture because they lack the element of invention.[83]

Subsequent to the *D'Arcy* decision, Gageler and Nettle JJ's reasoning was considered in *MLA* which was more relevantly concerned with method claims. In that case, Beach J noted that, save for one of the claims, the reasoning in *D'Arcy* did not assist Meat &

[80] See, eg, *D'Arcy* (n 30); *MLA* (n 43); *Sequenom* (n 44).
[81] See, eg, *D'Arcy* (n 30); *MLA* (n 43); *Sequenom* (n 44).
[82] *D'Arcy* (n 30) 385 [137] (Gageler and Nettle JJ).
[83] Ibid 395 [165] (Gageler and Nettle JJ).

Livestock Australia Ltd's arguments against the validity of the respondent's claims in its patent application.[84]

In particular, Beach J emphasised the importance of the distinction between a product claim and a method claim which applies a naturally occurring phenomenon. Given his Honour's earlier quoted comments regarding the nature of the claim (especially that it involved 'the practical *application* of a naturally occurring phenomenon to a *particular use*'),[85] there was no reason to suggest the said claim had failed the manner of manufacture requirement. In addition, his Honour emphasised that the wordings of a claim ought not to be disregarded under the guise of having regard to the 'substance' of what is claimed.[86] As such, claims must be construed as a whole and in light of relevant prior art.

This same reasoning was later applied by Beach J in *Sequenom*, which he considered similar to *MLA*. According to his Honour, 'both cases were concerned with claims to methods of identifying or detecting a nucleic acid having a particular characteristic, not the nucleic acids or the information encoded by such nucleic acids per se'.[87] As with *MLA*, Beach J found that the claimed invention in *Sequenom* resulted in the creation of an artificially created state of affairs and was itself of economic significance.[88] Accordingly, the claimed invention was patentable since it fell within the concept of manner of manufacture and satisfied the first two criteria identified in *D'Arcy*.[89]

It should be noted that the claim in dispute in *Sequenom* actually involved a claimed method for detecting the presence of fetal nucleic acids (cffDNA)[90] in non-cellular components of a maternal serum or plasma sample. [91] In his analysis, Beach J sought to emphasise that the applicant's (Sequenom Inc) claim was not to the product or presence of cffDNA but rather to a method by which the discovery of the existence of cffDNA can be put to practical use

[84] *MLA* (n 43) 207 [433].
[85] Ibid 211 [455].
[86] Ibid 210-11 [454].
[87] *Sequenom* (n 44) 98 [477].
[88] Ibid 101 [494], 102 [499].
[89] Ibid 103 [503].
[90] As explained in the glossary of terms, cffDNA (cell free fetal DNA) refers to non-cellular DNA (i.e. DNA that is outside a cell) obtained from a fetus: ibid 4 [23].
[91] Ibid 1 [1], 38 [195].

such as in sex determination, detection of paternally-inherited sequences and screening for chromosomal aneuploidies.[92]

Given Beach J's conclusion in both cases, it would appear that claims relating to the isolation and cultivation of living cells as well as cellular/biological processes involved in the fabrication of bioprinted constructs may be patentable if they are novel, involve an inventive step, and amount to a new process or method of bringing about an artificially created state of affairs of economic significance.[93] While some commentators had questioned whether the claims in *MLA* involved anything more than a method of identifying an association that already existed,[94] the appeal to the Full Court as noted earlier did not include the manner of manufacture question.[95] As such, Beach J's conclusion in both cases remains the current position of the law subject to the outcome of the *Sequenom* appeal to the Full Court.[96]

3.4 Exclusions from Patentability

While it would appear that bioprinted constructs and some bioprinting processes might potentially be patentable subject matter, it is important to note that inventions amounting to patentable subject matter may nonetheless be excluded from patentability by virtue of specific or general exclusion provisions. These include exclusions pertaining to 'diagnostic, therapeutic and surgical methods for the treatment of humans or animals',[97] the contrary to law and general inconvenience proviso in Australia, and the *ordre public*/morality exclusion contained in the *TRIPS Agreement* and the *EPC*.

Accordingly, this section examines whether bioprinted constructs and bioprinting processes could be excluded from patentability notwithstanding their status as patentable subject matter. This is especially in light of the ethical controversies relating to bioprinting as identified in the preceding chapter.[98]

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[92] Ibid 39 [200]-[201], 96 [463].
[93] *MLA* (n 43) 212 [462]; *Sequenom* (n 44) 84 [396].
[94] Dreyfuss, Nielsen and Nicol (n 39) 576.
[95] See chapter five (section 5.4.2) for a comparison of this decision with the approach taken by the courts in the United States of America.
[96] Judgment has been reserved in *Ariosa Diagnostics, Inc v Sequenom, Inc* (File No VID875/2019) since 30 June 2020.
[97] *TRIPS Agreement* (n 1) art 27(3)(a).
[98] See chapter two (section 2.6)

3.4.1 Methods of Treatment

One aspect of bioprinting which has hitherto not being examined for patentability is bioprinting *in situ*. Unlike the more common form of bioprinting, where fabrication occurs outside the body, bioprinting *in situ* involves the 'direct printing of bioinks to create or repair living tissues or organs at a defect site in a clinical setting'.[99] Accordingly, beyond the preparatory stages, all other aspects of fabrication (including maturation) and usage occur within the body. To this end, bioprinting *in situ* can be regarded as a method of treatment of the human body.

Whereas art 27(3) of the *TRIPS Agreement* provides that members may exclude from patentability: diagnostic, therapeutic and surgical methods for the treatment of humans or animals, there is no specific provision to that effect in the *Patents Act*. Nevertheless, the courts have had to grapple with questions relating to the patentability of methods of treatment in Australia.

In 1938, in *Maeder v Busch,* Latham CJ expressed doubt as to whether a claim for a new method of conducting an operation upon a part of the human body could in itself be regarded as a 'manner of manufacture'.[100] This sentiment was later echoed by the High Court in *NRDC* when it stated that 'the exclusion of methods of surgery and other processes for treating the human body may well lie outside the concept of invention because the whole subject is conceived as essentially non-economic'.[101] It would seem that the Court's argument in this instance was founded on what it considered to be the likely failure of methods of treatment to satisfy the second limb of the manner of manufacture requirement test – eonomic endeavour. However, in later decisions, there appeared to be a shift towards reliance on the general inconvenience proviso to ground an exclusion of methods of treatment from patentability if needed.[102]

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[99] Satnam Singh et al, '*In Situ* Bioprinting – Bioprinting from Benchside to Bedside?' (2020) 101 *Acta Biomaterialia* 14.
[100] *Maeder v Busch* (1938) 59 CLR 684, 699.
[101] *NRDC* (n 19) 275.
[102] *Joos v Commissioner of Patents* (1972) 126 CLR 611, 623 ('*Joos*') (In this case, a cosmetic treatment having a commercial application was held to be patentable.); *Advanced Building Systems Pty Ltd v Ramset Fasteners (Aust) Pty Ltd* (1998) 194 CLR 171, 190 [34]. This is similar to how case law in New Zealand initially excluded methods of medical treatment of humans from patentability on the grounds that they did not satisfy the manner of manufacture requirement under *Patents Act 1953* (NZ). See, eg, *Pfizer Inc. v The Commissioner of Patents* [2005] 1 NZLR 362.

Nevertheless, it would appear from subsequent decisions upholding claims directed to methods of treatment that there has been another shift towards acceptance that methods of treatment are patentable.[103] In *Anaesthetic Supplies Pty Ltd v Rescare Ltd* ('*Rescare*'),[104] which was concerned with an invention for the treatment of a chronic sleep disorder, the court clarified that earlier statements regarding the patentability of methods of treatment were obiter and therefore not binding. In the opinion of Lockhart J (Wilcox J agreeing), there was no reason in principle why a method of treatment of the human body could not constitute a manner of manufacture within the context defined in *NRDC*.[105] This was especially in light of the fact that Parliament had chosen not to introduce a provision excluding methods of treating the human body in the *Patents Act* despite it being excluded in other jurisdictions at the time.[106]

Furthermore, in *Apotex Pty Ltd v Sanofi-Aventis Australia Pty Ltd,* it was held that irrespective of previously held views, methods of treatment (especially the use of pharmaceutical drugs) can no longer be considered as 'essentially non-economic'.[107] In the event that a method of medical treatment meets all other requirements for patentability and satifies the *NRDC* test of contributing to useful art by having economic utility, such is patentable under the *Patents Act.*[108]

However, although not deciding the issue, Crennan and Kiefel JJ sought to emphasise the distinction 'between a method of treatment which involves a hitherto unknown therapeutic use of a pharmaceutical (having prior therapeutic uses) and the activities or procedures of doctors (and other medical staff) when physically treating patients'.[109] The latter, in their Honours' view, are 'essentially non-economic'.[110] Neither are they 'susceptible' or 'capable' of industrial application.[111] Thus, their Honours considered that to the extent that such treatments involve a process/method, they are unlikely to satisfy the test for patentability

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[103] *Rescare* (n 29); *Apotex* (n 29); *Bristol-Myers Squibb Co v FH Faulding & Co Ltd* (2000) 97 FCR 524 ('*Bristol-Myers*').
[104] *Rescare* (n 29).
[105] Ibid 19.
[106] Ibid 19.
[107] *Apotex* (n 29) 23 [50] (French CJ). In his dissenting judgment, Hayne J found that a method of prevention or treatment of human disease is not a proper subject for the grant of a patent. In his opinion, the resulting product from such a process is beyond the ambit of a 'manner of manufacture' within the meaning of s 6 of the *Statute of Monopolies*: at 47 [164]-[165].
[108] Ibid 73 [286] (Crennan and Kiefel JJ).
[109] Ibid 73 [287] (Crennan and Kiefel JJ).
[110] Ibid.
[111] Ibid.

because they are incapable of being practically applied in commerce or industry.[112] It is of course arguable whether this reasoning accords with present realities given the fact that such services evidently have commercial and industrial application.

Nevertheless, in the absence of any further authority on this point, it would thus appear that Crennan and Kiefel JJ's comments provide some justification for excluding surgical procedures such as transplanting bioprinted constructs and bioprinting *in situ* from patentability. This would, however, not extend to other methods of treatment that occur outside the human body such as the printing process, and treatment of cells and bioprinted constructs. At the same time, it is important to recognise that unlike transplantation, bioprinting *in situ* actually presents a new approach to treatment in that living cells are directly printed in the human body. It combines physical treatment on the patient (which, according to Crennan and Kiefel JJ, is an 'essentially non-economic' activity) with the printing process (an activity with economic utility). The question then is whether the economic utility of the printing process involved is sufficient to make bioprinting *in situ* patentable.

Arguably, the economic utility of the printing process involved should make bioprinting *in situ* patentable subject matter. This is because bioprinting *in situ* demonstrably results in the creation of an artificially created state of affairs and is itself of economic significance This is assuming that bioprinting *in situ* is also novel, inventive and capable of industrial application. While there might be moral objections to patentability given its significance in improving healthcare, it is important not to conflate such concerns with the question of patentability. As suggested by Barwick CJ in *Joos v Commissioner of Patents* ('*Joos*'), such concerns are better dealt with as a public policy consideration under the general inconvenience proviso.[113]

In any case, as has previously been explained under the requirements for patentable subject matter, there are scientific discoveries made in the 20th and 21st centuries, which may fall on or outside the boundaries of patentability determined by case law.[114] This may very well

[112] Ibid.
[113] *Joos* (n 102) 623.
[114] See section 3.3.

be one of such instances and the onus will be on the courts to determine whether bioprinting *in situ* has sufficient economic utility to make it patentable.

3.4.2 Ethically Informed Exclusions and the General Inconvenience Proviso

At the international patent regime level, art 27(2) of the *TRIPS Agreement* provides that:

> Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect *ordre public* or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law.

However, as previously noted, the *TRIPS Agreement* merely sets out minimum standards for intellectual property protection amongst member states. Thus, leaving some discretion to member states to determine how these standards are formulated and expressed at national or regional level. Accordingly, it is unsurprising to note that the three jurisdictions appear to approach the subject matter of exclusions differently.

Whereas art 53(a) of the *EPC* contains provisions similar to art 27(2) of the *TRIPS Agreement* (as will be explored further in the next chapter), the Australian patent regime retains the general inconvenience proviso contained in s 6 of the *Statute of Monopolies* by virtue of s 18(1)(a) and sch 1 of its *Patents Act*.[115] Given the *Statute of Monopolies* predates the *TRIPS Agreement* and forms the basis of modern patent laws in many common law jurisdictions including Australia and the USA,[116] it is useful to begin the consideration of ethically informed exclusions from this standpoint. This is especially as an understanding of the origins of the general inconvenience proviso provides additional insight into how the proviso might apply to bioprinting.

Accordingly, this section traces the origins of the general inconvenience proviso from the 1500s in the United Kingdom ('UK'), to its current application under the Australian patent regime. The positions under the *EPC* and the USA are considered separately in subsequent chapters.

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[115] *Patents Act* (n 17).
[116] Bernard Lo and Lindsay Parham, 'Ethical Issues in Stem Cell Research' 30 *Endocrine Reviews* 204.

Furthermore, this section examines the recommended shift away from the proviso towards a contemporary exclusion clause similar to the *ordre public* and morality exclusion in accordance with Australia's international obligations.[117] In addition, this section also considers the factorial approach developed in *D'Arcy,* given the Court's statement that it may be that one or more of the identified factors would inform the general inconvenience proviso.[118]

It should be emphasised at this juncture that the status of an invention as morally offensive in itself or otherwise is distinct from whether the act of patenting it is morally offensive. It is also worth stating that this section does not focus on the debate about the role of ethics or morality in patent law. Rather it proceeds from the standpoint that ethics and morality are a part of patent law and as such bioprinted constructs must be examined for compliance.

3.4.3 Origins of the General Inconvenience Proviso

Whilst the application of the *Statute of Monopolies* in the UK has generally been superseded by the *Patents Act* of 1977 (which brought the UK's patent laws in line with the *EPC*),[119] the *Statute of Monopolies* remains the basis of modern patent laws in many common law jurisdictions including Australia and the USA.[120] In particular, s 6 is central to the tests for patentability in Australia by virtue of s 18(1)(a) and sch 1 of its *Patents Act.*[121] As such, it is important to consider the general inconvenience proviso when contemplating the patentability of bioprinted constructs.

Section 6 of the *Statute of Monopolies* states that

> Provided also and be it declared and enacted that any declaration before mentioned shall not extend to any letters patent and grants of privilege, for the term of 14 years or under hereafter to be made of the sole working or making of any manner of new manufacture within this realm to the true and first inventor and inventors of such manufactures which others, at the time of making such letters or grant, shall not use, *so as also they be not contrary to the law, nor mischievous to the state, by raising prices of commodities at home or hurt of trade or generally*

[117] Advisory Council on Intellectual Property, *Patentable Subject Matter* (Final Report, December 2010) <https://www.ipaustralia.gov.au/sites/g/files/net856/f/acip_final_report_patentable_subject_matter_archived.pdf> >, 18 (Recommendation 9) 'Patentable Subject Matter'.
[118] *D'Arcy* (n 30) 351 [28].
[119] *Patents Act 1977* (UK).
[120] Lo and Parham (n 116).
[121] *Patents Act* (n 17).

> *inconvenient;* the said fourteen years to be accounted from the date of the first letters patent, or grant of such privilege hereafter to be made, but that the same shall be of such force as they should be if this Act had never been made, and of none other (emphasis added).

The origins of the proviso contained in s 6 does not however begin with the *Statute of Monopolies*. Prior to its enactment, it was the practice of monarchs to grant monopolies in the form of letters patent (that is, open letters) with the purpose of stimulating the establishment of new industries within the realm. In a way, this encouraged skilled migration as some beneficiaries were artisans from foreign countries skilled in trades not otherwise practised in England.[122] As the trades were relatively unknown to England, it was acceptable to grant those artisans exclusive rights over the practice of their trades for a limited period of time as reward for their ingenuity and the risk they bore by introducing new trades that could potentially benefit the economy. In return, it was expected that there would be some form of apprenticeship during the exclusive period such that at its expiration, others would have acquired new skills with which they could support themselves and their families.[123] Essentially, letters patents were aimed at creating sustainable employment and economic development opportunities for the local English industry.[124]

On the other hand, however, granting monopolies over existing trades including any improvements to the trade was generally frowned upon as it was held to be antithetical to the public good and generally inconvenient.[125] A monopoly over an existing trade would have concentrated practice of such trade in the hands of the 'patentee' to the exclusion of others who had hitherto been practising the same trade, effectively putting them out of work. The lack of competition would have also created artificial scarcity and led to an unjustifiable increase in prices. In essence, it would have resulted in unnecessary hardship on the community by harming free trade where there was no logical reason to do so. Thus,

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[122] E Wyndham Hulme, 'History of the Patent System Under the Prerogative and at Common Law' (1896) 12 *Law Quarterly Review* 141; Ramon A Klitzke, 'Historical Background of the English Patent Law' (1959) 41 *Journal of the Patent Office Society* 615; Ben McEniery, 'Patent Eligibility and Physicality in the Early History of Patent Law and Practice' (2016) 38 *University of Arkansas at Little Rock Law Review* 175.
[123] Klitzke (n 122).
[124] See Chris Dent, '"Generally Inconvenient": The 1624 Statute of Monopolies as Political Compromise' (2009) 33 *Melbourne University Law Review* 415; Hulme, 'History of the Patent System Under the Prerogative and at Common Law' (n 122); Klitzke (n 122).
[125] Klitzke (n 122); William L Letwin, 'The English Common Law Concerning Monopolies' (1954) 21 *University of Chicago Law Review* 355.

the proviso derives its existence from the tension between the grant of monopolies and free trade under common law.

Nevertheless, there are records of instances where monopolies over existing trades were granted during the reigns of Queen Elizabeth I and King James I, much to the dismay of the public. Some of these grants, which were considered an abuse of royal privileges, were later successfully challenged and either revoked by the Crown or invalidated by the courts when they came to be vested with the power to do so. One of such instances was *Matthey's case* in which a patent to Richard Matthew over knife-handles made of diverse pieces of horn mixed with yellow or white plate was invalidated after a challenge by the Cutlers' Company who argued that the patent was for a slight improvement on an old industry.[126] Similarly, the Court of Exchequer disallowed the claims of the assignees of the patent of Humfry & Shutz on the ground that the differences between their ore-sifting apparatus imported from overseas and that already in use at Mendip (a district in England) was insufficient to justify a monopoly.[127]

These types of grants, in addition to abuses of monopoly privileges by the beneficiaries, created tension between Parliament and the Crown. Indeed, grievances about how odious some monopolies granted by the Crown were and how it affected their constituents, in that it raised the prices of several goods such as steel, starch, playing cards, glasses and pots, formed the core of many parliamentary debates.[128] Whilst there were attempts to limit the powers of the Crown through legislation in Parliament, many parliamentarians were reluctant to pass any bill that would appear to oppose the powers of the Crown. This attitude is unsurprising as parliaments at the time existed at the pleasure of the Crown.[129] In any event, such legislation would have required the Crown's approval and its application would have been subject to the Crown's discretionary powers even if approved.[130]

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[126] Hulme, 'History of the Patent System Under the Prerogative and at Common Law' (n 122); J W Gordon, *Monopolies by Patents and the Statutable Remedies Available to the Public* (Stevens and Sons Limited, 1897).
[127] Hulme, 'History of the Patent System Under the Prerogative and at Common Law' (n 122).
[128] Simonds d'Ewes, 'Journal of the House of Commons: November 1601' in *The Journals of All the Parliaments During the Reign of Queen Elizabeth* (Irish University Press, 1682) 622; Heywood Townshend, 'Proceedings in the Commons, 1601: November 21st - 25th' in *Historical Collections: Or, An Exact Account of the Proceedings of the Four Last Parliaments of Q. Elizabeth* (T Basset, W Crooke and W Cademan, 1680) 236; Klitzke (n 122).
[129] Dent (n 124).
[130] d'Ewes (n 128); Townshend (n 128); 'House of Lords Journal: 1 December 1621' in *Journal of the House of Lords 1620-1628* (His Majesty's Stationery Office, 1767-1830) vol 3, 176.

On separate occasions, both monarchs (that is, Queen Elizabeth I and King James I) made statements about being more conscientious in the exercise of their powers. For instance, in response to a petition from Parliament regarding the abuse of monopolies, Elizabeth I promised to address the grievances raised, failing which Parliament could enact a law.[131] She also recalled some monopolies and in 1601 relinquished her right to determine the validity of her grants in her own courts (the Court of Star Chamber)[132] to the common law courts.[133] Subsequently, the *Case of Monopolies*[134] (commonly known as *Darcy v Allen* ('*Darcy*')) was decided. Edward Darcy, groom of the Queen's Privy Chamber had been granted the exclusive right to manufacture, import and sell playing cards even though their manufacture was already an established trade in England. Inevitably, the patent was 'infringed', and Darcy brought a claim against one of the alleged infringers, Allen. The case was decided in Allen's favour on the grounds that monopolies were against the law as they raised prices, reduced the quality of goods and affected employment. Although the patent was granted by the Queen in 1598, the case was not decided by the King's Bench until after the Queen's death in 1603, during the reign of King James I.

This did not however deter the King from granting further odious monopolies as seen in the *Ipswich Taylor's case.*[135] In that case, a group of tailors in Ipswich chartered by the King brought an action against William Sheninge, a tailor who practised his trade in Ipswich despite not having completed an apprenticeship with the corporation and also not being a member of the clothworkers corporation. It was decided that although the Crown could create such corporations, its power did not extend to creating a monopoly harmful to free trade. This case was decided in 1615, after James I had issued a Declaration[136] (also known as the Book of Bounty) in 1610 which restated the common law attitude towards odious monopolies.

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[131] d'Ewes (n 128); Townshend (n 128).
[132] Steven G Calabresi and Larissa Price, 'Monopolies and the Constitution: A History of Crony Capitalism' (Faculty Working Paper 214, Northwestern University School of Law, 2012) <http://scholarlycommons.law.northwestern.edu/facultyworkingpapers/214>
[133] Gordon (n 126); Klitzke (n 122).
[134] *Case of Monopolies* (1603) 11 Co Rep 84b; 77 ER 1260; *Darcy v Allin* (1603) Noy 173; 74 ER 1131.
[135] *Ipswich Taylors' case* (1614) 11 Co Rep 54; Godb 253; 78 ER 147.
[136] *A Declaration of His Majesties Royall Pleasure, in What Sort He Thinketh Fit to Enlarge: Or Reserve Himselfe in Matter of Bountie* (Robert Barker, 1610).

Even though James I subsequently issued a proclamation in 1621 revoking a number of monopolies, the abuse of power did not stop and eventually, the *Statute of Monopolies* was passed. The wordings of the *Statute of Monopolies*, including s 6, were in fact inspired by the Book of Bounty.[137] As with the Book of Bounty, the *Statute of Monopolies* simply codified common law rules about monopolies and patents, especially in terms of the exclusions contained in s 6.[138] It is thought that the similarities between the *Statute of Monopolies* and the Book of Bounty was a deliberate attempt to obtain the King's consent.[139] Accordingly, some authors describe the *Statute of Monopolies* as a political compromise between the Crown and Parliament over the exercise of royal authority.[140]

In explaining the *Statute of Monopolies*, Edward Coke, who penned the original draft[141] and was involved in the *Darcy* case, noted that:

> A monopoly is an institution or allowance by the King by his grant, commission, or otherwise to any person or persons, bodies politique, or corporate, of or for the sole buying, selling, making, working or using of anything, whereby any person or persons, bodies politique, or corporate, are sought to be restrained of any freedom, or liberty that they had before, or hindered in their lawful trade.[142]

According to him, the rationale against monopoly can be traced to Deuteronomy 24:6.[143] In that passage, Moses admonished the Israelites not to take a millstone as security for a loan as that would amount to taking away the debtor's source of livelihood. Applying that logic, Coke reasoned that a man's trade is the source of his livelihood. The grant of a monopoly over an existing trade would take away not only a man's trade, but also his life,

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[137] 'House of Commons Journal: 19 April 1624' in *Journal of the House of Commons 1547-1629* (His Majesty's Stationery Office, 1802) vol 1; Gordon (n 126).
[138] Dent (n 124); E Wyndham Hulme, 'History of the Patent System Under the Prerogative and At Common Law A Sequel' (1900) 16 *Law Quarterly Review* 44; Chris R Kyle, "But a New Button to an Old Coat': The Enactment of the Statute of Monopolies, 21 James I cap.3' (1998) 19 *The Journal of Legal History* 203; Klitzke (n 122); Justine Pila, 'The Common Law Invention in its Original Form' (2001) (3) *Intellectual Property Quarterly* 209.
[139] Gordon (n 126).
[140] Dent (n 124); Thomas B Nachbar, 'Monopoly, Mercantilism and the Politics of Regulation' (2005) 91 *Virginia Law Review* 1313.
[141] Kyle (n 138).
[142] Edward Coke, *Third Part of the Institutes of the Laws of England: Concerning High Treason, and Other Please of the Crown and Criminall Causes* (M Flesher, W Lee and D Pakeman, 1644).
[143] Ibid.

and would consequently be odious.[144] Thus, a monopoly grant would be (generally) inconvenient if it turned many labouring men into idleness.[145]

From Coke's analysis and the cases identified above, it would appear that the phrase 'generally inconvenient' as it was then interpreted meant something that hampered the ability of people to participate in a trade and earn a living. In other words, the phrase as applied, had a public interest connotation. There was nothing to suggest it extended to questions of morality arising from patenting.

In 1907, a separate morality clause was introduced into the UK *Patents Act* alongside the general inconvenience proviso, which was retained by reference to s 6 in the definition of the term 'invention'.[146] As an aside, it should be noted that, by 1977, the UK had altogether discarded any reference to s 6 in its *Patents Act.*[147] The importance of the introduction of a separate morality clause alongside the general inconvenience proviso in 1907 is that it appears to support the school of thought that the general inconvenience proviso is insufficient to ground an ethical exclusion.

Notwithstanding, it is important to consider how the general inconvenience proviso has been interpreted in Australia before it can be concluded whether the proviso is insufficient to ground an ethical exclusion in Australia.

3.4.4 The General Inconvenience Proviso and Morality in Australia: *Patents Act 1903* (Cth) - *Patents Act 1952* (Cth)

On 22 October 1903, the Australian Federal Parliament passed the first Australian *Patents Act*,[148] which was modelled after its UK counterpart.[149] Accordingly, the same definition of 'invention' in the context of s 6 of the *Statute of Monopolies* as was contained in the UK

[144] Ibid.
[145] Ibid.
[146] *Patents and Designs Act 1907*, 7 Edw 7, c 29, s 75, 93. In particular, s 75 provides that '[t]he comptroller may refuse to grant a patent for an invention, or to register a design, of which the use would, in his opinion, be contrary to law or morality'.
[147] *Patents Act 1977* (UK).
[148] *Patents Act 1903* (Cth).
[149] *Patents, Designs, and Trade Marks Act 1883* 46 & 47 Vict, c 57.

Act, was retained in the Australian Act.[150] Similarly, a separate morality clause as was applicable in the UK at the time was also contained in the 1903 Act.[151]

Whilst some Members of Parliament had argued for a modern definition of 'invention' given the interpretative difficulties faced with the definition in the UK,[152] it was generally agreed that the s 6 definition be retained. According to Parliament, Australia stood to benefit from over 300 years of judicial precedents which had rendered the meaning 'precise and clear' in comparison to the USA where their 'modern' definition had yet to be fully tested judicially.[153]

In the absence of any special consideration of the general inconvenience proviso in these discussions, it would thus appear that the intention of Parliament was for the proviso to be interpreted in accordance with its known application in the UK. Indeed, this was the case in two separate applications brought under the subsequent *Patents Act* of 1952,[154] where reference was made to the UK decision of *Rolls-Royce Ltd's Application*.[155] It should be borne in mind at this juncture that the separate morality clause which was contained in the *Patents Act* of 1903 was for reasons that are unclear, omitted from the *Patents Act* of 1952.[156] This was despite the fact that the UK *Patents Act 1949,* which the *1952 Act* was modelled after, contained a separate morality clause.[157]

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[150] Ibid, s 46; *Patents Act 1903* (Cth) s 4.

[151] *Patents, Designs, and Trade Marks Act 1883* 46 & 47 Vict, c 57, s 86 provides that "[t]he comptroller may refuse to grant a patent for an invention, or to register a design or trade mark, of which the use would, in his opinion, be contrary to law or morality. Letters patent have always contained a clause that the grant is to be void if it be "contrary to law or prejudicial or inconvenient to our subjects in general"". *Patents Act 1903* (Cth) s 118 provides that '[t]he Commissioner may refuse to grant a patent for an invention of which the use would in his opinion be contrary to law or morality'.

[152] Commonwealth, *Parliamentary Debates*, Senate, 15 July 1903, 2118 (Gregor McGregor), 2119 (George Pearce); Commonwealth, *Parliamentary Debates*, Senate, 13 August 1903, 3543 (George Pearce); Commonwealth, *Parliamentary Debates*, House of Representatives, 29 September 1903, 5509 (Henry Higgins) (John Watson) (King O'Malley).

[153] Commonwealth, *Parliamentary Debates*, Senate, 15 July 1903, 2080 (James Drake), 2117 (James Drake), 2118 (Richard O'Connor) (Albert Gould); Commonwealth, *Parliamentary Debates*, Senate, 13 August 1903, 3543 (James Drake); Commonwealth, *Parliamentary Debates*, House of Representatives, 29 September 1903, 5509 (Alfred Deakin).

[154] It should be noted that the same definition of the term 'invention' had been retained under the 1952 Act: *Patents Act 1952* (Cth) s 6.

[155] *Rolls-Royce Ltd's Application* (1963) 80 RPC 251 ('*Rolls-Royce Ltd's Application*').

[156] *Patents Act 1952* (Cth) s 155(1)(a) provides that '[t]he Commissioner may refuse to accept an application and complete specification or to grant a patent for an invention the use of which would be contrary to law'.

[157] *Patents Act 1949*, 12 13 &14 Geo 6, c 87, s 10(1)(b) provides that '[i]f it appears to the comptroller in the case of any application for a patent – (b) that the use of the invention in respect of which the application is made would be contrary to law or morality; he may refuse the application'.

Nevertheless, in *Rolls-Royce Ltd's Application*, an application had been made under the UK *Patents Act 1949*,[158] for a method of operating an aircraft powered by gas turbine engines which would reduce engine noise at the material part of the take-off climb. Lloyd-Jacob J in refusing the application stated that even where a manner of new manufacture had been disclosed in a patent application (which was not the case in this application), the application would still be subject to the generally inconvenient test. According to him,

> It must be additionally borne in mind that, even where a manner of new manufacture is disclosed in a patent application, s. 6 of the *Statute of Monopolies* excluded grants which are mischievous to the State by being generally inconvenient. The responsibility of a pilot of an aircraft in flight carrying scores of passengers is already sufficiently onerous without adding to his burden the task of avoiding infringement of a statutory monopoly in the operation of his standard engine controls unless the justification for grant is reasonably manifest.[159]

These comments were subsequently referred to in decisions by the Australian Patent Office to refuse two separate applications. The first was for claims relating to computer programs in *The British Petroleum Co Ltd's Application*[160] where the Hearing Officer Mr I B Asman stated that 'even if programming were to be considered as being "a manner of new manufacture", it would still not come within the definition of invention given in the Act' further to Lloyd-Jacob J's comments quoted above.[161] He went on to add that:

> Computer programming is a relatively young art and, although many stratagems and simplifications have been devised so far, a much greater number may be expected to be devised in the future. It would certainly be mischievous to the State and generally inconvenient if, after investing a million dollars in a computer, the owner were to find himself prevented from operating it efficiently, or in any other manner he may wish, or with any degree of privacy or secrecy he may desire.[162]

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[158] Section 101 of the Act defines 'invention' in reference to s 6 of the *Statute of Monopolies*: ibid.
[159] *Rolls-Royce Ltd's Application* (n 155) 255.
[160] *The British Petroleum Co Ltd's Application* (1968) 38 AOJP 1020.
[161] Ibid 1021.
[162] Ibid 1021.

The second decision, incidentally by the same Hearing Officer, was in respect of an application claiming a method of operating a computer. In refusing the application, the Hearing Officer stated that further to s 6 of the *Statute of Monopolies*,

> It would indeed be very inconvenient if a person having purchased, or hired, at great expense a machine capable of performing various functions in any desired sequence as may be needed and directed, were to be prevented from the use of some sequences or instructions.
>
> Moreover, many computers were, or still are, the subject of letters patent. Section 69 provides that the effect of a patent is to grant to the patentee the exclusive right "… to make, use, exercise and vend the invention in such manner as he thinks fit, so that he shall have and enjoy the whole profit and advantage accruing by reason of the invention during the term of the patent." A patent having been issued in those terms, it would clearly be generally inconvenient and mischievous to the state if the Commissioner were to issue further patents effectively depriving the patentee from the use of his invention as he thinks fit, or depriving him from the whole profit and advantage accruing by reason of the invention.[163]

Other instances where the generally inconvenient proviso was considered include *Clayton Furniture Ltd's Application* ('*Clayton*')[164] for an improved lunch box and *V S Clark's Application* ('*V S Clark*')[165] for cover strips for glazing arrangements. In *Clayton*, the Hearing Officer explained that issuing a patent over the claimed invention, which was not novel, would have the effect of turning ordinary routine activities into infringements.[166] The ensuing state of affairs according to him, 'would obviously be mischievous to the State and generally inconvenient and, accordingly, cannot fall within the scope of protection envisaged by s 6 of the *Statute of Monopolies*'.[167] On the other hand, in *V S Clark*, it was considered mischievous to the State and generally inconvenient to issue a patent for the claim which had been found to be far too broad and indefinite.[168] Consequently, the

[163] *Telefon A/B L M Ericsson's Application* [1975] FSR 49, 56-7.
[164] (1965) 35 AOJP 2303 ('*Clayton*').
[165] (1969) 39 AOJP 1638 ('*V S Clark*').
[166] *Clayton* (n 164) 2305.
[167] Ibid 2305.
[168] *V S Clark* (n 165) 1639.

applicant was directed to lodge a statement of proposed amendments which was allowed, with the application and specification subsequently accepted.

Considering the inventions as claimed in all of the above decisions were found to be inherently unpatentable and therefore did not constitute manners of new manufacture, it would seem that the comments made in respect of the generally inconvenient proviso are to be treated as obiter. This is because, by virtue of s 6 of the *Statute of Monopolies* and as can be inferred from Lloyd-Jacob J's comment quoted earlier, the general inconvenience proviso only applies when a claimed invention is found to constitute a manner of new manufacture capable of being patented. In the event that a manner of new manufacture is not disclosed, the question of whether or not the grant of a patent over said 'invention' would be generally inconvenient does not arise. Notwithstanding, it is worth paying attention to those comments as they provide an insight into likely interpretations of the proviso and how it could potentially apply to bioprinting.

Drawing from the facts of the aforementioned cases and the comments made, a number of public policy concerns can be treated as falling within the purview of the proviso. These include the likelihood of inadvertent infringement; over-patenting of new technologies; subsequent patents that limit the scope of earlier patents; lack of novelty and overly broad patents. Together, these concerns can be summarised under the broad headings of novelty and general access by the public and other innovators. Whilst this approach appears to be in concert with historical interpretations of the proviso, as evidenced by the cases decided prior to the *Statute of Monopolies*, changes to patent laws at the time in question warrant a closer examination of the validity of this approach.

At the time the cases were decided, and even before then, the requirement for novelty had been distinctly identified as one of the three main criteria for patentability alongside inventiveness and usefulness.[169] The options of compulsory licensing and revocation for non-working had also been introduced to address concerns about access.[170] In light of these developments, the reasonable assumption would be a commensurate revision to the scope and application of the general inconvenience proviso reflective of those changes. Such a revision would have meant that concerns about lack of novelty, in particular, would

[169] *Patents Act 1903* (Cth) ss 7(2), 41, 56(e), 88(4), 89; *Patents Act 1952* (Cth) ss 48, 59(1)(h), 100(1)(e),(g)-(h).
[170] *Patents Act 1903* (Cth) s 87; *Patents Act 1952* (Cth) ss 108-112.

not have been contemplated under the proviso. Although the effect of a grant in these cases would have been inconvenient given the lack of novelty, the lack of novelty should have been dealt with solely under the technical heading of novelty since it had been provided for in the Act. There was no reason to have considered applying the proviso since the requirements for patentability had not been met. As explained earlier, the proviso operates solely to exclude patentable inventions and not non-patentable inventions (since these are already excluded). In essence, the notion that the proviso might apply where there are concerns about novelty is unsubstantiated and should not be considered as an indication of how the proviso might apply to bioprinting-related inventions or indeed any invention. Moreover, IP Australia has since clarified in its Patent Examiner's Manual that – '[w]here general inconvenience appears to be an issue, examiners should consider whether the appropriate objection is really one of anticipation or that the invention does not lie in the technical realm'.[171]

For concerns about access, on the other hand, this is a significant issue that extends well beyond the mere availability of safeguards such as compulsory licensing and revocation for non-working. Whilst the issue of access will be examined extensively later on in chapter seven, it will suffice at this juncture to state that attempts to address concerns about access within the patent system appear to be in direct conflict with the overarching purpose of the patent system which is to reward inventors with exclusive rights. A by-product of this exclusive rights is often limitation of access to the patented invention. That is not to say concerns about access are not valid, but rather that those concerns need to be carefully balanced against the purpose of the patent system. Failing which, the purpose of the patent system might very well be defeated.

Nonetheless, as concerns about access carry with them an implied assumption of patentability and are also a matter of public policy, it is perhaps appropriate that they are considered under the proviso. However, in the above cases, the concern appeared largely focused on the fear of infringement, which again is a by-effect of a patent grant. As Heerey

[171] Australian Patent Office, '2.9.3.3 General Inconvenience', *Patent Manual of Practice & Procedure* (Web Page, 10 November 2014) <http://manuals.ipaustralia.gov.au/patents/national/patentable/2.9.3.3_general_inconvenience.htm>.

J noted in the more recent case of *Welcome Real-Time SA v Catuity Inc* ('*Welcome Real-Time SA*'):

> [b]ut if an invention otherwise satisfies the requirement of s 18 it can hardly be a complaint that others in the relevant field will be restricted in their trade because they cannot lawfully infringe the patent. The whole purpose of patent law is the granting of monopoly.[172]

Thus, it would appear that not all concerns about access are suited for consideration under this proviso. The difficulty, however, lies in identifying which are suited for such consideration. In line with IP Australia's directive, a good rule of thumb would be to first consider whether there are specific mechanisms (such as compulsory licensing, revocation for non-working and research/experimental exemptions) available within patent and related laws to address the particular concern. It is irrelevant whether the mechanisms when applied provide the preferred result. What is most important is that there exists a definite response to the concerns raised. This will of course require correct identification and proper phrasing of the concern. Only in the absence of an applicable mechanism should the proviso be considered.

Altogether, while the concerns raised under the proviso so far could have and were indeed decided by reference to other technical grounds, it would appear that the inevitable conclusion is that public policy concerns ought to be contemplated under this proviso. This position is further reinforced by the observations of Barwick CJ in *Joos* where he stated that if he were to discover and express a basis for excepting a claim for medical treatment, he 'would place the exception, if it so to be maintained, on public policy as being in the language of the *Statute of Monopolies*, "generally inconvenient"…'.[173]

The unanswered question, however, remains - what kind of public policy concerns are contemplated under this proviso? Does it include ethical questions pertaining to morality arising from patenting an invention? To this end, this chapter now turns to the enactment of the current *Patents Act* alongside the growth of biotechnology in Australia.

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[172] (2001) 113 FCR 110, 138 [132] ('*Welcome Real-Time SA*').
[173] *Joos* (n 102) 623.

3.4.5 *Patents Act 1990* (Cth) and the Growth of Biotechnology in Australia

Up until 1990, it would appear that biological/genetic materials were generally patentable in Australia. Nevertheless, by the time the *Patents Act* was passed in 1990, concerns about such patenting had reached a crescendo. It is unclear whether there were ever any attempts to invoke the general inconvenience proviso to address these concerns. Given Senator John Richard Coulter's speech during the debate of the 1990 Patents Bill in Parliament, however, it is highly unlikely this occurred.

In his speech, the Senator expressed the growing concern held by many Australians about the lack of ethical considerations in the Patent Bill given technological advancements at the time and social attitudes towards those technologies.[174] He explained patenting genetic/biological material as 'prostituting the very substance of life, prostituting for commercial gain the very essence of life itself'.[175] This he considered repugnant and an ethical question of the highest order which ought to have been addressed in the Bill.[176] To this end, he sought an amendment to s 18 which dealt with the definition of patentable material, to exclude genetic/biological material from patenting.[177] It should be emphasised that the Senator was not opposed to patenting the techniques for doing so, however.[178] As some life forms were patentable in Australia at the time, there was concern that a broad exclusion, as proposed, would have the unfavourable effect of preventing the patenting of some useful life forms such as live vaccines, which pose little to no ethical concern.[179] Ultimately, s 18 was amended to exclude human beings, and the biological processes for their generation from patentability instead.[180]

Curiously, in all of this, there was no reference to the general inconvenience proviso and its possible application to the concerns raised. This is especially because, as noted earlier, the separate morality exclusion clause contained in the *1903 Act*[181] had, for some unknown

[174] Commonwealth, *Parliamentary Debates*, Senate, 22 August 1990, 1911-3 (John Coulter).
[175] Ibid 1912 (John Coulter).
[176] Ibid.
[177] Commonwealth, *Parliamentary Debates*, Senate, 17 September 1990, 2478-81,83 (John Coulter).
[178] Commonwealth, *Parliamentary Debates*, Senate, 20 September 1990, 2653 (John Coulter).
[179] Commonwealth, *Parliamentary Debates*, Senate, 17 September 1990, 2480 (John Coulter) (Peter Baume).
[180] *Patents Act* (n 17) s 18(2); Commonwealth, *Parliamentary Debates*, Senate, 20 September 1990, 2654 (Brian Harradine).
[181] *Patents Act 1903* (Cth) s 118.

reason, been omitted from the *1952 Act*[182] and, subsequently, the *1990 Act,*[183] despite comments about maintaining coherency between Australian and UK patent laws.[184] It could very well be that the lack of reference to the general inconvenience proviso in the debates associated with the introduction of the *1990 Act* was simply an oversight. On the other hand, it could be that it was an implicit acknowledgment on the part of Parliament that the proviso was insufficient to deal with ethical concerns about the morality of patenting certain inventions. If the latter, it is surprising that Parliament chose to introduce the narrower exception in s 18(2), as opposed to possibly reintroducing the broader morality exclusion clause previously contained in the *1903 Act*. This is especially in light of the fact that Australia at the time was also engaged in negotiating the *TRIPS Agreement*, which, as noted earlier, contains a general morality exclusion clause.[185] Whatever the case may be, this was a missed opportunity to provide clarity on the scope of the proviso in relation to ethical concerns about morality.

It would thus appear that all of these actions and inaction have eventually culminated in the prevailing judicial reluctance to engage with the proviso, as exemplified in the following cases, despite precedent indicating that public policy concerns likely fall under the proviso. In *Rescare*[186] for instance, the majority failed to make a definite pronouncement in respect of the appellant's argument that the claimed invention for medical treatment was generally inconvenient within the *Statute of Monopolies*. The appellant had argued that two of the claims were generally inconvenient, primarily because it was in the public interest that the invention be published and freely available.[187] In his minority judgment, however, Sheppard J acknowledged the importance of the appellant's argument. His Honour stated that, in his opinion, granting a monopoly over a potentially life-saving treatment as claimed seemed generally inconvenient and was a ground for invalidity of the claims in issue.[188] He went on to add that in light of the recent *TRIPS Agreement*, the question on validity of

[182] *Patents Act 1952* (Cth) s 155(1)(a).
[183] *Patents Act* (n 17) s 51(1)(a) provides that '[t]he Commissioner may refuse to accept a patent request and specification, or to grant a patent for an invention the use of which would be contrary to law'.
[184] Commonwealth, *Parliamentary Debates*, House of Representatives, 3 June 1952, 1241 (Howard Beale); Commonwealth, *Parliamentary Debates*, Senate, 22 May 1952, 690 (John Spicer); Commonwealth, *Parliamentary Debates*, Senate, 29 May 1952, 1018 (Nicholas McKenna).
[185] Commonwealth, *Parliamentary Debates*, House of Representatives, 1 June 1989, 3480 (Barry Jones).
[186] *Rescare* (n 29).
[187] Ibid 17-18.
[188] Ibid 41.

methods of medical treatment on whatever grounds (that of general inconvenience or that they are not proper subject matter of a valid grant) was best left to Parliament to legislate upon.[189] This was further to the observations of Lockhart J that Parliament had the opportunity to exclude methods of medical treatment when it enacted the *1990 Act* but failed to do so.[190] Ultimately, as with the cases decided prior to 1990, the claims failed for reasons other than that they were generally inconvenient.

Notwithstanding, the trial judge in *Bristol-Myers Squibb Co v FH Faulding & Co Ltd* found Sheppard J's obiter in *Rescare* persuasive enough to rule that petty patents for administration of an anti-cancer drug in specified periods were generally inconvenient within the meaning of s 6 of the *Statute of Monopolies.*[191] On appeal, however, the Full Court unanimously held that the trial judge had erred in holding that the patents were invalid on the ground of general inconvenience, given historical precedent and the view of the majority in *Rescare.*[192] Finkelstein J added that it was not for judges to resolve moral questions nor should legal principles be ascertained by reference to standards of ethics or morality.[193] Citing the United States Supreme Court decision in *Diamond v Chakrabaty*,[194] he opined that exclusions from patentability on the grounds of public policy ought to be dealt with by Parliament and not Courts as it was too complex and controversial an issue.[195] Anticipating that some might be wont to consider this a dereliction of duties, Finkelstein J went on to state that his position was not an abdication of duties as such decisions were simply not the function of the Court.[196] He nevertheless acknowledged that public interest matters are contemplated under the proviso.

The general inconvenience proviso was again raised by the respondents in *Welcome Real-Time SA.*[197] They argued that the patent claimed (which was for a process and device for operation of smart cards in connection with traders' loyalty programs) was generally inconvenient as it placed a restraint on other traders in developing and operating loyalty

[189] Ibid 41.
[190] Ibid 19.
[191] *Bristol-Myers Squibb Co v FH Faulding & Co Ltd* (1998) 41 IPR 467.
[192] *Bristol-Myers* (n 103).
[193] Ibid 559-60 [100].
[194] *Diamond v Chakrabarty*, 447 US 303, 308-10 (1980).
[195] *Bristol-Myers* (n 103) 569 [140]-[142].
[196] Ibid 569 [141]-[142].
[197] *Welcome Real-Time SA* (n 172).

and incentive schemes which were 'a commonplace way of doing business and had been so for many years in both the real and on line worlds'.[198] By stating that the schemes were commonplace, the respondents were in a way rephrasing their argument that the claimed invention lacked novelty. As explained earlier, the requirements that an invention be novel and not generally inconvenient are distinct with the latter dependent on the existence of the former. However, unlike the other cases discussed previously, the Court found that the patent in this case did not lack novelty and was on other additional grounds valid. Accordingly, it was appropriate for the Court in this instance to consider the question of general inconvenience. Unfortunately, beyond stating that the respondent's argument was contradictory to the purpose of the patent system and therefore rejected,[199] the Court provided no useful guidance on the application of the proviso.

On the one hand, while it would seem that the courts have generally failed to make any definitive pronouncement on the meaning and scope of the general inconvenience proviso so far, it would also appear that the courts have not been given the opportunity to do so as the proviso, when pleaded, is often as an alternative should other arguments based on technical aspects of patent law fail. To date, there has been no reported case where the proviso was raised as a standalone argument. There have also been instances where parties eschewed reliance on the proviso, making it impossible for the courts to expound on its interpretation.[200] Given that these cases were ultimately decided on other technical grounds, it is perhaps of little significance that the proviso was not pleaded.

Thus, with the uncertainty surrounding the scope and application of the general inconvenience proviso in Australia, it is difficult to predict to what extent, if any, the proviso will be relevant to the ethical challenges presented in patenting bioprinted constructs and related processes. This is notwithstanding the High Court's comments regarding the relationship between the factorial approach and the general inconvenience proviso.[201]

[198] Ibid 138 [131].
[199] Ibid 138 [131]-[132].
[200] *D'Arcy* (n 30); *Apotex* (n 29).
[201] *D'Arcy* (n 30) 351 [28].

In the meantime, however, recourse might be found under the aforementioned amendment to s 18(2) of the *Patents Act* intended to exclude genetic/biological material from patenting.

3.4.6 *Patents Act 1990* (Cth) s 18 (2) – Scope and Application

Section 18(2) [202] provides that human beings, and the biological processes for their generation, are not patentable inventions. The *Act* however fails to define what is meant by 'human beings' or the 'biological processes for their generation'. An initial reading of this clause in conjunction with an understanding of how bioprinting works would indicate that the most relevant aspect of this clause to patenting bioprinting would be 'biological processes for their generation'. This is because bioprinting in its current and anticipated form appears to be more concerned with fabricating body parts rather than human beings as a whole. Moreover, human beings are not 'inventions' capable of being patented. Nevertheless, it is pertinent to understand the meaning of both terms in order to ascertain the extent to which this exclusion might apply to bioprinting.

For this, some guidance is to be found in the decision of the Deputy Commissioner of Patents in *Re Luminis Pty Ltd and Fertilitescentrum AB.*[203] In said case, the applicants had filed an application for claims to an invention that involved using a substance they had discovered to increase the viability of embryos. During examination, the examiner objected to their claims for a method of growing preblastocyst human embryos on the grounds that such claims were a step along the path of generating human beings and as such excluded from patentability by virtue of s 18(2). The applicants argued that their method of invention was in fact a method of treatment since it was only applied after the human being had been created and could therefore not be caught by the provisions of s 18(2).

In order to ascertain whether or not the claimed method involved biological processes for the generation of a human being, it was important to first determine at what point in the reproductive process a human being is created. Thus, the Deputy Commissioner stated as follows:

> Accordingly, in my view the correct interpretation of s 18(2) is ascertained by recognising a human being as being in the process of generation … from the time of the processes

[202] *Patents Act* (n 17).
[203] *Re Luminis Pty Ltd and Fertilitescentrum AB* (2004) 62 IPR 420.

> that create a fertilised ovum (or other processes that give rise to an equivalent entity) up until the time of birth.
>
> The prohibition of "human beings" in my view is a prohibition of patenting of any entity that might reasonably claim the status of a human being. Clearly a person that has been born is covered by this exclusion. But to the extent that there is a process of generation of a human being that lasts from fertilisation to birth, I consider that a fertilised ovum and all its subsequent manifestations are covered by this exclusion.
>
> The prohibition of "biological processes for (the generation of human beings)" clearly covers all biological processes applied from fertilisation to birth—so long as the process is indeed one that directly relates to the generation of the human being. I also consider the exclusion of biological processes includes the processes of generating the entity that can first claim a status of human being. For example, processes for fertilising an ovum; processes for cloning at the four–cell stage by division; processes for cloning by replacing nuclear DNA.[204]

In the end, the Deputy Commissioner concluded that the claimed method as applied to an embryo was for a process that directly related to the generation of a human being and therefore within the ambit of s 18(2). This would appear a logical conclusion given debates regarding the status of embryos as human beings.[205] To hold that the generation of a human being ends at fertilisation would be to effectively categorise embryos as human beings – a position which remains contentious among scientists, philosophers, and theologians. Moreover, the term 'generation' implies an ongoing process, which continues up to the point it can be said a human being exists. Unless it can be said with sufficient certainty that an embryo is a human being, it would seem that any biological process that occur between fertilisation and birth (when it is certain that a human being exists) should rightfully be considered ineligible for patenting by virtue of s 18(2). This is in so far as the capacity for development into a human being exists.

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[204] Ibid 430 [36]-[38].

[205] See generally Helga Kuhse, 'A Report from Australia: When A Human Life Has Not Yet Begun - According to the Law' (1998) 2(4) *Bioethics* 334; Robert P George and Patrick Lee, 'Embryonic Human Persons. Talking Point on Morality and Human Embryo Research' (2009) 10(4) *EMBO Reports* 301; John Janez Miklavcic and Paul Flaman, 'Personhood Status of the Human Zygote, Embryo, Fetus' (2017) 84(2) *The Linacre Quarterly* 130.

Subsequently, the same Deputy Commissioner was confronted with interpreting s 18(2) again in *Re Woo-Suk Hwang.*[206] This was in respect of an application for a method of producing hybrid embryos derived by nuclear transfer using human and bovine cells.[207] He held that the claimed method fell within the exclusion of s 18(2) being a method for generating a human being. It was irrelevant that the ovum had been artificially post-activated, or that a mitochondrial DNA which was entirely bovine had been used. The claimed invention was also refused under s 50(1)(a)[208] as noted earlier.

Relying on both decisions, IP Australia stated in 2014 that amongst other things, the following would be excluded from patentability under s 18(2):

i. zygotes, blastocysts, embryos and foetuses.
ii. totipotent human cells, including those cells that are the products of nuclear transfer procedures.
iii. processes or methods of growing or culturing fertilised ova, zygotes or embryos including methods for obtaining embryonic stem cells which comprise a step(s) for making an embryo. The exclusion applies regardless of the manner in which the embryo is generated (whether by fertilisation of gametes, or nuclear transfer, or activation of gametes, or parthenogenesis[209] etc.)[210]

However, in 2016, IP Australia ruled that blastocysts formed via parthenogenic activation of unfertilised human egg cells (oocytes) do not have the potential to develop into human beings and are therefore not caught under the s 18(2) exclusion.[211] This was in respect of an application submitted by International Stem Cell Corporation for methods of producing human embryonic stem cells from oocytes through a process known as parthenogenesis, and the use of those stem cells in the generation of synthetic cornea. The examiners had objected that the claimed methods involved biological processes for the generation of

[206] (2004) AIPC 92-031.
[207] Ibid.
[208] *Patents Act* (n 17).
[209] The term parthenogenesis is defined as 'the production of an embryo from a female gamete in the absence of any contribution from a male gamete, with or without the eventual development into an adult'. Nathalie Rougier and Zena Werb, 'Minireview: Parthenogenesis in Mammal' (2001) 59 *Molecular Reproduction and Development*.
[210] Australian Patent Office, '2.9.3.5 Human Beings and Biological Processes for Their Generation', *Patent Manual of Practice & Procedure* (Web Page, 10 November 2014) <http://manuals.ipaustralia.gov.au/patents/national/patentable/2.9.3.5_Human_Beings_and_Biological_Processes_for_their_Generation.htm>.
[211] *Re International Stem Cell Corp* (2016) 123 IPR 142.

human beings and were therefore excluded from patentability under s 18(2). In arriving at his conclusion, the Delegate of the Commissioner of Patents noted that the important consideration was whether 'the formation of a blastocyst via parthenogenic oocyte activation represent a "process that directly relates to the generation of a human being"'.[212]

Furthermore, with regard to the patentability of claimed methods which include a step involving a biological process for the creation of a human being, the Delegate of the Commissioner of Patents noted that:

> Thus, when interpreting s 18(2), I must apply the interpretation that would best achieve the purpose of the Act. In doing so, I may consider the mischief that Parliament was trying to solve… Having regard to the deliberations described therein, I consider that the exclusion of biological processes where a (potentially human) entity is created, and is subsequently used (or even destroyed to allow the use of the cells produced) for another purpose, provides a clear representation of the type of mischief that Parliament was addressing. Put another way, it would be inconsistent with the intended purpose of s 18(2) if the inclusion of additional steps following the production of a human being or human embryo resulted in the claim circumventing the s 18(2) exclusion.[213]

As explained in chapter two, different cell types such as xenogeneic, embryonic, adult/somatic or induced pluripotent stem cells are used in bioprinting. In light of the aforementioned decisions, it would appear that s 18(2) could potentially affect bioprinting process claims pertaining to the production of embryonic stem cells. While such processes in themselves may be ineligible for patenting, depending on how the embryo is generated and whether it has the potential to develop into a human being, it should be remembered that there are other processes/methods involved in bioprinting. The question then is whether such additional processes embodying ineligible embryonic stem cells will also be considered ineligible for patenting by association. Another question is whether the use of such embryonic stem cells will impact the patentability of bioprinted constructs.

Further to the Delegate of the Commissioner of Patents' comment in *Re International Stem Cell Corp*, it would appear that such additional bioprinting processes may potentially be

[212] Ibid 147 [28].
[213] Ibid 146 [22].

considered ineligible for patenting in so far as they include a step producing a potential human being. By implication, this could also extend to bioprinted constructs embodying embryonic stem cells produced via an ineligible biological process. In essence, any method or product claim which includes a step involving a biological process for the creation of a human being is potentially ineligible for patenting by virtue of s 18(2), since to hold otherwise would be to circumvent the provisions of s 18(2).

However, considering that such additional bioprinting processes and indeed the resulting bioprinted construct appear independent of the stem cells used, it is unlikely that any of the related claims will necessarily include a step involving the production of embryonic stem cells. This argument is bolstered by the fact that other cell types (xenogeneic, adult/somatic or induced pluripotent stem cells), do not appear excluded from patentability by virtue of s 18(2).[214]

3.4.7 Current State of the Law - Attempts at Legislative Reform

Having considered the extent of the general inconvenience proviso and s 18(2), it is equally imperative to consider the general state of the law regarding ethically informed exclusions. This is especially so with ongoing discussions in Australia about the possibility of amending the *Patents Act* to include an ethical exclusion clause in compliance with its international obligations under the *TRIPS Agreement*, which permits member countries to

> exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect ordre public or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law.[215]

Pursuant to a reference from the then Attorney-General in 2002 to undertake a review of intellectual property rights over genes and genetic and related technologies, with a particular focus on human health issues, the Australian Law Reform Commission ('ALRC') conducted an inquiry and submitted its report in 2004. In its report, the ALRC acknowledged the existence of the general inconvenience proviso but noted that it had

[214] Australian Patent Office, '2.9.3.5.1 Stem Cells', *Patent Manual of Practice & Procedure* (Web Page, 10 November 2014) <http://manuals.ipaustralia.gov.au/patents/national/patentable/2.9.3.5.1_stem_cells.htm>.
[215] *TRIPS Agreement* (n 1) art 27(2).

rarely been relied upon alone as a ground for invalidity and as such, its use to ground exclusion for social and ethical reasons was arguable and unclear.[216] The ALRC pointed to the difficulty the European Patent Office has encountered in applying the *ordre public*/morality exclusion clause as well as its limited successes, all of which will be examined in the next chapter, in recommending that such proposed amendment was unnecessary. This was particularly the case because it would not address concerns about the implications of patenting genetic materials or technologies for research and access to healthcare. Instead, it recommended that 'social and ethical concerns should be addressed primarily through direct regulation of the use or exploitation of a patented invention'.[217] It also recommended an independent review of the appropriateness and adequacy of the 'manner of manufacture' test for patentability with a particular focus on the 'general inconvenience' requirement.[218]

Subsequently, the now defunct Advisory Council on Intellectual Property ('ACIP') was requested by the Minister for Innovation, Industry, Science and Research to conduct said review of patentable subject matter.[219] In its report dated 23 December 2010, the ACIP urged that the Australian patent system must take account of both economic and ethical matters in determining what is patentable.[220] It nevertheless advised that ethical concerns pertaining to access to beneficial technologies are better dealt with through legislative and non-legislative mechanisms (such as compulsory licensing, experimental use, patent pools and other targeted government programs) rather than the test for patentability.[221] With regard to ethical concerns about patenting undesirable and offensive technologies, or where the commercial exploitation in itself is undesirable and offensive, it recommended they be dealt with by a combination of general and specific exclusion clauses.

On the use of specific exclusion clauses, ACIP noted that whilst they provided transparency and certainty, they were often inflexible and proposed changes would have to operate retrospectively in order to have any significant impact.[222] Thus, rather than recommending the introduction of new specific clauses in the absence of a clear need,

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[216] Australian Law Reform Commission, *Genes and Ingenuity: Gene Patenting and Human Health* (Report 99, 29 June 2004) <http://www.alrc.gov.au/publications/report-99>, 179 [7.48].
[217] Ibid 191 (Recommendation 7-1).
[218] Ibid 132 (Recommendation 6-2).
[219] 'Patentable Subject Matter' (n 117).
[220] Ibid 29.
[221] Ibid 6.
[222] Ibid 14.

ACIP simply recommended that the specific exclusions contained in s 18(2)-(3) dealing with humans, plants and animals be retained.[223]

With regard to the use of general exclusion clauses, ACIP noted that there was an overlap between the manner of manufacture test and other tests for patentability which had contributed to the uncertainty surrounding the general inconvenience proviso. To this end, it recommended that the proviso be removed. In its place, it suggested a general exclusion for inventions, 'the commercial exploitation of which would be wholly offensive to the ordinary reasonable and fully informed member of the Australian public'.[224] This position is contrary to ALRC's recommendation not to amend the *Patents Act* to expand existing circumstances in which social and ethical concerns may be taken into account in granting patents.

The choice of language for the proposed general exclusion clause was informed by the ACIP's opinion that directly importing the wording of art 27(2) of the *TRIPS Agreement* would be difficult to interpret in the Australian context. It argued that by using the reasonable person test, which is considered an objective concept, the issue of subjective evaluations faced in Europe or countries with exclusions similar to art 27(2) would be avoided.[225] This is in addition to the use of what it considers 'neutral terms' allowing for flexibility in interpretation given the transient nature of societal values. In its opinion, the interpretation of such a test will, through case law, be clarified over time by the Australian courts.[226]

With regard to the limitation of the exclusion to only 'commercial exploitation', ACIP noted that such limitation was in line with the exclusive right conferred by a patent grant - to (commercially) exploit an invention.[227] Since granting a patent might in effect be perceived as government endorsing an invention, it is only appropriate that a patent grant be withheld where commercial exploitation of such invention would be offensive to the Australian public. However, it cautioned that such an approach would only deter exclusive

[223] Ibid 15 (Recommendation 6).
[224] Ibid 18 (Recommendation 9).
[225] Ibid 64-67.
[226] Ibid 67.
[227] Ibid 68.

exploitation which is conferred by patents, and not the act of exploitation in general.[228] In the same vein, ACIP also noted that a general exclusion clause would also not address any ethical concern about the invention itself.[229] Accordingly, it recommended that ethical concerns about inventions in themselves be dealt with by other areas of law.[230]

In 2011, the Australian Government accepted the recommendations of the ACIP regarding the introduction of a new general exclusion clause amongst other recommendations but noted that any proposed amendment would need to be consistent with the country's international obligations.[231] It undertook to develop legislation to give effect to the recommendations adding that such legislation would be subject to the same public consultation process as the Intellectual Property Laws Amendment (Raising the Bar) Bill 2011. However, in spite of the public consultation conducted by IP Australia in 2013 and a failed attempt at amending the *Patents Act* to prevent the patenting of biological materials identical to or substantially identical to materials existing in nature,[232] the proposed exclusion clause was not considered when the Productivity Commission undertook an inquiry into Australia's intellectual property arrangements in 2016.[233] It remains to be seen if and when any amendment introducing a general exclusion clause will be made.

Assuming Parliament were to implement the recommendation of the ACIP, it is doubtful whether the exclusion clause would have any significant impact on patenting bioprinting and indeed many other similar technologies. Even the ACIP acknowledged this in its report when it noted that:

> [w]e do not expect a significant number of inventions to be excluded on this ground. The exclusion will only apply in exceptional circumstances, where the *commercial exploitation* of

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[228] Ibid.
[229] Ibid.
[230] Ibid.
[231] 'Government Response - Patentable Subject Matter', *IP Australia* (Web Page, 21 April 2016) <https://www.ipaustralia.gov.au/about-us/public-consultations/archive-ip-reviews/ip-reviews/government-patentable-subject>.
[232] 'Consultation on Proposed Objects Clause and Patentability Exclusion', *IP Australia* (Web Page) <https://www.ipaustralia.gov.au/about-us/public-consultations/consultation-proposed-objects-clause-and-patentability-exclusion>; Patent Amendment (Human Genes and Biological Materials) Bill (No 2) 2010 (Cth).
[233] Productivity Commission, *Intellectual Property Arrangements* (Inquiry Report No 78, 23 September 2016) <http://www.pc.gov.au/inquiries/completed/intellectual-property/report>.

> the invention involves something which is wholly offensive to the ordinary reasonable and fully informed member of the Australian public.[234]

This is unsurprising giving the choice of words. For the exclusion to apply, the commercial exploitation of the invention must be wholly offensive. In other words, the offensiveness of the invention is hinged on commercial exploitation. Unfortunately, this emphasis on 'commercial exploitation' appears to limit the application of the provision in such a way that may not have been intended.[235]

It should be noted that the right to exploit any invention, whether or not patented, is subject to regulatory approval outside of the patent regime. For instance, bioprinted constructs used for therapeutic purposes in Australia will likely fall under the regulatory regime administered by the Therapeutic Goods Administration. Thus, what patents confer on right holders is the 'exclusive' right of exploitation as opposed to a mere right of exploitation. This means that an invention may be prohibited from being sold irrespective of the fact that a patent grant has been issued for it. In its current form, the proposed exclusion clause appears to be concerned with whether commercial exploitation in general and not exclusive commercial exploitation (which is what patents confer) is offensive. This would appear to extend beyond the rights conferred by the grant of a patent - the right to exclude others.

While patents may be used to regulate technologies to the extent that they confer exclusive rights of exploitation, it is important for such regulations to remain within the confines of rights afforded by a patent grant. Thus, in this instance, a more appropriate approach would perhaps have been to qualify the term 'commercial exploitation' with 'exclusive' thus reading 'exclusive commercial exploitation'. In doing so, it is probable that the exclusion clause would conceivably have a more significant impact on addressing concerns about access, which appears to be at the heart of objections to patenting certain technologies.

It is often not the exploitation that is offensive or odious, but rather the exclusive rights accompanying the grant of a patent. In all of the aforementioned cases, there were no

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[234] 'Patentable Subject Matter' (n 117) 69.

[235] See Deryck Beyleveld, Roger Brownsword and Margaret Llewelyn, 'The Morality Clauses of the Directive on the Legal Protection of Biotechnological Inventions: Conflict, Compromise and the Patent Community' in Richard Goldberg and Julian Lonbay (eds), *Pharmaceutical Medicine, Biotechnology and European Law* (Cambridge University Press, 2000) 157, 165-67, 179.

objections to the actual commercial exploitation of the inventions per se. Instead, many of the objections were founded on arguments about the unfairness of exploitation being concentrated in the hands of a single person/entity irrespective of limits on duration.

Thus, if the proposed exclusion clause were to read 'exclusive commercial exploitation' then it might be possible to exclude bioprinted constructs from patentability on the grounds that exclusive commercial exploitation is wholly offensive given the prospects of the technology as identified in chapter two. Otherwise, as it stands, neither the general inconvenience clause nor the proposed general exclusion clause appears to impact the patentability of bioprinted constructs or related processes.

3.4.8 Contrary to Law

Another provision worth considering (albeit of limited relevance to the issue of ethics) is the contrary to law provision, which has its origins in s 6 of the *Statute of Monopolies* discussed above.[236] Section 50(1)(a) of the *Patents Act* provides that the Commissioner may refuse to accept a request and specification relating to a standard patent, or to grant a standard patent for an invention the use of which would be contrary to law. According to IP Australia, this encompasses 'statute law, including regulations and ordinances, and case law'.[237]

According to case law,

> [a]n invention 'contrary to law' may be either (1), one the primary use of which would be a criminal act, punishable as a crime or misdemeanour, or, (2), one the use of which would be an offence by reason of its being prohibited under by-laws or regulations made for police and administrative purposes.
>
> Inventions belonging to the former class would always be refused protection. As regards the latter class, the nature and possible uses of the invention and the exact terms of the prohibition would have to be considered in each case.[238]

Where an invention could be used for both lawful and unlawful purposes, there is evidence to suggest a patent could be granted nonetheless.[239] This is further buttressed by IP

[236] See generally Dent (n 124) 444-5.
[237] Australian Patent Office, '2.9.3.1 Contrary to Law', *Patent Manual of Practice & Procedure* (Web Page, 24 December 2020) <http://manuals.ipaustralia.gov.au/patent/2.9.3.1-contrary-to-law > ('*2.9.3.1 Contrary to Law*').
[238] *Official Rulings* 1923 C (1923) 40 RPC Appendix iv.
[239] *Pessers and Moody v Haydon & Co.* (1909) 26 RPC 58.

Australia's direction that objections should only be taken under s 50(1)(a) where 'an unlawful use, but no lawful use, of an invention has been disclosed'.[240] In doing so, 'regard must be had to whether the invention is primarily devised or intended for a lawful, or for an unlawful, use'.[241]

In *Re Woo-Suk Hwang*,[242] which was concerned with a method of producing hybrid embryos, the Deputy Commissioner of Patents noted that s 20 of the *Prohibition of Human Cloning Act 2002* (Cth) ('*Prohibition of Human Cloning Act*') made it an offence to create a chimeric or hybrid embryo.[243] Although there was the possibility that the invention could be used lawfully in mammals other than humans, both the description and claims of the application concerned were specific in the application of the invention to humans only.[244] In arriving at this decision, the Deputy Commissioner emphasised that s 50(1)(a) is a discretionary provision with refusal to occur only in the clearest circumstances.[245] In particular, regard must be had to 'whether the relevant law is of an ephemeral nature - that is, whether it is reasonable to expect that what is illegal today will be illegal throughout the term of the patent'.[246] As the invention was clearly contrary to the *Prohibition of Human Cloning Act*, which provision the Deputy Commissioner considered unlikely to be ephemeral, it was held that the application should be refused under s 50(1)(a) for being contrary to law.[247]

Although there is currently no law prohibiting the production of bioprinted constructs, the *Prohibition of Human Cloning Act* and the *Research Involving Human Embryos Act 2002* (Cth) establish a number of offences in relation to the use of embryos. It is therefore possible that bioprinting-related inventions embodying embryonic stem cells could potentially be refused under s 50(1)(a) if they are in breach of any of the aforementioned Acts. This will of course depend on how the claims are drafted.

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[240] *2.9.3.1 Contrary to Law* (n 238).
[241] Ibid.
[242] (2004) AIPC 92-031.
[243] Now ss 17-18. Ibid [13]–[14].
[244] Ibid [17].
[245] Ibid [18].
[246] Ibid.
[247] Ibid.

3.5 Conclusion

From a review of existing legislation and case law, it would appear that bioprinted constructs and bioprinting processes are generally capable of satisfying the patentable subject matter requirement in Australia. This is primarily because bioprinting involves the creation of an artificial state of affairs with economic significance. There is also the fact that bioprinting stems from tissue engineering wherein patents have previously been granted for engineered tissue constructs. The implication of this is that the plurality's factorial approach in *D'Arcy* appears to be of limited significance, since bioprinted constructs do not appear to belong to a new class of claim.

Nevertheless, it is equally important to consider the impact patenting aspects of bioprinting could have on research and clinical applications. This is especially so for patenting bioprinted constructs. While the *Patents Act* allows for inventions to be excluded on the grounds of general inconvenience, this proviso does not appear likely to ground an exclusion for bioprinted constructs from patentability. Neither does the proposed general exclusion clause, which purports to exclude inventions for which their commercial exploitation is considered wholly offensive. This is because while monopolising the exploitation of bioprinted constructs might be considered offensive to some, the very act of exploiting bioprinted constructs is unlikely to be considered offensive or generally inconvenient given the cost implications of fabricating same.

To this end, a possible compromise regarding the patentability of bioprinted constructs and indeed other controversial life forms is to consider limiting the proposed exclusion clause to instances where '*exclusive* commercial exploitation' will be wholly offensive as opposed to 'commercial exploitation' in general. This would better accord with the rights conferred by patents – an exclusive (not general) right of exploitation. It would also be responsive to the fact that exploitation is often not the issue with patented inventions, but rather the fact that the right of exploitation has been monopolised.

Chapter 4

4 State of the Law on Patentability – *European Patent Convention*

4.1 Introduction

This thesis, as noted in the preceding chapter, examines the patentability of bioprinted constructs and related processes in three jurisdictions with divergent approaches to the question of patentability. Thus, having examined the position in Australia in the preceding chapter and concluded that bioprinted constructs and related processes appear generally patentable in that jurisdiction, this chapter considers the same issue of patentability albeit from the *European Patent Convention* ('*EPC*')[1] perspective.

The purpose of this analysis is twofold: to consider the patentability of bioprinted constructs and related processes under the *EPC*, and to consider whether the differences in legislative provisions between the *EPC* and the Australian *Patents Act 1990* (Cth) have any significant bearing on the patentability of bioprinted constructs and related processes. This is especially in light of the fact that, unlike Australia, the exceptions to patentability under the *EPC* align more closely with those of the *Agreement on Trade-Related Aspects of Intellectual Property Rights* ('*TRIPS Agreement*' or '*Agreement*').[2] In other words, as with the *TRIPS Agreement*, the *EPC* expressly excludes from patentability methods of treatment, and inventions the commercial exploitation of which are contrary to *ordre public* or morality.[3] Indeed, this difference between the *EPC* and the Australian *Patents Act 1990* (Cth) provides an opportunity to assess the extent to which varying approaches to ethically informed exceptions produce similar or different results within the context of bioprinting. This is all the more so when the markedly different approach in the United States of America ('USA') is subsequently considered in chapter five.

As the *EPC* is a regional *patent* treaty operating alongside national patent laws of European countries signatory to it, this chapter begins with an overview of the European patent

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[1] *Convention on the Grant of European Patents*, signed 5 October 1973, 1065 UNTS 255 (entered into force 7 October 1977) ('*EPC*').

[2] *Agreement on Trade-Related Aspects of Intellectual Property Rights*, signed 15 April 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, 1869 UNTS 299 (entered into force 1 January 1995) ('*TRIPS Agreement*').

[3] Aside from these express exclusions, the *EPC* also provides that the following subject matter are not patentable as such: discoveries, scientific theories and mathematical methods; aesthetic creations; schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers; and presentations of information: *EPC* (n 1) art 52(2).

system and its relationship with national patent regimes. Thereafter, this chapter examines the threshold for patentability under the *EPC* and assesses the patentability of bioprinted constructs and related processes against this threshold. As noted in the preceding chapter, an invention may be excluded from patentability notwithstanding that it is otherwise patentable subject matter. Accordingly, the section on patentable subject matter is followed by an examination of exceptions to patentability as contained in the *EPC*. This is considered in the context of bioprinting.

It should be emphasised at this juncture that given the interconnectedness between this chapter and the preceding chapter, much of the analysis regarding the nature of bioprinted constructs and related processes carry over into this chapter. This is notwithstanding differences in legislative provisions between the *EPC* and the Australian *Patents Act 1990* (Cth).

Ultimately, this chapter concludes that, other than the express exclusion of methods of treatment, which may likely extend to *in situ* bioprinting as well as inventions embodying embryonic stem cells, bioprinted constructs and related bioprinting processes appear generally patentable under the *EPC*. As it stands, the *ordre public* and morality exception appears to have limited impact on the patentability of bioprinted constructs and related bioprinting processes given indications of how strictly the exception is expected to be interpreted.

4.2 The European Patent System and the *European Patent Convention*

Many of the substantive provisions contained in the *EPC* can be traced back to the *Convention on the Unification of Certain Points of Substantive Law on Patents for Invention* ('*Strasbourg Convention*').[4] In itself, the *Strasbourg Convention* arose from a desire by members of the Assembly of the Council of Europe to establish a European Patent Office ('EPO').[5] To achieve this, it was decided that there had to be a (partial) unification of substantive patent law across member states. Accordingly, the Committee of Experts designated to prepare

[4] *Convention on the Unification of Certain Points of Substantive Law on Patents for Invention*, opened for signature 27 November 1963 ETS No 47 (entered into force 1 August 1980); Christopher Wadlow, 'Strasbourg, the Forgotten Patent Convention, and the Origins of the European Patents Jurisdiction' (2010) 41 *International Review of Intellectual Property and Competition Law* 123; Eda Kranakis, 'Patents and Power: European Patent-System Integration in the Context of Globalization' (2007) 48 *Technology and Culture* 689, 705.
[5] Kranakis (n 4) 704.

the draft convention undertook a comparative study of the laws and regulations governing industrial rights in member states of the Council of Europe and, more particularly, of the texts and juridical decisions on the subject of novelty and patentability.[6]

Whilst the *Strasbourg Convention* was eventually signed in 1963, it was not until 1977 that the EPO was set up.[7] This was further to art 4 of the *EPC* which established the European Patent Organisation and provided for two organs of said Organisation, namely: the EPO and the Administrative Council.[8] Whereas it is the responsibility of the EPO to grant European patents (that is, patents granted by virtue of the *EPC*), the Administrative council is responsible for supervising the EPO.[9]

The idea of a single, harmonised system for the grant of patents across Europe arose from the cumbersome nature of filing patents across European States. Prior to the enactment of the *EPC*, applicants seeking to obtain patents across multiple European countries had to contend with filing multiple applications, which also had to be translated into different languages in some cases given the variety of spoken languages across Europe.[10] This was rather time-consuming and costly. As such, the Contracting States of the *EPC* sought to develop a system which allowed for the protection of inventions via 'a single procedure for the grant of patents and by the establishment of certain standard rules governing patents so granted'.[11]

This culminated in the *EPC*, which has the *Paris Convention*,[12] the *Patent Cooperation Treaty*,[13] and the International Patent Institute ('IIB') as its precursors.[14] As of today, there are currently 38 member states of the European Patent Organisation.[15] It should be emphasised, however, that membership of the European Patent Organisation is separate

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[6] Wadlow (n 4).
[7] 'Legal Foundations', *European Patent Office* (Web Page, 5 April 2019) <https://www.epo.org/about-us/foundation.html>.
[8] Ibid.
[9] *EPC* (n 1) art 2, 4(3).
[10] 'The History of the EPO', *European Patent Office* (Web Page, 19 December 2018) <https://www.epo.org/about-us/timeline.html> ('*The History of the EPO*'); Kranakis (n 4) 701.
[11] *EPC* (n 1) Preamble.
[12] *Paris Convention for the Protection of Industrial Property,* opened for signature 20 March 1883*,* 828 UNTS 305 (entered into force 7 July 1884).
[13] *Patent Cooperation Treaty,* opened for signature 19 June 1970*,* 1160 UNTS 231 (entered into force 24 January 1978).
[14] The IIB which was established to achieve cooperation in patent searching and archiving was subsequently integrated into the European Patent Organisation: *The History of the EPO* (n 10); Kranakis (n 4) 704.
[15] 'Member States of the European Patent Organisation', *European Patent Office* (Web Page, 19 March 2019) <https://www.epo.org/about-us/foundation/member-states.html>.

and distinct from the European Union ('EU'). Thus, whilst countries such as Albania, Iceland, Liechtenstein, Monaco, North Macedonia, Norway, San Marino, Serbia, Switzerland and Turkey are members of the European Patent Organisation, they are not members of the EU.[16]

The *EPC* is a multilateral treaty which effectively harmonises substantive conditions for patentability and exceptions to patentability across Contracting States.[17] Thus, rather than filing multiple applications in each Contracting State, the *EPC* allows applicants to file a single patent application with the EPO for a European patent which is deemed as designating all the Contracting States of the *EPC*.[18] In this vein, the *EPC* also affords applicants the benefit of a supranational patent search and examination system.[19]

Appeals from the decisions of the Receiving Section, Examining Divisions, Opposition Divisions and the Legal Division of the EPO may be made to the Boards of Appeal. [20] In turn, the Boards of Appeal may refer decisions on points of law to the Enlarged Board of Appeal.[21] The Enlarged Board of Appeal is also responsible for deciding petitions for review of the decisions of the Boards of Appeal and giving opinions on points of law referred to it by the President of the EPO.[22] It should however be noted that whilst the EPO is responsible for granting European patents, such patents are nonetheless subject to the national patent law in each of the Contracting States for which the patent is granted.[23]

Additionally, it is important at this juncture to highlight the *Implementing Regulations* to the *EPC*[24] and the *Directive on the Legal Protection of Biotechnological Inventions* ('*Biotech Directive*'),[25] as their provisions are equally relevant to the discourse contained in this chapter. By virtue

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[16] Ibid; 'About the EU: Countries', *European Union* (Web Page, 28 July 2020) <https://europa.eu/european-union/about-eu/countries_en>.
[17] Kranakis (n 4) 708; See generally *EPC* (n 1) art 52-74.
[18] *EPC* (n 1) art 79(1).
[19] Kranakis (n 4) 708; *EPC* (n 1) art 90-98.
[20] *EPC* (n 1) art 21; The Boards of Appeal, which are headed by the President of the Boards of Appeal consist of the Enlarged Board of Appeal, the Legal Board of Appeal and 28 Technical Boards of Appeal European Patent Office, 'FAQ - Boards of Appeal', *European Patent Office* (Web Page, 24 November 2010) <https://www.epo.org/about-us/boards-of-appeal/faq-boards-of-appeal.html> ('*FAQ - Boards of Appeal*').
[21] *EPC* (n 1) art 22.
[22] *EPC* (n 1) art 22.
[23] *EPC* (n 1) art 2(2).
[24] *Implementing Regulations to the Convention on the Grant of European Patents* (as last amended by decision of the Administrative Council of the European Patent Organisation of 14 December 2016 (CA/D 17/16)) ('*Implementing Regulations*').
[25] *Directive 98/44/EC of 6 July 1998 on the Legal Protection of Biotechnological Inventions* [1998] OJ L 213/13 ('*Biotech Directive*').

of art 164 of the *EPC*, the *Implementing Regulations* are considered an integral part of the *EPC*. They contain supplementary provisions used in defining, interpreting and developing the provisions of the *EPC*. In the event of a conflict between provisions, however, those of the *EPC* supersede those of the *Implementing Regulations*.[26]

On the other hand, although originally a product of the EU and therefore not legally binding on the EPO, the *Biotech Directive* was incorporated in the *Implementing Regulations* by the EPO's Administrative Council in 1999.[27] In addition, the EPO has stated that it 'voluntarily follows the rulings of the European Court of Justice on the correct interpretation of the Directive, and has incorporated such rulings into its working practice in biotechnology'.[28] This is further to a recognition of the fact that in establishing common European standards for the definition and protection of biotechnological inventions, the *Biotech Directive* has fundamentally affected *EPC* rules on patentability.[29] Whilst there was a demand to formally revise the *EPC* in this regard, it has been suggested that such a revision would have been near impossible as it would have required ratification by national parliaments of the Contracting States, which would have been difficult to obtain given the controversial nature of the *Biotech Directive*.[30]

The *Biotech Directive* originated as a result of growing concerns about the patentability of biotechnological inventions across Europe.[31] At the time, European and international biotechnology companies had begun an intense lobbying campaign aimed at challenging the EPO's restrictions on biotechnology patents.[32] This was compounded by the perceived lack of national support for biotechnology patents especially with countries like France prohibiting biotechnological patents covering human deoxyribonucleic acid ('DNA').[33] There was also a growing concern amongst European governments and the European Commission with regard to the long-term consequences of European biotechnology

[26] *EPC* (n 1) art 164.
[27] Kranakis (n 4) 722; 'Biotechnology Patents at the EPO', *European Patent Office* (Web Page, 19 May 2020) <https://www.epo.org/news-issues/issues/biotechnology-patents.html>.
[28] 'Biotechnology Patents at the EPO' (n 27); *Implementing Regulations* (n 24) rule 26 also provides that the *Biotech Directive* shall be used as a supplementary means of interpretation of the *EPC* for biotechnological inventions.
[29] Kranakis (n 4) 722.
[30] Ibid.
[31] Ibid 720-1; Robin Whaite and Nigel Jones, 'Biotechnological Patents in Europe - The Draft Directive' (1989) 11 *European Intellectual Property Review* 145, 145.
[32] Kranakis (n 4) 721.
[33] Ibid.

companies shifting their research operations to the USA given what was perceived as the latter's more liberal stance to biotechnology patents.[34]

The *Biotech Directive* was therefore considered a useful mechanism for addressing these concerns. Nevertheless, it should be noted that the process of passing the *Biotech Directive* was protracted and complex given widely differing views on key issues such as patenting human genetic material, ethics and morality.[35] In fact some member States of the EU such as France, Italy and Netherlands vehemently opposed its passage because it allowed patents on living things.[36]

4.3 Patentable Subject Matter under the *EPC*

Having considered the role of the *EPC* in harmonising substantive patent laws in Contracting States, it is useful to now turn to the matter of what constitutes patentable subject matter under the *EPC*. Article 52(1) of the *EPC* provides that inventions in all fields of technology shall be eligible for patents provided they are new, involve an inventive step and are susceptible of industrial application. However, rather than defining the term 'invention' (as in Australia and the USA), art 52(2), which interpretation is discussed in the next section, simply provides that the following, in particular, shall not be regarded as patentable inventions if claimed as such:

a) discoveries, scientific theories and mathematical methods;
b) aesthetic creations;
c) schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers;
d) presentations of information.[37]

The *Implementing Regulations* further provide that an invention must be of 'technical character' to the extent that it must relate to a technical field, must be concerned with a technical

[34] Ibid 721-2; Whaite and Jones (n 31) 145.
[35] Kranakis (n 4) 720-1; Nigel Jones, 'Biotechnological Patents In Europe - Update on the Draft Directive' (1992) 14 *European Intellectual Property Review* 455; Nigel Jones, 'The New Draft Biotechnology Directive' (1996) 18 *European Intellectual Property Review* 363; Margaret Llewelyn, 'The Legal Protection of Biotechnological Inventions: An Alternative Approach' (1997) 19 *European Intellectual Property Review* 115. See also Jessica C Lai, 'Gene-Related Inventions in Europe: Purpose- vs. Function-Bound Protection' (2015) 5(4) *Queen Mary Journal of Intellectual Property* 4.
[36] Kranakis (n 4) 720-1; Jones, 'Biotechnological Patents In Europe - Update on the Draft Directive' (n 35); Jones, 'The New Draft Biotechnology Directive' (n 35); Llewelyn (n 35).
[37] *EPC* (n 1) art 52(3) further provides that '[p]aragraph 2 shall exclude the patentability of the subject-matter or activities referred to therein only to the extent to which a European patent application or European patent relates to such subject-matter or activities as such'.

problem, and must have technical features in terms of which the matter for which protection is sought can be defined in the claim.[38] Thus, for an invention to be patentable, it must be concrete and involve a 'technical teaching'.[39] Technical teaching in this context refers to 'an instruction addressed to a technically skilled person as to how to solve a particular technical problem using particular technical means'.[40]

4.3.1 Bioprinted Constructs

Based on the threshold for patentability highlighted above, it would appear that there are two considerations involved in ascertaining whether bioprinted constructs amount to patentable subject matter - whether they fall within the exclusions contained in art 52(2) as noted above, and whether they satisfy the technical character requirement. It would nevertheless appear that these two considerations are in fact linked given traditional understanding that the items listed in art 52(2) inherently lack technical character since they are of abstract and theoretical nature.[41] Accordingly, the test for determining the patent-eligibility of an invention under the *EPC* is to ascertain whether a claimed invention possesses a technical character.[42]

Although the terms 'technical' or 'technology' in themselves remain undefined so as to allow some degree of flexibility in their interpretation,[43] it has been noted that technical character of an invention may result either from the physical features of an entity or from the use of technical means for a method. In particular, the Boards of Appeal notes in a

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[38] *Implementing Regulations* (n 24) rules 42(1)(a), (1)(c), 43(1); European Patent Office, *Guidelines for Examination in the European Patent Office* (November 2019 ed, 2019), part G-I, para 2(ii) ('*Guidelines for Examination in the European Patent Office*').

[39] Ibid part G-II, para 1.

[40] 'Patents for Software? European Law and Practice', *European Patent Office* (Web Page, 26 November 2013) <https://www.epo.org/news-issues/issues/software.html>; *Estimating Sales Activity/Duns Licensing Associates* [2008] OJ EPO 2/46 ('*Estimating Sales Activity/Duns Licensing Associates*').

[41] Stefan V Steinbrener, 'Patentable Subject Matter Under Article 52(2) and (3) EPC: A Whitelist of Positive Cases from the EPO Boards of Appeal—Part 1' (2018) 13 *Journal of Intellectual Property Law & Practice* 13, 14; *Estimating Sales Activity/Duns Licensing Associates* (n 40); *Modellieren eines Prozessnetzwerks/Xpert* [2006] T 0930/05; Timo Minssen and Marc Mimler, 'Patenting Bioprinting-Technologies in the US and Europe – The 5th Element in the 3rd Dimension' in Rosa Maria Ballardini, Marcus Norrgård and Jouni Partanen (eds), *3D printing, Intellectual Property and Innovation – Insights from Law and Technology* (Wolters Kluwer, 2017); Jessica C Lai, 'Myriad Genetics and the BRCA Patents in Europe: The Implications of the U.S. Supreme Court Decision' (2015) 5 *UC Irvine Law Review* 1041, 1046.

[42] Lai (n 41) 1046; Justine Pila, 'Dispute over the Meaning of "Invention" in Article 52(2) EPC - The Patentability of Computer-Implemented Inventions in Europe' (2005) 36 *IIC: International Review of Industrial Property and Copyright Law* 173.

[43] Steinbrener (n 41) 15; Justine Pila, 'Article 52(2) of the Convention on the Grant of European Patents: What did the Framers Intend? A study of the Travaux Preparatoires' (2005) 36 *International Review of Intellectual Property and Competition Law* 755; Reinier B Bakels, 'Should Only Technical Inventions be Patentable, Following the European Example?' (2008) 7 *Northwestern Journal of Technology and Intellectual Property* 50, 55.

case relating to a claimed method aimed at 'identifying optimum fuel bundle loading arrangements in a nuclear reactor core' that

> [t]echnical character may be provided through the technical implementation of the method, resulting in the method providing a tangible, technical effect, such as the provision of a physical entity as the resulting product or a non-abstract activity, such as through the use of technical means.[44]

Thus, in the case under deliberation, it was noted that

> technical character would be provided through the technical implementation of the method, resulting in the method providing a tangible, technical effect, such as the provision of a physical entity, eg a reactor core loaded according to a given design, or a non-abstract activity, such as through the use of technical means. The claimed method, however, lacks such a technical implementation.[45]

It should, however, be noted that technical character does not imply any new contribution to prior art.[46] As provided for in the *EPC*, the requirements of invention, novelty, inventive step, and susceptibility of industrial application are separate and independent criteria which ought to be considered separately.[47] At the same time, it is useful to note that whilst the technical character of an invention may be determined without considering novelty, 'novelty and inventive step can only be established on the basis of the technical features of the invention'.[48]

Accordingly, some have noted that in light of the narrow approach adopted in interpreting the technical character requirement such that 'any technical aspect is sufficient to establish patent-eligibility', some fundamental issues pertaining to patentability as a whole have been transferred to the second hurdle of patentability.[49] This is especially in respect of the requirement of inventive step which is beyond the scope of this thesis to analyse in the context of bioprinted constructs, as such analysis is claim-dependent.[50]

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[44] T 0914/02 [2005] ('T 0914/02'); Steinbrener (n 41).
[45] T 0914/02 (n 44).
[46] *Estimating Sales Activity/Duns Licensing Associates* (n 40).
[47] Ibid.
[48] Ibid.
[49] Steinbrener (n 41) 14.
[50] Ibid; Lai (n 41) 1069.

Furthermore, with regard to the list contained in art 52(2), it has been repeatedly emphasised that art 52(3), which restricts the art 52(2) exclusions to 'such subject-matter or activities as such', exists solely to deter a broad interpretation of art 52(2).[51] In particular, art 52(3) was introduced to ensure that anything patentable in Contracting States prior to the *EPC* remained patentable under the *EPC*.[52] Thus, the non-exhaustive list of items contained in art 52(2) are only excluded when claimed 'as such', that is, in some kind of 'pure' form.[53]

This would seem to imply that 'mixed' inventions, comprising of both technical and non-technical features, are potentially eligible for patenting. According to the Boards of Appeal, it is possible for a non-technical feature to interact with technical elements so as to produce a technical effect, which should count as contribution to the technical character of invention.[54] Thus, given technical character is a legal requirement of invention, claimed inventions linked to items contained in art 52(2) are patent-eligible in so far as they have technical character.[55]

This position was further reinforced by the Enlarged Board of Appeal in a case involving the use of known compounds as friction reducing additives in lubricant compositions.[56] In that case, the Enlarged Board of Appeal noted that 'the fact that the idea or concept underlying the claimed subject-matter resides in a discovery does not necessarily mean that the claimed subject-matter is a discovery "as such"'. [57] It is only when the claimed invention relates to any of the items contained in art 52(2) 'as such' that the exclusion from patentability applies. Therefore, in order to ascertain whether an invention is claimed 'as such' further to art 52(2), the claim has to be construed so as to determine the technical features of the invention (that is, the features which contribute to the technical character of the invention).[58]

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[51] *Estimating Sales Activity/Duns Licensing Associates* (n 40); G 0002/12 [2016] OJ EPO A27.
[52] *Estimating Sales Activity/Duns Licensing Associates* (n 40).
[53] Steinbrener (n 41) 14.
[54] *Estimating Sales Activity/Duns Licensing Associates* (n 40).
[55] Ibid.
[56] *Friction reducing additive/Mobile Oil III* [1990] OJ EPO 4/93 ('*Friction reducing additive/Mobile Oil III*').
[57] Ibid.
[58] *Estimating Sales Activity/Duns Licensing Associates* (n 40); *Friction reducing additive/Mobile Oil III* (n 56).

In the context of biotechnology (which bioprinted constructs relate to given they comprise living cells),[59] it is equally important to consider the relevant portions of the *Implementing Regulations* dealing with biotechnological inventions. This is even more so as it has been noted that art 52(2)(a) of the *EPC* ought to be interpreted in accordance with rule 29(2) of the *Implementing Regulations*, which places emphasis on whether the invention as claimed has been obtained by a technical process.[60]

To this end, rule 27(a) of the *Implementing Regulations* provides that biotechnological inventions are patentable if they concern biological material[61] that is isolated from its natural environment or is produced by means of a technical process, even if it previously occurred in nature. Rule 29 further provides that

1) The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.
2) An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element'.[62]

Given earlier analysis of bioprinting and its origins in this thesis, it would appear that bioprinted constructs ordinarily satisfy the technical character requirement.[63] This is because bioprinting as a whole is connected with technical fields (such as the life sciences and engineering), and aimed at addressing the shortcomings of earlier technologies in those fields as well as the shortage of human tissue for *in vitro* research and clinical applications. Moreover, it is expected that claims for bioprinted constructs will contain technical features pertaining to the manner of fabrication which ought to satisfy the technical teaching requirement.

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[59] Biotechnological inventions are 'inventions which concern a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used': *Implementing Regulations* (n 24) rule 26 (2).
[60] *Mutation/University of Utah* [2008] T 0666/05 ('*Mutation/University of Utah*'); *Relaxin/Howard Florey Institute* [2002] T 0272/95 ('*Relaxin/Howard Florey Institute*').
[61] *Implementing Regulations* (n 24) rule 26(3) defines biological material as 'any material containing genetic information and capable of reproducing itself or being reproduced in a biological system'.
[62] Similar to *Biotech Directive* (n 25) art 5; *Breast and ovarian cancer/University of Utah* [2007] T 1213/05; *Method of diagnosis/University of Utah* [2008] T 0080/05; *Mutation/University of Utah* (n 60); *Relaxin/Howard Florey Institute* (n 60).
[63] Phoebe Li, '3D Bioprinting Technologies: Patents, Innovation and Access' (2015) 6 *Law, Innovation and Technology* 282; Minssen and Mimler (n 41).

With regard to the issue of bioprinted constructs embodying living cells which exist in nature, it has been noted that while substances occurring freely in nature are merely discoveries and consequently unpatentable, such could potentially be patent-eligible under certain circumstances.[64] In particular,

> if a substance found in nature has first to be isolated from its surroundings and a process for obtaining it is developed, that process is patentable. Moreover, if this substance can be properly characterised by its structure and it is new in the absolute sense of having no previously recognised existence, then the substance *per se* may be patentable.[65]

Thus, considering bioprinted constructs represent a significant departure from their starting points as living cells isolated from tissue samples, it is arguable that they have no previously recognised existence. Whilst they are designed to replicate their naturally occurring counterparts structurally and functionally, it is important to recall that bioprinted constructs are produced via a technical process that involves the use of artificial materials in addition to living cells and other natural materials. This act of human intervention as argued in the preceding chapter, ought to distinguish bioprinted constructs from their naturally occurring counterparts.

To the extent, however, that bioprinted constructs may embody embryonic stem cells, which appear excluded from patentability by virtue of rule 29(1), it is debatable whether constructs embodying such cells will be considered patentable subject matter. This is especially so when the provisions of rule 28(a)of the *Implementing Regulations* are considered. According to rule 28(a), patents shall not be granted in respect of biotechnological inventions which concern the uses of human embryos for industrial or commercial purposes. As this provision is in furtherance to art 53(a) of the *EPC* dealing with the *ordre public* and morality exclusion, further consideration of the patentability of bioprinted constructs embodying embryonic stem cells is reserved for that section of this chapter.[66]

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[64] *Howard Florey/Relaxin* [1995] EPOR 541; *Guidelines for Examination in the European Patent Office* (n 38) part G-II, para 3.1.
[65] *Howard Florey/Relaxin* (n 64).
[66] See below section 4.4.2.

4.3.2 Bioprinting Process Claims

As with the analysis on the patentability of bioprinted constructs under the *EPC*, it appears that the patentability of bioprinting process claims is equally to be determined by whether such processes have technical character. In addition, with bioprinting processes potentially being categorised as biotechnological inventions by virtue of rule 26(2)-(3) of the *Implementing Regulations*, the provisions of rule 27(c) are equally relevant in this regard. According to rule 27(c), biotechnological inventions concerning microbiological or other technical process, or a product obtained by means of such a process other than a plant or animal variety are patentable under the *EPC*.[67] The reference to technical processes, which is most relevant to bioprinting process claims, would seem to reinforce the technical character requirement earlier discussed.

In the preceding chapter, a number of bioprinting processes were identified and categorised into two distinct stages – fabrication and usage. Whereas processes identified under usage of the construct include methods of using bioprinted constructs in *in vitro* research and medical treatment of humans, processes under the fabrication stage include the isolation and cultivation of living cells, biological/cellular processes, preparation of materials, printing methods, and maturation of the finished construct.

To the extent that the patentability of methods of treatment is explicitly dealt with by the *EPC*, further consideration of their patentability is reserved for the relevant section of this chapter.[68] This would also apply to further analysis of biological processes involving embryonic stem cells.[69] Accordingly, this section focuses on the remaining processes which do not fall within the aforementioned exclusions from patentability. These include the use of bioprinted constructs in *in vitro* research, isolation and cultivation of living cells, cellular/biological processes, preparation of materials, printing methods, and maturation of the finished construct.

On the whole, it would appear that many of aforementioned bioprinting processes will likely satisfy the technical character requirement given they involve the use of technical means for a method.[70] This would arguably include claims relating to the isolation and

[67] *Broccoli/Plant Bioscience* [2012] OJ EPO 3/130; *Tomatoes/State of Israel* [2012] OJ EPO 3/206.
[68] See below section 4.4.1.
[69] See below section 4.4.2.
[70] T 0914/02 (n 44); Steinbrener (n 41); Minssen and Mimler (n 41).

cultivation of living cells, given the Enlarged Board of Appeal's comment that 'the fact that the idea or concept underlying the claimed subject-matter resides in a discovery does not necessarily mean that the claimed subject-matter is a discovery "as such"'. [71] Whilst the isolation and cultivation of living cells involve naturally occurring phenomena, there is also the technical aspect of isolating the cells and creating suitable conditions for their cultivation.

On the other hand, it is unlikely that cellular/biological processes in themselves will be considered eligible for patenting under the *EPC* since such processes would likely fall under the art 52(2)(a) exception.

4.4 Exceptions to Patentability

From the preceding section, it is apparent that bioprinted constructs and many related bioprinting processes are in themselves likely to satisfy the technical character requirement for patentable subject matter. Nevertheless, as with many biotechnological inventions, it would appear that the patentability of bioprinted constructs and related processes ultimately hinge on the exceptions contained in art 53(a), (c) of the *EPC* which provide thus:

> European patents shall not be granted in respect of:
>
> (a) inventions the commercial exploitation of which would be contrary to "ordre public" or morality; such exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States;
>
> (c) methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body; this provision shall not apply to products, in particular substances or compositions, for use in any of these methods.

Accordingly, this section examines the applicability of these exceptions to bioprinted constructs and related processes.

4.4.1 Methods of Treatment

Unlike Australia, but similar to art 27(3)(a) of the *TRIPS Agreement*, surgical, therapeutic and diagnostic methods for treatment of the human or animal body are expressly excluded

[71] *Friction reducing additive/Mobile Oil III* (n 56).

from patentability in Europe.[72] This does not, however, extend to products, in particular substances or compositions, used in any of these methods.[73] As noted by the Enlarged Board of Appeal, the provisions of art 53(c) are clear and unambiguous such that there is a distinction between method claims directed to therapeutic treatment and claims to products for use in such methods.[74] Whereas the latter are patentable provided they fulfil the other requirements of patentability such as novelty and inventiveness, the former are absolutely forbidden in order to allow physicians to act unfettered.[75] Accordingly, this provision does not appear to extend to bioprinted constructs in themselves, nor the printing apparatus.

It should be noted that the three alternative methods of treatment contained in art 53(c) (that is, surgical, therapeutic and diagnostic methods) are separate and different in scope. Thus, a method claim will be excluded from patentability under art 53(c) if it 'comprises or encompasses at least one feature defining a physical activity or action' that constitutes any of the listed three alternative methods of treatment.[76]

Perhaps, most relevant to bioprinting are surgical treatments and methods of therapy to a lesser extent. This is because methods of therapy concern 'the curing of a disease or malfunction of the human or animal body and cover prophylactic treatment such as immunisation against a certain disease'.[77] This could also potentially encompass treatments related to the implantation of bioprinted constructs. On the other hand, surgical treatments have been described by the Enlarged Board of Appeal as embracing 'those interventions which, whatever their specific purpose, give priority to maintaining life and health of the human or animal body on which they are performed' such as performing a lumbar puncture to deliver epidural injections.[78]

As bioprinting has the potential to be applied in human enhancement, it is important to emphasise that surgical treatments in the context of art 53(c) are not confined to surgical

[72] *EPC* (n 1) art 53(c).
[73] *EPC* (n 1) art 53(c).
[74] *Dosage regime/Abbott Respiratory* [2010] OJ EPO 10/456.
[75] Ibid.
[76] *Treatment by surgery/Medi-Physics* (G 0001/07) [2011] OJ EPO 3/134 ('*Treatment by surgery/Medi-Physics*').
[77] *Diagnostic methods* (G 0001/04) [2006] OJ EPO 5/334 ('*Diagnostic methods*').
[78] *Treatment by surgery/Medi-Physics* (n 76); *Diagnostic methods* (n 77).

methods pursuing a therapeutic purpose.[79] According to the Enlarged Board of Appeal, 'neither the legal history nor the object and purpose ("*ratio legis*") of the exclusions from patentability in Article 53(c) *EPC* justify a limitation of the term "treatment by surgery" to curative surgery'.[80] In particular, it noted that

> as regards serious and risky surgical interventions, e.g. in cosmetic surgery, organ transplantation, embryo transfer, sex change operations, sterilisation and castration, i.e. surgical methods which require considerable professional medical expertise to be carried out and involve serious health risks even when carried out with the required professional care and expertise, the ratio legis of the exclusion, i.e. to free practitioners from being potentially hampered by patents in the application of the best possible treatment on their patients, does apply, is important and calls for their exclusion from patentability.[81]

Furthermore, with regard to the level of interaction with the human or animal body contemplated by art 53(c), the Enlarged Board of Appeal has stated that this provision 'does not require a specific type and intensity of interaction with the human or animal body'.[82] It is therefore possible for such interaction to be either invasive or non-invasive.[83] However, method steps carried out *in vitro* in a laboratory without any interaction with the animal or human body are not excluded by virtue of art 53(c).[84]

Consequently, the Guidelines for Examination provide that unlike the exclusions in art 52(2)-(3) which apply if the subject matter is claimed as such:

> a method claim is not allowable under art 53(c) if it includes at least one feature defining a physical activity or action that constitutes a method step for treatment of the human or animal body by surgery or therapy. In that case, whether or not the claim includes or consists of features directed to a technical operation performed on a technical object is legally irrelevant to the application of art 53(c).[85]

This would seem to suggest that surgical procedures such as transplanting bioprinted constructs and bioprinting *in situ* are potentially excluded from patentability since they are

[79] *Treatment by surgery/Medi-Physics* (n 76).
[80] Ibid.
[81] Ibid.
[82] *Diagnostic methods* (n 77).
[83] Ibid.
[84] Ibid.
[85] *Guidelines for Examination in the European Patent Office* (n 38) part G-II, para 4.2.1; *Treatment by surgery/Medi-Physics* (n 76).

practised on the human body.[86] This is notwithstanding that bioprinting *in situ* in particular presents a novel approach to medical treatment, which would otherwise render it potentially patent-eligible. On the other hand, surgical methods performed on bioprinted constructs prior to implantation will, however, likely not be caught by this exception since they are not practised on the human body.[87]

Whilst bioprinting *in situ* is potentially excluded from patentability as a method of treatment because it is practised on the human body, another important consideration that would otherwise ground their exclusion under art 53(c) is the overall premise for the exception. According to the Enlarged Board of Appeal and the EPO, the rationale for excluding methods of treatment from patentability stems from socio-ethical and public health considerations in ensuring that medical practitioners are not constrained by patents in the performance of related duties.[88] Accordingly, if patents were to be granted for methods of bioprinting *in situ*, such a grant could potentially have the impact of limiting any form of printing *in situ* irrespective of the construct being printed or the type of printing apparatus used. In turn, this could compromise the quality of treatment received by patients since medical personnel would be overly cautious about the method of printing adopted even if the situation were to require otherwise. Allowing such a situation to occur would defeat the intent of excluding methods of treatment from patentability.

In the same vein, although the rationale for excluding methods of treatment is to ensure medical and veterinary practitioners are not constrained in their duties, it has been noted that methods of treatment excluded by virtue of art 53(c) are not restricted to those carried out by medical or veterinary practitioners.[89] Instead, the exclusion in art 53(c) is directed specifically to methods and not persons carrying out the method.[90] In the context of bioprinting, this would seem to imply that methods of treatment carried out by pre-programmed bioprinters are also caught by this provision in so far as they are carried out on the human or animal body.

[86] Li (n 63); Minssen and Mimler (n 41).
[87] Minssen and Mimler (n 41).
[88] *Guidelines for Examination in the European Patent Office* (n 38) part G-II, para 4.2.1; *Second medical indication/EISA* (G 0005/83) [1985] OJ EPO 3/64; *Diagnostic methods* (n 77); *Treatment by surgery/Medi-Physics* (n 76).
[89] *Diagnostic methods* (n 77).
[90] Ibid.

4.4.2 The *Ordre Public*/Morality Exclusion

Prior to the passage of the *EPC*, patent laws across Europe such as the *Austrian Law of August 1852* and the *Italian Patent Law of January 1864* excluded from patentability inventions considered contrary to existing law or incapable of being worked for reasons of public interest, health, morals or safety.[91] Indeed, at the time the *Strasbourg Convention* was being considered, all the European countries involved confirmed that ethical exclusions formed a part of their national patent laws.[92] This was further to a questionnaire distributed as part of the earlier mentioned comparative study undertaken by the Committee of Experts.[93] Amongst other things, member states had been asked to confirm whether inventions contrary to law and morality were excluded from patentability in their national patent laws.[94]

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[91] Lionel Bently et al, *Exclusions from Patentability and Exceptions and Limitations to Patentee's Rights: Introduction*, SCP/15/3 (2 September 2010) annex I <http://www.wipo.int/meetings/en/doc_details.jsp?doc_id=141352>.

[92] Committee of Experts on Patents, Council of Europe, 'Reply to the Questionnaire drawn up by the Bureau of the Committee of Experts on Patents, from the point of view of the Austrian legislation' (EXP/Brev (53) 16, 4 July 1953); Committee of Experts on Patents, Council of Europe, 'Reply to the Questionnaire drawn up by the Bureau of the Committee of Experts of the Council of Europe from the view point of the Danish legislation' (EXP/Brev (53) 11, 21 April 1953); Committee of Experts on Patents, Council of Europe, 'Reply to the Questionnaire drawn up by the Bureau of the Committee of Experts of the Council of Europe, from the point of view of the Dutch legislation' (EXP/Brev (53) 2, 15 January 1953); Committee of Experts on Patents, Council of Europe, 'Reply to the Questionnaire drawn up by the Bureau of the Committee of Experts from the point of view of the French legislation' (EXP/Brev (53) 4, 10 February 1953); Committee of Experts on Patents, Council of Europe, 'Reply to the Questionnaire drawn up by the Bureau of the Committee of Experts of the Council of Europe from the point of view of legislation in Greece' (EXP/Brev (53) 8, 31 March 1953); Committee of Experts on Patents, Council of Europe, 'Reply to the Questionnaire drawn up by the Bureau of the Committee of Experts of the Council of Europe from the point of view of legislation in Ireland' (EXP/Brev (53) 14, 15 May 1953); Committee of Experts on Patents, Council of Europe, 'Reply to the Questionnaire drawn up by the Bureau of the Committee of Experts of the Council of Europe, from the point of view of the Italian legislation' (EXP/Brev (53) 12, 7 May 1953); Committee of Experts on Patents, Council of Europe, 'Reply to the Questionnaire drawn up by the Bureau of the Committee of Experts on behalf of the Luxembourg legislation' (EXP/Brev (53) 5, 2 March 1953); Committee of Experts on Patents, Council of Europe, 'Reply to the Questionnaire drawn up by the Bureau of the Committee of Experts of the Council of Europe from the point of view of legislation in Norway' (EXP/Brev (53) 9, 7 April 1953); Committee of Experts on Patents, Council of Europe, 'Reply to the Questionnaire drawn up by the Bureau of the Committee of Experts of the Council of Europe, from the point of view of the Swedish legislation' (EXP/Brev (53) 10, 13 April 1953); Committee of Experts on Patents, Council of Europe, 'Reply given on the basis of the Swiss legislation to the Questionnaire drawn up by the Bureau of the Committee of Experts of the Council of Europe' (EXP/Brev (53) 6, 12 March 1953); Committee of Experts on Patents, Council of Europe, 'Reply to the Questionnaire drawn up by the Bureau of the Committee of Experts on Patents from the point of view of the Turkish legislation' (EXP/Brev (53) 15, 19 May 1953); Committee of Experts on Patents, Council of Europe, 'Reply to the Questionnaire drawn up by the Bureau of the Committee of Experts of the Council of Europe from the point of view of legislation in the United Kingdom' (EXP/Brev (53) 7, 17 March 1953); Committee of Experts on Patents, Council of Europe, 'Reply to the Questionnaire drawn up by the Bureau of the Committee of Experts from the point of view of the Belgian legislation' (EXP/Brev (53) 17, 12 August 1953).

[93] See above section 4.2.

[94] Committee of Experts on Patents, Council of Europe, 'Questionnaire drawn up by the Bureau of the Committee of Experts of the Council of Europe' (EXP/Brev (53) 3, 15 January 1953).

With member states confirming the existence and extent of a public interest/morality clause in their national laws, an *ordre public*/morality exclusion clause was included in the *Strasbourg Convention*. Article 2(a) of the *Strasbourg Convention* provides thus:

> The Contracting States shall not be bound to provide for the grant of patents in respect of:
>
> a. inventions the publication or exploitation of which would be contrary to *ordre public* or morality, provided that the exploitation shall not be deemed to be so contrary merely because it is prohibited by a law or regulation;[95]

It is from this provision that art 53(a) of the *EPC* derives its existence.[96] It provides as follows:

> European patents shall not be granted in respect of:
>
> (a) inventions the commercial exploitation of which would be contrary to "ordre public" or morality; such exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States;

Rule 28 of the *Implementing Regulations* further sets out a non-exhaustive list of biotechnological inventions excluded from patentability by virtue of art 53(a) namely:

a) processes for cloning human beings;
b) processes for modifying the germ line genetic identity of human beings;
c) uses of human embryos for industrial or commercial purposes; and
d) processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes.[97]

This section will now examine the interpretation of these provisions and their likely application to bioprinting.

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[95] It should be noted that the choice of the French term 'ordre public' to cover public interest concerns was to bring the *Strasbourg Convention* in line with the *European Convention on Establishment*, opened for signature 13 December 1955 ETS No 19 (entered into force 23 February 1965).

[96] Initially, the wordings contained in art 53(a) of the *EPC* were the same as art 2(a) of the *Strasbourg Convention*. However, in 2000, the provision was amended to bring it in line with art 27(2) of the *TRIPS Agreement* and art 6(1) of the *Biotech Directive*. Notwithstanding, the application still remains the same.

[97] Similar to *Biotech Directive* (n 25) art 6(2).

4.4.2.1 *European Patent Convention* art 53(a) - *Ordre Public* and Morality

At the time the *Strasbourg Convention* was drafted, it was proposed that the term '*ordre public'* be interpreted in a narrow sense or the sense generally given to it in continental countries.[98] Hence, the *Strasbourg Convention* did not propose any definition for the term, nor was there any proposed for the term 'morality'. The onus of interpretation was therefore left to national courts and patent offices which was perhaps logical given the absence of a consensus on the definition of either concept.[99]

Similarly, at the time the *EPC* was drafted, the *EPC* Working Party also elected not to define either term so as not to counter principles of national law.[100] This same attitude appears to have been maintained in the *Biotech Directive* and the *TRIPS Agreement*, which although containing similar provisions, equally do not provide any working definition for either concept.

It should be emphasised at this juncture that the terms *ordre public* and morality are two distinct concepts irrespective of any overlap that may seem to exist. As Beyleveld and Brownsword note, reading both concepts as synonyms ridicules the notion that the French concept of *ordre public* has no English equivalent.[101] Indeed, while earlier drafts of the *TRIPS Agreement* suggested the use of 'public order'*,* the feeling was that the phrase did not adequately capture the essence of the *ordre public* concept.[102] That is not to say the term cannot be explained, but rather it seems to embody a variety of concepts, for which there is no sufficiently descriptive term.

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[98] Committee of Experts on Patents, Council of Europe, 'Draft Report by the Committee of Experts to the Committee of Ministers on the Meeting held at Strasbourg from 2nd to 5th May 1961' (EXP/Brev (61) 2 Revised, 8 May 1961); Committee of Experts on Patents, Council of Europe, 'Revised Draft Report by the Committee of Experts to the Committee of Ministers on the Meeting held at Strasbourg from 2nd to 5th May 1961' (EXP/Brev (61) 2, 5 May 1961).
[99] See generally Deryck Beyleveld and Roger Brownsword, *Mice, Morality and Patents* (Common Law Institute of Intellectual Property, 1993) 53-74; *Plant Genetic Systems/Glutamine synthetase inhibitors* [1995] EPOR 357 ('*Plant Genetic Systems/Glutamine synthetase inhibitors*').
[100] Patents Working Party, European Economic Community, 'Proceedings of the 1st Meeting of the Patents Working Party held at Brussels from 17 to 28 April 1961' (IV/2767/61-E, 3 May 1961), 7-8.
[101] Beyleveld and Brownsword (n 99). See also UNCTAD-ICTSD, 'Patents: Ordre Public and Morality' in *Resource Book on TRIPS and Development* (Cambridge University Press, 2005) 375; Philip W Grubb and Peter R Thomsen, *Patents for Chemicals, Pharmaceuticals and Biotechnology* (Oxford University Press, 5th ed, 2010); Benjamin D Enerson, 'Protecting Society from Patently Offensive Inventions: The Risk of Reviving the Moral Utility Doctrine' (2004) 89 *Cornell Law Review* 685; *Plant Genetic Systems/Glutamine synthetase inhibitors* (n 99); Daniel Gervais, *The TRIPS Agreement: Drafting History and Analysis* (Thomson Reuters, 4th ed, 2012).
[102] Gervais (n 101) 435.

Nonetheless, the *ordre public* concept has been interpreted as akin to the English concept of 'public policy',[103] which 'concerns fundamentals from which one cannot deviate without endangering the institutions of a given society'.[104] According to the Technical Board of Appeal,[105] a generally accepted explanation of the *ordre public* concept is that it

> covers the protection of public security and the physical integrity of individuals as part of society. This concept encompasses also the protection of the environment. Accordingly, under Article 53(a) *EPC*, inventions the exploitation of which is likely to breach public peace or social order (for example, through acts of terrorism) or seriously to prejudice the environment are to be excluded from patentability as being contrary to 'ordre public'.[106]

In the same case, the Technical Board of Appeal also noted with regards to the concept of morality, that

> [t]he concept of morality is related to the belief that some behaviour is right and acceptable whereas other behaviour is wrong, this belief being founded on the totality of the accepted norms which are deeply rooted in a particular culture. For the purposes of the *EPC*, the culture in question is the culture inherent in European society and civilisation. Accordingly, under Article 53(a) *EPC*, inventions the exploitation of which is not in conformity with the conventionally-accepted standards of conduct pertaining to this culture are to be excluded from patentability as being contrary to morality.[107]

These statements were made in respect of an opposition lodged against a patent granted for inventions relating to herbicide-resistant plants and plant material on the grounds that such grant was contrary to art 53(a)-(b) and inherently unpatentable under art 52. With regard to patentability under art 53(a), the appellants argued the invention as claimed was contrary to *ordre public* because of the environmental concerns it posed, and contrary to morality because of concerns about the dominion by man over the natural world.

On the matter of *ordre public*, the Technical Board of Appeal found that no conclusive evidence had been presented to support the appellant's argument that the exploitation of

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[103] *Patents Act 1977* (UK) ss 1(3)-(4), which contains similar exclusions uses the term 'public policy' as opposed to '*ordre public*'.
[104] Gervais (n 101) 436.
[105] The Technical Boards of Appeal decide mainly on questions relating to the granting of and opposition to European patents under the *EPC*, but not on questions of patent infringement: *FAQ - Boards of Appeal* (n 20).
[106] *Plant Genetic Systems/Glutamine synthetase inhibitors* (n 99) 366 [5].
[107] Ibid 366 [6].

the invention would seriously prejudice the environment.[108] It noted that potential risks cannot be anticipated merely on the basis of disclosure in the patent specification.[109] In any event, the right to exploit patented inventions is often conditional upon regulatory approval which typically occurs after the grant of a patent when a realistic assessment of risks can take place.[110] On the matter of morality, the Technical Board of Appeal found that there was no indication of misuse or destructive use suggesting the invention was contrary to morality.[111] To this end, the invention as claimed was not caught by the provisions of art 53(a).

Further to the appellants' reliance on a survey and opinion poll to establish that the claim in dispute was objectionable under art 53(a), the Technical Board of Appeal noted that results of surveys and opinion polls are not determinative of patentability under art 53(a) because they are relative, susceptible to manipulation, biased and do not necessarily reflect *ordre public* concerns or moral norms. In any event, the fact that a section of people oppose the grant of a patent over a subject-matter is not a sufficient criterion for establishing contrariness under art 53(a) since an invention is not unpatentable simply because it is contrary to law.[112]

Additionally, in terms of what test to apply in determining whether a claimed invention is excluded from patentability by virtue of art 53(a), the Technical Board of Appeal emphasised that the tests utilised in the present case (the unacceptability test) and other cases considered below are not exhaustive or applicable in all cases as each case is to be decided on its merits.[113] The implication of this is that there is no general test for assessing patentability under art 53(a).

Earlier, in the *Oncomouse* case, Examiners from the EPO had to consider whether a patent application for a transgenic mouse developed for use in cancer research contravened the provisions of article 53(a). Initially, the Examining Decision refrained from addressing this issue under the notion that moral considerations had no place in patent law.[114] However,

[108] Ibid 372-373 [18.6]-[18.8].
[109] Ibid 371 [18.4].
[110] Ibid 371 [18.2] [18.4].
[111] Ibid 370 [17.1]-[17.3].
[112] Ibid 368-69 [15].
[113] Ibid 368 [13], 373 [18.8].
[114] *Harvard/Onco-mouse* [1990] 1 EPOR 4 ('*Harvard/Onco-mouse*').

upon remand of the case by the Technical Board of Appeal, the Examining Division was forced to consider whether the application had indeed violated article 53(a). Using the balancing test which weighs the benefit of an invention against its costs, the Examining Division concluded that the invention was not in contravention of art 53(a) as the anticipated benefits to humanity outweighed moral concerns about suffering caused to the animal.[115] Consequently, a patent was granted for the application despite controversies surrounding the invention.

The *Oncomouse* case is particularly instructive in the differing results produced in other jurisdictions silent on moral considerations in their patent laws. In the USA, the invention had been successfully patented prior to the European case. On the other hand, the invention was denied patent grant in Canada by the Supreme Court on the grounds that higher life forms are not patentable because they are neither a 'manufacture' or 'composition of matter' within the meaning of 'invention' in s 2 of its *Patent Act*.[116] According to the majority, the term 'manufacture' is generally understood as denoting a non-living mechanistic product/process in the context of the *Act*.[117] This would therefore exclude living creatures such as the Oncomouse. The majority also considered that the words 'composition of matter' as used in the *Act* do not encompass higher life forms such as the Oncomouse.[118] This is all the more so as the words follow 'art, process, machine and manufacture' and ought to be restricted to the same genus as those preceding words, which do not imply living creatures.[119]

Whilst the majority conceded that the fertilized, genetically altered Oncomouse egg was an invention, they denied the resulting Oncomouse was patentable because the biological process that followed was devoid of human intervention[120] - a logic the minority found untenable.[121] The majority pointed out that by adopting an exhaustive definition of invention as 'any new and useful art, process, machine, manufacture or composition of matter' as opposed to 'anything new and useful made by man', Parliament had not intended

[115] Ibid; *Transgenic animals/Harvard* [2006] O J EPO 1/15 ('*Transgenic animals/Harvard*').
[116] *Harvard College v Canada (Commissioner of Patents)* [2002] 4 SCR 45.
[117] Ibid.
[118] Ibid.
[119] Ibid.
[120] Ibid 126-27 [162].
[121] Ibid 59 [3].

for higher life forms to be patentable.[122] In any case, the *Act* was ill-equipped to deal with the challenges that arise from patenting higher life forms.[123]

This decision was however won by a slim majority (5-4) with the minority stating that the proper question was not whether Parliament intended to make higher life forms patentable (which they could not have foreseen at the time), but rather whether Parliament intended for the *Act* to extend to inventions not anticipated at the time of its enactment.[124] Since the intention was to encourage new and useful inventions, and the Commissioner of Patents had not been given discretion to refuse a patent on any grounds (including morality, public interest or public order), the minority were of the view that having met the statutory criteria, the respondents were 'by law' entitled to a patent for their invention.[125]

The minority's position in this matter appears to be more tenable given that whether or not Parliament could have foreseen patent applications for higher life forms, it could nevertheless have chosen to include moral considerations as part of the examination process. By choosing otherwise, it would appear that the intention was for inventions to be assessed solely by whether they fit within the *Act*'s definition of invention. It was not for the Court to import external factors for consideration even if it felt that the *Act* was ill-equipped to deal with the challenges that arise from patenting higher life forms. If the fertilized, genetically altered Oncomouse egg was deemed an invention, it is difficult to comprehend how the resulting Oncomouse was deemed otherwise. This would suggest that at some point between fertilization and maturation, the Oncomouse lost its status as an invention. The implication of this rather unsustainable conclusion is that it is possible for an invention to lose its status of patentability.

Returning to the interpretation of art 53(a), it is instructive to note that the balancing test adopted by the EPO in *Oncomouse* produced different results in an application for a transgenic mouse, which was to be used in testing products to treat human baldness.[126] A gene had been introduced into said mouse in order to induce baldness for this purpose.

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[122] Ibid.
[123] Ibid.
[124] Ibid 62[10].
[125] Ibid 62-3 [10].
[126] World Intellectual Property Organisation, 'Bioethics and Patent Law: The Case of the Oncomouse' (2006) (3) *WIPO Magazine* 16 ('Bioethics and Patent Law: The Case of the Oncomouse'); Robin Nott, 'The Biotech Directive: Does Europe Need A New Draft?' (1995) 17 *European Intellectual Property Review* 563, 565-6.

Weighing up the anticipated benefits of curing baldness and harm suffered by the mouse, the EPO concluded that the latter outweighed the former and, as such, the exploitation of the invention would be contrary to morality and could not therefore be eligible for patenting.[127] This case represents one of the few instances in which the morality clause has been successfully invoked,[128] which is unsurprising given the official stance of the EPO that the exception 'is likely to be [successfully] invoked only in rare and extreme cases'.[129]

In its approach to assessing whether an invention has violated art 53(a), the EPO has emphasised that balancing competing interests is only one of many tests that may be applied.[130] According to the EPO, 'a fair test to apply is to consider whether it is probable that the public in general would regard the invention as so abhorrent that the grant of patent rights would be inconceivable'.[131] In *Howard Florey/Relaxin*, the Opposition Division suggested that an invention which would satisfy this criteria is one that involves 'the patenting of human life, abuse of pregnant women, a return to slavery and the piecemeal sale of women to industry'.[132] This was further to the opponents' contention that 'the subject-matter of the disputed patent, insofar as it relates to a DNA fragment encoding human H2-relaxin and its precursors, offends against the provisions of Article 53(a)'.[133]

However, with regard to the assertion concerning slavery, the Opposition Division characterised the argument as betraying a fundamental misunderstanding of the effects of patents.[134] Patents confer exclusive rights over a patented invention for a limited period. Patents over human genes or products do not confer any right whatsoever to individual human beings.[135] Neither does the patenting of a human gene correspond to the patenting of human life as it would be impossible to recreate a human being from all its genes even if said genes were cloned and patented.[136] More so as 'DNA is not "life", but a chemical

[127] 'Bioethics and Patent Law: The Case of the Oncomouse' (n 126); Nott (n 126) 565-6.
[128] The ordre public/morality exception was unsuccessfully raised in *Plant Genetic Systems/Glutamine synthetase inhibitors* (n 99); *Howard Florey/Relaxin* (n 64).
[129] *Guidelines for Examination in the European Patent Office* (n 38) part G-II, para 4.1.
[130] *Plant Genetic Systems/Glutamine synthetase inhibitors* (n 99) 373 [18.8].
[131] *Guidelines for Examination in the European Patent Office* (n 38) part G-II, para 4.1.
[132] *Howard Florey/Relaxin* (n 64) 550 [6.3].
[133] Ibid 540 [6.1].
[134] Ibid 550-51 [6.3.3].
[135] Ibid.
[136] Ibid 551 [6.3.4].

substance which carries genetic information and can be used as an intermediate in the production of proteins which may be medically useful'.[137]

The different tests (that is, the unacceptability, balancing and the public abhorrence tests) referred to in the aforementioned cases reflect the difficulty inherent in formulating an accepted standard of morality for patentable subject matter.[138] This is perhaps unsurprising owing to many suggestions that examiners lack the technical expertise to consider matters of morality given their training lies in evaluating the technical merits of inventions.[139] In addition, Bagley also states that the tests are possibly unequal in ranking with the public abhorrence test posing the lowest hurdle to cross.[140] This is given the fact that very few inventions will be considered abhorrent as opposed to simply unacceptable.[141] On the other hand, the balancing test would likely pose the most difficult hurdle to cross given it requires evidence of concrete social disadvantages of the invention in order for it to be applied.[142]

Thus, while it is arguable that moral considerations should be taken into account in the granting of a patent, since it affords a state-sanctioned monopoly and should therefore be reflective of societal values,[143] it is questionable whether such balance between science and culture can truly be achieved, given interpretation of these exclusions has proven difficult in practice as evidenced by case law.[144] Moreover, while social, cultural, ethical and religious values may provide some insight into what a society considers morally acceptable, it should be noted that such values are not necessarily shared by every person within that society. This is especially as attitudes towards the patentability of certain technologies are often informed by personal beliefs, understanding of the technology as well as the context in which such questions about patentability are being asked.[145]

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[137] Ibid.
[138] Margo A Bagley, 'Patent First Ask Questions Later: Morality and Biotechnology in Patent Law' (2003) 45 *William & Mary Law Review* 469, 524; Llewelyn (n 35) 122.
[139] Minssen and Mimler (n 41); Evisa Kica and Nico Groenendijk, 'The European Patent System: Dealing With Emerging Technologies' (2011) 24 *Innovation: The European Journal of Social Science Research* 85, 87.
[140] Bagley (n 138) 523-4.
[141] Ibid 523-4.
[142] Ibid 523-4.
[143] Li (n 63); Kica and Groenendijk (n 139); Cynthia M Ho, 'Splicing Morality and Patent Law: Issues Arising from Mixing Mice and Men' (2000) 2 *Washington University Journal of Law and Policy* 247
[144] Kica and Groenendijk (n 139) 87; Ho (n 143).
[145] *Howard Florey/Relaxin* (n 64) 552 [6.4.4].

Moreover, the categorisation of what constitutes an immoral or morally acceptable invention is relative to time and space. That which was previously considered immoral could potentially be considered morally acceptable at a later date as evidenced by previous attitudes to the use of contraceptives in some countries.[146] As noted in the preceding chapter, refusing a patent over an invention does not prevent said invention from being commercially exploited. Rather, it only prevents such inventions from being commercially exploited with the backing of state-sanctioned monopolies.[147] In any case, it is impractical to ascertain morality at the time of invention as no one can say with certainty how an invention will be exploited.

Although it was hoped that the *Biotech Directive* might clarify the assessment of morality standards especially as the foregoing cases were decided prior to its enactment, this does not appear to be the case. This is because whilst art 6(2) of the *Biotech Directive* expanded on art 53(a) of the *EPC* by providing a non-exhaustive list of inventions that would violate art 53(a), art 6(1) of the *Biotech Directive* adopted language similar to art 53(a) of the *EPC*, which in itself had proven difficult to apply.[148] In fact, some commentators have suggested that rather than clarify the interpretation of the *ordre public*/morality exclusion, the inclusion of specific inventions to be prohibited has only created more uncertainty.[149] This is in light of the fact that subject to an amendment (which will most likely be difficult to achieve given the historical background of the *Biotech Directive*), their inclusion in the *Directive* creates an almost permanent bar to the future patentability of such inventions irrespective of prevailing moral attitudes at the time.[150]

Nevertheless, in the absence of an objective standard of assessing the concepts of *ordre public* and morality, it is possible that the rationale for their inclusion in patent legislations might offer some assistance in their interpretation. Thus, while the *TRIPS Agreement* and the *EPC* are silent on the rationale for introducing the *ordre public*/morality exception, it should be noted that recitals 16 and 38 of the *Biotech Directive* allude to the protection of

[146] Nott (n 126) 565; Ho (n 143) 281-2.
[147] Nott (n 126) 565; Ho (n 143) 285; Lydia Nenow, 'To Patent or Not to Patent: The European Union's New Biotech Directive' (2001) 23 *Houston Journal of International Law* 569.
[148] Ho (n 143) 274; Llewelyn (n 35) 122; Nenow (n 147) 593.
[149] Ho (n 143) 281-2, 284; Llewelyn (n 35) 122; Nenow (n 147) 593-4.
[150] Ho (n 143) 281-2, 284; Llewelyn (n 35) 122; Nenow (n 147) 593-4.

human dignity and integrity.[151] Additionally, the EPO also notes that the purpose of this exception is to deny protection to inventions likely to induce riot or public disorder, or to lead to criminal or other generally offensive behaviour.[152]

Therefore, in evaluating the patentability of bioprinted constructs and related bioprinting processes, it is important to consider whether the grant of a patent would be an affront to the protection of human dignity and integrity. This is notwithstanding that some commentators have questioned the extent to which recitals 16 and 38 of the *Biotech Directive* would influence the interpretation of art 53(a) given their non-inclusion in the substantive text particularly in light of the list contained in art 6(2).[153] In addition, it is equally important to consider whether the existence of bioprinted constructs and related bioprinting processes have the propensity to incite generally offensive behaviour. Before considering this, however, it is useful to examine how rule 28 of the *Implementing Regulations* which pertain to the application of art 53(a) to biotechnological inventions has been interpreted and applied.

4.4.2.2 *Implementing Regulations* to the *EPC* rule 28 - Biotechnological Inventions

As noted earlier, it is arguable whether the subsequent inclusion of examples of inventions excluded under art 53(a) through the implementation of the *Biotech Directive* has resolved questions of what constitutes an acceptable standard of morality.[154] Not only are the *Implementing Regulations* silent on the morality test applied to arrive at these examples, some of the terms used such as 'human embryo' have proven particularly challenging to define.[155]

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[151] *Biotech Directive* (n 25) recitals 16, 38.
[152] *Guidelines for Examination in the European Patent Office* (n 38) part G-II, para 4.1.
[153] Ho (n 143) 279.
[154] See above section 4.4.2.1.
[155] See generally *International Stem Cell Corporation v Comptroller General of Patents* (C-364/13) [2015] OJ C 65/7 ('*International Stem Cell Corporation*'); *Oliver Brüstle v Greenpeace eV* (C-34/10) [2011] ECR I-9849 ('*Brüstle*'); Tony Howard, 'The Legal Framework Surrounding Patents for Living Materials' in Johanna Gibson (ed), *Patenting Lives: Life Patents, Culture and Development* (Ashgate, 2008) 9, 18; Martin Heyer and Tade Matthias Spranger, 'The European Court of Justice's Decision Regarding the Brüstle Patent and Its Implications for the Legality of Stem Cell Research Within the European Union' (2013) 22 *Stem Cells and Development* 50; Ella O'Sullivan, 'International Stem Cell Corp v Comptroller General of Patents: The Debate Regarding the Definition of the Human Embryo Continues' (2014) 36(3) *European Intellectual Property Review* 155; Sigrid Sterckx, 'The WARF/Stem Cells Case Before the EPO Enlarged Board of Appeal' (2008) 30(12) *European Intellectual Property Review* 535; Julian Hitchcock and Clara Sattler de Sousa e Brito, 'Should Patents Determine When Life Begins?' (2014) 36(6) *European Intellectual Property Review* 390; Paolo Stazi, 'European Union: Comment on "International Stem Cell": The EU Court of Justice Revisits the Patentability of Processes for the Production of Human Stem Cells' (2015) 46(6) *International Review of Intellectual Property and Competition Law* 740.

While it does not claim to be an exhaustive list, rule 28 of the *Implementing Regulations,* which is a restatement of art 6(2) of the *Biotech Directive,* is focused solely on biotechnological inventions to the exclusion of other types of inventions that could potentially be problematic. Out of all the exclusions listed, para (c), dealing with uses of human embryos for industrial or commercial purposes, appears to be the only exclusion relevant to bioprinting and as such will be the focus of this section.[156]

In order to ascertain its application to bioprinting given the possible use of embryonic stem cells, it is important to first understand what constitutes a 'human embryo'. In the absence of a definition contained in the *EPC*, the Court of Justice of the European Union ('CJEU')[157] was confronted with the task of interpreting this concept, amongst other things, in *Oliver Brüstle v Greenpeace eV* ('*Brüstle*').[158]

In that case, the CJEU ruled that the concept of the human embryo must be understood in a wide sense as covering any human ovum as soon as it is fertilised, since fertilisation marks the commencement of the process of development of a human being.[159] Accordingly, it defined the term as including 'a non-fertilised human ovum into which the cell nucleus from a mature human cell has been transplanted and a non-fertilised human ovum whose division and further development have been stimulated by parthenogenesis'.[160] This definition was formulated based on the expert evidence before the court, which indicated that the ovum in question appeared 'capable of commencing the process of development of a human being', due to the effect of the technique used to obtain it.[161] The CJEU also added that an invention is not patentable in Europe if its implementation requires the prior destruction of human embryos or their prior use as starting material.[162]

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[156] Minssen and Mimler (n 41); Li (n 63).
[157] The CJEU is responsible for interpreting European Union ('EU') laws such as the *Biotech Directive* in order to ensure harmonious application across all EU countries: 'Court of Justice of the European Union (CJEU)', *European Union* (Web Page, 26 March 2020) <https://europa.eu/european-union/about-eu/institutions-bodies/court-justice_en>.
[158] *Brüstle* (n 155): The CJEU was actually called to interpret *Biotech Directive* (n 25) art 6(2).
[159] Ibid.
[160] Ibid.
[161] The CJEU, however, failed to rule on whether a stem cell obtained from a human embryo at the blastocyst stage constitutes a 'human embryo' within the meaning of *Biotech Directive* (n 25) art 6(2)(c), but instead referred the interpretation back to the referring court.
[162] *Brüstle* (n 155).

However, in *International Stem Cell Corporation*,[163] the CJEU clarified its position on the status of parthenogenetically-activated oocytes.[164] It held that their classification as human embryo is dependent on whether they possess the inherent capacity of developing into a human being. If they lack such capacity, then they do not constitute human embryos. In *Brüstle*, the expert opinion presented had showed that the human parthenote used was capable of developing into a human being. However, in the current case, the information provided showed that a human parthenote, by virtue of the technique used in its production, is incapable of commencing the process of developing into a human being. It was ultimately for the referring court to determine whether the human parthenote used in this case had the inherent capacity to develop into a human being.

It would thus appear that the CJEU adopted a definition similar to that of Australia in that the status of an embryo is dependent on its capacity to develop into a human being.[165] Nevertheless, it is worthy to note at this juncture that by virtue of its wording, the application of rule 28(c) would appear broader than the equivalent Australian provision. Whereas rule 28(c) refers to 'uses of human embryos for industrial or commercial purposes', s 18 (2) *Patents Act 1990* (Cth) refers to 'human beings and the biological processes for their generation'.

This would seem to imply that inventions embodying embryos are not exempted from patentability in Australia by virtue of s 18(2). However, it should be recalled that IP Australia has advised that such an interpretation would be 'inconsistent with the intended purpose of s 18(2) if the inclusion of additional steps following the production of a human being or human embryo resulted in the claim circumventing the s 18(2) exclusion'.[166] Accordingly, it would appear that differences in legislative provisions notwithstanding, s

[163] *International Stem Cell Corporation* (n 155).
[164] Parthenogenesis refers to 'the production of an embryo from a female gamete without any genetic contribution from a male gamete and with or without eventual development into an adult'. Thus, parthenogenetically-activated oocytes are oocytes (immature ovum) which have been artificially stimulated under non-sperm conditions using parthenogenetic activation technology. This provides an alternative source of embryo for experimental research: R A Reatty, 'Parthenogenesis in Vertebrates' in C B Metz and Monroy A (eds), *Fertilization* (Academic Press, 1967) vol I, 413; Bao-Sheng Han and Jun-Ling Gao, 'Effects of Chemical Combinations on the Parthenogenetic Activation of Mouse Oocytes' (2013) 5 *Experimental and Therapeutic Medicine* 1281.
[165] See chapter 3 (3.4.6).
[166] *Re International Stem Cell Corp* (2016) 123 IPR 142, 146 [22].

18(2) and rule 28(c) are likely to be applied in a manner that results in inventions embodying embryonic stem cells being excluded from patentability.

Under the *EPC*, this would mean that bioprinted constructs and related bioprinting processes may potentially be excluded from patentability if they involve the use of embryonic stem cells.[167] However, as noted in chapter three, it is unlikely that claims for either bioprinted constructs or related bioprinting processes will necessarily include a step involving the production of embryonic stem cells. This is because bioprinted constructs and related bioprinting processes operate independently of the stem cell types used, as opposed to the claimed inventions in *International Stem Cell Corporation and Brüstle*, which were directly linked to the production of embryonic stem cells. Moreover, as others have noted, the exclusion in rule 28(c) is limited to human embryonic stem cells and does not extend to non-human stem cells or non-embryonic stem cells.[168] To this end, it is uncertain the extent to which rule 28(c) will affect the patentability of bioprinted constructs and related bioprinting processes especially if there is no reference to the stem cell types used in the claims.

4.4.2.3 Applying the *Ordre Public*/Morality Exclusion Clause to Bioprinted Constructs and Related Bioprinting Processes

Although there are specific exclusions directed towards biotechnological inventions, these exceptions do not appear likely to have any significant impact on the patentability of bioprinted constructs and related bioprinting processes. This is largely due to the fact that while such bioprinting-related inventions may embody embryonic stem cells, which appear to be the focus of the biotechnological exceptions, their existence is not dependent on embryonic stem cells, given the variety of stem cells available for use (such as xenogeneic, adult/somatic or induced pluripotent stem cells).

Accordingly, art 53(a) remains a predominant factor in the patentability of bioprinted constructs and related bioprinting processes. This is further to comments by the EPO that where an invention does not fall under one of the aforementioned categories, it must be

[167] Minssen and Mimler (n 41); Li (n 63).
[168] See, eg, Andrew Sheard, 'Patenting Stem Cell Technologies in Europe' (2014) 5(3) *Cold Spring Harbor Perspectives in Medicine* a021089.

examined more closely under the *ordre public* or morality exception.[169] The challenge, however, with excluding either invention on the grounds of *ordre public*/morality is that bioprinted constructs and related bioprinting processes are undoubtedly beneficial.

From the aforementioned cases, it is apparent that an invention otherwise considered objectionable will be considered patent eligible if there is at least one beneficial use which outweighs any risk.[170] As is evident from previous explanations about the potential applications of bioprinting, bioprinted constructs and related bioprinting processes arguably satisfy this requirement. This is especially because unlike the aforementioned cases which were concerned with suffering to animals and the environment, the use of bioprinted constructs either in *in vitro* research or clinical applications do not appear to contemplate suffering to humans much more the environment. Bioprinting goes beyond mere experimentation on animals to fabricating constructs that could potentially be implanted in humans. Whilst there are present concerns about the safety and efficacy of bioprinted constructs particularly as relates to implantation in humans, it is unlikely that bioprinted constructs will be implanted in humans if they pose a risk. At the same time, their use in *in vitro* research also requires a minimum level of safety given the results from such research will likely be translated into clinical applications in the form of cosmetics, drugs or medical treatment. This is notwithstanding that safety cannot reasonably be ascertained at the point of patent grant.

Furthermore, it is questionable whether the grant of a patent for bioprinted constructs in particular can be equated with actions such as slavery, torture and rape which are considered affront to the protection of human dignity and integrity so as to justify an exception from patentability. Like DNA, bioprinted constructs are neither 'life' or 'humans' against whom these actions may be perpetrated. While the grant of a patent certainly raises concerns about monopolising and commercialising body parts, it has been argued in this thesis that unlike naturally occurring body parts, bioprinted constructs are artificial creations notwithstanding the use of living cells and reliance on biological processes. Considering that the *EPC* permits the grant of patents for elements (including gene

[169] See also *Biotech Directive* (n 25) recital 38; *Harvard/Onco-mouse* (n 114); *Use of embryos/WARF* [2009] O J EPO 5/306.
[170] *Harvard/Onco-mouse* (n 114); *Transgenic animals/Harvard* (n 115); *Plant Genetic Systems/Glutamine synthetase inhibitors* (n 99).

sequences) isolated from the human body or otherwise produced by means of a technical process, it is difficult to justify how the patenting of bioprinted constructs would be an affront to the protection of human dignity and integrity whilst the patenting of elements isolated from the body is acceptable. More so as the exclusive rights afforded by the grant of patents are limited to the patented invention for a period of time.

Whether or not patents are granted, there will likely be a strong demand for bioprinting-related inventions as a whole. In addition, it is unlikely that there will be any objection to consideration being charged for bioprinted constructs given all that is involved in their fabrication. This is so even in countries where payment for tissues or organs is considered abhorrent.

Thus, as it stands, it is unlikely that art 53(a) would be sufficient grounds to justify an exclusion of bioprinted constructs and related bioprinting processes from patentability.

4.5 Conclusion

For an invention to constitute patentable subject matter under the *EPC*, it must satisfy the technical character requirement. Given previous analysis about the nature of bioprinting, it would appear that bioprinted constructs and related bioprinting processes ordinarily satisfy this technical character requirement and are as such patentable subject matter. This result would appear to coincide with the conclusion reached under the Australian analysis. Whilst the requirement for patentable subject matter in Australia is predicated on establishing the invention is a 'manner of manufacture', the creation of something artificial involving human intervention appears to underlie the patentable subject matter requirement in both jurisdictions.

Similarly, bioprinting-related inventions embodying the use of embryonic stem cells which have the capacity to develop into human beings are potentially excluded from patentability under the *EPC* as in Australia. The difficulty with this, however, is that while bioprinted constructs and related bioprinting processes may involve the use of embryonic stem cells, their operation is independent of the cell type used. As such it is possible there is no indication of specific cell types contained in patent claims. The emphasis in patent claims will likely be on the fabrication process and the finished construct as opposed to the origin of every single element used.

Nevertheless, there appears to be a departure between the Australian and *EPC* position regarding methods of treatment, which is unsurprising given the *EPC* expressly excludes methods of treatment unlike Australia. Thus, whilst the position regarding the patentability of methods of treatment particularly *in situ* bioprinting remains uncertain in Australia, bioprinting methods of treatment including *in situ* bioprinting are potentially excluded from patentability under the *EPC* in so far as they are practised on the human or animal body.

While it might appear that the *ordre* public/morality exception might have more force compared to the Australian 'general inconvenience' provision in grounding an exception from patentability for bioprinted constructs, given particular concerns about the potential impact of their patenting, the evidence seems to suggest otherwise. Since inception, there have only been few instances where the *ordre* public/morality exception was successfully invoked. In fact, the EPO has acknowledged that it expects that the exception will only be successfully invoked in rare and extreme cases. Given the potential applications of bioprinting, this does not appear to be one of such extreme cases.

To this end, it would appear that the existence of a morality exclusion clause in the *EPC* has not produced results significantly different to that of Australia in terms of patentability. In fact, the only difference in patentability between both jurisdictions is that methods of treatment are specifically excluded under the *EPC*. In other respects, the results are the same notwithstanding variations in legislative provisions.

Chapter 5

5 State of the Law on Patentability – United States of America

5.1 Introduction

So far, with the exception of methods of medical treatment, it would appear that the differences between the Australian and the *European Patent Convention* ('*EPC*')[1] legislative provisions on patentability have had limited impact on the patentability or otherwise of bioprinted constructs and related bioprinting processes. In general, bioprinted constructs and related bioprinting processes appear to satisfy the patentable subject matter requirements in both jurisdictions to the extent that they do not embody embryonic stem cells. Additionally, despite concerns about the morality of patenting bioprinted constructs given its approximation to patenting life forms and human cloning, neither the general inconvenience proviso in Australia nor the *ordre public*/morality exception in the *EPC* appear sufficient to ground an exception for bioprinted constructs.

To this end, a review of the patent eligibility requirements in the United States of America ('USA') offers a useful opportunity to not only ascertain the patentability of bioprinted constructs and related bioprinting processes in that jurisdiction, but to also consider the impact any variation in legislative provisions might have on their patentability in comparison to Australia and the *EPC*. This is especially in view of the USA's perceived liberal approach to granting biotechnology patents on the one hand,[2] and recent judicial pronouncements which may potentially negate said liberal approach on the other hand.[3]

Given the USA's apparent openness to granting biotechnology patents, it is useful to begin this chapter with a historical background of the country's patent system. In itself, this allows for greater understanding of the USA's patent system and recent developments in that regard. Thereafter, this chapter considers the threshold for patentable subject matter

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[1] *Convention on the Grant of European Patents*, signed 5 October 1973, 1065 UNTS 255 (entered into force 7 October 1977).

[2] Eda Kranakis, 'Patents and Power: European Patent-System Integration in the Context of Globalization' (2007) 48 *Technology and Culture* 689, 721-2; Robin Whaite and Nigel Jones, 'Biotechnological Patents in Europe - The Draft Directive' (1989) 11 *European Intellectual Property Review* 145, 145.

[3] *Association for Molecular Pathology v Myriad Genetics Inc,* 569 US 576 (2013) ('*AMP*'); *Illumina Inc v Ariosa Diagnostics Inc*, 952 F 3d 1367 (Fed Cir, 2020) ('*Illumina Inc*'); *In re Roslin Institute (Edinburgh)*, 750 F 3d 1333 (Fed Cir, 2014) ('*In re Roslin Institute*'); *Mayo Collaborative Services v Prometheus Laboratories Inc*, 566 US 66 (2012) ('*Mayo*').

in the USA, and examines the patentability of bioprinted constructs and related bioprinting processes against the established threshold.

It should be emphasised from the onset, however, that unlike Australia and the *EPC*, the USA does not explicitly provide for an ethically informed exclusion clause. Neither does it provide a method of medical treatment exception.[4] At best, there exists the judicially created concept of 'moral utility' and the recently passed *Leahy-Smith America Invents Act* ('*AIA*'), which provides that claims directed to or encompassing human organisms (including human embryos and foetuses) are ineligible for patent protection.[5] Accordingly, the section on exceptions to patentability focuses primarily on the concept of 'moral utility' and the *AIA*.

Effectively, this chapter sums up the analysis on the patentability of bioprinted constructs and related bioprinting processes in the three jurisdictions under consideration. It concludes that while bioprinted constructs and related bioprinting processes may otherwise be patent eligible subject matter in the USA, recent developments in that country appears to place their patentability in doubt. This is especially surprising given that the USA's historical acceptance of biotechnology patents has long influenced other jurisdictions' approach to biotechnology patents.

5.2 The Patent System in the United States of America

Long before the first *Patent Act* titled '*An Act to promote the progress of useful Arts*' was passed by the United States Congress in 1790,[6] private exclusive rights over inventions were granted by colonial governments to inventors.[7] This included the exclusive right to utilise a new process of making salt for 10 years granted to Samuel Wilson by the Massachusetts General Court in 1641, which is often described as the first patent granted in America.[8]

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[4] Although 35 USC § 287(c) exempts from infringement a medical practitioner or related health care entity's performance of a medical activity, the term 'medical activity' is however limited to the performance of a medical or surgical procedure on a body and does not include: (i) the use of a patented machine, manufacture, or composition of matter in violation of such patent; (ii) the practice of a patented use of a composition of matter in violation of such patent; or (iii) the practice of a process in violation of a biotechnology patent. 35 USC § 287(2)(A).

[5] *Leahy-Smith America Invents Act*, Pub L No 112–29 § 33, 125 Stat 284, 340 (2012) ('*AIA*').

[6] *Patent Act*, Ch 7, 1 Stat 109, 109-112 (1790).

[7] Herbert J Hovenkamp, 'The Emergence of Classical American Patent Law' (2016) 58 *Arizona Law Review* 263, 267

[8] United States Census Office, *Manufactures of the United States in 1860; Compiled from the Original Returns of the Eighth Census, Under the Direction of the Secretary of the Interior* (Government Printing Office, 1865); Lucy Eisenberg, 'The Origins of Patent and Copyright Law' (2008) 23 *Bill of Rights in Action* .

Thereafter, with increasing requests for the grant of exclusive rights, it was considered more prudent to develop standardised laws governing the grant of such exclusive rights.[9] This culminated in the enactment of general patent laws by individual states - the first of which was passed by the state of South Carolina in 1784 titled '*An Act for the Encouragement of Arts and Sciences*'.[10] Although the primary focus of the Act was the protection of literary property, it also provided that '[i]nventors of useful machines shall have a like exclusive privilege of making or vending their machines for the like term of 14 years, under the same privileges and restrictions hereby granted to, and imposed on, the authors of books'.[11]

However, whilst patent grants continued to increase in the 1780s, with many states granting patents on similar terms for a period of mostly 14 years, it became apparent that a national patent system was required to simplify the application process and reduce costs.[12] Accordingly, when the Constitutional Convention convened in 1787 to amend the Articles of Confederation, an intellectual property clause was included in the new *United States Constitution* signed later that year.[13] It provided that '[t]he Congress shall have power ... To promote the progress of science and useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries'.[14]

Subsequently, the first *Patent Act* was passed by the United States Congress in 1790. This was further to the address to Congress by the new president, George Washington, who said 'that you will agree with me in opinion that there is nothing which can better deserve your patronage than the promotion of science and literature'.[15] Section 1 of the *Act* provided that

> upon the petition of any person or persons to the Secretary of State, the Secretary or the department of war, and the Attorney General of the United States, setting forth, that he, she, or they, *hath or have invented or discovered any useful art, manufacture, engine, machine, or device, or any improvement therein not before known or used*, and praying that a patent may be granted therefor, it shall and may be lawful to and for the said Secretary of State, the Secretary for

[9] Eisenberg, 'The Origins of Patent and Copyright Law' (n 8).
[10] Ibid; 'Historical Notes' (1908) 9 *The South Carolina Historical and Genealogical Magazine* 55.
[11] Eisenberg, 'The Origins of Patent and Copyright Law' (n 8).
[12] Ibid.
[13] Ibid.
[14] *United States Constitution* art I § 8 cl 8.
[15] Gerhard Peters and John T Woolley, 'George Washington, First Annual Address to Congress', *The American Presidency Project* (Web Page) <https://www.presidency.ucsb.edu/node/203158>.

> the department of war, and the Attorney General, or any two of them, if they shall deem the invention or discovery *sufficiently useful and important*, to cause letters patent to be made out in the name of the United States, to bear teste by the President of the United States, reciting the allegations and suggestions of the said petition, and describing the said invention or discovery, clearly, truly and fully, and thereupon granting to such petitioner or petitioners, his, her or their heirs, administrators or assigns *for any term not exceeding fourteen years, the sole and exclusive right and liberty of making, constructing, using and vending to others to be used, the said invention or discovery* …[16]

Over time, the definition of statutory subject evolved such that in 1793, the *Patent Act* provided that

> when any person or persons, being a citizen or citizens of the United States, shall allege that he or they *have invented any new and useful art, machine, manufacture or composition of matter, or any new and useful improvement on any art, machine, manufacture or composition of matter, not known or used before the application*, …[17]

Subsequently, in 1836, the *Patent Act* was amended to read:

> That any person or persons *having discovered or invented any new and useful art, machine, manufacture, or composition of matter, or any new and useful improvement on any art, machine, manufacture, or composition of matter, not known or used by others before his or their discovery or invention thereof*, and not, at the time of his application for a patent, in public use or on sale, with his consent or allowance, as the inventor or discoverer; and shall desire to obtain an exclusive property therein, …[18]

By 1952, the word 'art' was replaced with the word 'process' and § 101 of the *Patent Act* provided 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.[19]

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[16] *Patent Act*, Ch 7, § 1, 1 Stat 109, 110 (1790) (emphasis added).
[17] *Patent Act*, Ch 11, § 1, 1 Stat 318, 318-321 (1793) (emphasis added).
[18] *Patent Act*, Ch 357, § 6, 5 Stat 117, 119 (1836) (emphasis added); A similar definition was contained in *Patent Act*, Ch 230, § 24, 16 Stat 198, 201 (1870).
[19] Whereby 'invention' means 'invention or discovery', and 'process' means 'process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material': *Patent Act*, Ch 950, § 100(a)-(b), 101, 66 Stat 792, 797 (1952) (emphasis added).

This same definition of statutory subject matter is retained in 35 USC § 101.[20] In addition, the term for patents has since been extended to 20 years and a new requirement that the invention be non-obvious was introduced alongside existing requirements of novelty and usefulness.[21]

It has been emphasised that, by virtue of the *Constitution*,[22] the powers granted to Congress are confined to the promotion of the progress of science and the useful arts.[23] As such, patent monopolies are not to be freely granted. Rather, for an invention to warrant patent grant, it must be such that pushes the frontiers of chemistry, physics, and the like in order to make a distinctive contribution to scientific knowledge.[24] In addition, 'it has to be of such quality and distinction that masters of the scientific field in which it falls will recognize it as an advance'.[25] Since patents serve a higher end, which is the advancement of science: their role 'is to add to useful knowledge' and not 'subtract from former resources freely available to skilled artisans'.[26]

The agency currently responsible for granting patents in the USA is the United States Patent and Trademark Office ('USPTO').[27] Appeals made against examiner decisions in respect of patent applications are heard by the Patent Trial and Appeal Board ('PTAB'),[28] which is an organ of the USPTO.[29] In the event that the determination by the PTAB is unsatisfactory to the applicant, further appeal can be made to the Court of Appeals for the Federal Circuit ('Federal Circuit').[30] Alternatively, a civil action may be filed against the Director in the United States District Court for the District of Columbia.[31]

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[20] 35 USC (2018).
[21] 35 USC § 101, 154 (a)(2) (2018).
[22] *United States Constitution* art I § 8 cl 8.
[23] *A & P Tea Co v Supermarket Equipment Corp*, 340 US 147, 154 (1950) ('*A & P Tea Co v Supermarket Equipment Corp*').
[24] Ibid.
[25] *A & P Tea Co v Supermarket Equipment Corp* (n 23) 155.
[26] *A & P Tea Co v Supermarket Equipment Corp* (n 23) 152, 155 (1950).
[27] 'General Information Concerning Patents', *United States Patent and Trademark Office* (Web Page, October 2015) <https://www.uspto.gov/patents-getting-started/general-information-concerning-patents#heading-1> ('*General Information Concerning Patents*'); 'Records of the Patent and Trademark Office', *The U S National Archives and Records Administration* (Web Page, 15 August 2016) <https://www.archives.gov/research/guide-fed-records/groups/241.html>.
[28] This was formerly the Patent Office Board of Appeals and later, Board of Patent Appeals & Interferences.
[29] *General Information Concerning Patents* (n 27).
[30] Ibid.
[31] Ibid.

The Court of Appeals for the Federal Circuit, which was created by Congress in 1982, was the result of a merger between the United States Court of Customs and Patent Appeals and the appellate division of the United States Court of Claims.[32] It is an appellate court with national jurisdiction over a number of subject areas including patents.[33] Effectively, it has exclusive jurisdiction over appeals from the PTAB as well as appeals from civil actions in district courts of the United States relating to patents.[34] As such, its decisions in that regard are binding throughout the country, and subject to review by the Supreme Court, the grant of which is discretionary.[35]

5.3 Patentable Subject Matter in the United States of America

As noted earlier, 35 USC § 101 provides that '[w]hoever 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'. This section examines the Supreme Court's evolving interpretation of this provision and its application to life sciences.

5.3.1 *Diamond v Chakrabarty*

In the seminal case of *Diamond v Chakrabarty* which is particularly instructive on patenting life forms in the USA,[36] the Supreme Court was tasked with interpreting 35 USC § 101. In particular, it was required to determine whether a man-made genetically engineered bacteria capable of breaking down crude oil constituted a 'manufacture' or 'composition of matter'.[37]

Earlier, the patent application claim for the bacteria had been denied by a patent examiner on the grounds that: (a) it was a product of nature; and (b) living matter are not patentable under 35 USC § 101. Whilst the Patent Office Board of Appeals (pre-PTAB) rejected that the bacteria were a product of nature given they were not naturally occurring; it affirmed the Examiner's decision to reject the application on the second ground. This was based on its conclusion that, further to a review of the legislative history of the *Plant Patent Act of*

[32] 'Court Jurisdiction', *United States Court of Appeals for the Federal Circuit* (Web Page) <http://www.cafc.uscourts.gov/the-court/court-jurisdiction> ('*Court Jurisdiction*').
[33] 28 USC § 1295 (2018).
[34] 28 USC § 1295 (2018).
[35] *Court Jurisdiction* (n 32).
[36] *Diamond v Chakrabarty*, 447 US 303 (1980).
[37] *Diamond v Chakrabarty* (n 36) 307.

1930,[38] in which patent protection was extended to certain asexually reproduced plants, § 101 was not intended to cover living things such as laboratory created micro-organisms.[39] Subsequently, this decision was reversed by the Court of Customs and Patent Appeals (pre-Federal Circuit). In particular, it emphasised that the fact that microorganisms are alive is without legal significance to patent law.[40]

Subsequently, the Commissioner of Patents and Trademarks sought *certiorari* from the Supreme Court against the decision of the Court of Customs and Patent Appeals, which was granted by the Supreme Court. In interpreting § 101, the Supreme Court in a 5-4 ruling noted that it had previously cautioned courts not to read into patent law limitations and conditions that the legislature had not expressed.[41] Given statutory rules of interpretation, it was required that the terms 'manufacture' and 'composition of matter' be interpreted according to their dictionary meaning or common usage.[42] Thus, the term 'manufacture' is to be interpreted as meaning 'the production of articles for use from raw or prepared materials by giving to these materials new forms, qualities, properties, or combinations, whether by hand-labor or by machinery' whilst 'composition of matter' as 'compositions of two or more substances and … all composite articles, whether they be the results of chemical union, or of mechanical mixture, or whether they be gases, fluids, powders or solids'.[43]

Additionally, the Supreme Court noted that in choosing such expansive terms, Congress had intended for patent laws to be given a wide scope of interpretation.[44] This was supported by the legislative history of the *Patent Act* of 1973 which defined statutory subject matter as 'any new and useful art, machine, manufacture, or composition of matter, or any new or useful improvement [thereof].'[45] According to the Supreme Court, the *Act* itself embodied its author Thomas Jefferson's philosophy that 'ingenuity should receive a liberal encouragement'.[46]

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[38] *Plant Patent Act of 1930*, Pub L No 245, 46 Stat 376
[39] *Diamond v Chakrabarty* (n 36) 306.
[40] *Diamond v Chakrabarty* (n 36) 306.
[41] *Diamond v Chakrabarty* (n 36) 308.
[42] Ibid.
[43] Ibid.
[44] *Diamond v Chakrabarty* (n 36) 308-10.
[45] *Patent Act*, Ch 11, § 1, 1 Stat 318, 318-321 (1793).
[46] *Diamond v Chakrabarty* (n 36) 308.

Thus, whilst the word 'art' was replaced with 'process' in 1952,[47] the rest of Jefferson's language was left intact – meaning the statutory definition was to retain its wide scope of interpretation. Moreover, a review of the Committee Reports accompanying the amended *Act* indicated that it was Congress intention for subject matter to 'include anything under the sun that is made by man'.[48] Nonetheless, having always been held non-patentable, laws of nature, physical phenomena and abstract ideas are not to be included under this broad interpretation.[49]

With regard to the claim before it, the Supreme Court held that it was to 'non-naturally occurring manufacture or composition of matter a product of human ingenuity "having a distinctive name, character and use"'.[50] In particular, it held that the patentee 'has produced a new bacterium with *markedly different characteristics* from any found in nature and one having the potential for significant utility. His discovery is not nature's handiwork, but his own; accordingly it is patentable subject matter under § 101'.[51]

Regarding the petitioner's argument that patentability of such inventions should be left to Congress, since genetic technology was unforeseeable by Congress at the time the *Act* was enacted, the Supreme Court responded that while it was for Congress and not the courts to define limits of patentability, courts bear the responsibility of interpreting the law once defined.[52] Where the law is ambiguous, courts are to be guided by the legislative history and statutory purpose of the law.[53] However, in the present case, § 101 could not be described as being ambiguous simply because it is broad.[54] More so when it was Congress' intention for the provision to be interpreted broadly so as to fulfil the constitutional goal of promoting science and the useful arts, and anticipate unforeseeable inventions.[55] To hold otherwise would be to leave unforeseen inventions without protection, which would defeat 'the core concept of the patent law that anticipation undermines patentability'.[56]

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[47] *Patent Act*, Ch 950, § 101, 66 Stat 792, 797 (1952).
[48] *Diamond v Chakrabarty* (n 36) 309.
[49] Ibid.
[50] *Diamond v Chakrabarty* (n 36) 309-10.
[51] Ibid.(emphasis added).
[52] *Diamond v Chakrabarty* (n 36) 315.
[53] Ibid.
[54] Ibid.
[55] Ibid.
[56] *Diamond v Chakrabarty* (n 36) 316 (1980).

Finally, the Supreme Court added that whilst there might be concerns about the potential risks of new technologies, that was for Congress to address by excluding such inventions from patentability.[57] In any event, the grant or denial of patents for such inventions is unlikely to halt any associated research or its attendant risks.[58]

It should be noted that the minority disagreed with the majority's conclusion in this case. The minority considered that there was no lacuna regarding the patentability of bacteria. By virtue of the enactment of the *Plant Patent Act of 1930*,[59] and the *Plant Variety Protection Act of 1970*,[60] the minority concluded there was evidence to suggest that Congress intended to exclude bacteria from patentability.[61] This is because if non-naturally living organisms were patentable under § 101, there would have been no need for separate legislations making agricultural 'human-made' invention patentable.[62] Thus, if bacteria were to become patentable, it was for Congress and not the Court to amend the law accordingly.[63]

Given the Supreme Court's decision not to limit the types of living organisms eligible for patent protection, it is unsurprising to note that the USA was considered more patent-friendly during the biotechnology boom in the 1970s and 1980s.[64] In fact, the Oncomouse patent which had generated controversy in Europe and Canada went unchallenged in the USA.[65] However, as one commentator has cautioned, 'as the biotechnology revolution continues, the line between what occurs in nature and the products and processes used by man to make something useful continues to blur'.[66]

This would seem the case with recent decisions, which would appear to have limited the USA's otherwise expansive definition of patentable subject matter.[67] In fact, it has been argued by some authors that the threshold for invention in the USA is perhaps now just as

[57] *Diamond v Chakrabarty* (n 36) 318.
[58] *Diamond v Chakrabarty* (n 36) 317.
[59] *Plant Patent Act of 1930*, Pub L No 245, 46 Stat 376.
[60] *Plant Variety Protection Act of 1970*, 7 USC §§ 2321-2583 (2018).
[61] *Diamond v Chakrabarty* (n 36) 319-22.
[62] Ibid.
[63] *Diamond v Chakrabarty* (n 36) 322.
[64] Kranakis (n 2) 721-2; Whaite and Jones (n 2) 145; Lucy Eisenberg, 'Patenting Life' (2008) 23 *Bill of Rights in Action* .
[65] Eisenberg, 'Patenting Life' (n 64).
[66] Ibid.
[67] *Alice Corporation Pty Ltd v CLS Bank International*, 573 US 208 (2014) ('*Alice*'); *AMP* (n 3); *Mayo* (n 3).

stringent as the other jurisdictions, if not more so.[68] This is with particular reference to the Supreme Court's decisions in *Mayo Collaborative Services v Prometheus Laboratories Inc* ('*Mayo*')[69] and *Association for Molecular Pathology v Myriad Genetics Inc* ('*AMP*'),[70] which are considered next.

5.3.2 *Mayo Collaborative Services v Prometheus Laboratories Inc*

The Supreme Court's comment in *Diamond v Chakrabarty* that laws of nature, physical phenomena and abstract ideas are generally ineligible subject matter because they are 'manifestations of nature …, free to all men and reserved exclusively to none'[71] is founded on what is generally referred to as the doctrine of pre-emption. In effect, the pre-emption doctrine seeks to exclude from patent protection claims which pre-empt the use of natural laws.[72]

Whilst the pre-emption doctrine had been considered in previous decisions,[73] the Supreme Court's decision in *Mayo*[74] seems to have recentred its importance in patent subject matter eligibility. More so as it forms an important consideration in the *Alice/Mayo* test, which will be considered shortly. Suffice to say at this juncture, however, the test is a two-part test which applies in respect of patent applications relating to the aforementioned judicial exceptions.[75]

In *Mayo*, the Supreme Court was concerned with the patent eligibility of claims which purported to apply natural laws in 'describing the relationship between the concentration in the blood of certain thiopurine metabolites and the likelihood that the drug dosage will be ineffective or induce harmful side-effects'.[76] Further to this, it reiterated its earlier position that laws of nature, physical phenomena and abstract ideas are not patentable

[68] Jessica C Lai, 'Myriad Genetics and the BRCA Patents in Europe: The Implications of the U.S. Supreme Court Decision' (2015) 5 *UC Irvine Law Review* 1041; Sarah E Fendrick and Donald L Zuhn Jr, 'Patentability of Stem Cells in the United States' (2015) 5(12) *Cold Spring Harbor Perspectives in Medicine* a020958.
[69] *Mayo* (n 3).
[70] *AMP* (n 3).
[71] *Diamond v Chakrabarty* (n 36) 308-10.
[72] *Mayo* (n 3) 72.
[73] See, eg, *O'Reilly v Morse*, 56 US 62 (1853); *Gottschalk v Benson*, 409 US 63 (1972) ('*Gottschalk*'); *Diamond v Diehr*, 450 US 175 (1981) ('*Diamond v Diehr*').
[74] *Mayo* (n 3).
[75] United States Patent and Trademark Office, *Manual of Patent Examining Procedure* (9th Edition, Revision 10.2019 (Last Revised June 2020) ed, 2020), ch 2100, s 2106 (Patent Subject Matter Eligibility) ('*Manual of Patent Examining Procedure*').
[76] *Mayo* (n 3) 72.

because they are the basic tools of scientific and technological work.[77] Additionally, monopolising them through the grant of patents would have the effect of potentially impeding innovation premised upon them rather than improving it.[78]

Nonetheless, the Supreme Court equally noted that as all inventions tend to embody laws of nature, natural phenomena, and abstract ideas at some point, it was important to restrict a too broad interpretation of this exclusionary principle. This is because holding otherwise would defeat patent law.[79] To this end, the Supreme Court emphasised that it is possible for an application of natural laws to be eligible for patent protection in so far as it embodies an inventive concept. That is, other elements or a combination of other elements sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself.[80]

It however warned that limiting the use of such applications to 'particular technological environments' or adding 'insignificant post solution activity' would not suffice to transform unpatentable natural laws into patent eligible applications of those laws.[81] Neither would adding 'conventional steps at a high level of generality to laws of nature, natural phenomena and abstract ideas'.[82] In addition, it noted that a process reciting a law of nature is unpatentable if the underlying law of nature is not patentable.[83] This is unless the process 'has additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself'.[84]

In the present case, the Supreme Court found that the claimed process was ineligible subject matter as it failed to transform 'unpatentable natural laws into patent eligible applications of those laws'.[85] In particular, the Supreme Court noted that

> the steps in the claimed processes (apart from the natural laws themselves) involve *well-understood, routine, conventional activity* previously engaged in by researchers in the field. At the

[77] *Mayo* (n 3) 71; *Gottschalk* (n 73) 67.
[78] *Mayo* (n 3) 71, 86.
[79] *Mayo* (n 3) 71.
[80] *Mayo* (n 3) 72-3.
[81] *Mayo* (n 3)73; *Diamond v Diehr* (n 73).
[82] *Mayo* (n 3) 82.
[83] *Mayo* (n 3) 77.
[84] Ibid.
[85] *Mayo* (n 3) 72.

same time, upholding the patents would risk disproportionately tying up the use of the underlying natural laws, inhibiting their use in the making of further discoveries.[86]

5.3.3 *Association for Molecular Pathology v Myriad Genetics Inc*

Further to *Mayo*, the Supreme Court was once again faced with adjudicating patent claims pertaining to the aforementioned judicial exclusions of laws of nature, physical phenomena and abstract ideas in *AMP*.[87] Although the Supreme Court had initially remanded *AMP* to the Federal Circuit for reconsideration in light of its decision in *Mayo*, it did not appear to establish a connection between both cases in its eventual decision.[88] This has been considered puzzling by some commentators in light of the fact that whereas the decision in *Mayo* was underlined by the 'laws of nature' doctrine, the decision in *AMP* was underlined by the 'products of nature' doctrine.[89] Nonetheless, the USPTO does not appear to have been perturbed by this lack of connection as it considers that courts have often described the terms 'laws of nature' and 'natural phenomenom' using other terms such as 'physical phenomena', 'scientific principles', 'natural laws', and 'products of nature'.[90] As such, the same general rules have been applied when assessing patent subject matter eligibility in that regard.[91]

The *AMP* case stemmed from concerns about freedom of speech and the implications of recognizing exclusive rights over genetic knowledge for patients, researchers, and science.[92] In that case, the Supreme Court was invited to rule on the validity of patents for isolated deoxyribonucleic acid ('DNA') sequences (that is, the BRCA1 and BRCA2 genes discovered by Myriad) associated with predisposition to breast cancers and ovarian cancers and for diagnostic methods of identifying mutations in those DNA sequences.[93]

As resolution of the case revolved around differentiating naturally occurring phenomena from non-occurring phenomena, the Supreme Court reiterated its earlier comments on

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[86] *Mayo* (n 3) 73 (emphasis added).
[87] *AMP* (n 3).
[88] Dan L Burk, 'The Curious Incident of the Supreme Court in Myriad Genetics' (2014) 90 *Notre Dame Law Review* 505, 506
[89] Ibid, 506; Rochelle C Dreyfuss, Jane Nielsen and Dianne Nicol, 'Patenting Nature - A Comparative Perspective' (2018) 5 *Journal of Law and the Biosciences* 550, 559-60
[90] *Manual of Patent Examining Procedure* (n 75) ch 2100, s 2106 (Patent Subject Matter Eligibility)
[91] Ibid.
[92] Dreyfuss, Nielsen and Nicol (n 89).
[93] *AMP* (n 3) 579-80.

limitations to the judicial exclusion of laws of nature, natural phenomena, and abstract ideas from patentability.[94] With regard to the case at hand, it noted that:

> It is undisputed that Myriad did not create or alter any of the genetic information encoded in the BRCA1 and BRCA2 genes. The location and order of the nucleotides existed in nature before Myriad found them. Nor did Myriad create or alter the genetic structure of DNA. Instead, Myriad's principal contribution was uncovering the precise location and genetic sequence of the BRCA1 and BRCA2 genes.[95]

In light of this, it was important for the Supreme Court to revisit its earlier decision in *Diamond v Chakrabarty*, particularly in relation to the markedly different characteristics requirement.[96] Ultimately, the Supreme Court found that the manner in which Myriad's claims were drafted indicated that the claims were concerned primarily with the genetic information encoded in the BRCA1 and BRCA2 genes, and not with the specific chemical composition of a particular molecule.[97] Thus, it was not enough that chemical bonds were severed by isolating the DNA thus creating a non-naturally occurring molecule.[98] Further, while Myriad's discovery of the precise location and sequences of the BRCA1 and BRCA2 genes may have been innovative, the act of isolating the genes from their surrounding material did not constitute an act of invention.[99] Hence, the Supreme Court unanimously ruled that the claimed isolated DNA sequences were ineligible for patenting because isolating DNA from its surrounding genetic material did not significantly add to the DNA's natural state and therefore did not qualify as non-naturally occurring.[100]

In contrast, however, the Supreme Court found that the claimed complimentary DNA ('cDNA') was non-naturally occurring and therefore patent eligible. This was because introns had been removed from the naturally occurring DNA resulting in an exons-only molecule, which did not exist in nature.[101] Whilst it was conceded that the nucleotide sequence of cDNA is dictated by nature and not the laboratory technicians, the Supreme

[94] *AMP* (n 3) 589-90.
[95] *AMP* (n 3) 590.
[96] *AMP* (n 3) 590-1.
[97] *AMP* (n 3) 593.
[98] *AMP* (n 3), 592.
[99] *AMP* (n 3) 591.
[100] *AMP* (n 3) 596.
[101] *AMP* (n 3) 594.

Court ruled that it was undisputed that the laboratory technician 'creates something new when cDNA is made'.[102] In particular, it noted that

> cDNA retains the naturally occurring exons of DNA, but it is distinct from the DNA from which it was derived. As a result, cDNA is not a "product of nature" and is patent eligible under §101, except insofar as very short series of DNA may have no intervening introns to remove when creating cDNA. In that situation, a short strand of cDNA may be indistinguishable from natural DNA.[103]

This decision has been criticised by many with suggestions that *AMP* imposes a bar to patenting all natural products as well as products which duplicate or come close to duplicating materials found in nature.[104] This is in part due to the fact that it leaves unclear how markedly different a synthetic molecule must be from its naturally occurring analog to be considered patentable.[105] Additionally, the decision has also been criticised for distinguishing genomic DNA and cDNA since they both encode identical information and their patenting has the potential to impede science.[106] This would seem to align with the Australian position that genomic DNA and cDNA are potentially ineligible for patenting given the substance of such claims are likely to be directed to genetic information that is similar to that in the genome of an organism.[107]

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[102] *AMP* (n 3) 595.
[103] *AMP* (n 3) 595.
[104] Dreyfuss, Nielsen and Nicol (n 89) 552.
[105] Ibid 561; Charles Lawson, 'Patenting Nucleic Acid Sequences: More Ambiguity from the High Court?' (2018) 25 *Journal of Law and Medicine* 741, 756-7; *AMP* (n 3) 596; Lai (n 68) 1064-6; Heidi Ledford, 'Myriad Ruling Causes Confusion' (2013) 498 *Nature* 281, 282; Sonya Davey et al, 'Interfacing of Science, Medicine and Law: The Stem Cell Patent Controversy in the United States and the European Union' (2015) 3 *Frontiers in Cell and Developmental Biology*; Ana Nordberg and Timo Minssen, 'A "Ray of Hope" for European Stem Cell Patents or "Out of the Smog into the Fog"? An Analysis of Recent European Case Law and How it Compares to the US' (2016) 47 *International Review of Intellectual Property and Competition Law* 138, 171
[106] Dreyfuss, Nielsen and Nicol (n 89) 560; Lawson (n 105) 757; Robert M Schwartz and Timo Minssen, 'Life after Myriad: The Uncertain Future of Patenting Biomedical Innovation and Personalised Medicine in an International Context' [2015] (3) *Intellectual Property Quarterly* 189, 206-7.
[107] *D'Arcy v Myriad Genetics Inc* (2015) 258 CLR 334, 371 [89], 418-9 [283] ('*D'Arcy*'); Australian Patent Office, '2.9.2.6 Nucleic Acids and Genetic Information', *Patent Manual of Practice & Procedure* (Web Page, 2 June 2020) <http://manuals.ipaustralia.gov.au/patents/national/patentable/2.9.2.6_Nucleic_acids_and_genetic_information.htm>; Australian Patent Office, '2.9.2.2 Principles for Examination', *Patent Manual of Practice & Procedure* (Web Page, 2 October 2018) <http://manuals.ipaustralia.gov.au/patents/adaptive_patents_manual/national/patentable/2.9.2.2_Principles_for_Examination.htm>.

Notwithstanding, the principles from *AMP* (particularly its the application of the markedly different characteristics requirement) remain relevant in assessing the patentability of inventions embodying 'products of nature'.

5.3.4 *Alice Corporation Pty Ltd v CLS Bank International*

Another important Supreme Court decision in assessing patent subject matter eligibility in relation to the aforementioned judicial exceptions is *Alice Corporation Pty Ltd v CLS Bank International* ('*Alice*').[108] This is especially with regard to the Supreme Court's application of the principles developed in *Mayo,* resulting in what is now referred to as the *Alice/Mayo* test, as highlighted earlier.

In *Alice*, the patent claims in suit were system, method and media claims implemented using a computer.[109] As the claims concerned abstract ideas, the Supreme Court reiterated its position on judicial exceptions with references to *Mayo* and *AMP* amongst other precedents.[110] In particular, it noted that

> [i]n *Mayo*, we set forth a framework for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts. *First, we determine whether the claims at issue are directed to one of those patent-ineligible concepts ... If so, we then ask, "[w]hat else is there in the claims before us?" ... To answer that question, we consider the elements of each claim both individually and "as an ordered combination" to determine whether the additional elements "transform the nature of the claim" into a patent-eligible application … We have described step two of this analysis as a search for an "inventive concept"—i.e., an element or combination of elements that is "sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself."*[111]

Further to its application of step one of the test to the claims at issue, it concluded that the claims were directed to a patent-ineligible concept (the abstract idea of intermediated settlement).[112] As such, it was required to proceed to step two of the test. Regarding this, the Supreme Court found that the claim elements, separately and as an ordered combination, failed to transform the abstract idea into a patent-eligible invention.[113] This

[108] *Alice* (n 67).
[109] *Alice* (n 67) 214.
[110] *Alice* (n 67) 216-8.
[111] *Alice* (n 67) 217-8 (emphasis added).
[112] *Alice* (n 67) 218.
[113] *Alice* (n 67) 221-226.

was because the steps involved did nothing more than 'require generic computer implementation to perform generic computer functions'.[114] In light of the Supreme Court's precedents, these were 'not "enough" to transform an abstract idea into a patent-eligible invention'.[115]

5.4 Applying the Subject Matter Eligibility Test to Bioprinted Constructs and Bioprinting Processes

Further to the above as well as additional case law (including those in which principles from the above cases were applied),[116] the USPTO has now developed a guideline for examiners in assessing subject matter eligibility. A summary of the steps involved is provided below.

i. **Step 1**: Establish which of the four statutory categories of invention mentioned in 35 USC § 101 (that is, process, machine, manufacture, or composition of matter) the claimed invention falls within.[117] In this regard, the USPTO advises that, as with genetically modified bacteria which satisfy both the composition of matter and manufacture categories, it is possible for a claimed invention to belong to more than one statutory category.[118]

ii. **Step 2**: This step encompasses the Supreme Court's two-part *Alice/Mayo* test mentioned earlier. As such, it is sub-divided into Step 2A and Step 2B.

   a) **Step 2A**: Consider whether the claim is directed to a judicial exception. Judicial exceptions in this regard include both existing and newly discovered judicial exceptions such as the laws of nature in *Mayo,* and the isolated DNA in *Myriad.*[119]

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[114] Ibid.
[115] *Alice* (n 67) 225-6.
[116] *Alice* (n 67); *AMP* (n 3); *Diamond v Chakrabarty* (n 36); *Diamond v Diehr* (n 73); *Mayo* (n 3); *ENFISH LLC v Microsoft Corp,* 822 F 3d 1327 (Fed Cir, 2016); *Bilski v Kappos*, 561 US 593 (2010); *TLI Communications v AV Automotive LLC*, 823 F 3d 607 (Fed Cir, 2016); *Eon Corp IP Holdings LLC v AT&T Mobility LLC*, 785 F 3d 616 (Fed Cir, 2015); *Intellectual Ventures I LLC v Capital One Bank (USA), N A*, 792 F 3d 1363 (Fed Cir, 2015); *Genetic Techs Ltd v Merial LLC*, 818 F 3d 1369 (Fed Cir, 2016); *Synopsys, Inc v Mentor Graphics Corp*, 839 F 3d 1138 (Fed Cir, 2016); *Ariosa Diagnostics, Inc v Sequenom, Inc*, 788 F 3d 1371 (Fed Cir, 2015) ('*Ariosa*'); *FairWarning IP, LLC v Iatric Sys, Inc*, 839 F 3d 1089 (Fed Cir, 2016); *Ultramercial, Inc v Hulu, LLC*, 772 F 3d 709 (Fed Cir, 2014); *In re Roslin Institute* (n 3); *RecogniCorp, LLC v Nintendo Co*, 855 F 3d 1322 (Fed Cir, 2017); *University of Utah Research Foundation v Ambry Genetics*, 774 F 3d 755 (Fed Cir, 2014) ('*University of Utah Research Foundation v Ambry Genetics*'); *McRO, Inc v Bandai Namco Games Am Inc*, 837 F 3d 1299 (Fed Cir, 2016); *Vanda Pharmaceuticals Inc v West-Ward Pharmaceuticals*, 887 F 3d 1117 (Fed Cir, 2018) ('*Vanda*'); *Rapid Litigation Management Ltd v CellzDirect, Inc*, 827 F 3d 1042 (Fed Cir, 2016) ('*Rapid Litigation Management Ltd*').
[117] *Manual of Patent Examining Procedure* (n 75) ch 2100, s 2104 (Requirements of 35 U S C 101), s 2106 (Patent Subject Matter Eligibility).
[118] Ibid ch 2100, s 2106 (Patent Subject Matter Eligibility).
[119] Ibid.

It should be noted that step 2A is a two-prong inquiry which involves determining 'whether a claim recites a judicial exception', and if so, determining 'if the recited judicial exception is integrated into a practical application of that exception'.[120]

As bioprinting relates to laws and products of nature, it is useful to limit a consideration of the USPTO's first prong inquiry in step 2A to this area.[121] Thus, it should be noted that the products of nature exception includes not just naturally occurring products, but also non-naturally occurring products which lack markedly different characteristics from any naturally occurring counterpart.[122] The 'markedly different characteristics' analysis is especially important when assessing the eligibility of non-naturally occurring products, as naturally occurring products are by their very nature excluded from patentability.[123] Generally, process claims are not subject to the markedly different analysis since they are process based. However, process claims reciting a nature-based product may be subject to the markedly different analysis if they are drafted in such a way that they focus on the product as opposed to the process.[124]

Depending on what is recited in the claim, the markedly different analysis involves a consideration of things such as the 'product's structure, function, and/or other properties' evaluated on a case-by-case basis.[125] To this end, it is important to select an appropriate naturally occurring counterpart(s) for conducting this analysis. Where the claimed invention is derived from a naturally occurring product such as with isolated genes, for instance, the naturally occurring product is the appropriate counterpart for conducting a markedly different characteristics analysis.[126] However, where there are multiple

[120] Ibid.
[121] Generally, the terms 'law of nature' and 'natural phenomenon' are used as inclusive of 'products of nature' in the USPTO's eligibility analysis under step 2A: ibid.
[122] Ibid; *University of Utah Research Foundation v Ambry Genetics* (n 115) 760; *In re Roslin Institute* (n 3) 1337.
[123] *Manual of Patent Examining Procedure* (n 75) ch 2100, s 2106 (Patent Subject Matter Eligibility).
[124] Ibid; *Rapid Litigation Management Ltd* (n 116) 1048-9.
[125] These include (i) biological or pharmacological functions or activities; (ii) chemical and physical properties; (iii) phenotype, including functional and structural characteristics; and (iv)structure and form, whether chemical, genetic or physical. *Manual of Patent Examining Procedure* (n 75) ch 2100, s 2106 (Patent Subject Matter Eligibility).
[126] Ibid.

counterparts, the most appropriate counterpart is the closest naturally occurring counterpart.[127]

In order to determine whether the characteristics of the claimed non-naturally occurring product are markedly different, it must be compared to the naturally occurring counterpart in its natural state.[128] Where the claimed product is found to possess at least one distinguishing characteristic from that of the naturally occurring counterpart, and the change is as a result of the applicant's efforts or influences, it would be held as markedly different and not reciting a product of nature exception.[129] Otherwise, it would be held as belonging to a product of nature exception requiring further analysis in prong two of Step 2A.[130]

As noted earlier, the second prong of the Step 2A inquiry involves determining 'if the recited judicial exception is integrated into a practical application of that exception'. According to the USPTO, '[a] claim that integrates a judicial exception into a practical application will apply, rely on, or use the judicial exception in a manner that imposes a meaningful limit on the judicial exception, such that the claim is more than a drafting effort designed to monopolize the judicial exception'.[131]

b) **Step 2B**: If, further to Step 2A Prong Two, the additional elements do not integrate the exception into a practical application, then it must be considered whether the claim recites additional elements that, individually and in combination, amount to significantly more than the judicial exception itself.[132] This involves searching for an 'inventive concept',[133] that is, something 'significantly more' than the recited judicial exception.[134] The analysis here is

[127] Ibid.
[128] Ibid.
[129] Ibid.
[130] Ibid.
[131] Ibid.
[132] Ibid.
[133] It should be noted that is different from the novelty and non-obviousness test for patentability: *Mayo* (n 3); *Manual of Patent Examining Procedure* (n 75) ch 2100, s 2106 (Patent Subject Matter Eligibility).
[134] *Manual of Patent Examining Procedure* (n 75) ch 2100, s 2106 (Patent Subject Matter Eligibility).

similar to Step 2A Prong Two in that they both involve an evaluation of a set of judicial considerations to ascertain whether the claim is eligible.[135]

5.4.1 Bioprinted Constructs

Further to the above, the first step in assessing the patentability of bioprinted constructs is a determination of whether bioprinted constructs belong to any of the four statutory categories. Given their physical/tangible form, as well as judicial definition of the terms 'manufacture'[136] and 'composition of matter'[137] which are most relevant to bioprinted constructs, it is safe to conclude that bioprinted constructs satisfy this requirement for ascertaining eligibility based on earlier analysis of the nature of bioprinted constructs in preceding chapters.

With regard to the second step, it is important to emphasise that analysis as to whether a claimed invention is non-naturally occurring is distinct from analysis as to whether said invention possesses markedly different characteristics from that of its naturally occurring counterpart. In other words, in addition to establishing that a claimed invention is non-naturally occurring, it must also be established separately that such an invention possesses markedly different characteristics from that of its naturally occurring counterpart. Thus, while earlier commentary on the patent-eligibility of bioprinted constructs seemed to have combined both analyses further to existing USPTO guidance at the time,[138] this is no longer the case. Accordingly, much of the analysis made distinguishing bioprinted constructs from their naturally occurring counterparts would now be more appropriately argued under the markedly different characteristics analysis.

Further to earlier analysis in this thesis about the nature of bioprinted constructs, it is firmly established that bioprinted constructs are non-naturally occurring. In themselves, they do not exist in nature. Rather, they are the result of a combination of natural and synthetic

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[135] Ibid.

[136] A manufacture is 'a tangible article that is given a new form, quality, property, or combination through man-made or artificial means': *Digitech Image Techs v Electronics for Imaging*, 758 F 3d 1344, 1349, (Fed Cir, 2014) ('*Digitech Image Techs*'); *Diamond v Chakrabarty* (n 36) 308.

[137] A composition of matter is a 'combination of two or more substances and includes all composite articles': *Digitech Image Techs* (n 136) 1348-9.

[138] Jasper L Tran, 'Patenting Bioprinting' (2015) 29 *Harvard Journal of Law and Technology Digest*; Timo Minssen and Marc Mimler, 'Patenting Bioprinting-Technologies in the US and Europe – The 5th Element in the 3rd Dimension' in Rosa Maria Ballardini, Marcus Norrgård and Jouni Partanen (eds), *3D printing, Intellectual Property and Innovation – Insights from Law and Technology* (Wolters Kluwer, 2017).

materials, as well as living cells. Furthermore, whilst there is some measure of reliance on intrinsic biological processes of cells, human intervention is also required at various stages of their fabrication. As such, they cannot be classified as naturally occurring.

Consequently, the next stage in assessing their patent eligibility is to consider whether bioprinted constructs possess any distinguishing characteristic from that of their naturally occurring counterpart. This involves identifying an appropriate counterpart and making a comparison between both products. In this regard, it is useful to consider the decision in *In re Roslin Institute*,[139] which offers some insight into how such analysis is to be carried out.

The *In re Roslin Institute* case was concerned with the patentability of cloned mammals. This ought to be contrasted with the Australian case of *Meat & Livestock Australia Limited v Cargill, Inc*, which was concerned with a claimed method for identifying a trait of a bovine subject from a nucleic acid sample of the bovine subject.[140] Whereas the method claims in *In re Roslin Institute* had been patented, the application for the cloned mammals had been rejected by the USPTO. In particular, the applicants had submitted claims for mammals produced via somatic cell nuclear transfer, involving removal of the nucleus of a somatic cell (egg or sperm) and implantation into an enucleated (without a nucleus) oocyte (an egg cell prior to maturation) in order to generate an embryo.[141] The resulting embryo is then implanted into a surrogate mammal, where it develops into a baby animal, which is an exact genetic replica of the adult mammal from which the somatic cell nucleus was taken.[142]

The Court (the Federal Circuit in this instance) used the mammals which had been replicated as the naturally occurring counterpart for the purpose of conducting the markedly different characteristics analysis. After comparing both, the Court found that the claimed clones were exact genetic copies of the donor mammals and did not possess markedly different characteristics from the donor mammals.[143] In particular, the Court noted that the primary innovation was 'the preservation of the donor DNA such that the clone is an exact copy of the mammal from which the somatic cell was taken'.[144] This was

[139] *In re Roslin Institute* (n 3).
[140] *Meat & Livestock Australia Limited v Cargill, Inc* (2018) 354 ALR 95 ('*MLA*').
[141] *In re Roslin Institute* (n 3) 1334.
[142] Ibid.
[143] *In re Roslin Institute* (n 3) 1337.
[144] Ibid.

similar to the situation in *AMP* where the genetic information was neither created nor altered.[145]

Additionally, the Court also found that even though phenotypic differences between the clones and the donor mammals were unclaimed, they were irrelevant in determining patentability because these were determined by environmental factors beyond Roslin's efforts.[146] Furthermore, with regard to Roslin's argument that its clones were markedly different from their original donor mammals because of 'differences in mitochondrial DNA, which originates from the donor oocyte rather than the donor nucleus', the Court found that there was nothing in the claims or specification, which indicated the clones were different in any relevant way from the donor sheep.[147] Nevertheless, the Court emphasised that it was possible for clones having the same DNA as the donor mammal to be patent eligible in so far as they possess markedly different characteristics from the donor animals.[148]

Given this decision and the USPTO guidance formulated from decided cases, it would thus appear that the appropriate counterpart for conducting the markedly different characteristics analysis in relation to bioprinted constructs are their naturally occurring counterparts. That is, if bioprinted breast tissue is claimed, for instance, the appropriate counterpart would be a similar naturally occurring breast tissue, and not the isolated cells from which they were fabricated.

This would seem to differentiate the analysis in the USA from that in Australia where artificiality can be determined by the 'labour required to create it [bioprinted constructs] and the physical differences between it [bioprinted constructs] and the raw natural material [cells] from which it [bioprinted constructs] is derived'.[149] The USA analysis is equally different from that of the *EPC* wherein the technical character of bioprinted constructs may be established by reference to its physical features,[150] as well as reference to technical

[145] Ibid.
[146] *In re Roslin Institute* (n 3) 1338.
[147] *In re Roslin Institute* (n 3) 1339.
[148] Ibid.
[149] *D'Arcy* (n 107) 382 [128].
[150] T 0914/02 [2005]; Stefan V Steinbrener, 'Patentable Subject Matter Under Article 52(2) and (3) EPC: A Whitelist of Positive Cases from the EPO Boards of Appeal—Part 1' (2018) 13 *Journal of Intellectual Property Law & Practice* 13.

features pertaining to the manner of fabrication which ought to satisfy the technical teaching requirement.

In terms of the characteristics to be compared, it should be emphasised that is claim dependent. As such, the analysis in this section is at best a broad overview of characteristics that might be compared. In particular, this section considers genetic structure and form as well as phenotype given the inherent nature of bioprinted constructs.

To the extent that genetic structure may be relevant in performing the markedly different characteristics analysis, it is unclear whether the appropriate naturally occurring product for comparison would have to be further narrowed. This is with respect to the fact that a combination of stem cells derived from human and animal donor tissue samples may be used in fabricating a single construct. Such a combination could potentially complicate the choice of an appropriate naturally occuring counterpart – whether human or animal.

Even then, it is unclear the extent to which bioprinted constructs retain the DNA of the original stem cells used in their fabrication. This is particularly so when induced pluripotent stem cells (iPSCs) are involved. As noted in chapter two, specialised stem cells may be reprogrammed into iPSCs for use in bioprinting. Already, there are studies suggesting that such iPSCs are susceptible to DNA damage, which may result in altered DNA.[151] In this case, there may be differences between the DNA of the original stem cells and the bioprinted constructs. This is, of course, not ignoring the fact that the primary innovation with bioprinting is the fabrication of constructs from stem cells and not the preservation of the donor stem cell or genetic identity contained therein.

While bioprinted constructs are intended to replicate their naturally occurring counterparts structurally and functionally, there is no evidence to suggest that they are intended to be genetic copies of their naturally occurring counterparts. To this end, it is questionable whether bioprinted constructs can properly be classified as clones of their naturally occurring counterparts. This is especially considering the fact that isolated stem cells are

[151] Qiang Bai et al, 'Embryonic Stem Cells or Induced Pluripotent Stem Cells? A DNA Integrity Perspective' (2013) 13 *Current Gene Therapy* 93; Minjie Zhang et al, 'Induced Pluripotent Stem Cells are Sensitive to DNA Damage' (2013) 11 *Genomics, Proteomics & Bioinformatics* 320.

combined with other materials, which genetic identity may not have been stripped, to produce the desired construct.

While the claimed clones in *In re Roslin Institute* derived from the fusion of the somatic cell nucleus of the animal cloned with an enucleated oocyte, bioprinted constructs involve more than isolating stem cells to reproduce the tissue from which it was derived. As noted in chapter two, stem cells used in the fabrication of bioprinted constructs may be reprogrammed cells sourced from tissues other than the tissue intended to be replaced. For instance, stem cells may be isolated from skin tissue to fabricate liver tissue. Even where stem cells are isolated from the tissue intended to be replaced, such stem cells undergo significant transformation assisted by human intervention before they result in bioprinted constructs.

Thus, whilst the decision in *In re Roslin Institute* means that any cloned stem cells used in bioprinting may in themselves be patent ineligible, it is unclear the extent to which this would affect bioprinted constructs.

In light of this, it may very well be that a better comparison is to be made between phenotypic characteristics: functional and structural characteristics such as shape, size, colour and behaviour. As such, it is instructive to consider the aforementioned earlier commentary about the differences between bioprinted constructs and their naturally occurring counterparts.[152] According to Tran, Minssen and Mimler, given bioprinted constructs in their current form differ structurally from their naturally occurring counterparts, this difference is enough to make them eligible subject matter for now.[153] However, if bioprinted constructs were ever to amount to an exact replica of their naturally occurring counterparts such that they are functionally and structurally similar, this might potentially render them ineligible subject matter.[154]

Given indications that all that is required to be considered markedly different is at least one distinguishing characteristic that is as a result of the applicant's efforts or influences, this thesis aligns with the position that bioprinted constructs are eligible subject matter in their current form. This is further to apparent structural and possibly functional differences

[152] Tran (n 138); Minssen and Mimler (n 138).
[153] Tran (n 138); See also Minssen and Mimler (n 138).
[154] Tran (n 138); Minssen and Mimler (n 138).

between bioprinted constructs and their naturally occurring counterparts. As noted in chapter two, issues of innervation and vascularisation still need to be addressed before bioprinted constructs can effectively be used in replacement of human tissues. With researchers uncertain about resolution of these matters, it is not clear whether bioprinted constructs will ever be exact replicas of their naturally occurring counterparts such that their eligibility is in doubt.

Nevertheless, considering that the markedly different characteristics analysis is conducted on a case-by-case basis with reference to the recited claims, patent-eligibility will ultimately rest on the manner in which the claims are drafted.

5.4.2 Bioprinting Process Claims

In the preceding chapters, a number of bioprinting processes were identified and examined for patentability. These included methods of using bioprinted constructs in *in vitro* research and medical treatment of humans, the isolation and cultivation of living cells, biological/cellular processes, preparation of materials, printing methods, and maturation of the finished construct. Out of all these processes, it was determined that the most uncertain with regards to patentability are the isolation and cultivation of living cells as well as cellular/biological processes involved in the fabrication of bioprinted constructs.

Following from earlier analysis of the threshold for patentable subject matter, it would appear that this conclusion is equally true for the USA. This is because such processes often embody laws of nature, which are otherwise patent ineligible. Accordingly, this section as with preceding chapters focuses predominantly on the isolation and cultivation of living cells as well as cellular/biological processes involved in the fabrication of bioprinted constructs.

Further to *Mayo* and *Alice* discussed earlier, the Federal Circuit has had to apply the *Alice/Mayo* test in a number of cases before it. One of such cases was *Ariosa Diagnostics, Inc v Sequenom, Inc* ('*Ariosa*')[155] which was concerned with a method for detecting paternally inherited cell-free fetal DNA ('cffDNA') in the plasma and serum of a pregnant woman.[156] In applying step one of the *Alice/Mayo* test, the Court found that the claimed method began

[155] *Ariosa* (n 116).
[156] *Ariosa* (n 116) 1373.

and ended with a natural phenomenon and as such was naturally occurring.[157] In particular, the claimed method began with obtaining cffDNA 'from a sample of maternal plasma or serum - a naturally occurring non-cellular fetal DNA that circulates freely in the blood stream of a pregnant woman', and ended with 'paternally inherited cffDNA, which is also a natural phenomenon'.[158]

As the claimed method was directed to a natural phenomenon, which is an ineligible subject matter, it was necessary for the Court to apply the second step. That is, it was necessary to consider whether the elements of the claim, individually and as an ordered combination, transformed the nature of the claim into a patent-eligible application. In this regard, the Court found that the claimed methods amounted to 'a general instruction to doctors to apply routine, conventional techniques when seeking to detect cffDNA'.[159] As the claimed methods were well-understood, conventional and routine, they were insufficient to transform the natural phenomenon of cffDNA into a patentable invention.[160] In light of this, the claimed methods were ineligible subject matter despite the fact that they amounted to 'a positive and valuable contribution to science'.[161]

This is in contrast to the conclusion reached by the Federal Court of Australia in *Sequenom Inc v Ariosa Diagnostics Inc*, which was decided afterwards.[162] There, Beach J found that the claimed method for detecting the presence of cffDNA in non-cellular components of a maternal serum or plasma sample resulted in the creation of an artificially created state of affairs and was itself of economic significance.[163] The claim, when considered as a whole, was not to the product or presence of cffDNA but rather to a method by which the discovery of the existence of cffDNA could be put to practical use such as in sex determination, detection of paternally-inherited sequences and screening for chromosomal aneuploidies.[164]

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[157] *Ariosa* (n 116).
[158] Ibid.
[159] *Ariosa* (n 116) 1377.
[160] *Ariosa* (n 116) 1376-7.
[161] *Ariosa* (n 116) 1380.
[162] *Sequenom Inc v Ariosa Diagnostics Inc* [2019] FCA 1011 ('*Sequenom*'); See also chapter three (section 3.3.2) for a discussion of this case.
[163] Ibid 101 [494], 102 [499].
[164] Ibid 39 [200] - [201], 96 [463].

Beach J found that the substance of the claim applied and followed on from the identification of a natural phenomenon, but was different to it.[165] The invention had built on the natural phenomenon to 'provide a new, inventive, useful, artificial method of detection of cffDNA', which was of economic significance.[166] Further, the claimed method provided a significant advantage over existing fetal DNA detection methods available at the priority date. [167] As Beach J noted, his decision differed from that of *Ariosa* in the USA because of the latter's 'dissection of the claims into their constituent parts', which is contrary to the Australian approach discussed in chapter three.[168]

On the other hand, in another case involving Ariosa Diagnostics, the Federal Circuit found the claimed methods in issue were not directed to a natural phenomenon. This was the case of *Illumina Inc v Ariosa Diagnostics Inc* ('*Illumina Inc*'),[169] which was concerned with 'methods of preparing a fraction of cffDNA that is enriched in fetal DNA'.[170] It should be noted that the claims in dispute claimed priority from a European patent application filed in 2003 and as such were unrelated to the claims in the earlier case.[171]

Prior to applying the *Alice/Mayo* test, the Court emphasised that the method claims in dispute were to methods of preparation and not diagnostic methods,[172] which have been held ineligible subject matter since *Mayo.*[173] Neither were they methods of treatment,[174] which are generally patentable in the USA.[175] Additionally, the Court also sought to distinguish *Illumina Inc* from *AMP*. Whereas *AMP* was concerned with isolated DNA sequences as opposed to the process for isolating them, *Illumina Inc* was concerned with the process of preparing a fraction of cffDNA not the cffDNA in itself.[176]

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[165] Ibid 99 [485].
[166] Ibid 99 [485].
[167] Ibid 102 [500].
[168] Ibid 107 [522].
[169] *Illumina Inc* (n 3).
[170] *Illumina Inc* (n 3) 1371.
[171] *Illumina Inc* (n 3) 1369, 1373.
[172] *Illumina Inc* (n 3) 1371.
[173] *Athena Diagnostics, Inc v Mayo Collaborative Services, LLC*, 927 F 3d 1333, 1352 (Fed Cir, 2019); *Athena Diagnostics, Inc v Mayo Collaborative Services, LLC*, 915 F 3d 743 (Fed Cir, 2019); *Cleveland Clinic Foundation v True Health Diagnostics LLC*, 859 F 3d 1352 (Fed Cir, 2017); *Cleveland Clinic Foundation v True Health Diagnostics LLC*, 760 F App'x 1013 (Fed Cir, 2019).
[174] *Illumina Inc* (n 3) 1371.
[175] *Vanda* (n 116); *Endo Pharmaceuticals Inc v Teva Pharmaceuticals USA, Inc*, 919 F 3d 1347 (Fed Cir, 2019); *Natural Alternatives International, Inc v Creative Compounds, LLC*, 918 F 3d 1338 (Fed Cir, 2019).
[176] *Illumina Inc* (n 3) 1373-4.

With regard to the eligibility of the claim, the Court concluded its application of the *Alice/Mayo* test in step one as it found that the claims in dispute were not directed to the natural phenomenom, but rather to a patent-eligible method that utilised it.[177] In particular, the Court found that the process steps changed the composition of the mixture, which resulted in a DNA fraction that was different from the naturally-occurring fraction in the mother's blood. Thus, the process had achieved 'more than simply observing that fetal DNA is shorter than maternal DNA or detecting the presence of that phenomenon'.[178] This was in contrast to *Ariosa* where 'the inventors in Ariosa discovered that cell-free fetal DNA exists, and then obtained patent claims that covered only the knowledge that it exists and a method to see that it exists'.[179]

Further to these decisions, it would appear that bioprinting methods of treatment including bioprinting *in situ* are potentially eligible subject matter in the USA. However, with regard to claims directed to cellular/biological processes, it is highly unlikely that these will be considered eligible given they are directed to natural phenomena. This is similar to the *EPC* position where such claims would be considered as likely falling under the art 52(2)(a) exception.

On the other hand, claims relating to the isolation and cultivation of living cells for use in the fabrication of bioprinted constructs, could potentially be eligible for patenting. This is similar to the position in Australia where it has been held that such claims may be patentable provided, of course, that they satisfy the standard patent criteria. This requires that they are novel, involve an inventive step, and amount to a new process or method of bringing about an artificially created state of affairs of economic significance.[180] Additionally, such claims are equally potentially eligible under the *EPC* further to the Enlarged Board of Appeal's comment that 'the fact that the idea or concept underlying the claimed subject-matter resides in a discovery does not necessarily mean that the claimed subject-matter is a discovery "as such"'.[181]

[177] *Illumina Inc* (n 3) 1372.
[178] Ibid.
[179] *Illumina Inc* (n 3) 1373.
[180] *MLA* (n 139) 212 [462]; *Sequenom* (n 162) 84 [396].
[181] *Friction reducing additive/Mobile Oil III* [1990] OJ EPO 4/93.

The eligibility of claims relating to the isolation and cultivation of living cells for use in the fabrication of bioprinted constructs in the USA would, however, depend on whether the claims are interpreted as being directed to a natural phenomena. In the event that they are, their eligibility will turn on whether the elements of the claim, individually and as an ordered combination, transform the nature of the claim into a patent-eligible application. Nevertheless, it is important to note that the isolation and cultivation of living cells in general is not a new phenomenon. As such, any method claimed must be innovative in order to qualify as eligible subject matter.

5.5 Exclusions from Patentability

A major distinction between the USA and the afore-examined jurisdictions (that is, Australia and the *EPC*) is its approach to exclusions from patentability. While it does not provide a method of medical treatment exception like Australia, the USA also does not explicitly provide for an ethically informed exclusion clause. At best, there exists the judicially created concept of 'moral utility' and the recently passed *AIA*, which provides that claims directed to or encompassing human organisms (including human embryos and foetuses) are ineligible for patent protection.[182]

Accordingly, this section focuses on the concept of 'moral utility' as well as the provisions of the *AIA*.

5.5.1 Moral Utility and the *Leahy-Smith America Invents Act*

From inception of its first federal patent law in 1790, the USA never provided for any ethical considerations to be taken into account in assessing patentability. Neither did the 1790 law contain any explicit reference to the *Statute of Monopolies*,[183] which appears to have influenced some of its provisions.[184] Instead, the judicially created concept of 'moral utility' stemming from Justice Story's interpretation of the utility requirement in *Lowell v Lewis*[185] was relied on to address ethical concerns in patent applications.

[182] *AIA* (n 4).
[183] *Statute of Monopolies 1623,* 21 Jac 1, c 3.
[184] Fredrik Neumeyer, 'Contribution to the History of Modern Patent Legislation in the United States and in France' (1956) 4 *Scandinavian Economic History Review* 126.
[185] *Lowell v Lewis*, 15 F Cas 1018, 1019 (C C D Mass, 1817) ('*Lowell*').

In that case, the defendant had argued that the term 'useful' as contained in the *Act*,[186] was to be interpreted as one of general utility such that the plaintiff's pump must supersede existing pumps.[187] Justice Story, however, disagreed saying the provisions of the *Act* did not contain 'any such qualification or reference to general utility'.[188] Rather,

> [a]ll that the law requires is, that the invention should not be *frivolous or injurious to the well-being, good policy, or sound morals of society. The word 'useful,' therefore, is incorporated into the act in contradistinction to mischievous or immoral.* For instance, a new invention to poison people, or to promote debauchery, or to facilitate private assassination, is not a patentable invention. But if the invention steers wide of these objections, whether it be more or less useful is a circumstance very material to the interests of the patentee, but of no importance to the public. If it be not extensively useful, it will silently sink into contempt and disregard.[189]

However, by the late 1970s, the moral utility doctrine had begun to be whittled away. This was especially demonstrated by the Patents and Trademarks Office Board of Appeals' ruling in *Ex parte Murphy* that an invention used solely for gambling was eligible for patenting.[190] Up until then, such inventions had routinely been denied patentability on the grounds of immorality.[191] Additionally, the courts also became increasingly reluctant to apply the doctrine.[192] They were generally of the opinion that it was for Congress and not the courts to impose moral limits on patentability if it deemed it necessary.[193] In particular, the Federal Circuit in *Juicy Whip Inc v Orange Bang Inc* stated that

> [t]he requirement of "utility" in patent law is not a directive to the Patent and Trademark Office or the courts to serve as arbiters of deceptive trade practices. Other agencies, such as the Federal Trade Commission and the Food and Drug Administration, are assigned the task of protecting consumers from fraud and deception in the sale of food products …

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[186] *Patent Act*, Ch 11, § 1, 1 Stat 318, 318-321 (1793).
[187] *Lowell v Lewis* (n 185) 1019.
[188] Ibid.
[189] Ibid (emphasis added).
[190] *Ex parte Murphy*, 200 U S P Q (BNA) 801 (Bd Pat App & Int 1977).
[191] *National Automatic Device Co v Lloyd*, 40 F 89, 89-90 (C C N D III, 1889); *Reliance Novelty Co v Dworzek*, 80 F 902, 903 (C C N D Cal 1897); *Schultze v Hotz*, 83 F 448, 449 (C C N D Cal, 1897).
[192] Benjamin D Enerson, 'Protecting Society from Patently Offensive Inventions: The Risk of Reviving the Moral Utility Doctrine' (2004) 89 *Cornell Law Review* 685; UNCTAD-ICTSD, 'Patents: Ordre Public and Morality' in *Resource Book on TRIPS and Development* (Cambridge University Press, 2005) 375; Cynthia M Ho, 'Splicing Morality and Patent Law: Issues Arising from Mixing Mice and Men' (2000) 2 *Washington University Journal of Law and Policy* 247; Margo A Bagley, 'Patent First Ask Questions Later: Morality and Biotechnology in Patent Law' (2003) 45 *William & Mary Law Review* 469
[193] *Juicy Whip Inc v Orange Bang Inc*, 185 F 3d 1364, 1367 (Fed Cir, 1999) ('*Juicy Whip Inc*'); *Diamond v Chakrabarty* (n 36) 317.

> Of course, Congress is free to declare particular types of inventions unpatentable for a variety of reasons, including deceptiveness. *Cf.* 42 U.S.C. § 2181(a) (exempting from patent protection inventions useful solely in connection with special nuclear material or atomic weapons). Until such time as Congress does so, however, we find no basis in section 101 to hold that inventions can be ruled unpatentable for lack of utility simply because they have the capacity to fool some members of the public.[194]

As discussed above,[195] by 1980, the Supreme Court ruled that other than laws of nature, physical phenomena and abstract ideas, anything under the sun made by man is patentable.[196] This seemingly sounded a death knell on the moral utility doctrine. Nevertheless, in 1998, the USPTO posited that 'inventions directed to human/non-human chimera could, under certain circumstances, not be patentable because, among other things, they would fail to meet the public policy and morality aspects of the utility requirement'.[197] That same year, though, the University of Missouri applied for a patent for an invention involving a method for producing a cloned mammal, which the USPTO granted in spite of opposition towards the grant.[198] Given what has been described as the USPTO's lack of authority to deny patents on morally controversial inventions,[199] it is not surprising to note that the USPTO's earlier statement regarding moral considerations is not reflected in the Manual of Patent Examining Procedure section dealing with the utility requirement.[200]

Notwithstanding, it is possible that the moral utility doctrine may be revived given the recently passed *AIA*, which provides that claims directed to or encompassing human organisms (including human embryos and foetuses) are ineligible for patent protection.[201] The provision, described as the Weldon amendment, was originally introduced by Hon Dave Weldon for the purpose of prohibiting the use of appropriated funds to issue patents

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[194] *Juicy Whip Inc* (n 193) 1368.
[195] See above section 5.3.1.
[196] *Diamond v Chakrabarty* (n 36) 308-10; *Whistler Corp v Autotronics Inc*, 14 U S P Q 2d 1885, 1886 (N D Tex, 1988)
[197] 'Facts on Patenting Life Forms Having a Relationship to Humans', *United States Patent and Trademark Office* (Web Page, 28 December 2012) <https://www.uspto.gov/about-us/news-updates/facts-patenting-life-forms-having-relationship-humans>.
[198] *US Patent Application No 6211429*, filed on 18 June 1998 (Issued 3 on April 2001).
[199] Bagley (n 192) 477-8.
[200] See *Manual of Patent Examining Procedure* (n 75) ch 2100 s 2107.
[201] *AIA* (n 4).

containing claims that encompassed human beings.[202] This was further to an amendment of the *Consolidated Appropriations Act*.[203]

It was noted by Weldon that the intent of the provision was to codify existing USPTO policy and practice of not approving patent claims directed to human organisms (including embryos and human foetuses).[204] As the Supreme Court's ruling in *Diamond v Chakrabarty* had invalidated USPTO policy against patenting living organisms, it was considered imperative to avoid such a situation with human beings, given ongoing biotechnological advancements which threatened to turn 'humans themselves into items of property, of manufacture and commerce'.[205]

In terms of the scope of the amendment, Weldon noted that it was intended to apply to:

> patents on claims directed to or encompassing a human organism at any stage of development, including a human embryo, fetus, infant, child, adolescent, or adult, regardless of whether the organism was produced by technological methods (including, but not limited to, in vitro fertilization, somatic cell nuclear transfer, or parthenogenesis). This … applies to patents on human organisms regardless of where the organism is located, including, but not limited to, a laboratory or a human, animal, or artificial uterus.[206]

Specifically, Weldon added that the term 'human organisms' did not include stem cells,[207] which would align with USPTO practice of issuing patents on stem cells (including embryonic stem cells).[208] While these are present in human organisms at every stage of development, they are not in themselves human organisms.[209] In particular, he noted that

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[202] 147 *Congressional Record* HE2417 (Dave Weldon) (daily ed, 21 November 2003).
[203] *Consolidated Appropriations Act of 2004*, Pub L No 108-199, 118 Stat 3.
[204] 157 *Congressional Record* HE1177-80 (Christopher Smith) (daily ed, 23 June 2011); 147 *Congressional Record* HE2417 (Dave Weldon) (daily ed, 21 November 2003).
[205] 157 *Congressional Record* HE1177-80 (Christopher Smith) (daily ed, 23 June 2011).
[206] Human organism in this regard includes organisms of the human species which incorporate one or more genes taken from a nonhuman organism, e.g., human-animal hybrid organisms: 157 *Congressional Record* HE1177-80 (Christopher Smith) (daily ed, 23 June 2011) (which reproduced Speech of Hon Dave Weldon of Florida in the House of Representatives Monday, December 8, 2003. Conference Report on H R 2673, Consolidated Appropriations Act, 2004 (House of Representatives December 8, 2003).
[207] Ibid.
[208] *US Patent Application No 5843780*, filed on 18 January 1996 (Issued on 1 December 1998); *US Patent Application No 6200806*, filed on 26 June 1998 (Issued on 13 March 2001); *US Patent Application No 7029913*, filed on 18 October 2001 (Issued on 18 April 2006).
[209] 157 *Congressional Record* HE1177-80 (Christopher Smith) (daily ed, 23 June 2011) (which reproduced Speech of Hon Dave Weldon of Florida in the House of Representatives Monday, December 8, 2003. Conference Report on H R 2673, Consolidated Appropriations Act, 2004 (House of Representatives December 8, 2003).

> This amendment should not be construed to affect claims directed to or encompassing subject matter other than human organisms, including but not limited to claims directed to or encompassing the following: *cells, tissues, organs,* or other bodily components that are not themselves human organisms including, but not limited to, stem cells, stem cell lines, genes, and *living or synthetic organs*); ...[210]

Whilst it has been noted that the new provision is intended to affirm the continued patentability of stem cells,[211] the impact of the decisions in the previously examined cases on their continued status as patent eligible subject matter must not be overlooked.[212] This is aside suggestions that the *AIA* appears to provide third parties with broader avenues to challenge stem cell patents before the USPTO.[213]

Already, there have been attempts to repeal patents on isolated stem cells by the Consumer Watchdog using the decision in *AMP* and the *AIA*.[214] Although this failed for lack of standing,[215] and as such did not address the patentability of stem cells, it foreshadows the likelihood of future challenges to the patentability of not only stem cells, but other biotechnological subject matter.[216]

Nevertheless, whilst the term 'human organism' is not defined in the *AIA*, it is questionable whether the courts will interpret it as encompassing stem cells given the provision's legislative history. This is notwithstanding comments that the absence of a definition renders the term human organism subject to a wide or narrow interpretation by the courts.[217] Given *AMP* and other decisions considered earlier, it may very well be that future challenges to the patentability of stem cells and indeed bioprinted constructs are resolved on those grounds without reference to the *AIA*.

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[210] Ibid (emphasis added).
[211] *Manual of Patent Examining Procedure* (n 75) ch 2100 s 2105.
[212] Fendrick and Zuhn Jr (n 68); Davey et al (n 105).
[213] Jacob S Sherkow and Christopher Thomas Scott, 'Stem Cell Patents after the America Invents Act' (2015) 16(5) *Cell Stem Cell* 461, 463.
[214] Fendrick and Zuhn Jr (n 68); Davey et al, (n 105).
[215] Federal Court challenges of patents require the existence of an actual case or controversy. In this instance, the Consumer Watchdog had neither been sued nor threatened to be sued by the owners of the patents (WARF). Thus, they lacked standing before the Federal Circuit.
[216] Fendrick and Zuhn Jr (n 68).
[217] Tran (n 138); Davey et al (n 105); 'Claims Directed to or Encompassing a Human Organism', *United States Patent and Trademark Office* (Web Page, 20 September 2011) <https://www.uspto.gov/sites/default/files/aia_implementation/human-organism-memo.pdf>.

In the meantime, however, there does not appear to be any legislative provision in the USA equivalent to the general inconvenience provision in Australia or the *ordre public*/morality exception under the *EPC*, which could potentially be invoked to exclude bioprinted constructs in particular from patentability.

5.6 Conclusion

It has been suggested that the decisions examined in this chapter have dramatically changed the USA's 'landscape for patenting products and processes tied to the natural world'.[218] In particular, that Australian and European laws are now arguably more permissive than those of the USA especially in the context of patenting genes and genetic diagnostic methods.[219]

While this may be the case, its impact on the future patentability of bioprinted constructs and related bioprinting processes remains uncertain. For now, bioprinted constructs appear eligible subject matter to the extent that they are not accurate replicas of their naturally occurring counterparts. In the event that scientists are ever able to accurately replicate naturally occurring tissues and organs, there is a possibility that such bioprinted constructs will be considered ineligible subject matter. This would seem to imply that the patent system in the USA deters the accurate replication of naturally occurring products since it requires non-naturally occurring products to be 'markedly different' from their naturally occurring counterparts. This is contrary to the position in Australia and under the *EPC*, where it appears that the very fact that bioprinted constructs are man-made is sufficient to warrant subject matter eligibility.

For related bioprinting processes on the other hand, it is difficult to predict whether these will be considered eligible subject matter. This is especially with respect to the isolation and cultivation of living cells which embodies natural phenomena. Whilst this conclusion may appear similar to the position in Australia and under the *EPC*, case law suggests that the threshold required from transforming claims directed to a natural phenomena into a patent-eligible application is rather high. Moreover, various methods of isolating and cultivating living cells have been in existence for a long time. As such, claims in that regard

[218] Dreyfuss, Nielsen and Nicol (n 89) 550.
[219] Schwartz and Minssen (n 106) 238; Lai (n 68) 1074.

may be considered well-understood, routine and conventional such that they are rendered ineligible subject matter.

With regard to cellular/biological processes, it is unlikely that claims in this area will in themselves be considered eligible subject matter since they amount to natural phenomena. Furthermore, given that methods of treatment claims have generally been held patent eligible in the USA, it is likely that bioprinting *in situ* will be considered eligible subject matter unlike under the *EPC* where methods of treatment are expressly excluded from patentability. This certainly offers more certainty in comparison to Australia where the position is unclear.

On the matter of bioprinted constructs embodying embryonic stem cells, this does not appear relevant in the USA since such cells are presently patentable. In any case, the legislative history of the *AIA* does not indicate any intention to depart from existing practice of the USPTO in this regard.

Finally, while the exclusion of human organisms under the *AIA* may appear to have been ethically motivated, its application cannot be equated to the general inconvenience provision in Australia or the *ordre public*/morality exception under the *EPC*. While those provisions could potentially be invoked to exclude bioprinted constructs in particular from patentability, the *AIA* provision is specifically directed at human organisms. According to its legislative history, this does not include cells, tissues, organs, living organs or synthetic organs.

Given how complicated it is to establish subject matter eligibility, it is perhaps insignificant that the USA does not provide for a general ethically informed exclusion clause. In any case, it has been argued in the preceding chapter that its existence under the *EPC* appears unlikely to have any effect on patenting bioprinting.

Chapter 6

6 Emerging Trends in Patenting Bioprinted Constructs

6.1 Introduction

Further to earlier analysis of the patentability of bioprinted constructs and related bioprinting processes in Australia, Europe (under the *European Patent Convention* ('*EPC*'))[1] and the United States of America ('USA'), it would appear that these inventions are potentially patent eligible subject matter provided they are not specifically excluded. Nevertheless, as noted in the preceding chapters, there are also some uncertainties regarding their status as patent eligible subject matter. This is especially so with regard to the status of bioprinted constructs and related bioprinting processes as natural phenomena, differences between bioprinted constructs and their naturally occurring counterparts as well as their embodiment of embryonic stem cells ('ESCs').

To this end, a patent landscaping exercise was conceived to test the conclusion that bioprinted constructs and related bioprinting processes are potentially eligible subject matter. Nevertheless, given the fact that the eligibility of bioprinting processes such as preparation of materials, configuration of printers, printing methods, and maturation of the finished construct appear relatively uncontested, a landscaping of these processes was considered unnecessary. Similarly, methods of treatment were also excluded from the landscaping because their eligibility as patentable subject matter is definitively dealt with under the *EPC* (where they are expressly excluded) and the USA (where they have generally been held to be eligible subject matter). This is notwithstanding the fact that their eligibility as patentable subject matter is uncertain in Australia.

Furthermore, whilst the eligibility of process claims for the isolation and cultivation of living cells as well as cellular/biological processes involved in the fabrication of bioprinted constructs remains uncertain, there is no evidence in existing literature to suggest that these processes are necessarily exclusive to bioprinting. The isolation and cultivation of living cells as well as reliance on cellular/biological processes appear to be practices generally

[1] *Convention on the Grant of European Patents*, signed 5 October 1973, 1065 UNTS 255 (entered into force 7 October 1977) ('*EPC*').

widespread across tissue engineering and regenerative medicine.[2] In addition, the actual bioprinting process draws from general three-dimensional printing processes, which are again not unique to bioprinting. Thus, while their patenting poses some ethical concern within the context of monopolising natural phenomena, it was ultimately decided to limit the patent landscape to bioprinted constructs per se.

This is all the more so as this thesis is primarily concerned with ethical challenges that arise specifically from patenting bioprinting and not tissue engineering or regenerative medicine as a whole. While chapters three, four and five examined the subject matter eligibility of the aforementioned bioprinting processes, this was done primarily for the purpose of engaging with the suggestion that bioprinting patents should be limited to the process/method of manufacture to the exclusion of bioprinted constructs. In addition, limiting the landscaping to bioprinted constructs and not bioprinting processes allowed for a more reasonable workload to test the extent to which claims of this nature are being filed and granted.

Although there have been patent landscaping exercises conducted in relation to bioprinting, these have been more general in coverage as opposed to specialised reports focused on specific types of bioprinting-related inventions.[3] Given most of the discussions about ethical concerns pertaining to patenting bioprinting revolve predominantly around the likely implications of patenting bioprinted constructs in the context of ownership and monopolisation,[4] it is important that a patent landscaping exercise focused exclusively on

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[2] See, eg, *AU Patent Application No* 2017200691, filed on 2 February 2017 (Granted on 5 September 2019) (Engineered liver tissues, arrays thereof, and methods of making the same) where the applicant notes in [00126]-[00127] of the desription section that '[t]he cell types used in the engineered liver tissues of the invention are suitably cultured in any manner known in the art. Methods of cell and tissue culturing are known in the art ... Appropriate growth conditions for mammalian cells in culture are well known in the art'.

[3] See, eg, Robert W Esmond and Deborah Sterling, 'Bioprinting: The Intellectual Property Landscape' in Aleksandr Ovsianikov, James Yoo and Vladimir Mironov (eds), *3D Printing and Biofabrication* (Springer International Publishing, 2016) 1; John F Hornick and Kai Rajan, 'The 3D Bioprinting Patent Landscape Takes Shape as IP Leaders Emerge', *3D Printing Industry* (Web Page, 7 July 2016) <https://3dprintingindustry.com/news/3d-bioprinting-patent-landscape-takes-shape-ip-leaders-emerge-84541/>; Marisela Rodríguez-Salvador, Rosa María Rio-Belver and Gaizka Garechana-Anacabe, 'Scientometric and Patentometric Analyses to Determine the Knowledge Landscape in Innovative Technologies: The Case of 3D Bioprinting' (2017) 12(6) *PLoS ONE*; Timothy Sheehan et al, 'Recent Patents and Trends in Bioprinting' (2011) 4 *Recent Patents on Biomedical Engineering* 26; Amy J C Trappey, Charles V Trappey and Kurt L C Lee, 'Tracing the Evolution of Biomedical 3D Printing Technology Using Ontology-Based Patent Concept Analysis' (2017) 29 *Technology Analysis & Strategic Management* 339.

[4] See, eg, Ippokratis Pountos, Nazzar Tellisi and Nureddin Ashammakhi, 'Three-Dimensional Bioprinting: Safety, Ethical, and Regulatory Considerations' in Murat Guvendiren (ed), *3D Bioprinting in Medicine: Technologies, Bioinks, and Applications* (Springer International Publishing, 2019) 191, 192-3; S Vijayavenkataraman, W F Lu and J Y H Fuh, '3D Bioprinting – An Ethical, Legal and Social Aspects (ELSA) Framework' (2016) 1-2 *Bioprinting* 11; Niki Vermeulen et al, '3D Bioprint Me: A Socioethical View of Bioprinting Human Organs and Tissues' (2017) *Journal of Medical Ethics*;

bioprinted constructs is conducted. This provides an opportunity not only to test the aforementioned conclusion, but also to consider the breadth of claims for bioprinted constructs.

Accordingly, this chapter begins with an overview of existing bioprinting patent landscape reports. It identifies that there is a gap in existing literature for a specialised patent landscape report focused on bioprinted constructs in light of ethical concerns about their patenting. In itself, this makes the landscaping exercise a novel and original contribution to general discourse about the patentability of bioprinted constructs.

Thereafter, the methodology employed in conducting the landscaping is explained. This is followed by an assessment of the limitations encountered and presentation of results. In presenting the results, an attempt is made to identify emerging patterns in the bioprinted constructs patent landscape, which will inform further discourse in the remainder of this thesis.

Finally, as a result of emerging patterns of dominance by Organovo and the USA, as well as the patenting of bioprinted constructs potentially embodying ESCs, this chapter concludes that a deeper analysis of the ethical implications of patenting bioprinting, as contemplated by this thesis, is especially important at this stage of the technology's development.

6.2 Background

Patent landscaping refers to a 'process whereby larger, specifically selected collections of patent documents (whether granted or otherwise) are analysed to derive important technical, legal and business information'.[5] The aggregation of information obtained from such exercise 'provides technical and commercial conclusions, such as macro-economic or geographic trends in innovation or identifying changes in activity or technology commercialization strategy – whether industry wide or from a single organization perspective'.[6] Furthermore, it provides 'context of the major actors and players within a

Timo Minssen and Marc Mimler, 'Patenting Bioprinting-Technologies in the US and Europe – The 5th Element in the 3rd Dimension' in Rosa Maria Ballardini, Marcus Norrgård and Jouni Partanen (eds), *3D Printing, Intellectual Property and Innovation – Insights from Law and Technology* (Wolters Kluwer, 2017).

[5] Nick Solomon and Pardeep Bhandari, *Patent Landscape Report on Assistive Devices and Technologies for Visually and Hearing Impaired Persons* (World Intellectual Property Organisation, 2015) 10.

[6] Ibid 11.

space as well as identifying more niche corporations or research institutions with expertise and interest in the field'.[7]

Thus, while there is no universally accepted definition of a patent landscape report, it can nevertheless be described as constituting 'an overview of patenting activity in a field of technology, in a specific geographical area'.[8] Patent landscape reports generally seek to answer specific policy or practical questions and present complex information in a clear and accessible manner.[9] In addition, patent landscape reports provide evidence of emerging trends in a specific industry which can be used to drive innovation and investment policies. It is therefore unsurprising to note that in recent years, there has been an uptake in the use of patent landscape reports by policymakers to 'build a factual foundation before considering high-level policy matters, especially in fields such as health, agriculture and the environment'.[10]

Within the bioprinting sphere, a number of researchers have conducted patent landscaping with the predominant objectives of identifying emerging patterns and potential patenting opportunities. In one such study by Hornick and Rajan, they note that as of June 2016, almost 950 granted patents and pending applications had been filed worldwide.[11] This comprises both bioprinting processes and products (including bioprinted constructs).

In their analysis, Hornick and Rajan report that a majority of these granted patents and pending applications are held by companies, with Organovo Inc holding the most.[12] Other top patent assignees identified include Koninklijke Philips, Wake Forest University, Hewlett-Packard Company, the University of Texas System, Medprin Regenerative Medical Technologies Co Ltd and Corning Incorporated.[13] Hornick and Rajan also found that a majority of the inventors were resident in the USA, China, Japan, South Korea and the United Kingdom (Australia ranked number 14 on this list).[14]

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[7] Ibid.
[8] Anthony Trippe, *Guidelines for Preparing Patent Landscape Reports* (World Intellectual Property Organization, 2015) 8.
[9] Ibid.
[10] Ibid 8.
[11] The search only includes issued patents and published applications. As such, the authors suggest that this number may not tell the whole story as there could be numerous unpublished applications that will increase the overall number: Hornick and Rajan (n 3).
[12] Ibid.
[13] Ibid.
[14] Ibid.

In another study conducted by Rodríguez-Salvador, Rio-Belver and Garechana-Anacabe, Organovo was again identified as a leading organisation in the patenting of bioprinting technologies followed by Tsinghua University, Therics LLC and Xi'an Jiaotong University.[15] In terms of the most prolific patenting countries,[16] China, the USA, Korea, Great Britain, France and Australia were identified as leaders in this area. However, it was noted that if inactive patent families were discarded from the computation, leaving only applications and granted patent families, the USA would outpace China as the most prolific patenting country.[17]

Further, Rodríguez-Salvador, Rio-Belver and Garechana-Anacabe identified the USA, China, Germany, South Korea, Japan, United Kingdom, Italy, Australia, Singapore and Portugal as the top 10 most prolific nations in 3D bioprinting publishing.[18] Queensland University of Technology in Australia tied with China's Zheijiang University for 10th most frequent organizational affiliations of the authors.[19] Otherwise, the USA and China dominated the list with four and three of the top 10 organisations tied to them respectively.[20] This report was prepared based on a review of 601 documents (grouped into 345 patent families)[21] pertaining to patents applications and grants from the year 2000 to mid-2016 across 140 countries.

Whilst there have been additional bioprinting patent landscape reports published by other researchers,[22] these have not been as detailed as the aforementioned two in their statistical analysis. Nevertheless, it is worthy to note that in one of the reports, Organovo was once again identified as the leading organisation in patenting bioprinting tissue technologies.[23]

Overall, the reviewed reports provide a general overview of the bioprinting patent landscape as a whole. None of the reports categorises the reviewed patent documents into the different types of bioprinting-related inventions identified in chapter three, such as

[15] Rodríguez-Salvador, Rio-Belver and Garechana-Anacabe (n 3).
[16] That is, countries where patents were first filed.
[17] Rodríguez-Salvador, Rio-Belver and Garechana-Anacabe (n 3).
[18] Ibid.
[19] Ibid.
[20] Ibid.
[21] That is, a group of either patent applications or publications protecting a single invention by a common inventor filed in multiple countries.
[22] Esmond and Sterling (n 3); Sheehan et al (n 3); Trappey, Trappey and Lee (n 3).
[23] Trappey, Trappey and Lee (n 3).

hardware, software, bioprinting materials, bioprinting processes and bioprinted constructs. Whilst this categorisation is acknowledged in one report, the authors only provide examples of patents issued in the different categories, without any statistical analysis of the applicants and number of granted patents or pending application in each category.[24]

In light of the reasons identified in the introduction to this chapter,[25] and in the absence of specific data on bioprinted constructs, the idea of a patent landscape limited to bioprinted constructs in Australia, Europe and the USA was developed. This is in addition to the fact that the inherent nature of bioprinted constructs raises significant ethical concerns about the implication of patenting human tissue and potentially organs.[26] Whilst many have raised concerns about the patentability of bioprinted constructs as well as the likely impact of patenting,[27] information about the exact nature of what is being patented has been conspicuously absent from such discourse.

Although it is possible to consider the ethical, legal and social implications of patenting bioprinting as it would appear from the growing body of literature in this field, much of the current discourse lacks the nuance that can only be achieved from a review of evidentiary data. With the information contained in this chapter, it is proposed that stakeholders and interested parties will be able to engage in a more holistic and balanced consideration of the issues arising from patenting bioprinting.[28] This is more so because of the insight it provides, not only into what is being patented and by whom, but also into the existence of partnerships between organisations in the fabrication of bioprinted constructs - the latter being especially important to the conversation on access.

Accordingly, the landscape report contained in this chapter serves to not only enhance the analysis in this thesis, but also aims to fill an identified gap in existing literature - the absence of a patent landscape report of bioprinted constructs. This makes the landscape report a novel and original output of this thesis.

[24] Esmond and Sterling (n 3).
[25] See above section 6.1.
[26] This is examined in chapter seven as part of the broader issue of access to bioprinting.
[27] See, eg, Pountos, Tellisi and Ashammakhi (n 4) 192-3; Vijayavenkataraman, Lu and Fuh (n 4); Vermeulen et al (n 4); Minssen and Mimler (n 4).
[28] Nevertheless, it should be emphasised that the legal analysis contained in this chapter is not intended to be relied upon for legal advice.

Given this background, the following have been identified as the overarching objectives of the patent landscaping undertaken in this chapter:

i. to confirm whether attempts have been made to patent bioprinted constructs in any or all of the jurisdictions of focus – Australia, Europe and the USA;
ii. to identify emerging trends and patterns of patenting activity – this includes what is being patented, the extent to which it is being patented and by whom; and
iii. to examine these trends and patterns in light of ethical exclusions and access considerations in the patent laws of the selected jurisdictions.[29]

6.3 Methodology

The patent search methodology adopted in this chapter is grounded in the case study research method, which is generally used in the social sciences.[30] Crowe et al define case study as a 'research approach that is used to generate an in-depth, multi-faceted understanding of a complex issue in its real-life context'.[31] Thus, the case study research method is especially useful when 'there is a need to obtain an in-depth appreciation of an issue, event or phenomenon of interest, in its natural real-life context'.[32]

Given the aforementioned objectives of the patent landscaping undertaken in this chapter, it would appear that the case study research method offers a useful tool in addressing the issues raised. In particular, the landscaping represents a combination of two types of case studies, namely: the instrumental type of case study, which helps understand something other than the particular situation; and the collective type of case study, which is useful for comparing multiple situations.[33] This is because the patent landscaping involves a review of the patent databases in Australia, Europe and the USA with a view to generating insight into the broader issue of the likely impact of patenting bioprinted constructs.

As far as patent landscaping is concerned, it has been suggested that there are three fundamental steps that must be undertaken in the design of any patent search methodology. These are:

[29] It should be noted that this third objective spans across the entire width of this thesis.
[30] Sarah Crowe et al, 'The Case Study Approach' (2011) 11(100) *BMC Medical Research Methodology*.
[31] Ibid.
[32] Ibid.
[33] Robert E Stake, *The Art of Case Study Research* (Sage Publications, 1995) 3-4.

i. selection of data sources and patent coverage;
ii. understanding and selection of appropriate patent classifications; and
iii. understanding and selection of appropriate terminology related to the subject matter.[34]

However, as evidenced by the search methodologies described in existing bioprinting patent landscape reports,[35] this process is not often strictly adhered to. This is especially so in relation to the use of patent classifications (step ii), which does not appear to have been relied upon. While patent classification codes 'represent a hierarchical means for sorting documents into technology subcategories', it has been noted that they rarely conform to the market or industry thoughts on technological categories.[36] This is further complicated by the use of different systems across different patent offices.[37] Even where the same classification system is used, there is the probability of the classification codes being applied differently.[38] Thus, while classification codes are relevant, it has been acknowledged that reliance on other methods such as the use of search terms may be more appropriate depending on the nature of the landscape report.[39]

Further to this, it is instructive to note that there is currently no specific patent classification for bioprinting. This is as opposed to printing or additive manufacturing (including three-dimensional printing), for instance, which fall between B41 – B44 and subclass B33Y, respectively of both the International Patent Classification ('IPC') scheme and the Cooperative Patent Classification scheme.[40] Neither is there a single class for human tissue and organs. For instance, although C12N 5/071 under the IPC covers vertebrate cells or tissues such as human cells or tissues, A61K 35/407 also covers liver and hepatocytes. While a search of both classes would return potentially relevant patent documents, the use of patent classifications would have returned an inordinate amount of irrelevant patent

[34] Solomon and Bhandari (n 5).
[35] Rodríguez-Salvador, Rio-Belver and Garechana-Anacabe (n 3); Trappey, Trappey and Lee (n 3).
[36] Trippe (n 8) 90.
[37] Ibid.
[38] Ibid.
[39] Ibid.
[40] Whereas the IPC scheme is used by IP Australia, the Cooperative Patent Classification scheme is used by the European Patent Office and the United States Patent and Trademark Office.

documents. There is also the probability that some relevant claims would have been missed if an appropriate classification code were inadvertently omitted.

Given the specific nature of the landscaping, it was therefore considered more efficient to limit the methodology for this patent landscape to steps (i) and (iii). In any event, relying primarily on the use of search terms derived from step (iii) allowed for a more comprehensive search since this effectively involved searching the entire database. Thus, it is not expected that omitting step (ii) would have any considerable impact on the results obtained.

6.3.1 Selection of Data Sources and Patent Coverage

Given the focus of this thesis on the aforementioned jurisdictions, it was considered appropriate to limit the search to the patent database of each jurisdiction as opposed to using a global database. Accordingly, the database used were:

i. AusPat for Australian patent applications.
ii. European Patent Register and Espacenet for European patent applications.
iii. United States Patent and Trademark Office ('USPTO') Patent Full-Text and Image Database ('PatFT') and Patent Application Full-Text and Image Database ('AppFT') for American patent applications.

Although the earliest patent application for bioprinted constructs found using this search strategy dates back to 2005, it was not considered necessary to set a start date for the search. This was to ensure as comprehensive a result as possible in accordance with objective (i), which is to confirm and identify what attempts have been made to patent bioprinted constructs in each of the three jurisdictions. Moreover, with the production of bioprinted constructs still in its nascent stage, it was anticipated that the results returned using this search strategy would be manageable.

It was nevertheless necessary to set a cut-off date for the end of the search so as to avoid an open-ended search that lacked certainty of time and results. A cut-off date of August 2019 was chosen to allow for a comprehensive collation and review of data. Thus, it is possible that at the time of submission, the filing status of some of the granted patents and pending applications may have changed. It should therefore be borne in mind that the data contained in the landscape report is valid as of August 2019.

It is useful at this juncture to provide an overview of each of the databases and their search capabilities as they differ to a slight degree.

a) Australia - AusPat (1904 – August 2019)

In comparison to the USPTO system, the Australian AusPat is a single search engine platform that contains details of patent applications lodged and granted in a single database. Additionally, patent applications that have been accepted, ceased, lapsed or withdrawn are also displayed in the search results.

In terms of its search capabilities, it allows for the inclusion of abstract, specification or full texts in the search conducted. The advantage of this is that it allows for a more thorough search of the database since the abstract, specification or full texts (where available), as well as the default search fields will be indexed for matches of the search terms.

b) Europe - European Patent Register and Espacenet (1782 - August 2019)

The European Patent Register provides comprehensive information on all published European patent applications through each stage of the granting process, and includes links to the national patent registers of many of the *EPC* Convention States.[41] It also provides direct links to the Espacenet page containing original documents of each patent application, as these are not contained in the Register. Espacenet is the European Patent Office's ('EPO') internet-based patent information search tool launched in 1998 as replacement for the ESPACE CD-ROMs on which patent documents were previously stored.[42] It contains up-to-date patent records from many patent authorities across the world including those of the *EPC* member states.[43]

Thus, given the focus on European patents, it was considered more pragmatic to conduct the initial search on the European Patent Register and then click through to the Espacenet page of the relevant patent application for the original patent documentation.

[41] 'European Patent Register', *European Patent Office* (Web Page, 15 May 2019) <https://www.epo.org/searching-for-patents/legal/register.html#tab-1>.
[42] '40-30-20-10 Anniversaries', *European Patent Office* (Web Page, 27 September 2018) <https://www.epo.org/searching-for-patents/40-30-20-10.html>.
[43] Ibid.

Similar to AusPat, the European Patent Register is a single search engine platform. However, unlike AusPat, it does not allow for the inclusion of abstract, specification or full texts in the search conducted. Instead, the search is limited to bibliographical fields such as title, inventor, applicant, opponent, representative, publication number or publication date depending on the search term used. The disadvantage of this is that if the search terms are not contained in any of the bibliographical fields, there is the likelihood of relevant patent applications being omitted from the search results. Indeed, this was one of the limitations encountered in the search conducted on European patents in particular.

c) USA - USPTO Patent Full-Text and Image Database (1790/1976 – August 2019) and Patent Application Full-Text and Image Database (2001 – August 2019)

Unlike AusPat and the European Patent Register, the United States' system provides for two separate databases for patent applications and granted patents. Whereas PatFT contains details of issued patents, AppFT is limited to published patent applications. In both databases, however, all of the text in the publication are searchable. This includes the inventor's name, published application's title, assignee's name, abstract, full description of the invention and the claims. This made the USA patent search for bioprinted constructs perhaps the easiest and most comprehensive of all the searches.

6.3.2 Understanding and Selection of Appropriate Terminology Related to the Subject Matter

As a number of researchers have previously conducted patent landscaping in the bioprinting sphere,[44] their reports provided a useful resource for the understanding and selection of appropriate terminology for this landscaping. Drawing from this, an initial list of search terms was compiled and tested in different query structures in the database of each jurisdiction. The purpose of this was to ascertain their suitability for the landscaping, and also identify additional search terms. With their suitability confirmed, the initial list and the additional search terms identified from the test served as the primary search terms used in this landscaping. These consisted of names of prominent institutions/organisations in the field as well as technical terms used in relation to bioprinting. Where appropriate, multiple search terms were used in a single search to refine the search results. Although

[44] Esmond and Sterling (n 3); Hornick and Rajan (n 3); Rodríguez-Salvador, Rio-Belver and Garechana-Anacabe (n 3); Trappey, Trappey and Lee (n 3).

exclusion terms are often used in patent searches to eliminate unwanted data, their use was considered unnecessary as the results returned from using the selected search terms were sufficiently specific and did not warrant such further refinement.

6.3.3 Collection Collation Method

In order to understand the steps taken in the collation and analysis of data, it is useful to provide an overview of the relevant components of the patent documents reviewed. These are:

i. **Abstract:** This has been described as 'a concise summary of the technical disclosure of a patent document enabling a reader to quickly ascertain the subject matter covered.'[45] It does, however, merely serve an informational purpose and ought not to be taken into account for any other purpose such as interpreting the scope of protection claimed in the patent document itself.[46] In many cases, the abstract is one of the key aspects of the patent document indexed in searches.

ii. **Applicant/Assignee:** The applicant is the entity or person which or who files an application for the grant of a patent, or in whose name an agent (representative) files such an application.[47] In the USA, it is common to see an assignee mentioned in patent documents. This is the person to whom the inventor has assigned his/her right in the invention.

    Generally, the applicant/assignee is the owner and holder of rights in a patent. Accordingly, any negotiation for the rights associated with a patented invention must be conducted with them.[48] While the identities of applicants/assignees may change over the lifecycle of a patent, it is nevertheless useful for study as it enables the identification of commercialising entities and collaborations within a technical area.[49]

[45] 'Handbook on Industrial Property Information and Documentation', *World Intellectual Property Organisation* (Web Page, June 2013) <https://www.wipo.int/standards/en/index.html> ('*Handbook on Industrial Property Information and Documentation*').
[46] Ibid.
[47] Ibid.
[48] Trippe (n 8) 17.
[49] Ibid.

iii. **Claims:** This is the 'part of a patent document which defines the matter for which protection is sought or granted'.[50] In patent documents, there are typically three kinds of claims: main, dependent and independent. The main claim, which is the first claim, is generally expected to include all the technical features of the invention.[51] Additional features not essential, but beneficial, are typically contained in dependent claims that refer to the main or any other claim.[52] Independent claims, on the other hand, are additional to but independent of the main claim or any other claim.[53] An example is the claim for a product created by the process contained in the main claim or vice versa. However, the principle of unity of invention must be observed for such independent claims to be accepted as part of a single application.[54]

iv. **Description/Specification:** The description is one of the essential aspects of patent documents which 'usually specifies the technical field to which the invention relates, includes a brief summary of the technical background of the invention and describes the essential features of the invention with reference to any accompanying drawings'.[55] In essence, it fulfils the disclosure aspect of the patent system.

Related to this is the specification section, which gives a detailed description of the invention, accompanied by claims. Where appropriate, the specification may also include drawings and formulae.[56]

As the description section generally contains a combination of information on the invention itself and historical information on similar inventions, it is often considered ambiguous for landscape analysis.[57] Accordingly, it is generally considered best to omit the description section from any analysis.[58] Nevertheless, for the purpose of this landscaping, a careful review of the description and

[50] *Handbook on Industrial Property Information and Documentation* (n 45).
[51] Trippe (n 8) 22.
[52] Ibid.
[53] Ibid.
[54] The principle of unity of invention mandates that an application must relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. Otherwise, the application must be divided: *Handbook on Industrial Property Information and Documentation* (n 45).
[55] Ibid.
[56] Ibid.

[58] Trippe (n 8) 21.

specification sections has been undertaken to ascertain the potential embodiment of ESCs and induced pluripotent stem cells ('iPSCs') in bioprinted constructs. This is further to earlier analysis of provisions excluding inventions embodying ESCs from patentability as well general ethical concerns arising from the use of ESCs.

v. **Inventors:** While details of inventors are not noted in this report, it is nonetheless useful to set out who an inventor is in relation to applicants/assignees. The inventor is the author of the invention who, by virtue of article 4ter of the *Paris Convention*,[59] reserves the right to be mentioned as such in the patent.[60] While the inventor may also be named as applicant on a patent application, it is not uncommon for a different person or entity to be named as applicant. As with applicants/assignees, studying inventors provides insight into potential experts and collaboration within a technical area.[61] Nevertheless, in light of the aforementioned objectives of this landscape and this thesis in general, the analysis of the patent landscape focuses on applicants/assignees to the exclusion of inventors.

vi. **Title of the Invention:** This refers to 'several words contained in the request part of the application indicating clearly, concisely and as specifically as possible the subject matter of the invention'.[62] Like the abstract, it is one of the key aspects of the patent document indexed in searches.

Having set out the above information, this section now turns to the steps taken in the collation of data for the patent landscape report.

Following the selection of appropriate search terminologies, a search for patent applications lodged and granted in each of the jurisdiction was conducted in the relevant databases. In the first instance, single term searches were conducted using each of the identified search terms. This involved entering search terms such as 'bioprint*', 'three-dimension*' and 'Organovo' into the text entry boxes in order to generate results. In some cases, such as with 'Organovo', for instance, the results returned were few and could easily be manually reviewed for relevance. In other cases, multiple search terms such as 'three-

[59] *Paris Convention for the Protection of Industrial Property,* opened for signature 20 March 1883*,* 828 UNTS 305 (entered into force 7 July 1884).
[60] *Handbook on Industrial Property Information and Documentation* (n 45).
[61] Trippe (n 8) 18.
[62] *Handbook on Industrial Property Information and Documentation* (n 45).

dimension* AND cell* AND print*' had to be used to refine the search results as the initial results returned were too large to be manually reviewed for relevance.

Ultimately, the search capabilities of each database determined the most effective search strategy for that particular database. With the USPTO databases, for instance, the use of single search terms such as 'bioprint*' generated comprehensive results as the full text of the patent documentation were indexed. While this meant fewer search terms were needed to review the USPTO database, it also meant that patent documentations had to be carefully reviewed for relevance since documents that had 'bioprint*' mentioned even just once in the reference section were included in the search results. In contrast, with AusPat and the European Patent Register, more search terms, usually a combination of two or more, had to be entered to generate a more comprehensive result. The implication of this was that not all the search terms identified in the master list were used in each database. Rather, the search terms used in each database were selected based on the search capabilities of each database.[63] It is unlikely that this action would affect the validity of the results obtained given earlier explanations about the varied nature of each database.[64]

In order to refine the results for each search string, the first step was to determine the status of the applications. This was especially important with AusPat and the European Patent Register as the results returned included applications at different stages of their lifecycle. Applications that had ceased, lapsed or been withdrawn were immediately discounted. The only relevant statuses for the search were filed/pending and granted. Given the earliest recorded patent filing for a bioprinted construct was in 2005, none of the applications were found to have expired.

Upon this initial refinement, the titles of the applications were reviewed for reference to tissues, organoids or methods of fabricating either. Applications that did not meet these criteria were immediately discounted. Thereafter, the abstract and the claim section of the remaining applications were reviewed to ascertain whether bioprinted constructs had been claimed in the application. In most cases, this was relatively easy to ascertain. In some cases,

[63] See Appendix A - C for the search terms used in each jurisdiction.
[64] See above section 6.3.1.

however, while it was clear that a biological construct was claimed, the method of production was uncertain.

Accordingly, where it was confirmed that biological constructs were claimed in the application, the description/specification section was then reviewed to ensure bioprinting was listed as a method of production. Although in some cases bioprinting was listed as only one of many methods or as a method for producing one aspect of the claimed construct, these applications were nevertheless included in the final results since they involved some measure of bioprinting. It should be clarified, however, that the reasoning behind reviewing the method of production was to ensure that only applications claiming tissue/organ constructs fabricated by bioprinting (that is, bioprinted constructs) were ultimately captured in the report.

Finally, the claim and description/specification sections were also reviewed for intended use as well as the embodiment of ESCs and iPSCs in the claimed invention. As noted earlier, this information is especially important as it relates to the ethical issues surrounding the patenting of bioprinted constructs.

6.4 Limitations and Comments

It should be emphasised, at this juncture, that the overarching objective of this landscaping was to understand the patent landscape of bioprinted constructs. Accordingly, while every effort was made to capture all patent applications for bioprinted constructs lodged and granted in the report, it is likely some may have been omitted inadvertently owing to some of the limitations noted below. Notwithstanding, it is highly unlikely that any such omissions would impact on the overall accuracy of the analysis reported in the next section.

A major limitation identified in relation to the search is that applications for bioprinted constructs were generally not immediately apparent on the face of the patent document. Many of the titles of the applications did not offer any indication as to whether bioprinting had been employed as a mode of production. For example, Australian patent 2011227282 is titled 'Multilayered vascular tubes', giving no indication as to the method of production. In some cases, a reading of the abstract and the claims did little to clarify the uncertainty. This meant a review of the description/specification section of each potentially relevant application was required. As noted earlier, the description/specification section is often

considered ambiguous for landscape analysis because it contains a combination of information on the invention itself and historical information on similar inventions.

Closely related to this is the fact that bioprinting is an offshoot of regenerative medicine and tissue engineering. Thus, while reference may have been made to regenerative medicine or tissue engineering in the patent documents, it was unclear, in some cases, whether this involved bioprinting. Generally, where there was no reference to bioprinting in any of its different nomenclatures (such as organ printing, additive manufacturing, layer-by-layer), the item was omitted from the final results. However, where there was some reference to bioprinting, including as one of the steps taken, such items were included in the final results.

In addition, some of the claims were overly general in their reference to bioprinted constructs without any more explanation as to whether a specific tissue construct was contemplated. This made it difficult to attempt any mapping of the specific tissues/organs being patented. It should be emphasised that while the claims were reviewed to ascertain that bioprinted constructs formed part of the claim, the landscaping did not involve a detailed analysis of the patent claims. This is in light of the complexity involved in analysing patent claims and the defined scope of the landscaping exercise.

In terms of interpreting the data and identifying emerging patterns, it should be emphasised that patent landscaping does not reveal patentee behaviour in terms of licensing. While some institutions or organisations might appear to be more prolific than others in filing patent applications, this is not conclusive as to how granted applications will be exploited. At best, the information gleaned from patent documents is only suggestive as to potential access issues. This is all the more so, where it appears that certain institutions or organisations might be dominating the field. Information about licence negotiations, grants and terms cannot reasonably be obtained from patent documents as such information is beyond the latter's purview. Any such information would have to be obtained from external sources. Hence, it is difficult to draw any definitive conclusion from the reviewed patent documents about the impact granted applications could potentially have on access.

Finally, while it was originally planned to undertake a comparison of the claims of similar patents granted across the three jurisdictions to determine how they might have been adapted to respond to limitations in local laws, this idea had to be reconsidered. This was

primarily due to the limited availability of information required to arrive at firm conclusions. In any event, a review of the results revealed that no single invention has been granted across all three jurisdictions. Even if they had been, comparing the claims would be a huge and complex undertaking for anyone not skilled in the art. It may very well also be the case that strategic decisions may have been made by applicants as to if, how and when to file in each of the three jurisdictions. It was therefore determined that there were too many variables to attempt any credible comparison.

6.5 Patent Landscape Report on Bioprinted Constructs

Overall, the results obtained from the patent landscaping of bioprinted constructs appear to be in concordance with the conclusion in chapter two that bioprinting is still in its developmental stages. Notwithstanding, it is evident that there are ongoing attempts to patent bioprinted constructs across all three jurisdictions, despite the viability of bioprinted constructs being uncertain.

In line with the objectives of this landscape exercise to provide a holistic overview of patenting of bioprinted constructs, this landscaping covered both granted patents and pending applications. It should be noted, however, that pre-grant (pending) applications, though providing evidence of filing activities, are not reliable indicators of property rights as they could potentially be refused, withdrawn or granted in limited form.[65] Such applications could also have been filed defensively with the intention of publicising the technical innovation so as to prevent others from obtaining patents over the subject matter.[66] Granted patents, on the other hand, are considered better quality indicators for innovation activities as the grant asserts that information is new and inventive compared to prior art.[67] Accordingly, the data for granted patents and pending applications are distinguished in this report.

In total, the USPTO holds the highest number of patent applications received and granted. Between 2005 and August 2019, the search reported in this chapter revealed that a total number of 71 applications for bioprinted constructs have been filed in the USA, of which 11 have been granted. This is followed by a total number of 26 applications received by

[65] Trippe (n 8).
[66] Ibid.
[67] Ibid.

the EPO, of which only two have been granted. Out of the three jurisdictions considered, IP Australia received the least number of applications (24), but has, however, granted more patents (eight) than the EPO. IP Australia also holds the highest number of applications granted in proportion to the total applications filed with a ratio of 1:3. Altogether, these results echo other authors' sentiments that bioprinting is still in early stages and, with the patenting process taking years, relatively few patents have been granted thus far.[68]

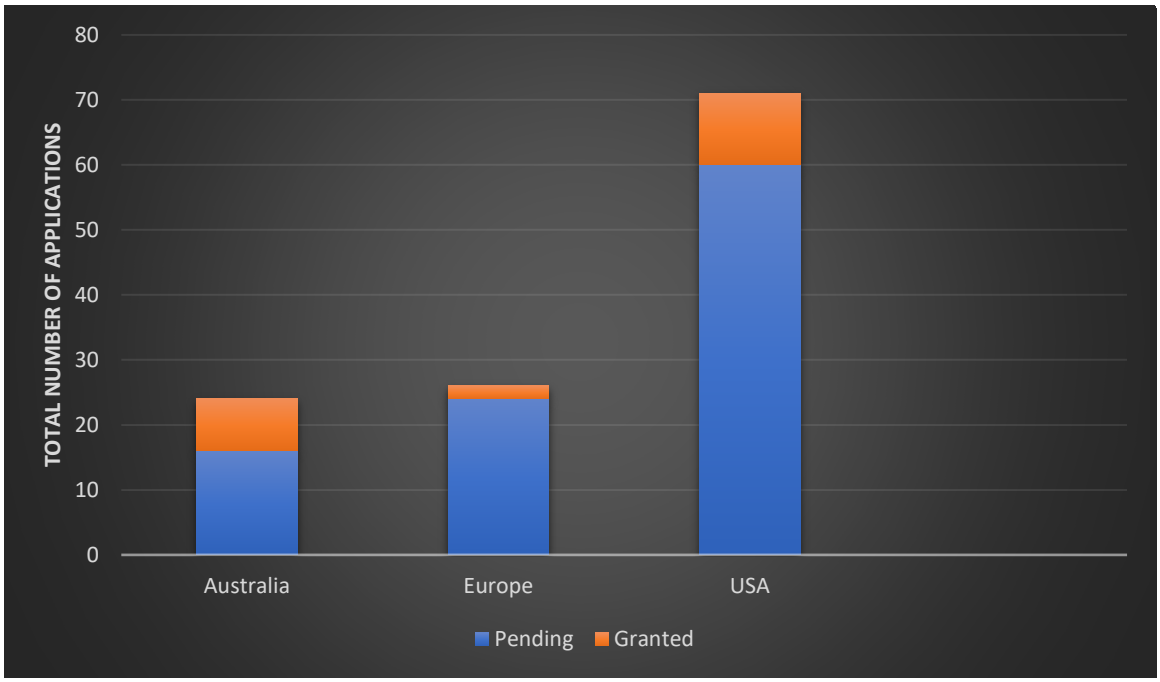

Figure 6.1: Total Filings

The remainder of this section will now examine closely the results obtained under identified headings.

6.5.1 Top Applicants/Assignees

In most patent landscape reports, including the aforementioned bioprinting patent landscape reports, it is common for the top five or 10 applicants/assignees to be identified. However, because of the limited number of applications, it was decided in this study that for an entity or person to be considered a top applicant/assignee, they must hold at least one granted patent and one pending application. Accordingly, the length of the list of top applicants/assignees varies across the three jurisdictions.

[68] Rodríguez-Salvador, Rio-Belver and Garechana-Anacabe (n 3).

In Australia, only four entities achieved this benchmark, whereas in Europe, the number increased to five. The USA, however, had 10 entities on the list of top applicants/assignees. Notwithstanding, across the three jurisdictions, Organovo holds the greatest number of filed and granted patents in each jurisdiction. In fact, in Europe, the only two granted patents for bioprinted constructs belong to Organovo. In Australia, Organovo owns more than half of relevant, granted patents, whilst in the USA, it owns a little over 35% of the granted patents.

Thereafter, the order of top applicants/assignees diverges across the three jurisdictions. The only other applicant/assignee that appears on the list of top applicants/assignees across all three jurisdictions is Wake Forest University. It ranks as second top applicant/assignee in Australia and the USA with a total of four and nine applications, respectively. In Europe, it is fourth on the list with a total of two applications. Of all these applications, only one has been granted and that is in the USA.

Although this section focuses on top applicant/assignee, it is interesting to note that, across the three jurisdictions, the list is dominated by organisations registered primarily in the USA. While no Australian institution appears on the list, one European institution (Cellink AB (Sweden)) does appear.

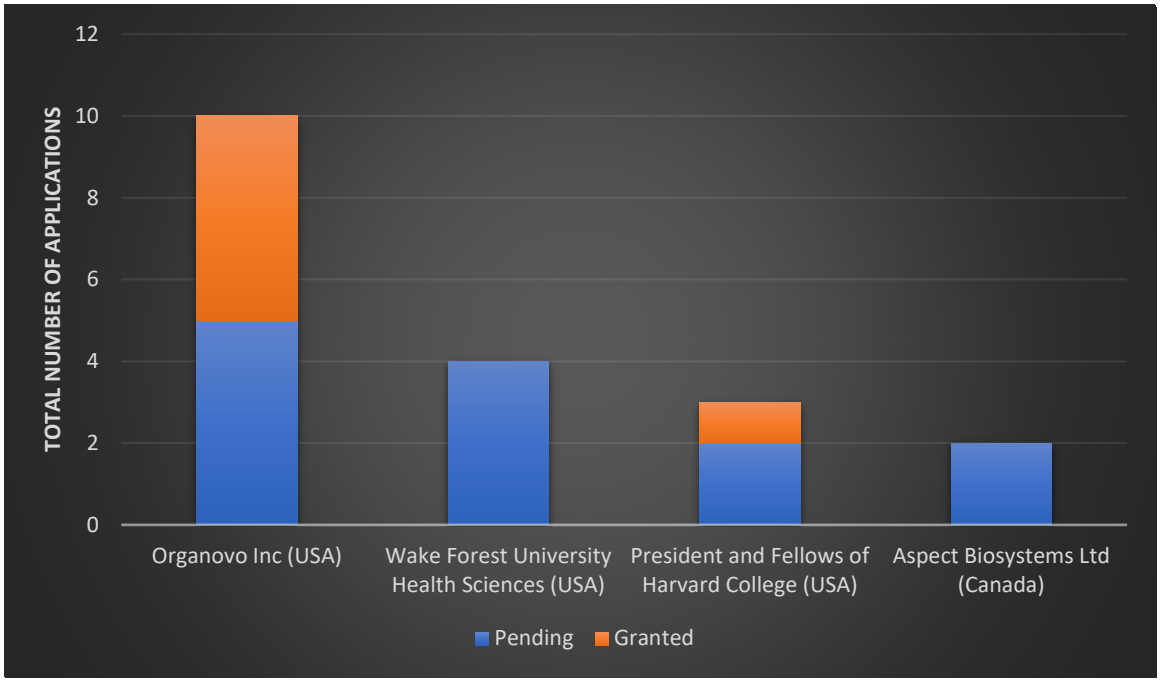

Figure 6.2: Top Applicants/Assignees in Australia

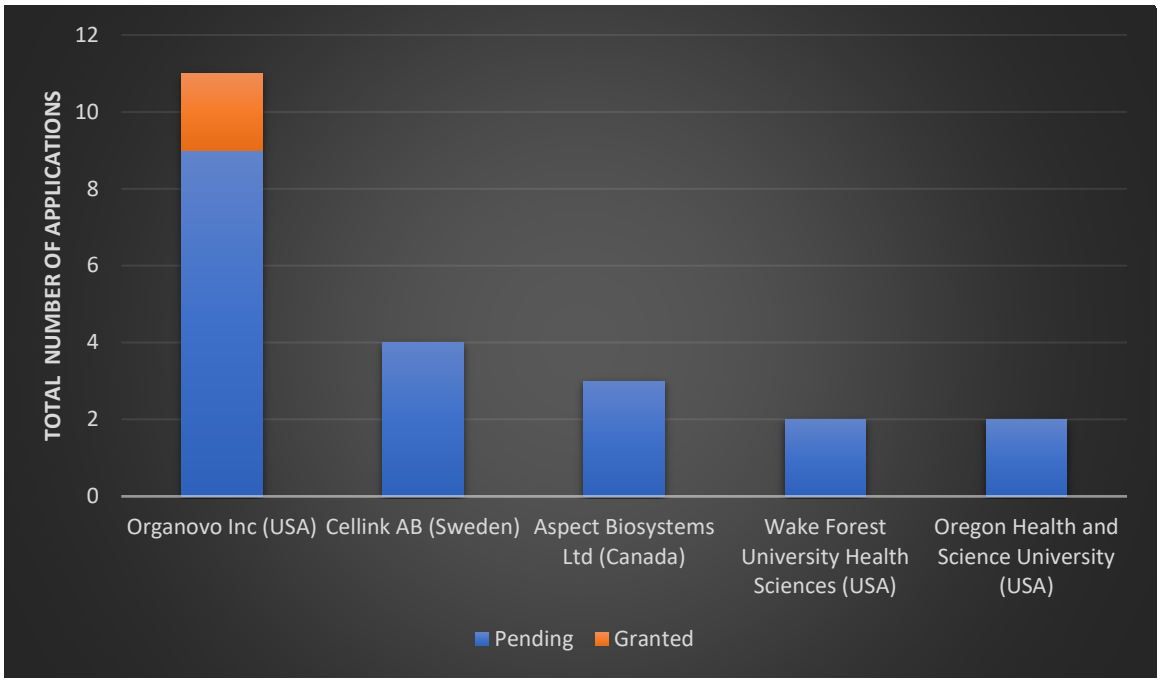

Figure 6.3: Top Applicants/Assignees in Europe

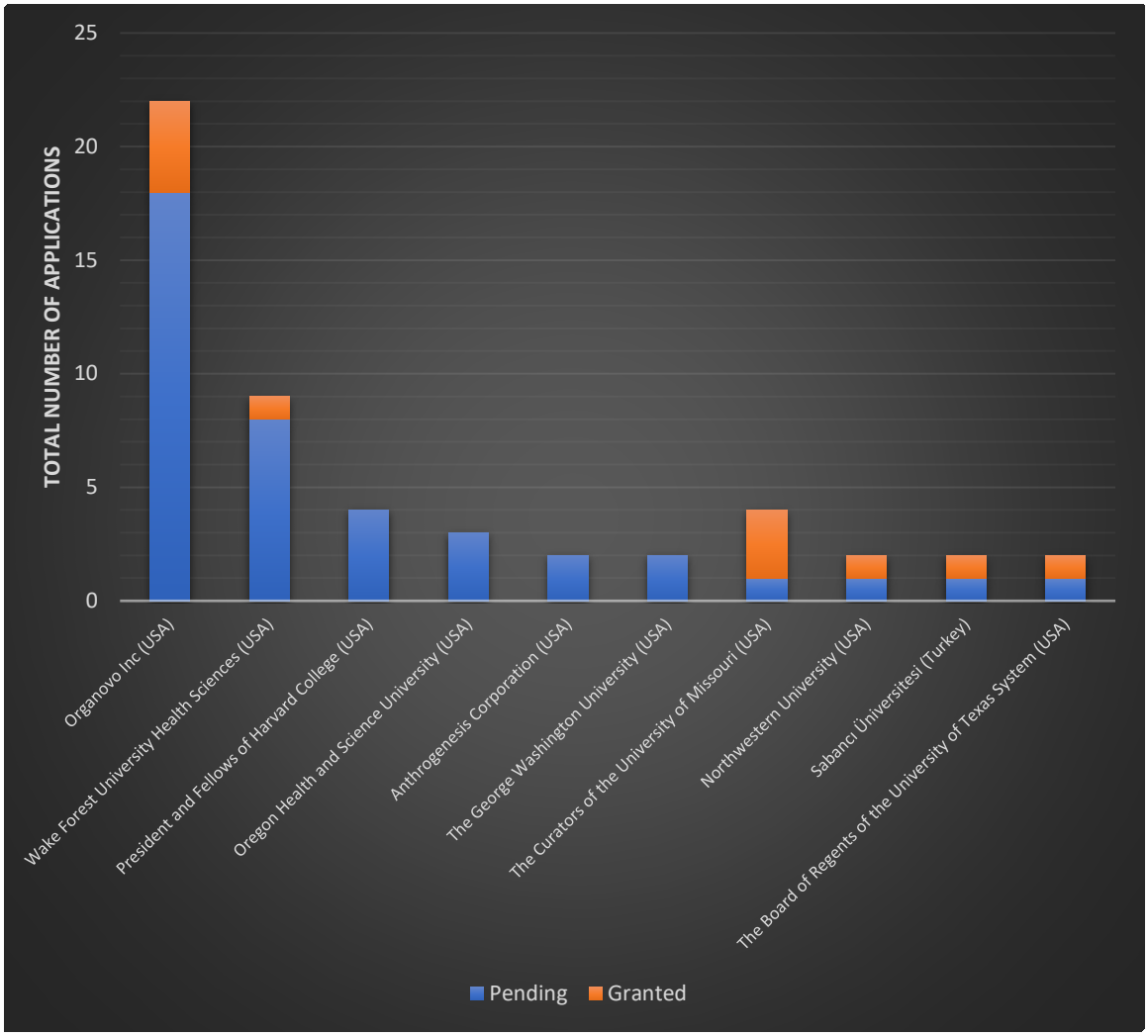

Figure 6.4: Top Applicants/Assignees in the United States of America

6.5.2 Type of Applicants/Assignees

Pursuant to further discourse about access to bioprinting presented in the next chapter, it was considered useful to identify any emerging patterns in the types of applicants/assignees seeking patent protection for bioprinted constructs. This is because of the insight it offers into the commercialising entities that are expected to be operating within any markets that might exist for bioprinted constructs. It should be noted that while the source of research and development funding is equally relevant to the discourse about access, such information is not provided in patent documents and would require further inquiries which are beyond the scope of this thesis.

From the results obtained, it would appear that patenting by for-profit organisations and academic institutions is prevalent across all three jurisdictions. However, in comparison to

Australia and Europe, more academic institutions appear to be filing for patents in the USA. This is likely due to the fact that across all three jurisdictions, most of the academic institutions applying originate from the USA with the exception of one from Australia, India and Turkey each, and two from Switzerland.

It is interesting to note that out of the two recorded applications for bioprinted constructs submitted by the Australian university (University of Queensland), neither was submitted in Australia. Instead, one was submitted in Europe and the other in the USA with the same title - Differentiation of Pluripotent Stem Cells to Form Renal Organoids.[69] Perhaps even more interesting is the fact that a similarly titled application was actually submitted in Australia by the University of Queensland prior to the applications in Europe and the USA.[70] However, while the application submitted in Australia claims a method of bioprinting whole kidneys and kidney tissue, it omits the claim for 'a bioprinted renal structure …', which is contained in both the *EPC* and USA application respectively.[71] As the landscaping was strictly focused on applications claiming bioprinted constructs, the Australian application was not included in the results since it was a purely method-based application. Nevertheless, the omission of the construct claim from the Australian application does arouse curiosity as to what may have informed this decision. While it is possible that the omission was in response to the legal environment in Australia which has previously been considered in chapter three, it should be noted that similar restrictions on the patentability of inventions embodying ESCs exist in Europe. This is in addition to the fact that only the *EPC* provides a general exclusion clause founded on morality.

Furthermore, in terms of partnerships between various types of applicants/assignees, it is worthy to note that Organovo appears to have submitted the greatest number of joint applications with other types of applicants/assignees. In particular, it holds a number of applications jointly filed with Oregon Health and Science University for breast tissue and

[69] *EPC Patent Application No EP3234108A1*, filed on 15 December 2015 - Differentiation of Pluripotent Stem Cells to Form Renal Organoids; *US Patent Application No 20190032020*, filed on 15 December 2015 - Differentiation of Pluripotent Stem Cells to Form Renal Organoids.
[70] *AU Patent Application No 2014277667*, filed on 15 December 2014 - Differentiation of Pluripotent Stem Cells to Form Renal Organoids.
[71] Compare *AU Patent Application No 2014277667*, filed on 15 December 2014 - Differentiation of Pluripotent Stem Cells to Form Renal Organoids with *EPC Patent Application No EP3234108A1*, filed on 15 December 2015 - Differentiation of Pluripotent Stem Cells to Form Renal Organoids; *US Patent Application No 20190032020*, filed on 15 December 2015 - Differentiation of Pluripotent Stem Cells to Form Renal Organoids.

tumour models – one in Australia (filed 2014), two in Europe (filed 2014 and 2017) and two in the USA (filed 2014 and 2018). This would appear pursuant to the partnership between Organovo and the Knight Cancer Institute at Oregon Health & Science University, announced in 2013, for the development of three-dimensional cancer models intended to advance discovery of novel cancer therapeutics.[72] Similarly, Organovo also filed an application for skin tissues with L'Oréal in 2015 - the same year it announced a collaborative research partnership with L'Oréal to develop 3-D printed skin tissue for product evaluation and other areas of advanced research.[73]

Finally, it is also worthy to highlight the fact that the only government entity to file an application for bioprinted constructs across the three jurisdictions is the United States of America, as represented by the Secretary Department of Health and Human Services. It holds one application in Australia, and another in Europe jointly filed with George Washington University, but none in the USA.

[72] 'Organovo and OHSU Knight Cancer Institute Announce Collaboration in Cancer Research', *Organovo* (Web Page, 30 January 2013) <https://ir.organovo.com/news-releases/news-release-details/organovo-and-ohsu-knight-cancer-institute-announce-collaboration>.

[73] Brittney Sevenson, 'L'Oréal USA & Organovo Team for 3D Printed Human Skin Tissue Research', *3DPrint.com* (Web Page, 7 April 2015) <https://3dprint.com/56475/loreal-organovo-skin-research/>; 'L'Oreal USA Announces Research Partnership with Organovo to Develop 3-D Bioprinted Skin Tissue', *Organovo* (Web Page, 5 May 2015) <https://organovo.com/05052015-2/>.

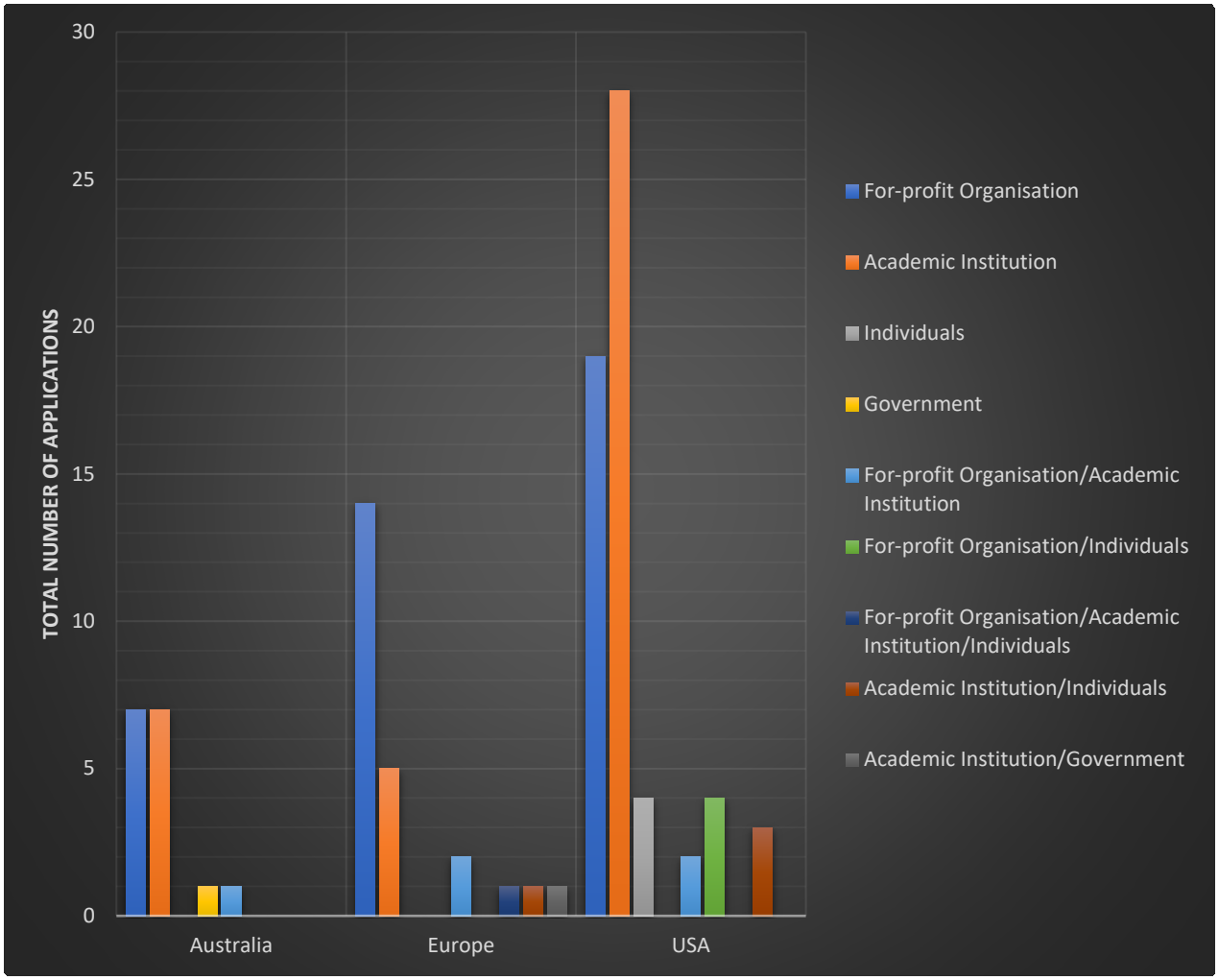

Figure 6.5: Type of Applicants/Assignees (Pending Applications)

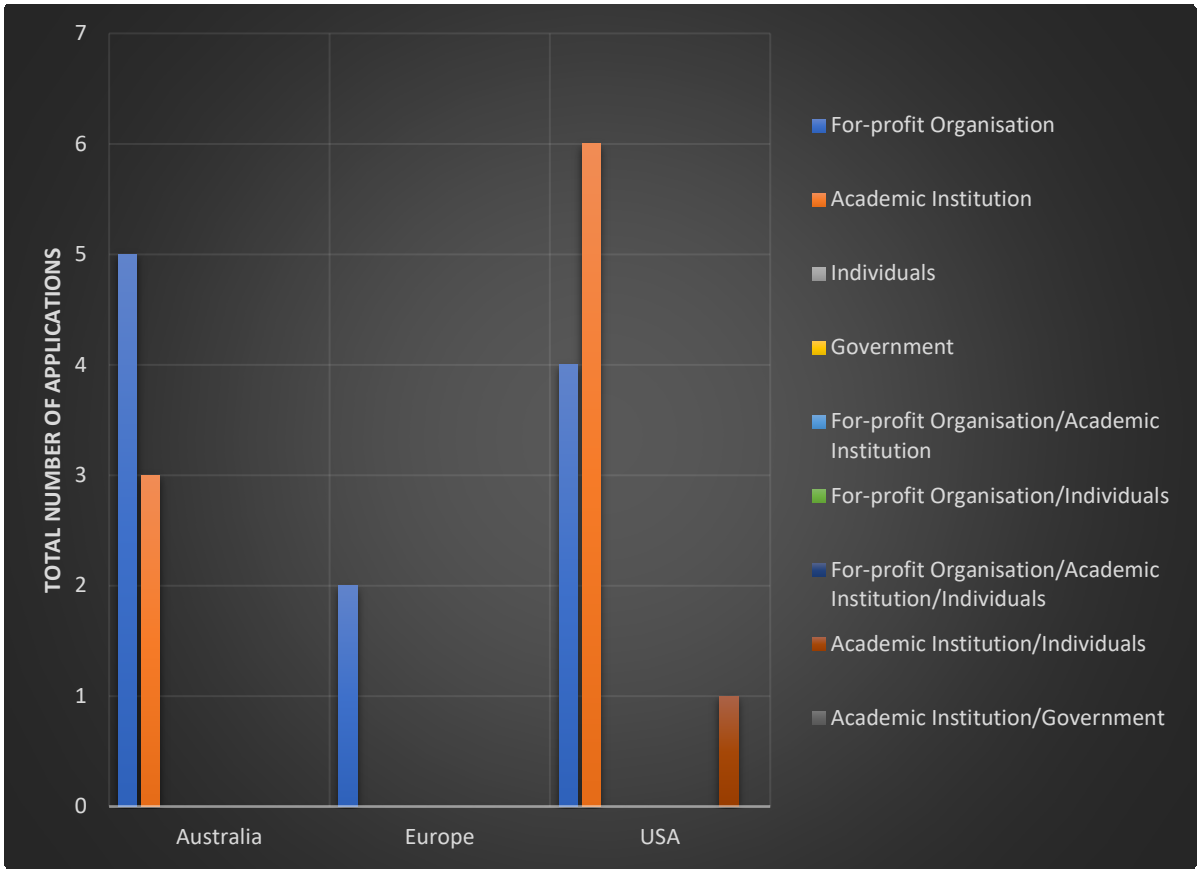

Figure 6.6: Type of Applicants/Assignees (Granted Patents)

6.5.3 Country of Origin of Applicants

This section examines the overall geographical spread of the country of applicants across the three jurisdictions. From the results obtained, it would appear that many patent applications for bioprinted constructs originate from applicants based in the USA. However, while one might be tempted to interpret this as meaning there is more innovation originating from the USA, care should be taken in reaching such conclusions in the absence of any conclusive evidence. This is all the more so as it is equally evident that there is on-going innovation in bioprinting across all three jurisdictions. In addition, the search methodology employed presents limitations in terms of what conclusions can be drawn. A broader search including all bioprinting-related inventions would have enabled more comprehensive conclusions.

It may very well be that, in comparison to their counterparts from other countries, applicants based in the USA are more inclined to patent as many inventions as they possibly can. It may also be because inventors from other countries are less inclined to patenting

their inventions, so as to ensure broader access. While this latter approach may appear noble, inventors need to be conscious of the implications of such choices on their freedom to research if other inventors are seeking patents for their inventions.

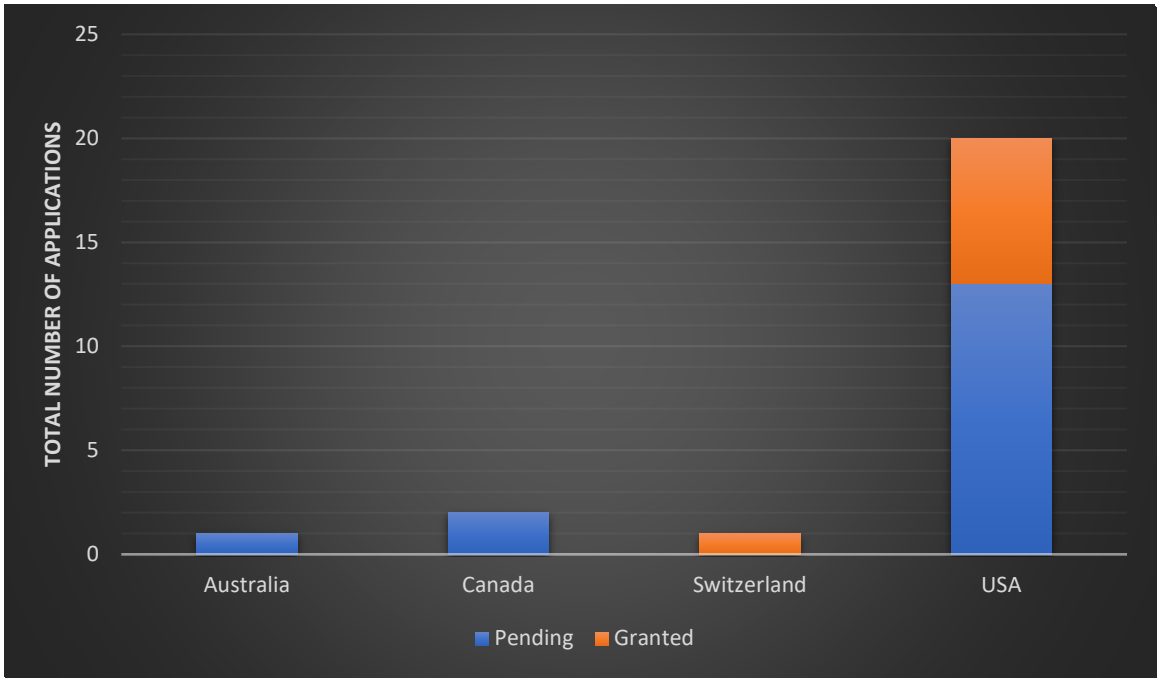

Figure 6.7: Country of Origin of Applicants (Australian Applications)

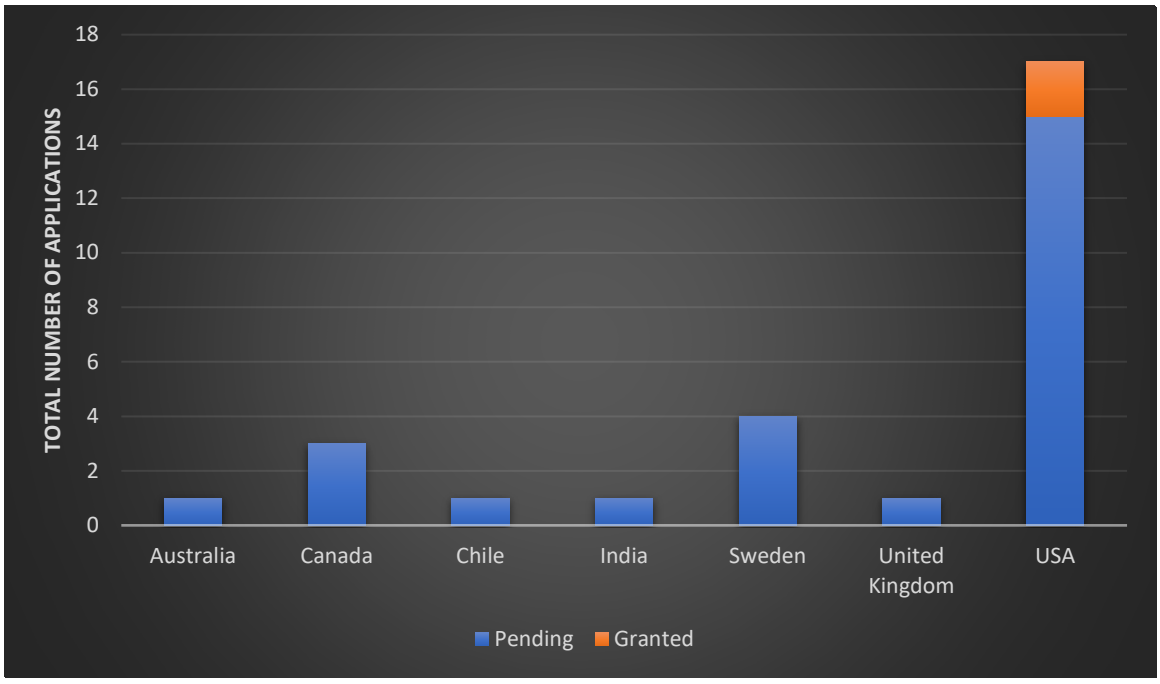

Figure 6.8: Country of Origin of Applicants (European Applications)

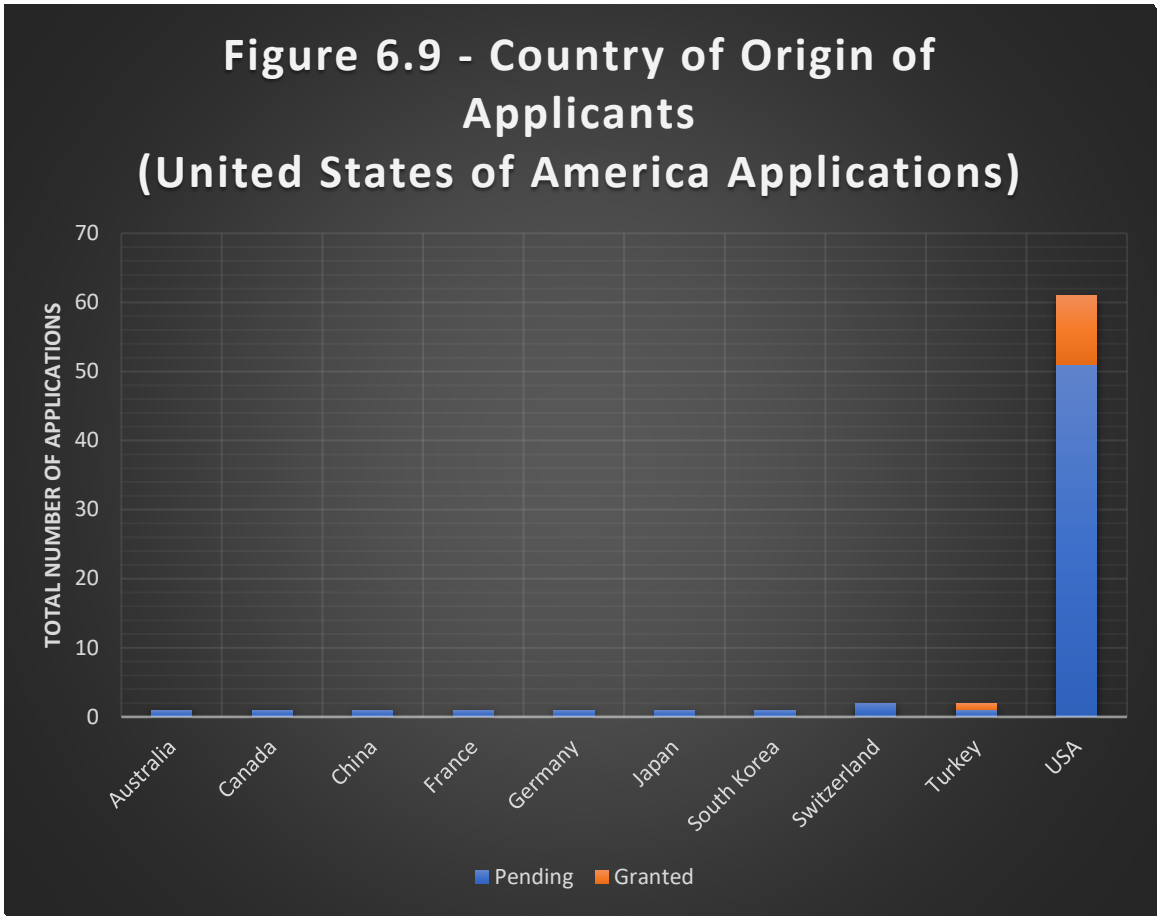

Figure 6.9: Country of Origin of Applicants (United States of America Applications)

6.5.4 Yearly Filings

From the results, there does not appear to be any apparent trend in filing common to the three jurisdictions. For instance, in 2016, IP Australia recorded its highest number of applications for bioprinted constructs with a total of eight applications filed, none of which had been granted at the end date for the landscaping analysis. This is followed by a total of five applications in 2017 of which one has been granted, and three in 2014, of which two have been granted.

In Europe, the EPO recorded its highest number of applications for bioprinted constructs in 2017 with a total of seven applications, none of which have been granted. This is followed by a total of five applications in 2018, none of which have been granted, and four in 2015, of which one has been granted.

Finally, in the USA, the USPTO recorded its highest number of applications for bioprinted constructs in 2016, with a total of 19 applications of which only one has been granted. This

is followed by a total of 14 applications in 2015, of which four have been granted, and eight applications each in 2014, 2017 and 2018. Out of these, only two of the eight filed in 2014 have been granted.

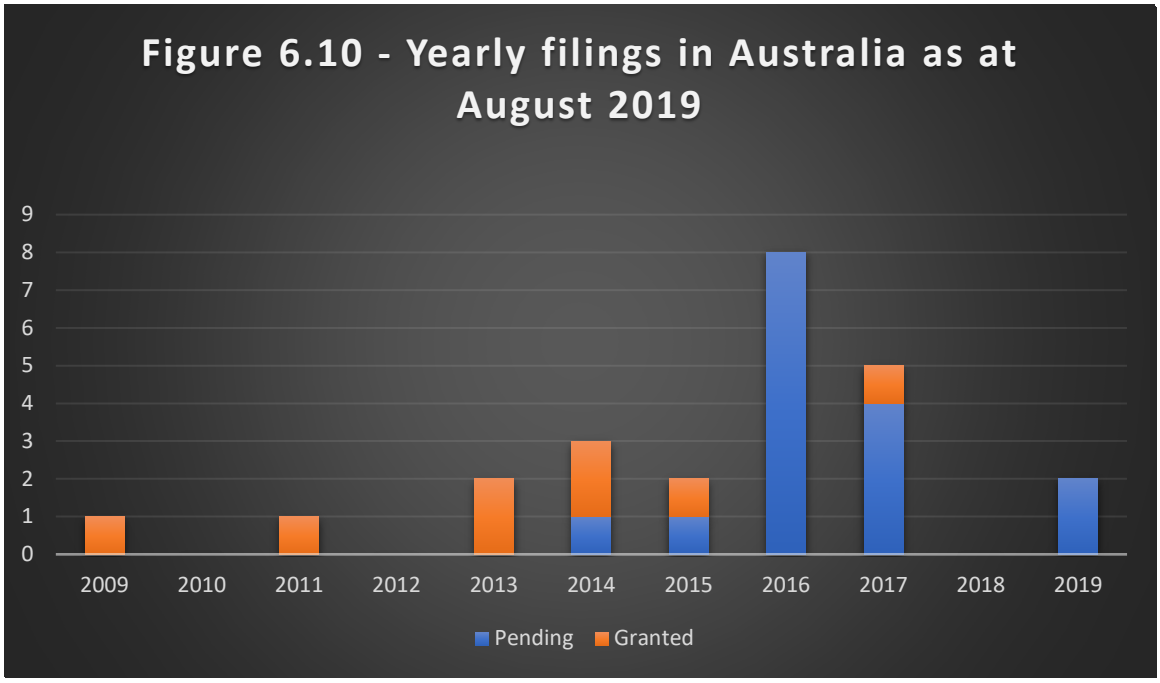

Figure 6.10: Yearly filings in Australia as of August 2019

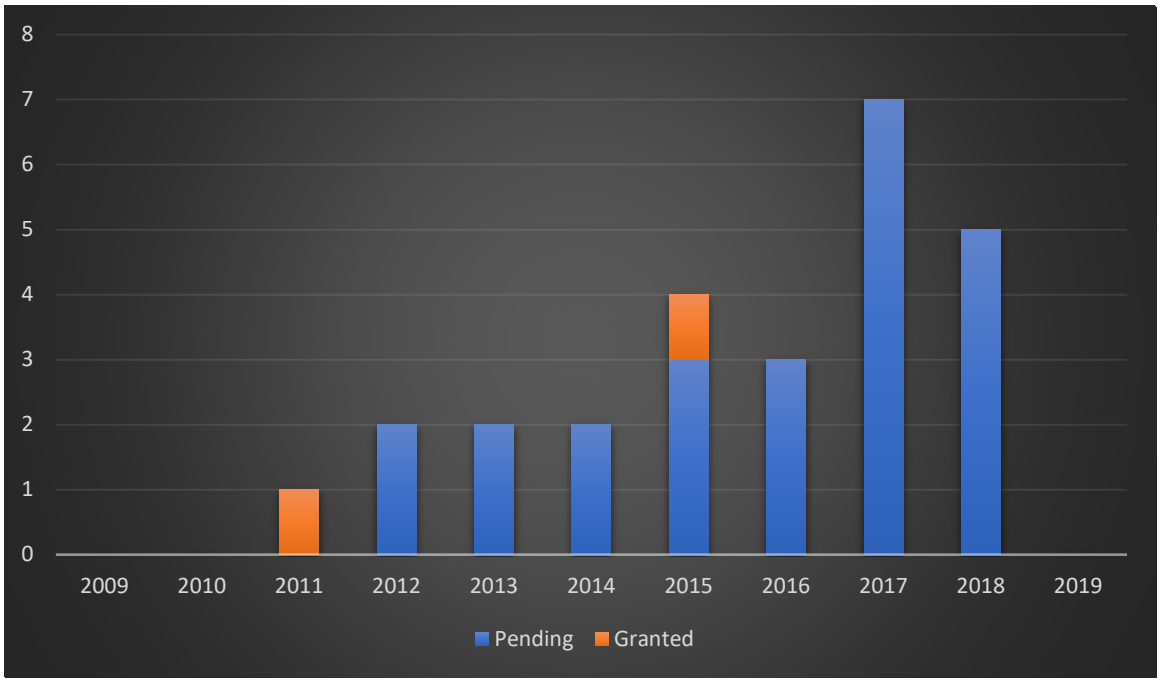

Figure 6.11: Yearly filings in Europe as of August 2019

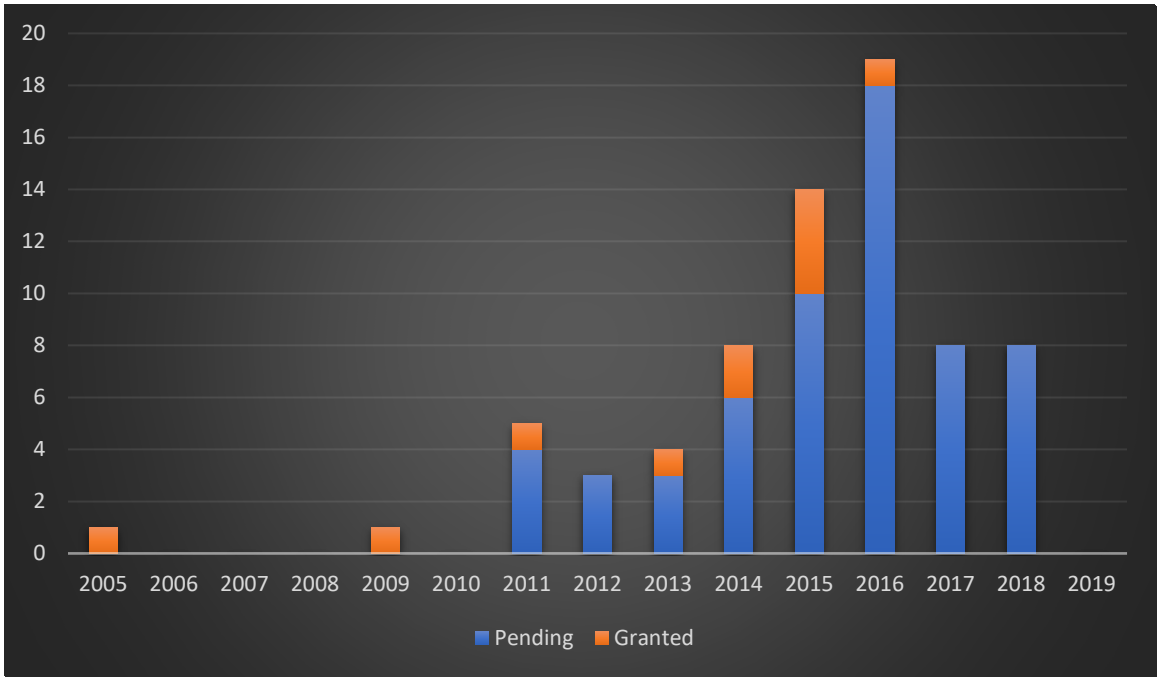

Figure 6.12: Yearly filings in the United States of America as of August 2019

6.5.5 Bioprinted Constructs Intended for Implantation

As noted in chapter two, bioprinting is not limited to the production of constructs solely for implantation in patients. Bioprinted constructs can also be used in *in vitro* studies for disease modelling and research, as well as drug discovery and animal testing. It was therefore unsurprising to note that these various uses of bioprinting were generally reflected in the patent documents.

Whereas some applications expressly identified implantation as a potential use of the claimed bioprinted constructs, others pertaining to cancer models, in particular, were expressed as being intended solely for use in *in vitro* studies. While both uses raise concerns about access, it should be noted that the patenting of bioprinted constructs intended for implantation in patients forms the substratum of concerns about monopolising and commercialising human tissue/organs.

Thus, it was considered beneficial to review the patent documents to determine the proportion of applications in which implantation was explicitly identified as a potential use. It was discovered across all three jurisdictions, whether pending or granted, that at least 50% of the applications explicitly identified implantation as a potential use of the claimed bioprinted constructs. This could be either by itself or as part of a larger tissue construct.

While it was unsurprising to note that patent applications for bioprinted constructs include those intended for implantation, the confirmation of this fact emphasises the importance and timeliness of examining the ethical implications of patenting bioprinting. As this chapter is primarily concerned with identifying emerging patterns, further discourse on the ethical implications of patenting bioprinted constructs intended for implantation will be reserved for the next chapter.

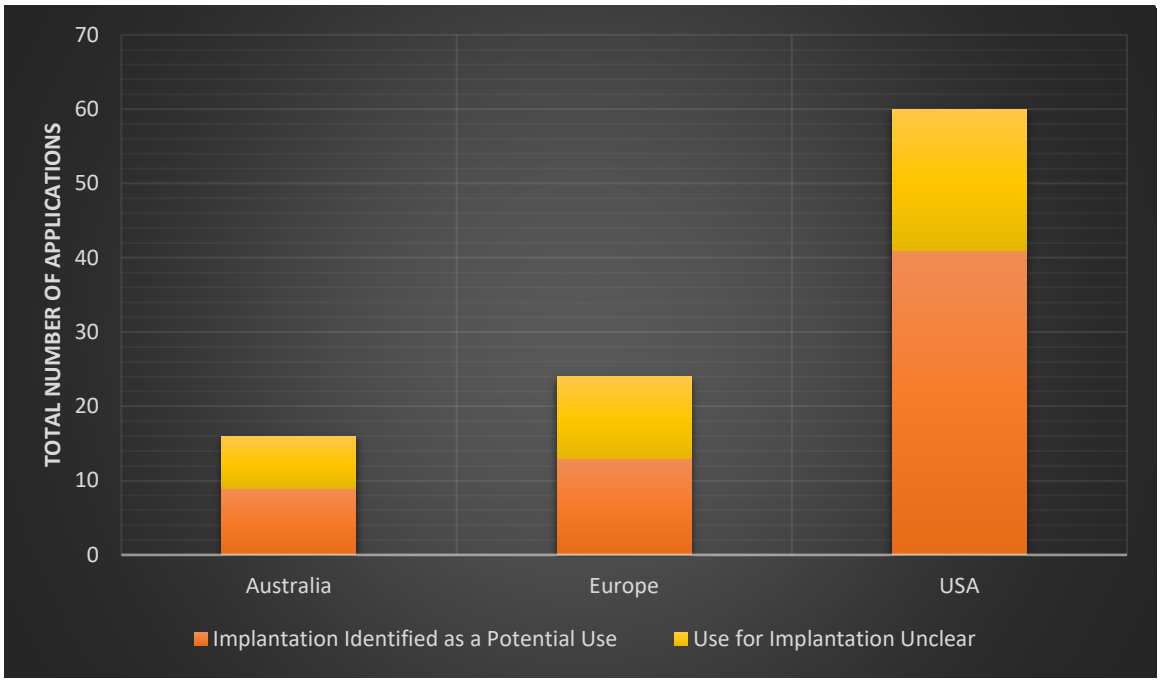

Figure 6.13: Proportion of Bioprinted Constructs Intended for Implantation (Pending Applications)

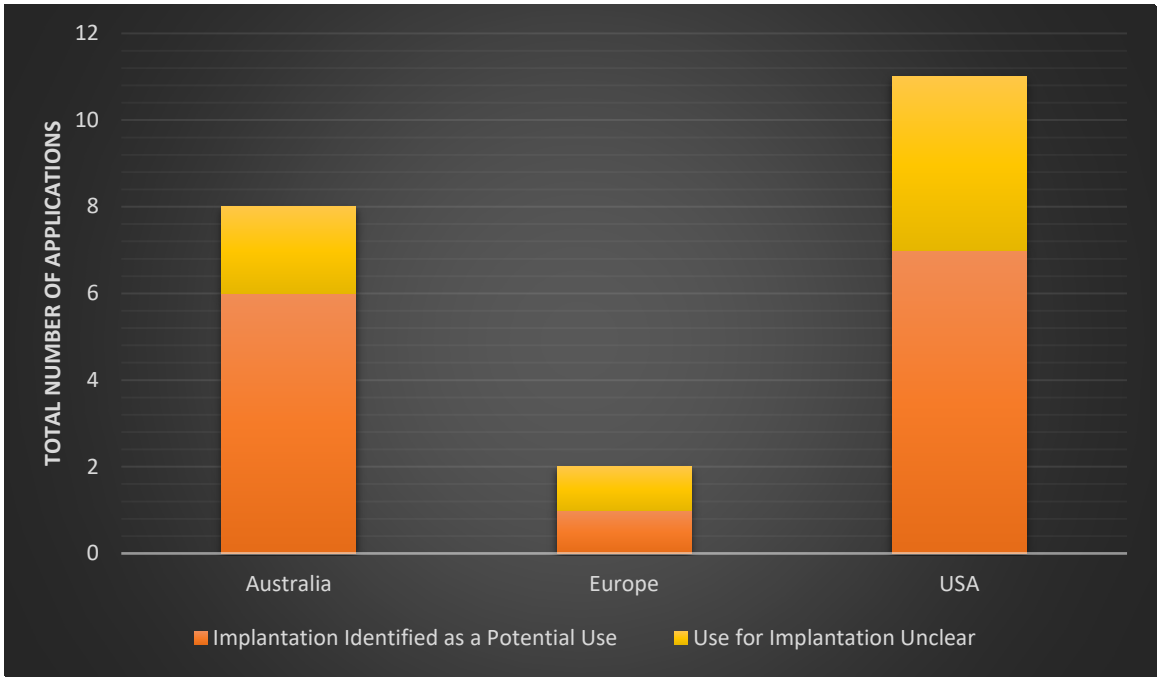

Figure 6.14: Proportion of Bioprinted Constructs Intended for Implantation (Granted Patents)

6.5.6 Embodiment of Embryonic and or Induced Pluripotent Stem Cells

Given bioprinting entails the use of stem cells, it is foreseeable that many of the claimed bioprinted constructs were described as potentially embodying various types of stem cells including ESCs and iPSCs. While it is debatable whether inventions embodying products of nature such as stem cells ought to be patentable, these are not generally excluded from patentability. However, as noted in chapters three to five, there are some express limitations on the patentability of inventions embodying ESCs, particularly in Australia and Europe. Accordingly, it was considered important to identify the proportion of applications explicitly expressed as likely to embody ESCs.

Data for applications expressed as likely to embody iPSCs were also coded for because of the prevailing view that iPSCs could potentially serve as a viable alternative to ESCs. It was therefore necessary to examine whether this view was reflected in the patent documents. However, a review of the applications revealed that, more often than not, the claimed constructs expressed as likely to embody ESCs were also expressed as likely to embody iPSCs as well. This made it difficult to code for the two stem cell types separately. Accordingly, both stem cell types were coded for together.

As with bioprinted constructs intended for implantation, it was discovered that, across the three jurisdictions, whether pending or granted, at least 50% of the applications explicitly referred to the likelihood of the claimed bioprinted constructs embodying ESCs and/or iPSCs. The remainder, whilst referring to the use of stem cells, did not explicitly state what type of stem cells were contemplated. Accordingly, this latter group was categorised as applications 'unclear if embodying ESCs and/or iPSCs'.

While it may very well be that the vagueness as to stem cell types was a deliberate attempt to circumvent restrictions on the patentability of inventions embodying ESCs in particular, it should be recalled that the fabrication of bioprinted constructs is not dependent on a particular stem cell type. It would therefore not be an aberration to omit the stem cell type contemplated since one stem cell type could potentially be substituted for another. Indeed, references to the potential embodiment of ESCs in the claims reviewed appeared more as examples of the various types of stem cells that could be used. In themselves, the claims were primarily concerned with the finished construct and the steps involved in their manufacture.

Consequently, the manner in which the claims have generally been drafted confirm earlier predictions in the preceding chapters that it is unlikely that claims for either bioprinted constructs or related bioprinting processes will refer explicitly to the use of ESCs given they can be fabricated using different types of stem cells. This ambiguity, of course, makes it difficult for patent offices to adequately enforce restrictions on the patentability of inventions embodying ESCs. This is especially as bioprinted constructs classified as falling under the category of applications 'unclear if embodying ESCs and/or iPSCs' could in fact actually embody ESCs and/or iPSCs upon fabrication.

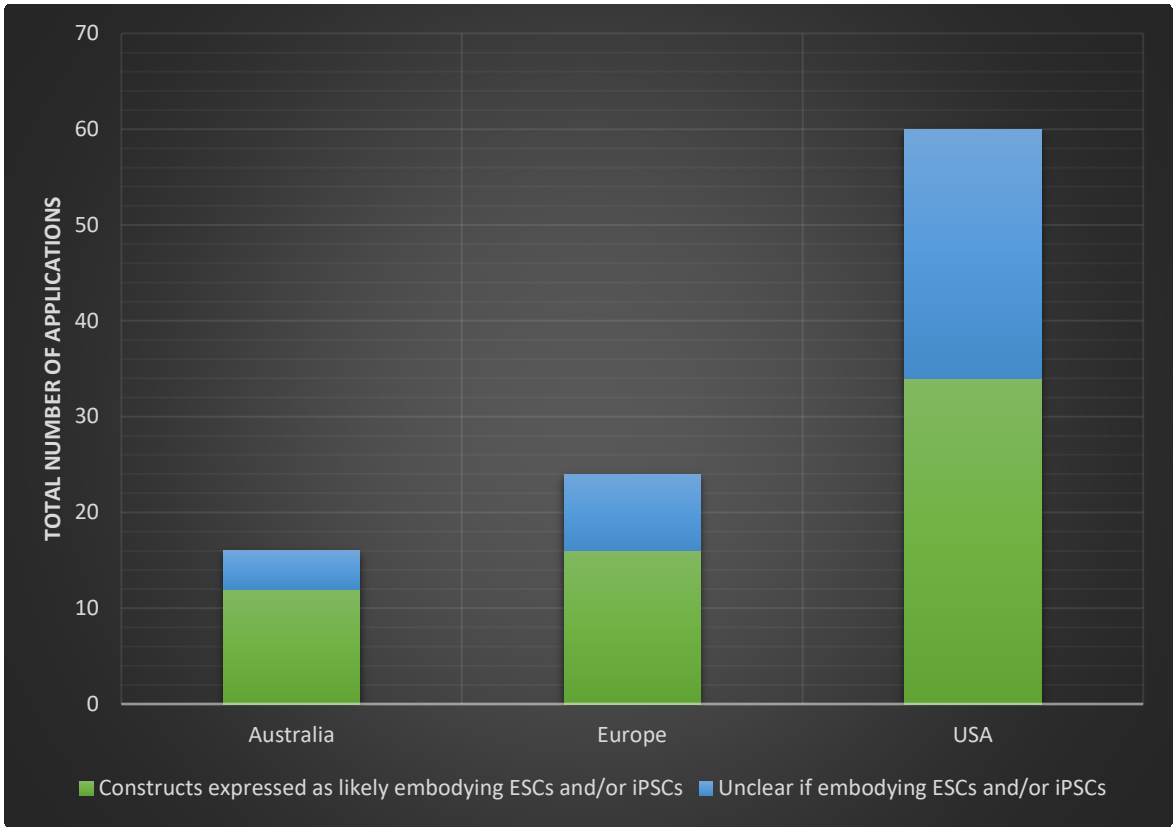

Figure 6.15: Proportion of Bioprinted Constructs Expressed as Likely Embodying ESCs and/or iPSCs (Pending Applications)

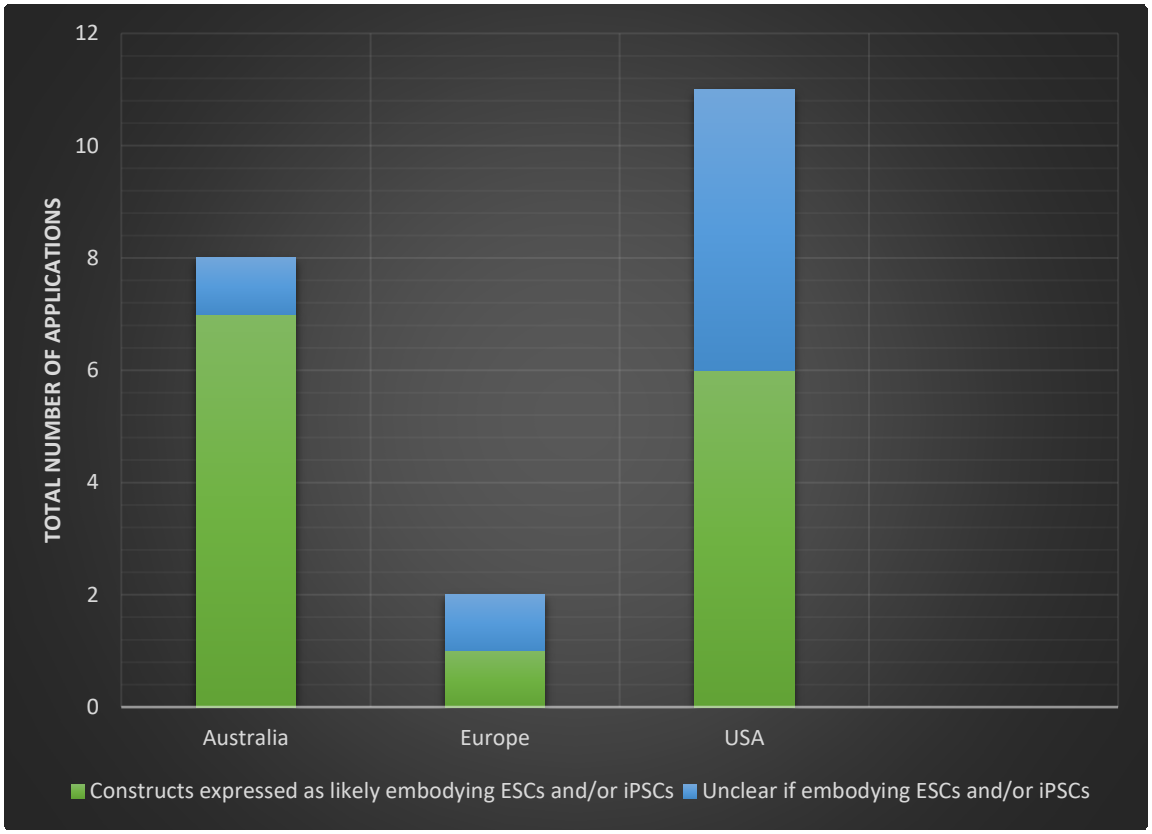

Figure 6.16: Proportion of Bioprinted Constructs Expressed as Likely Embodying ESCs and/or iPSCs (Granted Patents)

6.6 Conclusion

Further to objective (i) of the patent landscaping, the results obtained confirm that there are indeed ongoing attempts to patent bioprinted constructs in Australia, Europe and the USA. While the proportion of patents granted so far remains limited in comparison to the applications filed, it is evident that patents can and have been granted for bioprinted constructs, notwithstanding ethical objections which will be considered in the next chapter. However, it is possible that, as the technology develops and the jurisprudence on the patentability of inventions involving natural phenomena becomes further refined, there may be objections filed against the validity of such patents.

In addition, the results obtained confirm some of the conclusions reached in other aforementioned bioprinting patent landscape reports. In particular, they confirm that many applications for patenting inventions within the bioprinting sector originate from the USA. Furthermore, Organovo is a leading organisation in that regard. The results also reveal that a number of applications held by Organovo are in conjunction with other for-profit

organisations and academic institutions. This reiterates the point noted in chapter two that the ultimate realisation of bioprinting depends on a concerted effort between researchers in different fields. It also indicates a willingness on the part of Organovo to partner with other entities despite clearly being a dominating player in the industry. While this is promising in light of concerns about access, it is not necessarily indicative of how their patents will be exploited.

Additionally, the results reveal that, notwithstanding restrictions on the patentability of subject matter embodying ESCs in Australia and Europe in particular, some bioprinted constructs likely embodying ESCs (although of unascertainable origins) are being patented in those jurisdictions. As yet, however, there is no clear pattern on the types of constructs being patented. Claims range from general biological tissue and tissue models to specific tissues such as liver and breast tissues. At best, the results reveal research is ongoing into various types of tissues depending on the research expertise of inventors.

Overall, the results obtained emphasise the importance of a comprehensive analysis of the ethical implications of patenting bioprinting at this stage of its development. In accordance with objective (iii) of the landscaping, the information obtained from this landscaping analysis will inform further discourse on ethical exclusions and access considerations in the remainder of this thesis.

Chapter 7

7 Ethical Concerns Arising from Patenting Bioprinting

7.1 Introduction

Over the course of this thesis, a common thread seems to have emerged regarding bioprinting – the matter of ethics. This includes ethical concerns about the technology as well as ethical considerations relevant in assessing patentability. From the analysis on the law of patentability in chapters three to five and the patent landscape report in chapter six, it would appear that the types of ethical considerations generally taken into account in determining patentability are insufficient to exclude bioprinting-related inventions embodying natural phenomena from patentability per se. In light of this, it is imperative to consider how patents in the field of bioprinting might be exploited in a manner that balances the interests of all stakeholders and accommodates broader ethical perspectives.

In order to do so, however, it is important to first consider more fully the nature of the ethical concerns arising from patenting bioprinting albeit with particular emphasis on bioprinted constructs. This is because as noted in chapter six, while the patenting of process claims embodying natural phenomena poses ethical concerns about monopolising such natural phenomena, there is no evidence in existing literature to suggest that these processes are necessarily exclusive to bioprinting.[1] Furthermore, the patentability or otherwise of methods of treatment appears to be well settled law under the *European Patent Convention* ('*EPC*')[2] and in the United States of America ('USA'). As this thesis is primarily concerned with ethical challenges that arise specifically from patenting bioprinting, it is therefore important to limit the consideration of such ethical concerns accordingly.

To this end, it is useful at this juncture to distinguish between ethical concerns about bioprinting as a technology and ethical concerns arising from patenting bioprinting. Whereas ethical concerns about bioprinting as a technology arise directly from the nature of the technology, ethical concerns arising, from patenting bioprinting are those concerns that can be directly attributed to patenting whether in part or in whole. That is not to say,

[1] See chapter six (section 6.1).
[2] *Convention on the Grant of European Patents*, signed 5 October 1973, 1065 UNTS 255 (entered into force 7 October 1977).

however, that there is no overlap between such concerns, as exemplified by the issue of access and social justice.

For the purpose of this chapter, ethical concerns arising from patenting bioprinted constructs have been categorised as follows: impact on the patentability of future biotechnological innovations; commodification of life and the human body; and access. Each of these concerns is examined in this chapter, with the aim of determining whether they are sufficient to justify a reconsideration of patent grants for bioprinted constructs.

Although the aforementioned ethical concerns are not unique to bioprinting, a significant portion of this chapter is devoted to concerns about access. This is because as will be explained subsequently, access is likely to be the most significant ethical concern arising from patenting bioprinting. In light of the potential applications of bioprinting noted earlier in chapter two, this chapter identifies patient and researcher access as key aspects of access to bioprinting that need to be resolved. Accordingly, the section on access explores the rights to health and benefit from science as it relates to access to medicines. The responsibilities of states parties and non-state actors in the realisation of these rights are also explored in this regard. Thereafter, this chapter examines the existing flexibilities included in the *Agreement on Trade-related Aspects of Intellectual Property Rights* ('*TRIPS Agreement*' or '*TRIPS*')[3] and their relevance in improving patient and research access to bioprinting.

Overall, this chapter concludes that while concerns about the ethical impact of patenting bioprinted constructs are valid, these are not sufficient to justify an exclusion from patenting on the basis of ethical concerns. This is especially as concerns about the impact of patenting bioprinted constructs on the patentability of future biotechnological innovations and commodification of life and the human body relate to overall concerns about patenting biotechnological inventions in general.

With regard to concerns about access, this chapter concludes that existing *TRIPS* flexibilities appear to offer limited practical value to patient access in comparison to research access. Since the feasibility of implanting bioprinted constructs is still very much in doubt, the limited relevance of existing *TRIPS* flexibilities to patient access is not an

[3] *Agreement on Trade-Related Aspects of Intellectual Property Rights*, signed 15 April 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, 1869 UNTS 299 (entered into force 1 January 1995) ('*TRIPS Agreement*').

immediately pressing concern (though it might become more pressing in the near future). Improving research access, on the other hand, would appear to be a pressing concern given the realisation of the aims of bioprinting is ultimately dependent on this. Accordingly, it is important that challenges with implementing applicable *TRIPS* flexibilities are addressed.

7.2 The Ethical Implications of Patenting Bioprinting

The patent system has generally been described as a means of incentivising innovation and rewarding innovators for the financial risk undertaken in the course of research and development.[4] In addition, because patents are effectively state-sanctioned monopolies, they are viewed as lending legitimacy to patented inventions whilst also creating exclusivity around the manner in which such inventions are exploited.

As a result, the grant of patents for inventions deemed controversial or essential, particularly in the health sector, often arouses debates about the legitimacy of patenting certain inventions. In the field of biotechnology, these debates typically encompass concerns about the impact of patenting a particular invention on the patentability of future biotechnological innovations, commodification of life and the human body as well as concerns about access.[5]

Whilst biotechnology continues to evolve with the emergence of new technologies such as bioprinting, it has been noted that '[a]s emerging technologies converge, it becomes clearer that the ethical issues raised by these technologies are at core similar and familiar'.[6] This is notwithstanding that some ethical concerns may be more prevalent in one technology compared to another. In light of this, it has been argued that inventing a 'new kind of ethics for each new technology' is a waste of resources.[7] Instead, the focus should be on learning from 'previous debates and our previous successes and failures at responding to them, so

[4] Ted Schrecker et al, 'Ethical Issues Associated with Patenting Higher Life Forms' (Intellectual Property Policy Directorate, Industry Canada, 17 May 1997); David B Resnik, 'DNA Patents and Human Dignity' (2001) 29(2) *The Journal of Law, Medicine & Ethics* 152; Nuffield Council on Bioethics, *The Ethics of Patenting DNA - A Discussion Paper* (Nuffield Council on Bioethics, 2002) ('*The Ethics of Patenting DNA - A Discussion Paper*').

[5] Erik Parens, Josephine Johnston and Jacob Moses, 'Ethical Issues in Synthetic Biology: An Overview of the Debates' (SYNBIO 3, Woodrow Wilson International Centre for Scholars, 24 June 2009) <https://www.wilsoncenter.org/publication/ethical-issues-synthetic-biology>; Belinda Huang, 'Biotech Patents in Australia: Raising the Bar on the Generally Inconvenient Exception' (2013) 24 *Australian Intellectual Property Journal* 40; Timothy Caulfield, E Richard Gold and Mildred K Cho, 'Patenting Human Genetic Material: Refocusing the Debate' (2000) 1(3) *Nature Reviews Genetics* 227.

[6] Parens, Johnston and Moses (n 5) 4.

[7] Ibid.

as to better anticipate concerns and address problems'.[8] This is especially as many of these known ethical issues have not necessarily been resolved despite having been considered in other contexts in the past.[9]

Consequently, it should be stated from the onset that this chapter does not purport to reinvent the wheel by describing the ethical issues arising from patenting bioprinting as 'new'. Rather, this chapter draws from existing discourse about ethical concerns associated with patenting biotechnology in general. In doing so, this chapter employs the use of analogy in examining how these concerns relate to patenting bioprinting and whether the unique features of bioprinting present new considerations deserving of separate solutions. To this end, the aforementioned ethical concerns associated with patenting biotechnology are canvassed in this chapter. Overall, the aim of examining these ethical concerns is to ascertain whether they are sufficient to warrant a prohibition on patenting bioprinted constructs, or whether there are measures within the patent system that can be deployed to ameliorate the concerns.

It is important to note that whilst the act of patenting may generate ethical concerns, there are debates about whether such concerns ought to and can be appropriately addressed within the patent system.[10] This is particularly so in relation to concerns about access which appear to contradict the very essence of patents – the creation of a monopoly. While some argue that patenting ought to be classified as an ethically neutral act,[11] others argue that social and ethical concerns cannot be divorced from the patent system.[12]

Generally, proponents of value neutrality within the patent system argue that the patent system is not an appropriate forum for addressing ethical considerations because of the uncertainty ethical concerns introduce into the system. Thus, even if ethical exclusions were introduced in countries that did not already provide for them, there is the probability

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[8] Ibid 11.
[9] Ibid; Caulfield, Gold and Cho (n 5).
[10] See generally Shobita Parthasarathy, *Patent Politics: Life Forms, Markets, and the Public Interest in the United States and Europe* (University of Chicago Press, 2017) where the author explains that culture, politics and institutions influence the manner in which patent law is interpreted and applied.
[11] R Stephen Crespi, 'The Case for and Against the Patenting of Biotechnological Inventions' in Sigrid Sterckx (ed), *Biotechnology, Patents and Morality* (Ashgate Publishing, 2000).
[12] Schrecker et al (n 4); Peter Drahos, 'Biotechnology Patents, Markets and Morality' (1999) 21 *European Intellectual Property Review* 441; Abraham Drassinower, 'Property, Patents and Ethics: A Comment on Wendy Adams' "The Myth of Ethical Neutrality"' (2003) 39(2) (2003) *Canadian Business Law Journal* 214; Huang (n 5); Caulfield, Gold and Cho (n 5).

that such exclusions would be interpreted inconsistently thus making the law unpredictable.[13] More so because courts are perceived as lacking the institutional competence to determine matters of public interest and social policy.[14] As is evident from the analysis in chapters three to five, there is merit to this argument, considering that the availability of ethical exclusions in the Australian patent legislation as well as the *EPC* appears likely to have minimal impact on the patentability of bioprinted constructs.[15] This is supported by the manner in which these ethically informed exclusions have been interpreted by the courts and patent offices in the past.

On the other hand, opponents of value neutrality within the patent system such as Drahos argue that '[s]ince the whole point of patenting is to exclude others from access to informational resources of the patent, it is hard to see how patenting can be described as ethically neutral'.[16] In light of this, some have argued that the absence of neutrality is a compelling reason to address ethical issues within the criteria for patentability.[17]

Whilst this thesis agrees that the patent system is not ethically neutral and should as such incorporate ethical considerations, it is debatable whether all ethical concerns can and should be addressed at the point of establishing patent eligibility. The fact that there are concerns about how an invention might be exploited should not be determinative of whether or not that invention is patent eligible. This is especially because such concerns are often speculative at the point of establishing patent eligibility.[18] Patentability of an invention and the impact of patenting the invention, though related, are two distinct issues, which ought to be addressed separately.

It is on this premise that ethical concerns about the impact of patenting bioprinting are considered as a distinct issue in this chapter, separate from earlier considerations about patentability. Thus, this section now turns to an examination of each of the aforementioned concerns arising from patenting bioprinted constructs.

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[13] Huang (n 5).
[14] Ibid.
[15] See especially chapters three (section 3.4.2) and four (section 4.4.2).
[16] Drahos (n 12) 441.
[17] W A Adams, 'The Myth of Ethical Neutrality: Property, Patents, Animal Rights and Animal Welfare in *Commissioner of Patents v President and Fellows of Harvard College*' (2003) 39 *Canadian Business Law Journal* 181.
[18] Australian Law Reform Commission, 'Genes and Ingenuity: Gene Patenting and Human Health' (ALRC 99, Australian Law Reform Commission, 29 June 2004) <http://www.alrc.gov.au/publications/report-99> ('Genes and Ingenuity: Gene Patenting and Human Health').

7.2.1 Impact on the Patentability of Future Biotechnological Innovations

One of the earliest concerns about patenting biotechnological inventions starting with microorganisms was that it would set an undesirable precedence for patenting life forms. Thus, if patents were permitted for microorganisms, it was feared that it was only a matter of time before patents were granted over animals and eventually, human beings.[19] This is in essence the slippery-slope argument, which alleges that an acceptable practice will lead to an immoral practice.[20]

Whilst many jurisdictions including Australia, Europe and the USA have now expressly prohibited the patenting of human beings and the biological process for their generation,[21] concerns about the broader impact of patenting biotechnological inventions on life forms does not appear to have dissipated. This is because ever since transgenic animals and genetically modified organisms were held to be patentable, there has been an increasing push at the boundaries of patentability.[22] In particular, there have been an increasing number of attempts at patenting morally controversial inventions claiming human deoxyribonucleic acid ('DNA') sequences, human embryonic tissues and other genetic materials – some of which have been successful.[23]

Although many of the claimed inventions offer great promise in improving health care, they are nonetheless controversial in the sense that they either originate from morally controversial research such as the destruction of human embryos or they involve monopolisation of elements or parts of the human body.[24] Accordingly, the prevailing concern appears to be the extent to which such inventions ought to be protected by patents, if at all. This is premised on the notion that allowing patents for existing controversial

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[19] Carrie F Walter, 'Beyond the Harvard Mouse: Current Patent Practice and the Necessity of Clear Guidelines in Biotechnology Patent Law' (1998) 73 *Indiana Law Journal* 1025; Cyril R Vidergar, 'Biomedical Patenting: Permitted, but Permissible' (2003) 19 *Santa Clara High Technology Law Journal* 253.
[20] Scott Altman, '(Com)Modifying Experience' (1991) 65 *Southern California Law Review* 293; Schrecker et al (n 4).
[21] *Patents Act 1990* (Cth) s 18(2); *Implementing Regulations to the Convention on the Grant of European Patents* (as last amended by decision of the Administrative Council of the European Patent Organisation of 14 December 2016 (CA/D 17/16)) rule 28 ('*Implementing Regulations*'); *Leahy-Smith America Invents Act*, Pub L No 112–29 § 33, 125 Stat 284, 340 (2012).
[22] Walter (n 19); Drahos (n 12); R Stephen Crespi, 'An Analysis of Moral Issues Affecting Patenting Inventions in the Life Sciences: A European Perspective' (2000) 6(2) (2000/06/01) *Science and Engineering Ethics* 157; Huang (n 5).
[23] Huang (n 5).
[24] Margo A Bagley, 'Patent First Ask Questions Later: Morality and Biotechnology in Patent Law' (2003) 45 *William & Mary Law Review* 469.

inventions sets a (dangerous) precedent for the grant of patents for future biotechnological inventions, which might be even more controversial, yet essential to healthcare delivery.

Thus, with bioprinting, for instance, earlier grants of patents for artificially engineered tissue products would appear to have set a precedent for the patenting of bioprinted constructs. Indeed, this was one of the arguments advanced in favour of the patentability of bioprinted constructs in earlier parts of this thesis – that with bioprinting being an advancement on traditional tissue engineering and regenerative medicine techniques, it is debatable whether bioprinted constructs ought to be treated any differently from engineered tissue products fabricated via traditional means, which have already been patented. This is notwithstanding the fact that bioprinted constructs are more likely to resemble their naturally occurring counterparts structurally and functionally in comparison to other artificially engineered tissue products. At the same time, however, this structural and functional similarity does raise concern about how the grant of patents for bioprinted constructs might translate into attempts to patent naturally occurring tissues and organs.

Already, there are concerns that the level of inventiveness required for patenting biotechnology inventions is low. This is especially considering the fact that the act of isolating an element of the human body has been deemed sufficiently inventive to warrant the grant of a patent under the *EPC*.[25] Recent judicial decisions in Australia and the USA, however, seem to indicate a departure from this proposition in those countries.[26] Whilst patent regulators continue to struggle with striking a balance between rewarding innovation and protecting public interests,[27] some commentators have noted that applicants and scientific inventors appear to be dictating the scope of patent eligibility through their applications without regard to ethical or social concerns.[28] This is with particular reference to the situation in the USA, where the approach to determining patent eligibility has been described as one of 'patent first, ask questions later' in the absence of a general morality exclusion clause.[29]

[25] *Implementing Regulations* (n 20) rule 29(2)
[26] See chapters three (section 3.3) and five (section 5.3)
[27] Huang (n 5).
[28] Ibid; Bagley (n 24).
[29] Bagley (n 24).

Although it is important for the patent system to be flexible enough to accommodate the emergence of new technologies, it is equally important that the scope of patentability is not allowed to be dictated by individual researchers who are motivated by curiosity and less concerned with morality and other ethical considerations.[30] As Bagley succinctly notes, 'the interests and goals of individual researchers should not be substituted for, nor denominated as, the interests of society at large'.[31] Thus, whilst bioprinting may address pressing health needs, it is important to consider whether bioprinted constructs ought to be patented in light of the precedent patenting sets for future biotechnology inventions which involve elements or parts of the human body.

A potential solution in this regard, which has been canvassed for other biotechnology inventions, is the prohibition of further patents for bioprinted constructs. Of course, it is questionable whether such legislative intervention would operate retroactively so as to invalidate existing patents.[32] At the same time, for such a prohibition to have full effect, it would require that biotechnology patents as a whole are prohibited. This is because bioprinting is but a minute aspect of biotechnology innovation. If other related inventions are not expressly prohibited, then prohibiting the grant of patents for bioprinted constructs would do little to address the overarching slippery-slope concern that arises from patenting biotechnology inventions. In addition, such prohibition would also have to be agreed to globally. Otherwise, prohibition in one jurisdiction could have the detrimental effect of potentially inhibiting the growth of biotechnology in said jurisdiction in relation to other countries that permit patenting.[33]

The non-discrimination principle contained in art 27(1) of the *TRIPS Agreement* forbids provisions excluding, limiting, or distinguishing a class of patents in fields such as biotechnology from other technologies for the purpose of special regulation.[34] In any case, such special wholesale prohibition would likely fragment and complicate the law with regards to how new technologies are treated.[35] As they stand, the requirements for

[30] Maureen L Condic and Samuel B Condic, 'The Appropriate Limits of Science in the Formation of Public Policy', (2003) 17(1) *Notre Dame Journal of Law, Ethics & Public Policy* 157, 167.
[31] Ibid 511
[32] Ibid 516
[33] 'Genes and Ingenuity: Gene Patenting and Human Health' (n 18) 173 [7.23].
[34] Huang (n 5) 51; 'Genes and Ingenuity: Gene Patenting and Human Health' (n 18) 174 [7.25]
[35] 'Genes and Ingenuity: Gene Patenting and Human Health' (n 18) 174 [7.25]-[7.27]

patentability are drafted in a manner that is technology-neutral, which makes it easier for the patent system to adapt to new technologies.[36]

Furthermore, whilst a wholesale prohibition on biotechnology patents may address ethical concerns about the role of state-sanctioned monopolies in legitimising morally controversial biotechnology inventions, it does not fully address ethical concerns about the underlying research. As many commentators have noted, withholding patents for an invention is unlikely to halt further research in that field given a major motivation for researchers is often scientific curiosity.[37]

In addition, the prohibition of patents may also have unfavourable consequences particularly where the controversy does not arise from the underlying research, but with the type of invention that is being patented and the manner in which the patents are exploited. This is particularly so with bioprinting where the underlying research is not controversial as such. Although embryonic stem cells may be used in the fabrication of bioprinted constructs, these can be substituted for alternative types of stem cells (such as induced pluripotent stem cells) which do not attract any significant controversy as far as research and patenting are concerned. Moreover, given recent jurisprudence in this regard,[38] it is apparent that embryonic stem cells can be produced via other means that do not fall afoul of legislative prohibitions on patenting inventions embodying embryonic matter.[39]

Thus, if the patenting of bioprinted constructs were to be prohibited, it would not only disincentivise further research in a field that promises to revolutionise healthcare, society will also likely lose the benefit of disclosure of research afforded by the patent system.[40] Given the potential of bioprinting highlighted in chapter two, there is no apparent benefit to disincentivising research in this field so as to mitigate the patenting of future biotechnology inventions, which might be similar but even more controversial.

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[36] Ibid, 119 [6.18]
[37] Walter (n 19); Cynthia M Ho, 'Building a Better Mousetrap: Patenting Biotechnology in the European Community' (1992) 3 *Duke Journal of Comparative & International Law* 173; Bagley (n 24); *Diamond v Chakrabarty*, 447 US 303, 317 (1980) ('*Diamond v Chakrabarty*').
[38] *International Stem Cell Corporation v Comptroller General of Patents* (C-364/13) [2015] OJ C 65/7; *Re International Stem Cell Corp* (2016) 123 IPR 142.
[39] *Patents Act 1990* (Cth) s 18(2); *Implementing Regulations* (n 20) rule 28(c); *Leahy-Smith America Invents Act*, Pub L No 112–29 § 33, 125 Stat 284, 340 (2012).
[40] Bagley (n 24).

A better solution, instead, would be to limit the scope of patentability, which will be considered in later parts of this thesis dealing with developing a framework for an ethical approach to patenting bioprinting.

7.2.2 Commodification of Life and the Human Body

Another objection to patenting biotechnological inventions, which is also relevant to bioprinted constructs, is that patenting is perceived as incentivising the commodification of life. According to Altman, the term 'commodification' has several meanings which includes actions that 'violate a duty of respect for persons by treating the person as a thing that can be sold'.[41] It could also refer to actions that 'alter the sensibilities of people directly involved in market transactions by causing them to regard each other as objects with prices rather than as persons'.[42] Furthermore, commodification could also refer to a set of actions that 'alter the sensibilities of people who learn about or live in a society that permits the sale of persons but who do not participate in such transactions themselves'.[43]

Some commentators are of the opinion that allowing biotechnology patents 'might reinforce or alter undesirable attitudes toward both animals and human beings'.[44] In turn, this could result in a diminished moral respect for life and potentially engender human or animal suffering.[45] Likewise, there are concerns that humans and animals will be considered 'either as mere collections of biological information, or as objects (manufactures or compositions of matter), rather than as conscious beings and subjects of experience'.[46] This is closely linked to the perception that exclusive monopoly rights arising from the grant of patents in the biotechnology sector are akin to vesting ownership of life in patent holders, notwithstanding the fact that their claimed invention may relate to only a minute fraction of the human body.[47]

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[41] Altman (n 20) 295.
[42] Ibid 295-6.
[43] Ibid 296.
[44] Schrecker et al (n 4) 67.
[45] Ibid; Jean-Pierre Berlan, 'The Commodification of Life' (1989) 41(7) *Monthly Review* 24; Timothy Caulfield and Roger Brownsword, 'Human Dignity: A Guide to Policy Making in the Biotechnology Era?' (2006) 7(1) *Nature Reviews Genetics* 72; Vidergar (n 19); *Diamond v Chakrabarty* (n 37) 316.
[46] Schrecker et al (n 4) 67; See also Caulfield and Brownsword (n 46).
[47] Robert P Merges, 'Intellectual Property in Higher Life Forms: The Patent System and Controversial Technologies' (1988) 47 *Maryland Law Review* 1051; Schrecker et al (n 4); Huang (n 5).

Nevertheless, there are reasons to disagree with the notion that biotechnology patents can be equated with vesting ownership of life in any person or entity. As noted by the Opposition Division in *Howard Florey/Relaxin*, biotechnological inventions in themselves do not constitute life.[48] Moreover, patents confer negative rights to 'exclude others from making, using, or commercializing his or her invention'.[49] The exploitation of which is subject to other national laws and the right of other patent holders not to have their patents infringed.[50] This is in addition to the fact that patents are valid only for a limited period of time (usually 20 years) unlike ownership, which can exist in perpetuity.[51]

Yet, it is indisputable that patents are property rights, which confer an exclusive right of exploitation.[52] Thus, irrespective of whether patent rights may be equated with ownership rights, biotechnology patents are still rightfully considered as establishing property rights over life forms. In light of this, many consider biotechnological patents morally unacceptable because they involve the creation of property rights over life forms, which in turn exacerbates their commodification.[53] In the same vein, proponents of the sanctity of life doctrine also believe that biotechnology patents violate or at the very least, threaten the principle of human dignity.[54] This is because human beings are generally viewed as having intrinsic moral worth which implies that they ought to be treated as ends-in-themselves not a means to an end.[55]

To this end, many organisations and religious groups have consistently lobbied against the patenting of inventions claiming human tissue, embryos, stem cells and genes amongst others.[56] While some of these actions have been successful and have resulted in the emergence of legislative prohibitions on the patenting of certain life forms such as

[48] *Howard Florey/Relaxin* [1995] EPOR 541, 551 [6.3.4].
[49] Resnik (n 4) 153; See also R Stephen Crespi, 'Patenting and Ethics - A Dubious Connection' (2003) 85 *Journal of the Patent and Trademark Office Society* 31, 33-4.
[50] Resnik (n 4) 153.
[51] Merges (n 48); Schrecker et al (n 4).
[52] Schrecker et al (n 4).
[53] Merges (n 48); Caulfield and Brownsword (n 46) Timothy Caulfield and Audrey Chapman, 'Human Dignity as a Criterion for Science Policy' (2005) 2(8) *PLoS Med* e244; Drassinower (n 12); L Bently and B Sherman, 'The Ethics of Patenting: Towards A Transgenic Patent System' (1995) 3(3) *Med Law Rev* 275; Huang (n 5); Resnik (n 4); 'Genes and Ingenuity: Gene Patenting and Human Health' (n 18).
[54] Merges (n 48); Caulfield and Brownsword (n 46); Caulfield and Chapman (n 54); Drassinower (n 12); Bently and Sherman (n 54); Huang (n 5); Resnik (n 4); 'Genes and Ingenuity: Gene Patenting and Human Health' (n 18).
[55] Resnik (n 4).
[56] Bently and Sherman (n 54); Resnik (n 4).

embryonic stem cells,[57] many other actions have equally been unsuccessful. Consequently, concerns about patenting life forms and their subsequent commodification remain a topical issue.

In themselves, bioprinted constructs can be considered as life forms since they embody living cells and are designed to replicate their naturally occurring counterparts structurally and functionally. Therefore, their patenting raises similar concerns about commodification of the human body as other life forms. Nevertheless, as has previously been acknowledged by Resnik (a bioethicist), human beings are already treated as commodities, albeit incomplete commodities to the extent that they are assigned a market value as well as another type of value, which is intrinsic and cannot be measured in terms of a price.[58] This is as opposed to complete commodification where the subject matter is assigned only a market value.[59] Historically, the assignment of market value to humans has occurred in various forms including through the availability of life insurance policies, worker's compensation as well as the possibility of marketing of one's image.[60] Similarly, human tissues and organs have also been treated as commodities through the practice of sex selection, surrogacy, in vitro fertilization and other assisted reproductive technologies.[61]

In light of this, it is debatable whether the commodification of bioprinted constructs is any different from other aspects of human existence, which has previously been commodified. Unless of course, the true concern is with the fact that commodifying bioprinted constructs is one step further down a slippery slope into complete commodification where human life has only a market value and nothing more.[62] In which case, it is important to remember that while patents may legitimise the commodification of bioprinted constructs, commodification can occur independently of patents. Thus, any prohibition on patenting bioprinted constructs will probably not address underlying concerns about their commodification.

[57] Caulfield and Brownsword (n 46); Caulfield and Chapman (n 54).
[58] Resnik (n 4).
[59] Ibid.
[60] Ibid.
[61] Caulfield and Brownsword (n 46).
[62] Resnik (n 4).

Furthermore, there does not appear to be any evidence that biotechnology patents such as DNA patents, for instance, have altered attitudes towards the value of the human body.[63] In fact, there is some suggestion that contrary to popular belief, biotechnology patents may instead enhance ethical sensitivity as 'it would make us more aware of ethically questionable dimensions of our current attitudes'.[64] At the same time, it should not be forgotten that there is some evidence to suggest that patenting encourages private investment in research, which in turn promotes innovation and scientific discovery.[65] In the absence of clear evidence establishing that the risk of patenting outweighs its benefits,[66] caution must be taken in pushing for the abolition of biotechnology patents and indeed patents for bioprinted constructs. This is so as not to disincentivise investment into a much-needed area of research.

On the other hand, because bioprinted constructs are effectively human tissues and organs, their patenting further challenges continued opposition to the commodification of human tissue and organs. Although it has been extensively argued in earlier parts of this thesis that bioprinted constructs are not naturally occurring and therefore eligible patent subject matter, it is debatable whether this distinction will have any significant impact on oppositions to their commodification as human tissues and organs. As noted by Resnik in the context of DNA patenting, although isolated and purified sequences are not technically body parts since they do not exist in nature as such, it would be a semantic manoeuvre to disregard them as body parts since there is usually a high degree of homology between naturally occurring sequences and patented sequences.[67] Accordingly, Resnik argues that for all practical purposes, isolated and purified sequences are body parts and would likely be regarded as such by most people.[68] In the same vein, it would be disingenuous to discountenance bioprinted constructs as human tissue and organs considering they comprise of living cells and effectively replicate their naturally occurring counterparts structurally and functionally.

[63] Ibid; 'Genes and Ingenuity: Gene Patenting and Human Health' (n 18).
[64] Schrecker et al (n 4) 68.
[65] Resnik (n 4).
[66] Ibid.
[67] Ibid 159.
[68] Ibid.

As it stands, the sale of human tissues and organs is prohibited in many parts of the world. This is notwithstanding the fact that there exists a market for artificial body parts and medical devices.[69] In general, the sale of human tissues and organs is prohibited because of reasons associated with human dignity and concerns that it might lead to the exploitation of vulnerable members of society.[70] However, considering the requirements for fabricating bioprinted constructs, it is most certain that there will be a fee associated with the cost of fabricating desired constructs. In itself, this presents a moral dilemma for countries opposed to the commodification of human tissues and organs. This is particularly pronounced in instances where the claimed constructs are intended for implantation in human recipients as opposed to use in *in vitro* research. It remains questionable, however, whether it is acceptable for bioprinted constructs to be treated as a commodity in the context of *in vitro* research and not so in the context of implantation.

Nevertheless, whilst attaching a monetary value to bioprinted constructs is not objectionable as such, the patenting of such constructs adds an element of exclusivity, which will undoubtedly affect how bioprinted constructs are valued - at least for the lifetime of such patents. In such circumstances, it becomes difficult to reconcile prohibitions on the sale of naturally occurring human tissues and organs with the commercialisation of bioprinted constructs. This extends the argument by Altman that commodification has the capacity to alter sensibilities and attitudes.[71] For if bioprinted constructs, which effectively serve the same purpose as naturally occurring tissues and organs, can only be obtained for value, on what grounds can governments continue to justify the prohibition of the sale of naturally occurring human tissues or organs? In the event that implantable bioprinted constructs become a reality, would-be-donors may become resistant to the idea of voluntarily parting with their tissue/organs without compensation, knowing fully well that the only other alternative for recipients is to pay for the fabrication of bioprinted constructs. Of course, in countries where the sale of human

[69] Merges (n 48).
[70] J S Taylor, 'Black Markets, Transplant Kidneys and Interpersonal Coercion' (2006) 32(12) *Journal of Medical Ethics* 698; Zümrüt Alpinar-Şencan, Holger Baumann and Nikola Biller-Andorno, 'Does Organ Selling Violate Human Dignity?' (2017) 34(3) *Monash Bioethics Review* 189; Roberto Andorno, 'Buying and Selling Organs: Issues of Commodification, Exploitation and Human Dignity' (2017) 1 *Journal of Trafficking and Human Exploitation* 119.
[71] Altman (n 20) 295-6.

tissues and organs is permitted, this is likely to be less of an issue, just as it would be less of an issue where the bioprinted constructs are utilised for *in vivo* research.

Nonetheless, as with the overarching concerns about commodification, prohibiting the grant of patents for bioprinted constructs does little to address the dichotomy that arises from commercialising bioprinted constructs whilst prohibiting the sale of naturally occurring human tissues and organs.

7.2.3 Access

As far as biotechnology patents in general are concerned, perhaps the most prominent concern with regards to patenting is the matter of access. This is buttressed by many of the arguments advanced against patenting in some of the cases examined in earlier parts of this thesis. In addition, as previously explained, matters of access also appear to underlie concerns about the impact of patenting current biotechnology inventions on the patentability of future inventions to the extent that it involves apprehensions about the manner in which such patents might be exploited. Nevertheless, it is debatable whether access ought to be categorised as an ethical concern since the purpose of patent grants is to create monopoly, albeit for a limited period. In other words, it would appear that concerns about access contradict the very essence of the patent system – exclusivity. To this end, it is useful to first provide an overview of the concept of access.

In the context of healthcare, access has been described as 'a general concept that summarizes a set of more specific dimensions describing the fit between the patient and the healthcare system'.[72] Penchansky and Thomas identify these dimensions as – availability, accessibility, accommodation, affordability and acceptability.[73] While these dimensions tend to overlap, it is imperative to understand what each dimension refers to in order to appreciate the broader meaning of the encompassing concept of access. Thus, whereas *availability* refers to the adequacy of personnel, facilities, specialised programs and services to meet clients' needs, *accessibility* refers to the geographical proximity between the location of supply and the location of clients.[74] Further, *accommodation* refers to the manner

[72] Roy Penchansky and J William Thomas, 'The Concept of Access: Definition and Relationship to Consumer Satisfaction' (1981) 19 *Medical Care* 127, 128.
[73] Ibid 128-9.
[74] Ibid 128; See also Catherine G McLaughlin and Leon Wyszewianski, 'Access to Care: Remembering Old Lessons' (2002) 37 *Health Services Research* 1441.

in which supply resources are organised to meet the individual needs of clients as well as the clients' perception of their appropriateness, while *affordability* refers to the ability and willingness of clients to pay for services provided.[75] Finally, *acceptability* refers to client and provider attitudes about personal and practice characteristics of each other.[76]

In recent years, the notions of cultural acceptability and respect of medical ethics (such as informed consent) as well as the principles of non-discrimination and accessibility of reliable information have also been included as part of the dimensions comprising access.[77] Correspondingly, in the provision of medicines, particularly by states, there is a responsibility to ensure equality of access for all individuals and groups irrespective of sex, race, ethnicity and socio-economic status.[78] Patients and healthcare professionals must also be provided with access to accurate and reliable information about medicines in order to make well informed decisions about their use.[79] Likewise, the medicines provided must be of good quality and safe for use.

Nonetheless, there are uncertainties regarding whether there is an ethical obligation to provide access to healthcare, whose responsibility it is and to whom the responsibility is owed. In light of this, it is useful to examine the provisions of human rights instruments such as the *Universal Declaration of Human Rights* ('*UDHR*')[80] and the *International Covenant on Economic, Social and Cultural Rights*[81] ('*ICESCR*') as it relates to the right to health and the right to benefit from science.

a) The Right to Health

The right to health is to be understood as 'a right to the enjoyment of a variety of facilities, goods, services and conditions necessary for the realization of the highest attainable standard of health'.[82] Similar to the aforementioned dimensions of access conceived by

[75] Penchansky and Thomas (n 73) 128; See also McLaughlin and Wyszewianski (n 75).
[76] Penchansky and Thomas (n 73) 129; See also McLaughlin and Wyszewianski (n 75).
[77] Paul Hunt, *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health*, UN Doc A/61/338 (13 September 2006).
[78] Ibid.
[79] Ibid.
[80] *Universal Declaration on Human Rights*, GA Res 217A (III), UN GAOR, 3rd sess, 183rd plen mtg, UN Doc A/810 (10 December 1948).
[81] *International Covenant on Economic, Social and Cultural Rights*, opened for signature 16 December 1966, 993 UNTS 3 (entered into force 3 January 1976) ('*ICESCR*').
[82] Committee on Economic, Social and Cultural Rights, *General Comment No 14: The Right to the Highest Attainable Standard of Health (Article 12 of the International Covenant on Economic, Social and Cultural Rights)*, 22nd sess, Agenda Item 3 UN Doc E/C.12/2000/4 (11 August 2000) para 9 ('*General Comment No 14*').

Penchansky and Thomas, the right to health consists of four interrelated and essential elements, namely availability, acceptability, quality and accessibility (noting that accessibility also encompasses non-discrimination, physical accessibility, economic accessibility (affordability) and information accessibility).[83]

According to art 25 of the *UDHR* , 'everyone has the right to a standard of living adequate for the health and well-being of himself and of his family including … medical care'. Furthermore, art 12 of the *ICESCR* requires states parties to 'recognise the right of everyone to the enjoyment of the highest attainable standard of physical and mental health'.[84] Some of the steps required to be taken to achieve the full realization of this right include the creation of conditions which would assure medical service and medical attention to all in the event of sickness; and the prevention, treatment and control of epidemic, endemic, occupational and other diseases.[85] Whereas the control of diseases refers to the individual and joint efforts of states to make available relevant technologies amongst other activities,[86] the creation of conditions which would assure medical service and attention to all includes the appropriate treatment of prevalent diseases.[87]

In light of the above and with health defined as 'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity',[88] it has been suggested that access to medicine is not only a fundamental element of the right to health, but also that it is related to the enjoyment of other rights such as the right to life.[89] This is because,

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[83] Ibid para 12.

[84] See also *International Convention on the Elimination of All Forms of Racial Discrimination*, opened for signature 21 December 1965, 660 UNTS 195 (entered into force 4 January 1969) art 5(e)(iv); *Convention on the Elimination of All Forms of Discrimination Against Women*, opened for signature 18 December 1979, 1249 UNTS 13 (entered into force 3 September 1989) art 11(1)(f), 12; *Convention on the Rights of the Child*, opened for signature 20 November 1989, 1577 UNTS 3 (entered into force 2 September 1990) art 24; *European Social Charter (Revised)*, opened for signature 3 May 1996, ETS No 136 (entered into force 1 July 1999) art 11; *African Charter on Human and People's Rights*, opened for signature 27 June 1981, 1520 UNTS 217 (entered into force 21 October 1986) art 16; *Additional Protocol to the American Convention on Human Rights in the Area of Economic, Social and Cultural Rights ("Protocol of San Salvador")*, opened for signature 17 November 1988, 28 ILM 156 (entered into force 16 November 1999) art 10.

[85] *ICESCR* (n 82) art 12(2)(c)(d).

[86] *General Comment No 14*, UN Doc E/C.12/2000/4 (n 83) para 16.

[87] Ibid para 17.

[88] *Constitution of the World Health Organization*, signed 22 July 1946, 14 UNTS 185 (entered into force 7 April 1948).

[89] Paul Hunt, *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health*, UN Doc A/61/338 (n 78); O A Owoeye, 'Patents and the Obligation to Protect Health: Examining the Significance of Human Rights Considerations in the Protection of Pharmaceutical Patents' (2014) 21(4) *Journal of Law and Medicine* 900.

in itself, the right to health is interdependent yet fundamental to the exercise of other human rights including the right to development.[90]

b) Responsibilities of State Actors in Realising the Right to Health

At this juncture, it would appear that enabling access to healthcare is the primary obligation of states who are parties to the aforementioned human right instruments. This is in furtherance of their obligation under international human right documents to progressively achieve the full realization of the right to health amongst other human rights.[91] As with other rights, the right to health encompasses three levels of obligation on states parties, namely: the obligations to *respect*, *protect* and *fulfil*.[92]

Whereas the obligation to *respect* 'requires States to refrain from interfering directly or indirectly with the enjoyment of the right to health', the obligation to *protect* 'requires States to take measures that prevent third parties from interfering with art 12 guarantees'.[93] Finally, the obligation to *fulfil* comprises three further obligations: to facilitate, provide and promote. Together, this 'requires States to adopt appropriate legislative, administrative, budgetary, judicial, promotional and other measures towards the full realization of the right to health'.[94]

Of particular relevance to the discourse on access in this chapter is the obligation to *protect*. This includes duties to take measures (including the adoption of legislation) 'ensuring equal access to health care and health-related services provided by third parties; to ensure that privatization of the health sector does not constitute a threat to the availability, accessibility, acceptability and quality of health facilities, goods and services; and to control the marketing of medical equipment and medicines by third parties'.[95] Additionally, states are required to ensure that people's access to health-related information and services is not limited by third parties.[96]

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[90] *General Comment No 14*, UN Doc E/C.12/2000/4 (n 83) para 1; World Health Organization and Office of the United Nations High Commissioner for Human Rights, *The Right to Health: Factsheet No. 31* (2008) ('*The Right to Health: Factsheet No. 31*'); Anand Grover, *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health*, UN Doc A/HRC/17/25 (12 April 2011).
[91] *ICESCR* (n 82) art 2(1).
[92] *General Comment No 14*, UN Doc E/C.12/2000/4 (n 83) para 33.
[93] Ibid.
[94] Ibid.
[95] Ibid para 35
[96] Ibid.

Furthermore, states have a core obligation to ensure equitable distribution of all health facilities, goods and services.[97] For those lacking in means, it is incumbent on states to provide health insurance and health-care facilities.[98] In some countries, this obligation is discharged through national health subsidy schemes (albeit funded by taxpayers) like the National Health Service (United Kingdom), the Medicare Benefits Scheme and the Pharmaceutical Benefits Scheme (Australia), and Medicare and Medicaid (the USA).

While states are obliged to employ to the maximum their available resources in the realization of the right to health, it is recognised that some states may be unable to fulfil these obligations owing to resource constraints.[99] Accordingly, international co-operation between states parties has been recognised as essential in the realization of the right to health.[100] In particular, the Committee on Economic, Social and Cultural Rights ('CESCR') emphasizes that it is 'incumbent on States parties and other actors in a position to assist, to provide "international assistance and cooperation, especially economic and technical" which enable developing countries to fulfil their obligations' under the right to health.[101]

The obligation of states parties to work together to achieve the full realization of the right to health is further reinforced by art II of the *Declaration of Alma-Ata*,[102] which proclaims that the 'existing gross inequality in the health status of the people, particularly between developed and developing countries, as well as within countries, is politically, socially and economically unacceptable and is, therefore, of common concern to all countries'.

Accordingly, states are enjoined to facilitate access to essential health facilities, goods and services in other countries depending on the availability of resources.[103] States are equally enjoined to ensure that when concluding international agreements, such instruments do not adversely impact upon the right to health.[104] Neither should restrictions on the supply of medicines and medical equipment to other states ever be used as an instrument of

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[97] Ibid para 43
[98] Ibid para 19.
[99] Ibid para 47; *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health: Expert Consultation on Access to Medicines as a Fundamental Component of the Right to Health*, UN Doc A/HRC/17/43 (16 March 2011).
[100] *General Comment No 14*, UN Doc E/C.12/2000/4 (n 83) para 38.
[101] Ibid para 45.
[102] '*Declaration of Alma-Ata*' in *Primary Health Care: Report of the International Conference on Primary Health Care, Alma-Ata, USSR, 6-12 September 1978* (World Health Organization, 1978) 2.
[103] *General Comment No 14*, UN Doc E/C.12/2000/4 (n 83) para 39.
[104] Ibid.

economic and political pressure.[105] These comments are of particular significance when one considers the manner in which free trade agreements have been used by developed countries to compel developing countries to adopt more stringent intellectual property provisions (known as '*TRIPS*-plus') than afforded under the *TRIPS Agreement* itself.[106]

Unwillingness to fulfil any of these obligations by states either through direct action or insufficient regulation of third parties are deemed a violation of the right to health.[107] However, as with many of the other rights contained in the *ICESCR*, there are no immediate penalties attached to the violations of the right to health. This has lent credence to comments that, unlike civil and political rights which have long been recognised as justiciable, economic, social and cultural rights are non-justiciable.[108]

Nonetheless, case law from South Africa, India and various Latin American countries suggest that economic, social and cultural rights including the right to health are justiciable to some extent.[109] This is in addition to the enforcement of the right to health by regional courts such as Inter-American Court of Human Rights, the African Court of Human and Peoples' Rights and the European Court of Human Rights.[110] It would also appear that despite not ratifying the *ICESCR* and specifically protecting the right to health in its Constitution, courts in the USA have recognised the right to access medicines and health care facilities in a number of cases involving HIV-positive prisoners.[111]

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[105] Ibid para 41.

[106] Paul Hunt, *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health*, UN Doc A/61/338 (n 78); *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health: Expert Consultation on Access to Medicines as a Fundamental Component of the Right to Health*, UN Doc A/HRC/17/43 (n 100); Suerie Moon, 'Respecting the Right to Access to Medicines: Implications of the UN Guiding Principles on Business and Human Rights for the Pharmaceutical Industry' (2013) 15 *Health and Human Rights Journal*; Sara Joseph, *Blame it on the WTO? A Human Rights Critique* (Oxford University Press, 2011).

[107] *General Comment No 14*, UN Doc E/C.12/2000/4 (n 83) para 48-49, 51.

[108] Joseph (n 107).

[109] Ibid; Owoeye, 'Patents and the Obligation to Protect Health: Examining the Significance of Human Rights Considerations in the Protection of Pharmaceutical Patents' (n 90); *Minister of Health v Treatment Action Campaign* (No 2) [2002] 5 SA 721 (Constitutional Court); *Mullen v Union Territory of Delhi* [1981] 2 SCR 516; *Rodriguez v Caja Constarricense de Seguro Social* (Supreme Court of Justice of Costa Rica, Constitutional Chamber, Decision No 6096-97, 1997); *Bermudez v Ministerio de Sanidad y Asistencia Social* (Supreme Court of Justice of Venezuela, Decision No 916, 1999); *García Lopez v Southeast Metropolitan Health Service* (Court of Appeals of Santiago, Petition for Protection, No 2,614-99, 14 June 1999); *Ramirez v Instituto Mexicano del Seguro Social* (Plenary Court of Supreme Court of Justice, Amparo Decision 2231/97, April 2000); Rebecca Young, 'Justiciable Socio-Economic Rights? South African Insights into Australia's Debate' (2008) 15 *Australian International Law Journal* 181.

[110] See generally Owoeye, 'Patents and the Obligation to Protect Health: Examining the Significance of Human Rights Considerations in the Protection of Pharmaceutical Patents' (n 90); Joseph (n 107).

[111] *Montgomery v Pinchak* 294 F 3d 492 (2002); *Brown v Johnson* 387 F 3d 1344 (2004); *Smith v Carpenter* 316 F 3d 178 (2003).

Furthermore, it would appear that the *Optional Protocol to the International Covenant on Economic, Social and Cultural Rights* ('*Optional Protocol*')[112] adopted by the United Nations ('UN') General Assembly in 2008 confirms that economic, social and cultural rights are indeed potentially justiciable. This is because it provides for an individual complaint mechanism to the CESCR about violations of any of the rights set forth in the *ICESCR*. In fact, it has been suggested that the *Optional Protocol*, which came into force on 5 May 2013 will 'usher in a new era of justiciable global economic social and cultural rights'.[113] However, it should be noted that by virtue of art 8(4) of the *Optional Protocol*, the justiciability of these rights as contained in the *ICESCR* is subject to the discretion states parties have in adopting possible policy measures for their implementation.[114]

c) Responsibilities of Non-State Actors in Realising the Right to Health

On the other hand, albeit to a lesser extent than states, there appears to be a growing recognition of the role of non-state actors particularly pharmaceutical companies in the realization of the right to health.[115] This is by virtue of the industry pharmaceutical companies operate in, and the patents they hold. It has been argued by some that the right to health imposes an obligation on patentees of lifesaving medicines to do all that is within their power to ensure access.[116] In particular, the CESCR notes in its General Comment on the right to health that while only states are parties to the *ICESCR*, all members of society including the private business sector, have responsibilities regarding the realization of the right to health.[117] It, however, fails to identify what these responsibilities are.

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[112] *Optional Protocol to the International Covenant on Economic, Social and Cultural Rights*, 63rd see, Agenda Item 58 UN Doc A/RES/63/117 (5 March 2009, adopted 10 December 2008).
[113] Joseph (n 107) 29.
[114] Ibid.
[115] *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health*, UN Doc A/63/263 (11 August 2008); Paul Hunt, *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health*, UN Doc A/61/338 (n 78); *The Right to Health: Factsheet No. 31* (n 91); *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health: Expert Consultation on Access to Medicines as a Fundamental Component of the Right to Health*, UN Doc A/HRC/17/43 (n 100); See also Target 8.E of Millennium Development Goal 8 which is to provide access to affordable essential drugs in developing countries in co-operation with pharmaceutical companies 'United Nations Millennium Development Goals', *United Nations* (Web Page) <https://www.un.org/millenniumgoals/global.shtml>.
[116] *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health: Expert Consultation on Access to Medicines as a Fundamental Component of the Right to Health*, UN Doc A/HRC/17/43 (n 100).
[117] *General Comment No 14*, UN Doc E/C.12/2000/4 (n 83) para 42.

Further to this, Paul Hunt – UN Special Rapporteur on the right to the highest attainable standard of health (2002-2008) undertook a review of the policies and practices of pharmaceutical companies in relation to access to medicines and the right to health. In his reports, he noted that whilst there was a general acknowledgment of the indispensable role pharmaceutical companies play in enhancing access to medicines, states have equally criticised some practices and policies of pharmaceutical companies, which they perceive as posing an obstacle to their endeavours to enhance access to medicines.[118] The practices identified include high drug pricing, imbalanced research and development into diseases affecting developing countries, as well as lobbying for *TRIPS*-plus standards.

Accordingly, and further to numerous discussions with stakeholders including pharmaceutical companies, Hunt submitted that if the right to health is to be attained, the exact nature and scope of the human right responsibilities of pharmaceutical companies in relation to access to medicines needs to be clarified.[119] To this end, he developed the 'Human Rights Guidelines for Pharmaceutical Companies in relation to Access to Medicines' ('Guidelines') in consultation with stakeholders including pharmaceutical companies.[120] The central objective of these Guidelines is to provide guidance to pharmaceutical companies and interested stakeholders who wish to monitor companies and hold them to account.[121]

The Guidelines draw from widely accepted standards including instruments on medicines by the World Health Organization, and human rights principles enshrined in the *UDHR* such as non-discrimination, equality, transparency, monitoring and accountability.[122] Throughout the Guidelines, the human rights responsibilities of pharmaceutical companies (defined as including innovator, generic and biotechnology companies) in relation to access to medicines are repeatedly emphasised. It is also noted in the preamble that 'for the

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[118] *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health*, UN Doc A/63/263 (n 116); Paul Hunt, *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health*, UN Doc A/61/338 (n 78).

[119] *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health*, UN Doc A/63/263 (n 116); *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health: Expert Consultation on Access to Medicines as a Fundamental Component of the Right to Health*, UN Doc A/HRC/17/43 (n 100).

[120] The final version of the Guidelines is contained in the annex of the *Report of the Special Rapporteur on the Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health*, UN Doc A/63/263 (n 116).

[121] Ibid.

[122] Ibid.

purposes of the present Guidelines, medicines include active pharmaceutical ingredients, diagnostic tools, vaccines, biopharmaceuticals and other related health-care technologies',[123] which can arguably be interpreted as possibly including bioprinting since it is a healthcare technology within the biotechnology sector.

The Guidelines are grouped into thematic areas such as transparency, corruption, neglected diseases, patents and licensing, public-private partnerships, and pricing and ethical marketing, each followed by a brief commentary. While not legally binding, the thematic section on patents and licensing is noteworthy as it enjoins companies to respect the letter and spirit of the *Doha Declaration*[124] as well as the right of countries to utilise *TRIPS* flexibilities to the fullest, which will be considered later in this chapter.[125] In essence, pharmaceutical companies are requested not to 'seek to limit, diminish or compromise the "flexibilities" and other features of the intellectual property regime that are designed to protect and promote access to existing medicines'.[126] Pharmaceutical companies are also enjoined to waive test data where appropriate, and issue non-exclusive voluntary licences for all medicines in low-income and middle-income countries.[127]

Although the Guidelines is not legally binding, it is nevertheless worthy to note that pharmaceutical companies such as GlaxoSmithKline and Merck have objected to the Guidelines.[128] Whilst Merck conceded that 'pharmaceutical companies have a responsibility to offer assistance when social, political and economic conditions make it impossible for patients to receive life-saving therapies', and that they ought to 'leverage their expertise to help remove the barriers that stand between patients and the therapies they need', it also noted that several of the Guidelines were impractical and placed undue burden on companies.[129] In particular, Merck noted that the Guidelines did not address

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[123] *Human Rights Guidelines for Pharmaceutical Companies in relation to Access to Medicines*, preamble para q.
[124] *Doha Declaration on the TRIPS Agreement and Public Health,* WTO Doc WT/MIN(01)/DEC/2 (20 November 2001, adopted 14 November 2001) ('*Doha Declaration*').
[125] *Human Rights Guidelines for Pharmaceutical Companies in relation to Access to Medicines* (n 124) paras 26-27.
[126] Ibid commentary on Patents and Licensing theme.
[127] Ibid paras 30-31.
[128] For a critique of the Guidelines, see generally Moon (n 107); Jeffrey L Sturchio, 'Response from Merck & Co., Inc. to Human Rights Guidelines for Pharmaceutical Companies in Relation to Access to Medicines', *Merck* (Web Page, 29 February 2008) <https://www.merck.com/corporate-responsibility/docs/access_developing_response_feb08.pdf>; 'GlaxoSmithKline Statement in Response to Paul Hunt's Report on GSK', *GlaxoSmithKline* (Web Page, June 2009) <http://198.170.85.29/GSKresponse-to-Paul-Hunt-report-June-2009.pdf>.
[129] Sturchio (n 129).

underlying issues that prevent achieving the highest attainable standard of physical and mental health such as health system development in developing countries, the need for more health professionals, capacity building, storage and distribution of medicines.[130]

While it is indeed true that there are other underlying issues that prevent achieving the highest attainable standard of physical and mental health, this does not detract from the fact that pharmaceutical companies play a pivotal role in improving access to medicines. This is notwithstanding that the primary obligation to provide access ultimately lies with states. However, as Moon argues, it is necessary to delineate the differences between the responsibilities of states and pharmaceutical companies as 'conflating the responsibilities of State and non-state actors risks detracting attention away from state obligations, making it easier for governments to shirk their own obligations'.[131]

Thus, it would appear that while it is generally accepted that pharmaceutical companies have some role to play in the provision of access to medicines, such role might at best be encapsulated as being merely socially desirable as opposed to importing legally enforceable responsibilities. Until such roles are clarified, it would appear that states alone have the primary responsibility of ensuring access to medicine in furtherance of their responsibility to progressively realize the right to health.

d) Beneficiaries of the Right to Health

It would appear from a combined reading of the provisions of the *UDHR*, the *ICESCR* and other human right documents that every person regardless of sex, race, ethnicity and socio-economic status is entitled to the right to health. Consequently, it would appear that every person irrespective of sex, race, ethnicity and socio-economic status is entitled to access to medicines given its centrality to the realization of the right to health.

Nevertheless, it should be noted that legal nationality is a prerequisite for the enjoyment of the right to health by any person.[132] This is because the right to health and indeed many other human rights are guaranteed by states parties primarily to their citizens. Hence, the extent of access to the right to health (including access to medicines) within a national

[130] Ibid.
[131] Moon (n 107).
[132] Lindsey N Kingston, Elizabeth F Cohen and Christopher P Morley, 'Debate: Limitations on Universality: The "Right to Health" and the Necessity of Legal Nationality' (2010) 10 *BMC International Health and Human Rights* 11.

system will often be determined by an individual's citizenship or migration status in the country within which access is sought.[133] This is understandably so because a state's primary obligations are to its citizens and taxpayers.

e) The Right to Benefit from Science

Another right which has been advanced as crucial to the realisation of the right to health, and consequently, access to medicines, is the right to benefit from science.[134] This is because the realisation of the right to health depends on the availability of health facilities, goods and services, which is in turn dependent on the availability of scientific knowledge and information. Article 27 of the *UDHR* provides that '[e]veryone has the right freely to … share in scientific advancement and its benefits'. In addition, art 15(1)(b) of the *ICESCR* enjoins states parties to recognise the right of everyone to enjoy the benefits of scientific progress and its applications.

Despite its inclusion in the *UDHR* and the *ICESCR*, however, the extent of the right to benefit from science remains vague in the absence of a legal definition.[135] As such, there has been a tendency for governments to overlook the right in practice.[136] In light of this, the UN has undertaken a number of actions to clarify the scope and extent of this right.[137] This includes the report submitted by Farida Shaheed (Special Rapporteur in the Field of Cultural Rights) on the right to enjoy the benefits of scientific progress and its applications.[138]

In her report, Shaheed noted that the right to science connotes a right of access to science 'as a whole, not only to specific scientific outcomes or applications'.[139] This requires that

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[133] Ibid; Israel De Alba et al, 'Impact of U S Citizenship Status on Cancer Screening Among Immigrant Women' (2005) 20 *Journal of General Internal Medicine* 290.
[134] Farida Shaheed, *Report of the Special Rapporteur in the Field of Cultural Rights: The Right to Enjoy the Benefits of Scientific Progress and its Applications*, UN Doc A/HRC/20/26 (14 May 2012).
[135] Jessica M Wyndham and Margaret Weigers Vitullo, 'Define the Human Right to Science' (2018) 362(6418) *Science* 975.
[136] Ibid; Committee on Economic, Social and Cultural Rights, *Day of General Discussion - Discussion Paper*, 64th sess, Agenda Item 3 (24 September – 12 October 2018) ('*Day of General Discussion - Discussion Paper*'); Andrea Boggio et al, 'The Human Right to Science and the Regulation of Human Germline Engineering' (2019) 2(3) *The CRISPR Journal* 134.
[137] See, eg, Scientific and Cultural Organization United Nations Educational, *The Right to Enjoy the Benefits of Scientific Progress and its Applications* (UNESCO).
[138] Farida Shaheed, *Report of the Special Rapporteur in the Field of Cultural Rights: The Right to Enjoy the Benefits of Scientific Progress and its Applications*, UN Doc A/HRC/20/26 (n 135).
[139] Ibid 9 [26].

scientific knowledge, information and advances must be made accessible to all without discrimination further to art 2 of the *ICESCR*.[140] She also emphasised the importance of the right to have access to scientific knowledge in the realization of the right to science.[141] In particular, she noted that 'access to scientific information for researchers is essential'.[142]

Furthermore, the United Nations Educational, Scientific and Cultural Organization ('UNESCO') has also undertaken a series of consultative processes in preparation for drafting a general comment on art 15 of the *ICESCR* as relates to the right to enjoy the benefits of scientific progress and its applications.[143] The aim of the general comment is to 'provide authoritative guidance to States parties on the measures to be adopted to ensure full compliance with the right'.[144] To this end, a day of general discussion on art 15 of the *ICESCR* was organised by UNESCO in October 2018 to discuss the relationship between science and economic, social and cultural rights.[145] Ahead of the discussion, a series of questions were posed to stakeholders. This included questions about whether 'science' ought to be understood as including technology and technological development as well as whether 'benefits' ought to include other elements such as knowledge in addition to material results of scientific research.[146] In addition, questions about the justiciability of the right to benefit from science and its relationship with intellectual property rights were also posed.[147] Whilst acknowledging that the right to enjoy the benefits of scientific progress likely refers to the right of access to the material benefits of science such as drugs, treatment, agricultural improvements and other technologies, it was questioned whether this access also ought to include access to knowledge including education, publications and contents.[148]

As part of its response, the American Association for the Advancement of Science, noted that access 'is a fluid and bi-directional continuum, defined on one end as "access for

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[140] Ibid.
[141] Ibid 9 [27].
[142] Ibid 9 [28].
[143] 'Science as a Human Right: The Need of a Unified Concept', *United Nations Educational, Scientific and Cultural Organization* (Web Page, 30 November 2018) <https://en.unesco.org/news/science-human-right-need-unified-concept>
[144] *Day of General Discussion - Discussion Paper* (n 137).
[145] Ibid.
[146] Ibid.
[147] Ibid.
[148] Ibid.

general public" and on the other as "access for scientists.'"[149] The United Nations Development Program also noted that the right to science provides a unique opportunity to promote innovation and access to health technologies.[150] The realization of this right is, however, dependent on finding a balance 'between protecting moral and proprietary interests of inventors and addressing public health needs, stimulating competition and fostering innovation'.[151] Furthermore, the Treatment Action Group identified access to knowledge, to information, and to the tangible products of scientific advancement as a cornerstone of the right to benefit from science.[152] In particular, it noted that access was important to scientists and beneficiaries of scientific progress.[153]

Overall, it has been suggested by the scientific community that beyond the 'right to benefit from material products of science and technology', the right to science also includes the 'right to benefit from the scientific method and scientific knowledge, whether to empower personal decision-making or to inform evidence-based policy'.[154] In addition, the right also ought to encompass access to scientific knowledge and information by scientists as well as non-specialist audience.[155]

Recently, the general comment on art 15 of the *ICESCR* was adopted by the CESCR and it notes that the term 'benefits' refers to the material results of the applications of scientific research, scientific knowledge and information directly deriving from scientific activity, and the role of science in forming critical and responsible citizens who are able to participate

[149] The American Association for the Advancement of Science has been described as 'the world's largest multidisciplinary scientific membership organization with over 100,000 members worldwide in over 80 countries'. 'Submission: Right to Science from the American Association for the Advancement of Science', *American Association for the Advancement of Science* (Web Page, October 2018) <https://www.ohchr.org/Documents/HRBodies/CESCR/Discussions/2018/AmericanAssociationAdvancementScience.pdf>.

[150] 'UNDP Contribution to the UN Committee an Economic, Social and Cultural Rights - General Discussion on a Draft General Comment on Article 15 of the International Covenant on Economic, Social and Cultural Rights: On the Right to Enjoy the Benefits of Scientific Progress and its Applications', *United Nations Development Program* (Web Page, October 2018) <https://www.ohchr.org/Documents/HRBodies/CESCR/Discussions/2018/UNDP.PDF>.

[151] Ibid.

[152] 'Written Contribution by Treatment Action Group to the Day of General Discussion on Article 15 of the ICESCR: On the Right to Enjoy the Benefits of Scientific Progress and its Applications', *Treatment Action Group* (Web Page, October 2018) <https://www.ohchr.org/Documents/HRBodies/CESCR/Discussions/2018/TAG.docx>.

[153] Ibid.

[154] Wyndham and Vitullo (n 136); See also Boggio et al (n 137); Andrea Boggio and Calvin W L Ho, 'The Human Right to Science and Foundational Technologies' (2018) 18(12) *The American Journal of Bioethics* 69.

[155] Wyndham and Vitullo (n 136).

fully in a democratic society.[156] It also identifies access as an element of the right to benefit from science.[157] In particular, the general comment states that

> Accessibility means that scientific progress and its applications should be accessible for all persons, without discrimination. It has three dimensions: first, States parties should ensure that everyone has equal access to the applications of science, particularly when they are instrumental for the enjoyment of other economic, social and cultural rights. Second, information concerning the risks and benefits of science and technology should be accessible without discrimination. Third, everyone should have the open opportunity to participate in scientific progress, without discrimination. Thus, States parties should remove discriminatory barriers that impede persons from participating in scientific progress, for instance, by facilitating the access of marginalized populations to scientific education.[158]

The obligations of states parties in the realisation of the right to benefit from science are similar to the obligations highlighted under the right to health including the obligations to *respect*, *protect* and *fulfil*.[159] Furthermore, it is noted that this right is enforceable and justiciable.[160] States parties are therefore enjoined 'to establish effective mechanisms and institutions, where they do not already exist, to prevent violations of the right and to ensure effective judicial, administrative and other remedies for victims if such violations occur'.[161]

7.2.3.1 Interaction between the Patent System, the Right to Health and the Right to Benefit from Science

Having established the interconnectedness between access, the right to health and the right to benefit from science, it is crucial to now examine the interaction between these concepts and the patent system. This is in light of concerns that patents pose an obstacle to the realization of the right to health and the right to benefit from science.[162] Additionally, it

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[156] Committee on Economic, Social and Cultural Rights, *General Comment No 25 (2020) on Science and Economic, Social and Cultural Rights (Article 15 (1) (b), (2), (3) and (4) of the International Covenant on Economic, Social and Cultural Rights)* 67th sess, Agenda Item 3 UN Doc E/C.12/GC/25 (30 April 2020) 3 [8] ('*General Comment No 25*').
[157] Ibid 4 [17].
[158] Ibid 4 [17].
[159] Ibid 9-10 [41]-[50].
[160] Ibid 19 [89].
[161] Ibid [89].
[162] Phoebe Li, '3D Bioprinting Technologies: Patents, Innovation and Access' (2015) 6 *Law, Innovation and Technology* 282; Justice Michael Kirby, 'Playing God? Owing God? - Patenting and the Human Genome' (2003) 26 *University of New South Wales Law Journal* 770.

provides a framework for analysing how patenting might pose an ethical concern in accessing bioprinting.

Over the course of this chapter, it has been emphasised that patents are generally considered as incentivising innovation by virtue of the exclusivity afforded. In addition, it has been argued that patents assure protection of new products in the market and facilitate disclosure of scientific information, which is especially important in the healthcare sector.[163] Accordingly, patents are considered beneficial to the public because of their capacity to stimulate the development of new and improved treatments.[164]

At the same time, however, there are concerns that patent monopoly could in fact hinder the development of new and improved treatments for a number of reasons. These include the prevalence of upstream patents with broad claims, patent thickets and the difficulties associated with obtaining and negotiating licences to use patented inventions.[165] There are also concerns about the likelihood of research potentially infringing patents particularly in countries like the USA where there is no general statutory exemption for experimental use.[166] For patients seeking to access treatments, it has been noted that patents have the capacity to impede access through increased cost of treatment arising from exclusivity.[167] In turn, this has the effect of emphasising instances of social inequality because certain treatments are priced out of the reach of the common person.[168]

To this end, there have been many commentaries regarding the possibility of striking a balance between incentivising innovation and rewarding innovators on the one hand, and

[163] *The Ethics of Patenting DNA - A Discussion Paper* (n 4); Joseph (n 107); Rebecca S Eisenberg, 'Patents and the Progress of Science: Exclusive Rights and Experimental Use' (1989) 56 *University of Chicago Law Review* 1017.
[164] *The Ethics of Patenting DNA - A Discussion Paper* (n 4); Joseph (n 107).
[165] See generally Nuffield Council on Bioethics, *Emerging Biotechnologies: Technology, Choice and the Public Good* (Nuffield Council on Bioethics, 2012); Boggio and Ho (n 155); Committee on Economic, Social and Cultural Rights, *Protection of Intellectual Property under the TRIPS Agreement: Background Paper Submitted by the Secretariat of the World Trade Organization*, 24th sess, Agenda Item 3 UN Doc E/C.12/2000/18 (29 November 2000); 'Genes and Ingenuity: Gene Patenting and Human Health' (n 18); Dianne Nicol and Jane Nielsen, *Patents and Medical Biotechnology: An Empirical Analysis of Issues Facing the Australian Industry,* Occasional Paper 6 (Centre for Law and Genetics, 2003); Michael A Heller and Rebecca S Eisenberg, 'Can Patents Deter Innovation? The Anticommons in Biomedical Research' (1998) 280 *Science* 698; Carl Shapiro, 'Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard Setting' (2000) 1 *Innovation Policy and the Economy* 119.
[166] Jon F Merza and Mildred K Chob, 'What Are Gene Patents and Why Are People Worried about Them?' (2005) 8 *Community Genetics* 203; Caulfield, Gold and Cho (n 5); See also chapter five (section 5.4).
[167] *The Ethics of Patenting DNA - A Discussion Paper* (n 4); Joseph (n 107).
[168] Vidergar (n 19).

ensuring access to these innovations on the other hand.[169] In other words, what is needed is a balance between protecting patent rights and respecting the rights to health and benefit from science. In light of this, it is important to note the provisions of art 27(2) *UDHR* and art 15(1)(c) *ICESCR*, which enjoin states parties to recognise the right of everyone to the protection of moral and material interests resulting from any scientific production of which they are the author.

While some have suggested that these provisions imply that property rights such as patents are recognised as human rights,[170] the CESCR have sought to distinguish the rights of authors in art 15(1)(c) from broader intellectual property rights. They note that art 15(1)(c) rights are human rights which derive from the inherent dignity and worth of persons.[171] As human rights, they are therefore fundamental, inalienable and universal.[172] This can be contrasted with intellectual property rights which are temporary and can be revoked, licensed or assigned to a third party.[173] At the same time, 'intellectual property regimes primarily protect business and corporate interests and investments' in contrast to art 15(1)(c) rights, which 'safeguards the personal link between authors and their creations and between peoples, communities, or other groups and their collective cultural heritage, as well as their basic material interests which are necessary to enable authors to enjoy an adequate standard of living'.[174]

With regard to its relationship with other rights contained in the *ICESCR* as well as intellectual property rights, the CESCR note as follows:

> States parties should therefore ensure that their legal or other regimes for the protection of the moral and material interests resulting from one's scientific, literary or artistic

[169] See, eg, *The Ethics of Patenting DNA - A Discussion Paper* (n 4); Owoeye, 'Patents and the Obligation to Protect Health: Examining the Significance of Human Rights Considerations in the Protection of Pharmaceutical Patents' (n 90); *General Comment No 25*, UN Doc E/C.12/GC/25 (n 157); Farida Shaheed, *Report of the Special Rapporteur in the Field of Cultural Rights: The Right to Enjoy the Benefits of Scientific Progress and its Applications*, UN Doc A/HRC/20/26 (n 135); Kirby (n 163); Hans Morten Haugen, 'Patent Rights and Human Rights: Exploring their Relationships' (2007) 10 (2007/03/01) *The Journal of World Intellectual Property* 97; Philippe Cullet, 'Human Rights and Intellectual Property Protection in the TRIPS Era' (2007) 29 *Human Rights Quarterly* 403.

[170] Owoeye, 'Patents and the Obligation to Protect Health: Examining the Significance of Human Rights Considerations in the Protection of Pharmaceutical Patents' (n 90).

[171] Committee on Economic, Social and Cultural Rights, *General Comment No 17 (2005): The right of everyone to benefit from the protection of the moral and material interests resulting from any scientific, literary or artistic production of which he or she is the author (article 15, paragraph 1 (c), of the Covenant)*, 35th sess, UN Doc E/C.12/GC/17 (12 January 2006) 2 [1].

[172] Ibid.

[173] Ibid 2 [2].

[174] Ibid.

> productions constitute no impediment to their ability to comply with their core obligations in relation to the rights to food, health and education, as well as to take part in cultural life and to enjoy the benefits of scientific progress and its applications, or any other right enshrined in the Covenant. Ultimately, intellectual property is a social product and has a social function. States parties thus have a duty to prevent unreasonably high costs for access to essential medicines, plant seeds or other means of food production, or for schoolbooks and learning materials, from undermining the rights of large segments of the population to health, food and education. Moreover, States parties should prevent the use of scientific and technical progress for purposes contrary to human rights and dignity, including the rights to life, health and privacy, e.g. by excluding inventions from patentability whenever their commercialization would jeopardize the full realization of these rights. States parties should, in particular, consider to what extent the patenting of the human body and its parts would affect their obligations under the Covenant or under other relevant international human rights instruments.[175]

It would therefore appear that the rights to health and benefit from science ought to take precedence over patent rights.[176] This is in addition to arguments that 'intellectual property rights as private rights ought to give deference to public rights and public interest qualifications in the event of conflict' since modern legal foundations are founded on the principle that public interest always takes precedence over private rights that run contrary to it.[177] Furthermore, some authors have noted that the rights to health and benefit from science 'offers a more concrete basis for governments to balance their competing commitments in promoting scientific development on the one hand, and ensuring benefit sharing on the other'.[178]

Notwithstanding, arguments about the order of precedence between human rights and patent rights in the context of access reflect an underlying tension between both rights which is yet to be resolved satisfactorily. In particular, the *TRIPS Agreement* and prevalence

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[175] Ibid 9 [35].
[176] Sub-Commission on the Promotion and Protection of Human Rights, *Intellectual Property Rights and Human Rights*, Resolution 2000/7, 52nd sess, UN Doc E/CN.4/SUB.2/RES/2000/7 (17 August 2000) paras 3-4.
[177] Owoeye, 'Patents and the Obligation to Protect Health: Examining the Significance of Human Rights Considerations in the Protection of Pharmaceutical Patents' (n 90) 912. There are, however, arguments that private rights such as intellectual property serve a public interest. See, eg, Rebecca Tushnet, 'Intellectual Property as a Public Interest Mechanism' in Rochelle Dreyfuss and Justine Pila (eds), *The Oxford Handbook of Intellectual Property Law* (Oxford University Press, 2018) 95
[178] Boggio and Ho (n 155) 70.

of *TRIPS*-plus provisions in free trade agreements have been identified as posing significant threats to the realisation of the rights to health and benefit from science.[179] Yet, it has also been acknowledged that flexibilities contained in *TRIPS*, which allow for public health considerations in the implementation of national patent regimes may be utilised to resolve this tension.[180] They include exclusions from patentability,[181] exceptions to exclusive rights,[182] compulsory licensing,[183] and parallel importation/exhaustion of rights.[184]

The recommended use of these flexibilities would appear to align with the school of thought which views intellectual property rights and human rights as complementary.[185] For this school of thought, the principal way to resolve the tension between both rights in the arena of access to medicines is to interpret the *TRIPS Agreement* in a manner that is conducive to promoting and protecting the right to health and access to medicines.[186] This is reflected in the combined provisions of art 7 and 8 of the *TRIPS Agreement* which provide context for interpreting and implementing the *TRIPS Agreement*.[187] Article 7, which contains the objectives of the *TRIPS Agreement* provides that:

> The protection and enforcement of intellectual property rights should contribute to the 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.

Article 8, on the other hand, contains the *TRIPS Agreement* principles, which provides thus:

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[179] Farida Shaheed, *Report of the Special Rapporteur in the Field of Cultural Rights: The Right to Enjoy the Benefits of Scientific Progress and its Applications*, UN Doc A/HRC/20/26 (n 135) 15 [56].
[180] Ibid 16 [58]-[59].
[181] *TRIPS Agreement* (n 3) art 27(2), (3).
[182] *TRIPS Agreement* (n 3) art 30.
[183] *TRIPS Agreement* (n 3) art 31.
[184] See chapters three (section 3.4), four (section 4.4), and five (section 5.4)
[185] See generally Jennifer Anna Sellin, 'Does One Size Fit All? Patents, the Right to Health and Access to Medicines' (2015) 62 *Netherlands International Law Review* 445 paras 3-4; Sub-Commission on the Promotion and Protection of Human Rights, *Intellectual Property Rights and Human Rights*, UN Doc E/CN.4/SUB.2/RES/2000/7 (n 177); Committee on Economic, Social and Cultural Rights, *Protection of Intellectual Property under the TRIPS Agreement: Background Paper Submitted by the Secretariat of the World Trade Organization*, UN Doc E/C.12/2000/18 (n 166).
[186] Sellin (n 186); Committee on Economic, Social and Cultural Rights, *Protection of Intellectual Property under the TRIPS Agreement: Background Paper Submitted by the Secretariat of the World Trade Organization*, UN Doc E/C.12/2000/18 (n 166).
[187] Sellin (n 186); *Doha Declaration*, WTO Doc WT/MIN(01)/DEC/2 (n 125) para 5(a).

1. Members may, in formulating or amending their laws and regulations, adopt measures necessary to protect public health and nutrition, and to promote the public interest in sectors of vital importance to their socio-economic and technological development, provided that such measures are consistent with the provisions of this Agreement.
2. Appropriate measures, provided that they are consistent with the provisions of this Agreement, may be needed to prevent the abuse of intellectual property rights by right holders or the resort to practices which unreasonably restrain trade or adversely affect the international transfer of technology.

It has been noted that art 7 and 8 of the *TRIPS Agreement* reflect competing objectives and purposes of both creators and users of intellectual property across international borders, which need to be balanced.[188] More importantly, that these provisions are 'fundamental to an analysis of the object and purpose of the TRIPS Agreement'.[189] This is further to the application of the customary rules of interpretation of public international law to the *TRIPS Agreement*. In particular, the *Vienna Convention on the Law of Treaties*, which provide that 'a treaty shall be interpreted in good faith in accordance with the ordinary meaning to be given to the terms of the treaty in their context in light of its object and purpose'.[190]

Further, the *Doha Declaration* equally recognises that the *TRIPS Agreement* and public health are inextricably linked. In particular, para 4 provides that:

> … the *TRIPS Agreement* does not and should not prevent Members from taking measures to protect public health. Accordingly, while reiterating our commitment to the *TRIPS Agreement*, we affirm that the *Agreement* can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all.

[188] Susy Frankel, 'WTO Application of the Customary Rules of Interpretation of Public International Law to Intellectual Property' (2006) 46(2) *Virginia Journal of International Law* 365, 393.
[189] Susy Frankel, 'Some Consequences of Misinterpreting the TRIPS Agreement' [2009] (1) *The WIPO Journal* 35, 40. See also Alison Slade, 'The Objectives and Principles of the WTO TRIPS Agreement: A Detailed Anatomy' (2016) 53(3) *Osgoode Hall Law Journal* 948; Henning Grosse Ruse-Khan, 'A Comparative Analysis of Policy Space in WTO Law' (Research Paper No 08-02, Max Planck Institute for Intellectual Property, Competition and Tax Law, 2008); Peter K Yu, 'The Objectives and Principles of the TRIPS Agreement' (2009) 46 *Houston Law Review* 979.
[190] *Vienna Convention on the Law of Treaties*, opened for signature 23 May 1969, 1115 UNTS 331 (entered into force 27 January 1980) art 31-32.

In light of these provisions, it is useful to now consider access concerns that may arise from patenting bioprinting and the sufficiency of the *TRIPS* flexibilities in addressing these concerns.

7.2.3.2 Access Concerns in the Context of Patenting Bioprinting

Although bioprinting is still in its nascent stage, judging from concerns about the impact of patenting on access in the healthcare space as explained above, it is apparent that access could likely be a potential issue for bioprinting. This is more so in light of the patent landscaping report contained in chapter six. In that chapter, it was noted that the search results obtained suggest that the American company Organovo holds a sizable number of patents and applications for bioprinting-related inventions. This is in addition to the fact that the USA appears to be the most prolific country in patenting bioprinting.

Nonetheless, it should be noted that whilst the concentration of patents in a single entity or institution may increase the likelihood of access being restricted because they potentially control the marketplace, the spread of patents across multiple owners may equally impede access owing to what has been termed the 'tragedy of the anticommons'. [191] This effectively occurs 'when multiple owners each have a right to exclude others from a scarce resource and no one has an effective privilege of use'.[192] An anticommons effect can arise either as a result of the creation of 'too many concurrent fragments of intellectual property rights in potential future products' or as a result of 'permitting too many upstream patent owners to stack licenses on top of the future discoveries of downstream users'.[193]

At this stage of patenting bioprinting, however, it is difficult to predict how such patents might be exploited and the effect this would have on access. At best, it is useful to consider the parameters of access in the context of bioprinting and how the *TRIPS* flexibilities might be employed to address concerns arising. Drawing from the analysis above, it would appear that there are two distinct access issues to be considered in the context of patenting bioprinting. These are patient access to bioprinted constructs in furtherance of the rights to health and benefit from science, and research access for scientists in furtherance of the right to benefit from science.

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[191] Heller and Eisenberg (n 166); Nicol and Nielsen (n 166); Shapiro (n 166).
[192] Heller and Eisenberg (n 166) 698.
[193] Ibid 699.

As noted in chapter two, whilst the production of bioprinted constructs suitable for implantation is the ultimate goal for researchers, the feasibility of this is still in doubt. Accordingly, concerns about access in this regard are unlikely to generate any significant outcry in the short- and medium-term. Nonetheless, because there is evidence to suggest that bioprinted constructs meant for implantation are being patented and their patenting raises the most significant ethical concerns as far as patenting bioprinting is concerned, it is useful to highlight concerns that may arise in the event that implantable bioprinted constructs become a reality.

A major factor that may impede initial access to bioprinted constructs will likely be cost, in view of the fabrication process amongst other factors. This is further complicated by the availability of an alternative form of treatment – reliance on voluntarily donated tissues and organs. It was argued in chapter two that bioprinted constructs are likely to produce a better outcome for patients than donated tissues and organs because of the removed risk of immune rejection. However, this does not displace advancements made in the field of organ transplantation to minimise the risks of immune rejection.[194] Thus, although bioprinted constructs may provide a better outcome for patients, there remains an alternative form of treatment, albeit constrained by availability of supply. This, then, presents a dilemma for any argument in favour of making bioprinted constructs available at an affordable price.

It may very well be that the availability of bioprinted constructs frees up existing demand for donated tissue and organs such that those who can afford to have their desired constructs fabricated opt instead for bioprinting given anticipated better outcomes. At the same time, factors such as increase in population, extended lifespan and decrease in mortality rates may also increase demand for replacement body parts, meaning that there is still a shortage in supply of donated tissue and organs. This results in a situation where stakeholders have to consider whether access to bioprinted constructs is an essential aspect

[194] Michael Nasr, Tara Sigdel and Minnie Sarwal, 'Advances in Diagnostics for Transplant Rejection' (2016) 16 *Expert Review of Molecular Diagnostics* 1121; J Bamoulid et al, 'Advances in Pharmacotherapy to Treat Kidney Transplant Rejection' (2015) 16 *Expert Opinion on Pharmacotherapy* 1627; K E Lunsford, A S Barbas and T V Brennan, 'Recent Advances in Immunosuppressive Therapy for Prevention of Renal Allograft Rejection' (2011) 16 (Aug) *Current Opinion in Organ Transplantation* 390.

of realising the rights to health and benefit from science so as to require some form of market intervention.

On the other hand, it would appear that research access is the more pressing concern at this stage of bioprinting's development.[195] This is in view of the potential application of bioprinting in the areas of disease modelling and research; drug discovery and animal testing; and chronic diseases and tissue/organ transplantation. More so, as some authors have noted, the successful translation of bioprinting into clinical application so as to realise its full potential is largely dependent on co-operation across multiple disciplines given the complexity of the issues involved.[196]

7.2.3.3 *TRIPS* Flexibilities Examined

As has previously been noted, while patents confer an exclusive right of exploitation, there are safeguards within the patent system which can be used to address concerns about abuse of monopoly.[197] Accordingly, this section briefly examines each of the flexibilities contained in the *TRIPS Agreement* and assesses how any of these might be useful in addressing concerns about access especially as far as research access is concerned.

a) Article 6 - Exhaustion

By virtue of art 6 of the *TRIPS Agreement*, member states are permitted to adopt the principle of exhaustion of rights and parallel import best suited to their needs.[198] Under the principle of exhaustion of rights, otherwise known as first sale in the USA, patent holders lose further rights over patented products once placed on the market.[199] This allows for further resale of the patented product without infringing the rights of the patent holder. Accordingly, parallel importation refers to the 'import and resale in a country, without the consent of the patent holder, of a patented product that has been legitimately put on the market of the exporting country'.[200] It should, however, be noted that

[195] See below section 7.2.3.3 for an elaboration of research access as it relates to the *TRIPS* flexibilities.
[196] S Vijayavenkataraman, W F Lu and J Y Fuh, '3D Bioprinting of Skin: A State-of-the-Art Review on Modelling, Materials and Processes' (2016) 8(3) *Biofabrication* 032001; Sean V Murphy and Anthony Atala, '3D Bioprinting of Tissues and Organs' (2014) 32 *Nature Biotechnology* 773.
[197] Crespi, 'An Analysis of Moral Issues Affecting Patenting Inventions in the Life Sciences: A European Perspective' (n 22).
[198] See generally Irene Calboli and Edward Lee (eds), *Research Handbook on Intellectual Property Exhaustion and Parallel Imports* (Edward Elgar Publishing, 2016).
[199] Sisule Musungu and Cecilia Oh, *The Use of Flexibilities in TRIPS by Developing Countries: Can They Promote Access to Medicines?* (South Centre, 2006) 47.
[200] Ibid.

exhaustion of rights may be national, regional or international. Thus, parallel importation is only relevant to regional and international exhaustion. Where exhaustion is national, it would still be considered an infringement to import patented goods bought in another jurisdiction.

When one considers that this flexibility is intended to allow for transportation of patented products, it becomes apparent that such patented products must have a stable shelf-life amenable to transportation and storage, for example, medicinal drugs and hardware. It would also seem to imply that mass production is contemplated. However, owing to the inherent nature of bioprinted constructs, it is questionable whether they can be mass produced, transported and stored in a manner that makes them amendable to importation and exportation. More so, it is more likely that the constructs will be printed on-demand either for implantation or use in *in vitro* studies. This would imply that a flexibility which encourages transfer of technology and local capacity building would be more suited to improving access. While there are suggestions that the notion of parallel importing could potentially extend to files containing instructions to 3D print patented objects,[201] it is uncertain the extent to which this flexibility is relevant in improving access to bioprinting as a whole.

b) Article 27 – Patentable Subject Matter

The question of whether bioprinting-related inventions, particularly, bioprinted constructs could potentially be excluded from patent protection has been addressed in earlier portions of this thesis. For reasons explored in earlier portions of this chapter, it is unlikely that any country will seek to exclude bioprinted constructs from patenting so as to improve access. This is most especially the case given that improved accessibility does not necessarily flow from an absence of patents.

c) Article 30 - Exceptions to Rights Conferred

Article 30 of the *TRIPS Agreement* provides that:

[201] Susy Frankel and Daniel J Gervais, 'International Intellectual Property Rules and Parallel Imports' in Calboli, Irene and Edward Lee (eds), *Research Handbook on Intellectual Property Exhaustion and Parallel Imports* (Edward Elgar Publishing, 2016) 85, 86-7.

> Members may provide limited exceptions to the exclusive rights conferred by a patent, provided that such exceptions do not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties.

This provision was interpreted in a panel decision further to a complaint by the European Community about the regulatory review and stockpiling provisions in Canada's patent legislation, which allowed drug manufacturers to override the exclusive rights conferred on a patent owner in certain situations.[202] The panel held that in order to qualify for an exception under art 30, each of the three conditions stipulated therein must be fulfilled.[203] That is, the exception must be limited; it must not unreasonably conflict with normal exploitation of the patent; and it must not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties.

The panel further noted that the three conditions must be interpreted in relation to each other with each of the three presumed to mean something different from the other two, or else there would be redundancy.[204] In addition, art 7 and 8(1) of the *TRIPS Agreement* must be borne in mind when interpreting each of the conditions.[205] Thus, the term 'limited exception' is to be read as connoting a narrow exception - one which makes only a small diminution of the rights in question.[206] The focus in this regard is the extent to which the legal rights have been curtailed and not the size or extent of the economic impact.[207] It is the latter two conditions which are more particularly concerned with the economic impact of the exception.[208] In addition, the panel emphasised that 'legitimate interests' are not be equated with legal interests but rather defined as a 'normative claim calling for protection of interests that are "justifiable" in the sense that they are supported by relevant public policies or other social norms'.[209]

Some of the most widely adopted exceptions under art 30 in national patent laws include the early-working exception (also known as regulatory review exception), individual

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[202] Panel Report, *Canada - Patent Protection of Pharmaceutical Products*, WTO Doc WT/DS114/R (17 March 2000).
[203] Ibid [7.20].
[204] Ibid [7.21].
[205] Ibid [7.26].
[206] Ibid [7.30].
[207] Ibid [7.31].
[208] Ibid.
[209] Ibid [7.68]-[7.69].

prescriptions and experimental use.[210] As the early-working exception is primarily concerned with obtaining marketing approval of generic pharmaceutical products before the expiration of the corresponding patent, the applicability of this flexibility to bioprinted constructs, which are personalised and produced on-demand, is uncertain. So also, is the exception for individual prescriptions which 'allows the use of patented pharmaceutical products in the preparation of individual prescriptions'.[211]

On the other hand, an experimental use exception might be of significant relevance to researchers in particular, since it is aimed at addressing concerns about scientific and technological progress being hindered by the patent system.[212] This is further to earlier observations that one area of concern with patenting for researchers is the uncertainty about the extent to which their research might infringe an existing patent. It has been noted that such uncertainty has the effect of unduly hindering research and follow-on innovation in a field.[213] Additionally, research could also be hindered by patent holders refusing to either licence their inventions or charging exorbitant licence fees which would significantly increase the cost of research.[214]

To this end, it has been argued that an experimental use exception could effectively stimulate inventive activity since the burden of paying royalties has been removed, thus lowering the cost of research.[215] In any case, the fact that disclosure is required at the point of applying for a patent would appear to suggest that there is an intention for the information disclosed to be used even during the patent term.[216] Consequently, an experimental use exception would allow researchers to see how the invention works, test

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[210] Musungu and Oh (n 200).
[211] Ibid 55-6.
[212] Christopher Garrison, 'Exceptions to Patent Rights in Developing Countries' (Issue Paper No. 17, UNCTAD-ICTSD Project on IPRs and Sustainable Development, August 2006) <http://www.iprsonline.org/unctadictsd/docs/Garrison%20final.pdf> 4. See generally Chris Dent et al, 'Research Use of Patented Knowledge: A Review' (Working Paper No 2006/2, OECD Directorate for Science, Technology and Industry, 2006); Elizabeth A Rowe, 'The Experimental Use Exception to Patent Infringement: Do Universities Deserve Special Treatment?' (2006) 57 Hastings Law Journal 921; Cristina Weschler, 'The Informal Experimental Use Exception: University Research After Madey v. Duke University' (2004) 79(4) New York University Law Review 1536.
[213] 'Experimental Use Exemption from Patent Infringement', *IP Australia* (Web Page) <https://www.ipaustralia.gov.au/about-us/legislation/raising-bar-act/experimental-use-exemption-patent> ('*Experimental Use Exemption From Patent Infringement*').
[214] Susy Frankel, 'An Experimental Use Exception from Patent Infringement for New Zealand' (2009) 12 *Journal of World Intellectual Property* 446.
[215] Eisenberg (n 164).
[216] Ibid.

the validity of the patentee's claims, design around an invention or even improve upon the patented invention.[217]

Nevertheless, there are debates about the scope of such experimental use exceptions - whether the exception should apply to commercial or non-commercial research as well as the extent to which such exception ought to apply if commercial research is contemplated.[218] The difficulty in making this delineation, however, is the fact that what started out as non-commercial research could potentially result in a commercial product.[219] Further to this, there are concerns that experimental use exceptions could effectively deprive a patent holder of royalties that would otherwise have been received as well as shorten the expected duration of the patent holder's effective monopoly, since the cost of inventing around the patent would have been lowered for competitors.[220] In turn, this could have the opposite effect of undermining patent incentives.[221]

Whilst many countries do provide for an experimental use exception in one form or the other, its usefulness to researchers in the bioprinting space will depend ultimately on how the exception has been implemented at the national level. In Australia, for instance, the 'experimental use exception'[222] is said to apply 'for the predominant purpose of gaining new knowledge, or testing a principle or supposition about the invention'.[223] Thus, even if future commercialisation is being considered, the exemption will apply in so far as the primary purpose of the experiment is the improvement of a patented invention.[224] It is only when the main purpose of the experiment is commercialisation that the exception will not apply.[225]

On the other hand, in many European countries, experimental exceptions are limited to private and non-commercial use, and experimental purposes relating to the subject matter

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[217] Garrison (n 213) 4; Eisenberg (n 164).
[218] Garrison (n 213) 4; Frankel (n 215).
[219] Garrison (n 213) 4; Eisenberg (n 164).
[220] Eisenberg (n 164).
[221] Ibid.
[222] *Patents Act 1990* (Cth) s 119C provides that experimental purposes include, but are not limited to: (a) determining the properties of the invention; (b) determining the scope of a patent claim relating to the invention; (c) improving or modifying the invention; (d) determining the validity of the patent or of a patent claim relating to the invention; (e) determining whether the patent for the invention would be, or has been, infringed by the doing of an act.
[223] *Experimental Use Exemption From Patent Infringement* (n 214).
[224] Ibid.
[225] Ibid.

of the invention.[226] In the USA where the experimental (research) exemption is of common law origin,[227] the courts have sought to distinguish between commercial and non-commercial research. In particular, it was noted in *Madey v Duke University*, that the experimental use defence is 'very narrow and strictly limited to actions performed "for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry"'.[228] This excludes use that has the 'slightest commercial implication' or use in 'keeping with the legitimate business of the alleged infringer'.[229] Accordingly, it is unlikely that the experimental use exception will be of any particular significance to researchers in the bioprinting space in the USA if their research has any commercial implication.

The alternative is advocating for the introduction of additional flexibilities suited to the peculiar needs of bioprinting (including bioprinted constructs in particular) since art 30 permits a degree of flexibility in its application.[230] It would, however, be useful to clarify the scope of such exceptions and consider the social and economic benefits before any new exceptions are introduced.[231]

d) Article 31 - Other Use Without Authorization of the Right Holder

Article 31 permits the use of patents by the government or third parties authorised by the government, without the authorization of the right holder under specified circumstances. These include but are not limited to matters of emergency or extreme urgency, failure to work an invention in the local market, public non-commercial use, dependent patents and anti-competitive practices.[232] The authorisations issued under art 31 are generally referred to as 'compulsory licences'.

The *Doha Declaration* further recognises the right of World Trade Organization ('WTO') members to grant compulsory licences and the freedom to determine on what grounds

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[226] See, eg, *Patents Act 1977* (UK) s 60 (5)(a)-(b).
[227] *Whittemore v Cutter*, 29 F Cas 1120 (C C D Mass, 1813).
[228] *Madey v Duke University*, 307 F 3d 1351, 1362 (Fed Cir 2002) .
[229] Ibid.
[230] Musungu and Oh, (n 200) 57.
[231] Frankel (n 215).
[232] See generally Reto M Hilty and Kung-Chung Liu (eds), *Compulsory Licensing: Practical Experiences and Ways Forward* (Springer, 2015); Cynthia Ho, *Access to Medicine in the Global Economy: International Agreements on Patents and Related Rights* (Oxford University Press, 2011); Jerome H Reichman, 'Comment: Compulsory Licensing of Patented Pharmaceutical Inventions: Evaluating the Options' (2009) 37(2) *Journal of Law, Medicine and Ethics* 247; Padmanabha Ramanujam and Yugank Goyal, 'One View of Compulsory Licensing: Comparative Perspectives from India and Canada' (2014) 18(2) *Marquette Intellectual Property Law Review* 375, 377.

such licences are granted.[233] A major drawback of the art 31 provision originally was its restriction on use to the supply of domestic markets.[234] Accordingly, many members with limited manufacturing capacities in the pharmaceutical sector faced difficulties in making effective use of the compulsory licensing provisions. However, following a directive in para 6 of the *Doha Declaration* to the Council for *TRIPS* to address the matter of WTO members with insufficient or no pharmaceutical manufacturing capacities, the *TRIPS Agreement* was amended to include art 31bis, which permits members to grant special compulsory licences for the export of pharmaceutical products.[235]

Thus, unlike art 31, which refers generally to the use of patents without limitation as to type,[236] art 31bis appears confined to pharmaceutical products.[237] According to the WTO, the new article 31bis and its corresponding Annex and Appendix 'provide the legal basis for WTO members to grant special compulsory licences *exclusively for the production and export of affordable generic medicines*'.[238] Further, the newly introduced annex defines 'pharmaceutical product' for the purpose of art 31bis as 'any patented product, or product manufactured through a patented process, of the pharmaceutical sector needed to address the public health problems'.[239] This includes 'active ingredients necessary for its manufacture and diagnostic kits needed for its use'.[240] To this end, it is unlikely that bioprinted constructs will be covered under art 31bis.

Notwithstanding, art 31 provides for the issuance of compulsory licences of patents without limitation as to type. By virtue of art 31(c), which contains an example of semi-conductor technology, it would seem to imply that compulsory licences may equally be issued for any patented technology.[241] Thus, art 31 could potentially be used to justify the issuance of compulsory licences for patented bioprinting methods and processes. This

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[233] *Doha Declaration*, WTO Doc WT/MIN(01)/DEC/2 (n 125) para 5(b).
[234] *TRIPS Agreement* (n 3) art 31(f). See also Ho (n 233) 197-220; Ramanujam and Goyal (n 233) 380.
[235] It should be noted that the amended *TRIPS Agreement* is only binding on members that have accepted the Protocol of 6 December 2005 which inserted a new article 31bis into the *Agreement* as well as an Annex and Appendix. 'Amended *TRIPS Agreement*: *TRIPS Agreement* (as amended on 23 January 2017)', *World Trade Organization* (Web Page, 2020) <https://www.wto.org/english/docs_e/legal_e/31bis_trips_01_e.htm>; V K Unni, 'Compulsory Licensing of Pharmaceutical Patents in India: Whether the Natco Decision Will Meet the Global Benchmarks?' (2015) 37 *European Intellectual Property Review* 296, 297-8.
[236] Ho (n 233) 128-30.
[237] Ho (n 233) 204.
[238] Ibid (emphasis added).
[239] *TRIPS Agreement* (n 3) annex para 1(a).
[240] Ibid.
[241] *TRIPS Agreement* (n 3) art 31(c).

would assist greatly with transfer of technology and local capacity building mentioned earlier.[242]

As far as access to medicine is concerned, compulsory licensing is perhaps the most emphasised flexibility, in addition to parallel import. This has been attributed to the fact that these two flexibilities are 'probably the most practical means of addressing the access to medicines problem'.[243] Proponents of compulsory licensing believe that compulsory licensing can be used to prevent the abuse of patent monopoly, safeguard public welfare and address prevailing global health care issues.[244] On the other hand, there are suggestions that granting compulsory licences has the potential to not only harm patent holders, but also that it reduces incentives to innovate and invest in research and development.[245]

Nonetheless, it should be noted that the total number of instances in which compulsory licences have been issued globally has generally been low leading to suggestions that compulsory licensing is insufficient by itself to achieve public interest goals in light of procedures and poor implementation.[246] Although art 31 does not limit the instances in which compulsory licences can be issued, it has been noted that some of the conditions imposed by art 31 makes its implementation difficult, which might explain why compulsory licences have rarely been used.[247] These include the requirement that licensees undertake negotiations with the patent holder (although this may be waived in cases of national emergency or public non-commercial use), determination of adequate remuneration to be

[242] E Bonadio, 'Compulsory Licensing of Patents: the Bayer-Natco Case' (2012) 34(10) *European Intellectual Property Review* 719.
[243] Olasupo Owoeye, *Intellectual Property and Access to Medicines in Africa: A Regional Framework for Access* (Routledge, 2019) 5.
[244] Ramanujam and Goyal (n 233) 385.
[245] Ramanujam and Goyal (n 233) 378; Bonadio (n 244); R C Bird, 'Developing Nations and the Compulsory License: Maximizing Access to Essential Medicines while Minimizing Investment Side Effects' (2009) 37(2) *Journal of Law, Medicine and Ethics* 209.
[246] World Health Organization, World Intellectual Property Organization and World Trade Organization, *Promoting Access to Medical Technologies and Innovation: Intersections between Public Health, Intellectual Property and Trade* (2012) ('*Promoting Access to Medical Technologies and Innovation: Intersections between Public Health, Intellectual Property and Trade*'), Unni (n 237) 299; Ramanujam and Goyal (n 233) 406.
[247] J L Nielsen and Diane Nicol, 'Pharmaceutical Patents and Developing Countries: The Conundrum of Access and Incentive' (2002) 13 *Australian Intellectual Property Journal* 289; J L Nielsen et al, 'Another Missed Opportunity to Reform Compulsory Licensing and Crown Use in Australia' (2014) 25 *Australian Intellectual Property Journal* 74; Joseph (n 107); *Promoting Access to Medical Technologies and Innovation: Intersections between Public Health, Intellectual Property and Trade* (n 248).

paid to the right holder and decisions as to when to terminate the licence because the reasons for granting it have ceased to exist.[248]

Additionally, there are concerns about pressures from pharmaceutical companies as well as *TRIPS*-plus provisions in free trade agreements which further restrict the grounds for which compulsory licences can be issued.[249] An example of this is art 17.9.7 of the *Australia-United States Free Trade Agreement*[250] which restricts the issue of compulsory licences to cases involving anti-competitive conduct, public non-commercial use, national emergency, or other circumstances of extreme urgency. In particular, the latter three grounds are only available for use by the government, or third persons authorised by the government.

Yet, it has been suggested that the very existence of provision for compulsory licensing in patent legislation in itself might be enough to force patent holders into contractual negotiations, thus obviating any concerns about the implementation of art 31.[251] This is because patentees would most likely prefer to negotiate a licence rather than having one forced upon them. In the same vein, the existence of compulsory licensing also possibly gives licensees bargaining power in contract negotiations. Alternatively, the threat of issuing a compulsory licence could equally convince patent holders to supply the patented invention by itself at a lower price, which is more affordable to local consumers.[252]

7.3 Conclusion

The patenting of bioprinted constructs presents similar ethical concerns as the patenting of other biotechnological inventions. In general, these include concerns about the impact of patenting on the patentability of future biotechnological innovations; commodification of life and the human body; and access. However, whilst these concerns are valid, they are not such as to warrant an outright prohibition on patenting bioprinted constructs. In part,

[248] *TRIPS Agreement* (n 3) art 31(b), (g), (h), (j).
[249] Charles Lawson, 'Accessing and Affording Drugs Despite the Patent Barrier: Compulsory Licensing and Like Arrangements?' (2013) 24 *Australian Intellectual Property Journal* 94; Nielsen et al (n 249); Robert C Bird, 'Developing Nations and the Compulsory License: Maximizing Access to Essential Medicines While Minimizing Investment Side Effects' (2009) 37 *The Journal of Law, Medicine & Ethics* 209; Ho (n 233) 149-52, 237-8.
[250] *Australia-United States Free Trade Agreement*, signed 18 May 2004, [2005] ATS 1 (entered into force 1 Jan 2005).
[251] Nielsen and Nicol (n 234); Nielsen et al (n 249).
[252] Bonadio (n 244).

this is due to the fact that there are other factors besides the grant of patents which contribute to these concerns.

In addition, although there are concerns about the limited empirical evidence to support the assertion that patents incentivise innovation, it has been argued that this absence of evidence is not, in itself, sufficient to justify withholding patents.[253] This is because withholding patents could potentially result in lost national income and employment opportunities as investors gravitate towards jurisdictions with stronger patent protection regimes.[254] In the same vein, investors could also resort to trade secrecy, which can impede scientific progress owing to emphasis on secrecy as opposed to the benefit of disclosure that the patent system offers.[255]

Nonetheless, the grant of patents poses a significant obstacle to access, which is perhaps paradoxical since the purpose of the patent system is to vest exclusivity and consequently create monopoly. In itself, this presents a dilemma as to whether the implications of patent monopoly on access ought to and can reasonably be addressed within the patent system. Whilst states parties may choose to reward and incentivise innovation with patents, they also have an important obligation in realising the rights to health and benefit from science, as contained in international human rights instruments to which many of them are signatories. In view of the fact that access to medicines is considered an essential element to the realisation of the right to health, it is therefore important that every effort is made to improve access. This includes balancing the protection of patent rights against these human rights obligations.

To this end, it has been suggested that flexibilities contained in the *TRIPS Agreement* to which many of these states parties are also signatories, provide a useful tool in balancing the interests of stakeholders. In light of this, it was important for this thesis to consider the sufficiency of the *TRIPS* flexibilities in addressing concerns about access to bioprinting.

Overall, owing to the inherent nature of bioprinted constructs, it would appear that existing flexibilities offer limited practical value to enabling direct patient access to bioprinted constructs and engineered tissue in general. This is particularly so for parallel

[253] Schrecker et al (n 4).
[254] Ibid; Resnik (n 4).
[255] Resnik (n 4).

importation/exhaustion of rights which appears more suited to products with a stable shelf-life amenable to transportation and storage (such as medicinal drugs and hardware). Similarly, whilst art 31bis was introduced to address the matter of limited or non-existent local manufacturing capacity with regard to the issuance of compulsory licences for the supply of domestic markets, its use is limited to pharmaceutical products. In light of the fact that the feasibility of implantable bioprinted constructs is very much in doubt, it might very well be that this is not a pressing issue.

On the other hand, the provisions of art 30 and 31 relating to experimental use exceptions and compulsory licensing respectively offer more practical value in enabling research access. However, as noted in this chapter, the implementation of these provisions is fraught with some challenges. This is in light of the fact that experimental use exceptions are narrowly defined in some countries such that they would not apply where there is the slightest chance of commercial application. At the same time, there have been very limited instances in which compulsory licensing has been successfully implemented globally. Moreover, as Li warns, there are possible chilling effects associated with forced sharing under compulsory licensing.[256] This is not discounting the prevalence of *TRIPS*-plus provisions in free trade agreements which counteract the little flexibility afforded by *TRIPS*.[257]

Nevertheless, at this stage of its development, there needs to be a concerted effort to improve research access to bioprinting. This is not only because it is the most practical option, but also because of its capacity to translate into the development of additional processes and products, which would otherwise not have been available to patients. This is so even if such resulting inventions are subject to patent protection. In light of this, the concluding chapter considers a number of options which can be implemented in the quest for an ethical approach to patenting bioprinting. This is in recognition of the benefits associated with patenting bioprinting as highlighted earlier in chapter one.

[256] Li (n 160). This would, however, appear contrary to the economic theory justification for patents discussed in Dan L Burk and Mark A Lemley, 'Policy Levers in Patent Law' (2003) 89(7) *Virginia Law Review* 1575.
[257] Owoeye, *Intellectual Property and Access to Medicines in Africa: A Regional Framework for Access* (n 245).

8 Conclusion

The ability to fabricate functional human tissues and organs as afforded by bioprinting is undoubtedly a significant milestone in medical research. This is owing to its potential applications in the areas of disease modelling and research; drug discovery and animal testing; and chronic diseases and tissue/organ transplantation. Although the long-term goal of fabricating implantable tissues and organs remains uncertain in light of current challenges associated with the technology, it is evident that bioprinting has the capacity to revolutionise healthcare in the short- and medium-term. This is notwithstanding concerns about the ethics and safety of using xenogeneic and human embryonic stem cells; the safety and efficacy of bioprinted constructs; access and social justice; and possible use of bioprinted constructs for human enhancement.

In order to enjoy the full benefits of bioprinting, however, it is important that considerations about access are given due attention as the technology continues to develop. This is especially in view of the growth in the patent landscape for various bioprinting-related inventions such as printing hardware and software, bioprinting processes and methods of treatment, biomaterials, bioinks and bioprinted constructs. As has been noted in existing literature, whilst the grant of patents is generally considered useful in incentivising innovation and encouraging disclosure, it also has the capacity to impede access.[1] This includes patient access to the resulting products as well as access by other researchers to scientific knowledge and information.

Accordingly, this thesis set out to evaluate ethical concerns arising from patenting bioprinting and propose measures for the protection of bioprinting-related inventions which balance the interests of inventors and the public. As part of this overarching intention, this thesis sought to contribute two main things to existing knowledge – (i) an assessment of bioprinted constructs and related bioprinting processes as patent eligible subject matter; and (ii) a specialised patent landscape report focused exclusively on bioprinted constructs.

[1] Nuffield Council on Bioethics, *The Ethics of Patenting DNA - A Discussion Paper* (Nuffield Council on Bioethics, 2002) ('*The Ethics of Patenting DNA - A Discussion Paper*').

Overall, it would appear that, out of the various categories of bioprinting-related invention potentially eligible for patent protection, bioprinted constructs seem to be the most contentious as far as patenting is concerned, because of the overlap with patenting life forms and human cloning. To this end, this thesis focused predominantly on the patentability of bioprinted constructs (and related bioprinting processes, albeit to a lesser extent) and the impact of such patenting on access to the technology.

In particular, chapters three to five of this thesis examined the state of the law on patentability in relation to bioprinted constructs and related bioprinting processes across three jurisdictions with divergent approaches to the matter of patentability, namely: Australia, the *European Patent Convention ('EPC')*[2] system, and the United States of America ('USA'). In response to research questions (i) and (ii),[3] it was concluded that despite the differences in legislative provisions and judicial interpretation, bioprinted constructs appear to be prima facie patentable across all jurisdictions in their current form. In addition, the existence of ethically informed exceptions from patentability such as the *ordre public*/morality exception in the *EPC* and the general inconvenience proviso in Australia appears unlikely to have any significant impact on the patentability of bioprinted constructs. This is in spite of concerns about the morality of patenting life forms.

This conclusion was further substantiated by results from a patent landscaping for bioprinted constructs across the aforementioned three jurisdictions undertaken in relation to research question (iii).[4] The report of the landscaping, which is contained in chapter six, confirmed the existence of pending applications and granted patents for bioprinted constructs in Australia, Europe and the USA. Additionally, the results also indicate emerging patterns of dominance in patenting by American applicants/assignees, with the biotechnology company Organovo holding the greatest number of filed and granted patents in each jurisdiction.

Whilst such emerging patterns are not necessarily indicative of how patents will be exploited, it does emphasise the importance of contemplating the likely impact of patenting

[2] *Convention on the Grant of European Patents*, signed 5 October 1973, 1065 UNTS 255 (entered into force 7 October 1977).
[3] See chapter one (section 1.5).
[4] Ibid.

bioprinting vis-à-vis its anticipated benefits. To this end, further to research question (iv),[5] chapter seven examined a number of ethical concerns likely to arise from patenting bioprinting with a view to determining whether these are sufficient to justify a reconsideration of patent grants for bioprinted constructs. This included concerns about the impact of patenting bioprinting on the patentability of future biotechnological innovations, commodification of life and the human body as well as concerns about access by patients and researchers.

It was noted that whilst the first two concerns are valid, they are not peculiar to bioprinting. Instead, these concerns are generally prevalent across the biotechnology industry. As such, refusing patent grants for bioprinted constructs will do little to address the underlying concerns. More so as some of the concerns exist independently of the patent system.

In the same vein, it was further noted that refusing patent grants for bioprinted constructs will not make bioprinting any more accessible to patients and researchers, despite concerns that patents have the capacity to impede access. This is because, paradoxically, patents also have the capacity to stimulate the development of new and improved treatments which are beneficial to the public. Whilst trade secrecy provides an alternative form of protection, it is not a perfect solution for patients as it does not afford the benefit of disclosure that the patent system offers. Indeed, it is the promise of disclosure offered by the patent system which justifies the accompanying.[6]

Accordingly, it is important to strike a balance between incentivising innovation and rewarding innovators on the one hand, and ensuring access to these innovations on the other hand. This is especially in light of the fact that access is crucial to the realization of the right to health and the related right to benefit from science. Generally, the flexibilities contained in the *Agreement on Trade-related Aspects of Intellectual Property Rights* ('*TRIPS Agreement*') [7] (such as exclusions from patentability, exceptions to exclusive rights, compulsory licensing, and parallel importation/exhaustion of rights) have been regarded

[5] Ibid.

[6] The extent to which patents effect disclosure has, however, been questioned. See generally Dan L Burk, 'Patent Silences' (2016) 69(6) *Vanderbilt Law Review* 1603 for extensive discussion about the sufficiency of patent disclosure. See also Jeanne C Fromer, 'Patent Disclosure' (2009) 94 *Iowa Law Review* 539; Lisa Larrimore Ouellette, 'Do Patents Disclose Useful Information?' (2012) 25 *Harvard Journal of Law and Technology* 545.

[7] *Agreement on Trade-Related Aspects of Intellectual Property Rights*, signed 15 April 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, 1869 UNTS 299 (entered into force 1 January 1995).

as useful in achieving the balance between incentivising innovation and promoting access, since they allow for public health considerations in the implementation of national patent regimes.

However, in the context of bioprinting, this thesis notes that the flexibilities appear to offer limited practical value in enabling direct patient access to bioprinted constructs. This is because flexibilities such as parallel importation/exhaustion of rights appear to contemplate the mass production of patented products with a stable shelf-life that is amenable to transportation and storage. Similarly, whilst art 31bis was introduced to address the matter of limited or non-existent local manufacturing capacity with regard to the issuance of compulsory licences for the supply of domestic markets, its use is limited to pharmaceutical products. Given the fact that the feasibility of implantable bioprinted constructs remains in doubt, the impracticability of these flexibilities in the context of bioprinted constructs does not appear to be a pressing issue warranting immediate action.

Rather, the focus should be on improving access for use in research given the utility of bioprinting in other areas such as disease modelling and research as well as drug discovery and animal testing. Whilst research access may not be a present issue, it could easily become an issue as the patent landscape continues to grow. Thus, in response to research question (v),[8] this thesis identified the flexibilities pertaining to exceptions to exclusive rights and compulsory licensing as potentially useful in improving research access. It should, however, be borne in mind that the usefulness of these flexibilities hinges on their implementation at national level. In addition, it should also be noted that improved research access may not necessarily translate into improved patient access since the resulting inventions will potentially also be subject to patent protection. Nonetheless, improved research access should allow for diffusion of knowledge which will aid in resolving current challenges associated with the technology and consequently, the emergence of additional inventions beneficial to the public.

Likewise, this thesis recommends the following measures, which can be implemented by both states and non-state actors in improving access and assuaging public concerns about

[8] See chapter one (section 1.5).

patenting bioprinted constructs. These include limiting the scope of patents and industry-driven initiatives.

a) Limiting the Scope of Patents

An often-suggested solution to ethical concerns about patenting life forms and many other biotechnological inventions is limiting the scope of patents granted.[9] This is in response to concerns about the overly broad nature of some of the patent claims. Indeed, as exemplified by some of the cases considered in chapters three to five, concerns about access are often rooted in the breadth of patent claims. While some have proposed that patents for bioprinted constructs be limited to the process/method of manufacture as opposed to the constructs as well,[10] such proposed restrictions must be assessed for compliance with the non-discrimination principle contained in art 27 (1) of the *TRIPS Agreement*.

It has been noted that there are two forms of discrimination – de jure (specific fields of technology are carved out for special treatment), and de facto (rules that are facially neutral have disparate effects on particular subject areas).[11] Further to the drafting history of the *TRIPS Agreement*, which indicates the avoidance of blanket exclusion of specific types of patentable subject matter such as drugs, Dreyfuss and Dinwoodie suggest that art 27(1) is clearly aimed at de jure discrimination.[12] Thus, exclusions directed either generally at or to specific areas of biotechnology such as bioprinted constructs would violate the *TRIPS Agreement*.

At the same time, while de facto discriminations which bar patents on significant upstream applications in every field of technology may appear facially neutral without directly implicating art 27(1), its potentially disparate impact on different fields could still fall afoul of the literal interpretation of art 27(1).[13] This would seem to suggest then that both de

[9] Carrie F Walter, 'Beyond the Harvard Mouse: Current Patent Practice and the Necessity of Clear Guidelines in Biotechnology Patent Law' (1998) 73 *Indiana Law Journal* 1025; Timothy Caulfield, E Richard Gold and Mildred K Cho, 'Patenting Human Genetic Material: Refocusing the Debate' (2000) 1(3) *Nature Reviews Genetics* 227; *The Ethics of Patenting DNA - A Discussion Paper* (n 1) 73 [6.17].

[10] Jasper L Tran, 'Patenting Bioprinting' (2015) 29 *Harvard Journal of Law and Technology Digest* <https://jolt.law.harvard.edu/digest/patenting-bioprinting>.

[11] Graeme B Dinwoodie and Rochelle Cooper Dreyfuss, 'International Intellectual Property Law and the Public Domain of Science' (2004) 7(2) *Journal of International Economic Law* 431, 434; Panel Report, *Canada - Patent Protection of Pharmaceutical Products*, (17 March 2000) [7.94].

[12] Dinwoodie and Dreyfuss (n 11) 434.

[13] Ibid 435.

jure and de facto discrimination are barred under art 27(1).[14] Nonetheless, the World Trade Organization panel report in *Canada - Patent Protection of Pharmaceutical Products* suggest that an additional element (such as an intention to discriminate) is required to establish de facto discrimination.[15] This would seem to imply that a legitimate purpose might be sufficient to rebut allegations of de facto discrimination.[16] As noted by the panel, 'article 27 does not prohibit bona fide exceptions to deal with problems that may exist only in certain product areas'.[17]

While there might be legitimate arguments for excluding patents on bioprinted constructs, it is doubtful whether this would suffice to rebut allegations of discrimination under art 27(1) given historical literal interpretation of the *TRIPS Agreement*.[18] Besides, judging from the patent claims reviewed, it would appear that there has been no attempt to patent any bioprinted construct such as skin tissue in its entirety. Instead, applicants have sought to patent bioprinted constructs resulting from a specific method of fabrication, which is also claimed. Thus, it is possible for many patentees to hold a patent for skin tissue albeit fabricated by different methods. In itself, however, this could potentially create an anticommons effect if there are large numbers of patents with narrower claims. Unfortunately, the full extent of such claims can only be determined when they are tested in some way.

Nevertheless, this thesis recommends that such practice should be retained - that is, granting patents for bioprinted constructs in so far as it is dependent on a claimed method of fabrication. It is anticipated that by doing so, concerns about monopolisation of body parts will greatly be minimised since such patents will be method-based. At the same time, however, care must be taken to ensure that the scope of method claims is equally limited as broadly drafted method claims could have just as great a market effect as product claims.

Furthermore, given concerns that patenting of bioprinted constructs and related processes could potentially obscure the divide between patenting inventions and natural phenomena, this thesis also recommends that patent rules regarding patent eligibility be stringently

[14] Panel Report, *Canada - Patent Protection of Pharmaceutical Products*, WTO Doc WT/DS114/R (n 11).
[15] Panel Report, *Canada - Patent Protection of Pharmaceutical Products*, WTO Doc WT/DS114/R (n 11) [7.105].
[16] Dinwoodie and Dreyfuss (n 11) 436.
[17] Panel Report, *Canada - Patent Protection of Pharmaceutical Products*, WTO Doc WT/DS114/R (n 11) [7.92].
[18] Dinwoodie and Dreyfuss (n 11) 436.

applied. Already, it would appear that this approach is gaining ground in the USA with its threshold for invention becoming just as stringent as other jurisdictions.[19] Perhaps more than ever, it is important for patent offices and the judiciary to carefully consider what is required to transform natural phenomena into eligible inventions. This would ensure that useful research tools remain within the public domain as much as is possible.

b) Industry-Driven Initiatives and A Cautious Approach to Patenting Bioprinting

As noted in chapter seven, there is growing recognition of the role of non-state actors, particularly pharmaceutical (and biotechnology) companies, in the realization of the right to health by virtue of their operations. While the extent of their responsibilities remains to be clarified, it is certain that the task of improving access to medicine cannot be achieved without their co-operation.

At the same time, however, the results of the patent landscaping exercise undertaken in chapter six indicate patenting of bioprinting-related inventions is still very much in its infancy. While there are ethical concerns about the extent to which bioprinted constructs in particular ought to be patented, there does not appear to be any immediate significant issues regarding the appropriateness of what is currently being patented. Neither is there any evidence to indicate patents are being exploited in a manner that is detrimental to the growth of the bioprinting industry.

Rather, there is evidence of emerging collaborative activities between key players in the bioprinting industry, which is promising in this regard. For instance, Organovo, which holds the highest number of patents in the industry is reported to have signed a number of collaborative research agreements with private and public institutions such as Johnson & Johnson, L'Oréal, Merck & Co and the University of Queensland for the production and testing of bioprinted constructs.[20] Aspect Biosystems is also reported to have entered

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[19] Jessica C Lai, 'Myriad Genetics and the BRCA Patents in Europe: The Implications of the U.S. Supreme Court Decision' (2015) 5 *UC Irvine Law Review* 1041; Sarah E Fendrick and Donald L Zuhn Jr, 'Patentability of Stem Cells in the United States' (2015) 5(12) *Cold Spring Harbor Perspectives in Medicine* a020958.

[20] Brittney Sevenson, 'Organovo Signs Agreement with University of Queensland's Uniquest to 3D Print Kidney Tissue', *3DPrint.com* (Web Page, 23 May 2014) <https://3dprint.com/4251/organovo-queensland-3d-print-kidney/>; Brittney Sevenson, 'L'Oréal USA & Organovo Team for 3D Printed Human Skin Tissue Research', *3DPrint.com* (Web Page, 7 April 2015) <https://3dprint.com/56475/loreal-organovo-skin-research/>; Michael Molitch-Hou, 'Organovo Licenses Mini Kidneys for Bioprinting', *3D Printing Industry* (Web Page, 13 October 2015) <https://3dprintingindustry.com/news/organovo-licenses-mini-kidneys-for-bioprinting-59817/>; Michael Molitch-Hou, 'Organovo Signs Multi-Year 3D Bioprinting Deal with Pharma Giant Merck', *3D Printing Industry* (Web Page, 23 April 2015) <https://3dprintingindustry.com/news/organovo-signs-multi-year-3d-bioprinting-deal-with-pharma-

into collaborative research agreements with German InSCREENeX GmbH and Institute for Toxicology and Experimental Medicine, as well as DePuy Synthes Products Inc for the development of bioprinted tissue.[21] In addition, CELLINK is also reported to have signed a memorandum of understanding to explore the development of bioprinted liver and skin tissue models with the Adult Stem Cell Research Centre at Seoul National university.[22]

Consequently, it would be premature to advocate any specific solution to a problem that has yet to emerge. This is especially in view of the limited scope of the patent landscaping undertaken in chapter six, which did not involve a detailed analysis of the patent claims.[23] At best, the most effective strategy at this stage of patenting bioprinting is to keep a watching brief on patenting activities. In line with this, this thesis advocates a cautious approach to patenting bioprinting. This is all the more so because the primary focus of this thesis is addressing ethical concerns that arise from patenting and not so much patent use. In the event, however, that concerns similar to those that have arisen in other sectors of the biotechnology industry begin to emerge in the bioprinting sphere, it may be useful to consider the option of voluntary licensing strategies - most especially non-exclusive licensing, which is prevalent within the biotechnology industry.[24] By virtue of the nexus between bioprinting and biotechnology, there is good reason to believe similar licensing strategies might be effectively employed in bioprinting in addition to reliance on research exemptions.

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giant-merck-47415/>; Brittney Sevenson, 'Organovo and Johnson & Johnson Team to Evaluate 3D Bio-printed Tissue Use', *3DPrint.com* (Web Page, 24 July 2014) <https://3dprint.com/10171/organovo-johnson-johnson/>.

[21] 'Collaboration with Johnson & Johnson Innovation', *Aspect Biosystems* (Web Page, 5 January 2017) <https://www.aspectbiosystems.com/news-resources/collaboration-with-johnson-johnson-innovation>; 'Aspect Biosystems Partners with Fraunhofer and InSCREENeX on 3DBioRing Bioprinted Muscle Tissue', *3D Printing Media Network* (Web Page, 18 September 2017) <https://www.3dprintingmedia.network/aspect-biosystems-partners-fraunhofer-inscreenex-3dbioring-bioprinted-muscle-tissue/>.

[22] 'CELLINK and the Adult Stem Cell Research Center at Seoul National University Announce New Agreement for Bioprinting Research', *CELLINK* (Web Page, 22 March 2019) <https://cellink.com/cellink-and-the-adult-stem-cell-research-center-at-seoul-national-university-announce-new-agreement-for-bioprinting-research/>.

[23] See section 6.4 on the limitations of the patent landscaping.

[24] Dianne Nicol and Jane Nielsen, *Patents and Medical Biotechnology: An Empirical Analysis of Issues Facing the Australian Industry,* Occasional Paper 6 (Centre for Law and Genetics, 2003); John P Walsh, Ashish Arora and Wesley M Cohen, 'Effects of Research Tool Patents and Licensing on Biomedical Innovation' in Wesley M Cohen and Stephen A Merrill (eds), *Patents in the Knowledge-Based Economy* (The National Academies Press, 2003) 285.

Appendices

Appendix A: Australian Patent Landscape Search Report

a) Granted Patents

S/No	Patent No/Title	Inventor	Applicant	Filing Date/ Expiration Date
1.	2013277275 Engineered three-dimensional connective tissue constructs and methods of making the same	Shepherd, Benjamin R Presnell, Sharon C Evinger, Albert J	Organovo, Inc	Filed 19/06/2013 Exp 19/06/33
2.	2014236780 Engineered liver tissues, arrays thereof, and methods of making the same	Shepherd, Benjamin R Robbins, Justin B Gorgen, Vivian A Presnell, Sharon C	Organovo, Inc	Filed 13/03/2014 Exp 13/03/34
3.	2011227282 Multilayered vascular tubes	Khatiwala, Chirag Murphy, Keith Shepherd, Benjamin	Organovo, Inc	Filed 16/03/2011 Exp 16/03/31
4.	2017200691 Engineered liver tissues, arrays thereof, and methods of making the same	Shepherd, Benjamin R Robbins, Justin B Gorgen, Vivian A Presnell, Sharon C	Organovo, Inc	Filed 02/02/2017 (Effective date of patent – 13/03/2014) Exp 13/03/2014
5.	2014346959 Method of printing a tissue construct with embedded vasculature	Lewis, Jennifer Kolesky, David B Skylar-Scott, Mark Homan, Kimberly A Truby, Ryan L Gladman, Amelia Sydney	President and Fellows of Harvard College	Filed 04/11/2014 Exp 04/11/2034

S/No	Patent No/Title	Inventor	Applicant	Filing Date/ Expiration Date
6.	2009271223 Self-assembling multicellular bodies and methods of producing a three-dimensional biological structure using the same	Norotte, Cyrille Forgacs, Gabor Marga, Francoise Suzanne	The Curators of the University of Missouri	Filed 24/06/2009 Exp 24/06/2029
7.	2013249569 Devices, systems, and methods for the fabrication of tissue utilizing UV cross-linking	Murphy, Keith Dorfman, Scott Law, Richard Jin Le, Vivian Anne	Organovo, Inc	Filed 12/04/2013 Exp 12/04/2033
8.	2015359286 Graft scaffold for cartilage repair and process for making same	Kesti, Matti Zenobi-Wong, Marcy Müller, Michael	ETH Zürich	Filed 11/12/2015 Exp 11/12/2035

b) Filed Applications

S/No	Patent No/Title	Inventor	Applicant	Filing Date
1.	2019203265 Engineered liver tissues, arrays thereof, and methods of making the same	Shepherd, Benjamin R Robbins, Justin B Gorgen, Vivian A Presnell, Sharon C	Organovo, Inc	Filed 09/05/2019
2.	2017335841 Use of engineered renal tissues in assays	King, Shelby Marie Nguyen, Deborah Lynn Greene Presnell, Sharon C	Organovo, Inc	Filed 28/09/2017
3.	2015328173 Engineered renal tissues, arrays thereof, and methods of making the same	Nguyen, Deborah Lynn Greene King, Shelby Marie Presnell, Sharon C	Organovo, Inc	Filed 06/10/2015
4.	2014389440 Engineered three-dimensional breast tissue, adipose tissue, and tumor disease model	King, Shelby Marie Nguyen, Deborah Lynn Greene Gorgen, Vivian A Shepherd, Benjamin R Presnell, Sharon C Sears, Rosalie Allen-Petersen, Brittany Langer, Ellen	Oregon Health & Science University Organovo, Inc	Filed 06/06/2014
5.	2016340819 Methods of producing in vitro liver constructs and uses thereof	Atala, Anthony Bishop, Colin Mead, Ivy	Wake Forest University Health Sciences	Filed 14/10/2016
6.	2017306698 Blood brain barrier model and methods of making and using the same	Wicks, Robert T Atala, Anthony Nzou, Goodwell Wicks, Elizabeth E	Wake Forest University Health Sciences	Filed 04/08/2017

S/No	Patent No/Title	Inventor	Applicant	Filing Date
7.	2016339998 Multi-layer airway organoids and methods of making and using the same	Murphy, Sean V Atala, Anthony	Wake Forest University Health Sciences	Filed 14/10/2016
8.	2016206994 Multi-layer skin substitute products and methods of making and using the same	Atala, Anthony Jeong, Gayoung Yoo, James J Lee, Sang Jin Seol, Young-Joon	Wake Forest University Health Sciences	Filed 11/01/2016
9.	2016279941 Continuously bioprinted multilayer tissue structure	Beyer, Simon Mohamed, Tamer Pan, Sheng Wadsworth, Sam	Aspect Biosystems Ltd.	Filed 16/06/2016
10.	2017285788 Bioprinted meniscus implant and methods of using same	Wadsworth, Sam Beyer, Simon Mohamed, Tamer Walus, Konrad	Aspect Biosystems Ltd.	Filed 16/06/2016
11.	2017359330 3D vascularized human ocular tissue for cell therapy and drug discovery	Bharti, Kapil Song, Min Jae Quinn, Russell Louis	The United States of America, as represented by the Secretary Department of Health and Human Services	Filed 08/11/2017
12.	2016352873 Improved methods for tissue fabrication	Retting, Kelsey Nicole Nguyen, Deborah Lynn Greene Presnell, Sharon C King, Shelby Marie	Organovo, Inc	Filed 09/11/2016
13.	2016297675 Process for printing 3D tissue culture models	O'Mahony, Aidan Patrick Utama, Robert Hadinoto Fife, Christopher Michael	Inventia Life Science Pty Ltd	Filed 21/07/2016

S/No	Patent No/Title	Inventor	Applicant	Filing Date
		Atapattu, Lakmali Ribeiro, Julio Cesar Caldeira Kavallaris, Maria Gooding, John Justin		
14.	2017375956 Biomimetic implants	Koffler, Yacov Chen, Shaochen Tuszynski, Mark Zhu, Wei	The Regents of the University of California	Filed 12/12/2017
15.	2016226178 Methods of generating functional human tissue	Lewis, Jennifer A Skylar-Scott, Mark A Kolesky, David B Homan, Kimberly A Ng, Alex H M Church, George M	President and Fellows of Harvard College	Filed 03/03/2016
16.	2016257427 Tubular tissue construct and a method of printing	Lewis, Jennifer A Homan, Kimberly A Kolesky, David B Truby, Ryan L Skylar-Scott, Mark A	President and Fellows of Harvard College	Filed 04/05/2019

c) Search Terms

Search Terms	
Organovo	Cell* + *print* + three-dimension*
Koninklijke Philips	Cell* + *print* + three dimension*
Wake Forest University	Cell* + *print* + three d*
Hewlett-Packard Company	Cell* + *print* + three d
The University of Texas System	Cell* + *print* + three-d
Medprin Regenerative Medical Technologies Co Ltd	Cell* + *print* + three-d*
Corning Incorporated	Cell* + *print* + additive*
Aspect Biosystems Ltd	Cell* + *print* + freeform OR free-form
The University of Queensland	Cell* + *print* + desktop
SMR Patents S.a.r.l.	Cell* + *print* + manufactur*
Inventia Life Science Pty Ltd	Cell* + *print* + fabricat*
Mammadov, Asad MR	Cell* + bio-fabricat*
Zhejiang University	Cell* + biofabricat*
Shanghai University	Cell* + bio fabricat*
Northwestern Polytechnical University	Cell* + bio print*
Sichuan Revotek Biotechnology Co., Ltd.	Cell* + bioprint*
Psimedica Ltd	Cell* + bio-print*
Dai Nippon Printing Co., Ltd	Cell* + rapid prototyp* OR rapid-protoyp*
Massachusetts Institute of Technology	Cell* + layer by layer OR layer-by-layer
Celgene Corporation	Cell* + biomanufact* OR bio manufact* OR bio-manufact*
Seiko Epson Corporation	Cell* + tissue engineer*
University of Utah	Tissue engineer* + additive
Johnson & Johnson	Tissue engineer*
Regenovo Biotechnology	Tissue + 3d
Cell* AND print* AND tissue*	Tissue + 3-d
Cell* AND print* AND engineer*	3 d OR three-d OR three d
Biofab*	Three dimensional

Search Terms	
Biofab*	Additive Manufacturing
Bio-fab*	Regenerative medicine
Bio fab*	Biomedic* + tissue*
Bioprint*	Biomedic* + cell*
bio print*	Organ OR organoid + print*
bio-print*	Tissue + print
rapid prototyp*	Biomanufact*
Layer-by-layer	Cancer model
layer by layer	Renal OR kidney + engineer*
Biomanufact*	liver OR nerve OR eye OR ear + engineer*
Cell* + *print* + 3d	muscle OR embry* OR bone OR tissue OR organ OR blood vessel OR *scaffold* + engineer*
Cell* + *print* + 3-d	skin OR cartilage OR "vascular tubes" OR "bio* tube*" + engineer*
Cell* + *print* + 3 d	biological OR "biological structure*" OR "biological tube*" + engineer* OR print*

Appendix B: European Patent Convention Patent Landscape Search Report

a) Granted Patents

S/No	Patent No/Title	Inventor	Applicant	Filing Date/Expiration Date
1.	EP2547288 Multilayered vascular tubes	Khatiwala Chirag Murphy Keith Shepherd Benjamin	Organovo, Inc	Filed 16/03/2011 Exp 16/03/2031
2.	EP3204488 Engineered renal tissues, arrays thereof, and methods of making the same	Nguyen Deborah Lynn Greene King Shelby Marie Presnell Sharon C	Organovo, Inc	Filed 06/10/2015 Exp 06/10/2035

b) Filed Applications

S/No	Patent No/Title	Inventor	Applicant	Filing Date
1.	EP3538643 Engineered intestinal tissue and uses thereof	Retting, Kelsey Nicole Nguyen, Deborah Lynn Greene Madden, Lauran	Organovo, Inc	10/11/2017
2.	EP2756073 Engineered tissues for in vitro research uses, arrays thereof, and methods of making the same	Murphy, Keith Khatiwala, Chirag Dorfman, Scott Shepherd, Benjamin Presnell, Sharon Robbins, Justin	Organovo, Inc	12/09/2012
3.	EP2755599 Platform for engineered implantable tissues and organs and methods of making the same	Murphy, Keith Khatiwala, Chirag Dorfman, Scott Shepherd, Benjamin Presnell, Sharon	Organovo, Inc	12/09/2012
4.	EP2861270 Engineered three-dimensional connective tissue constructs and methods of making the same	Shepherd, Benjamin R Presnell, Sharon C Evinger, Albert J	Organovo, Inc	19/06/2013
5.	EP2970896 Engineered liver tissues, arrays thereof, and methods of making the same	Shepherd, Benjamin R Robbins, Justin B Gorgen, Vivian A Presnell, Sharon C	Organovo, Inc	13/03/2014
6.	EP3126490 Engineered three-dimensional breast tissue, adipose tissue, and tumor disease model	King, Shelby Marie Nguyen, Deborah Lynn Greene Gorgen, Vivian A Shepherd, Benjamin R	Organovo, Inc Oregon Health and Science University	06/06/2014

S/No	Patent No/Title	Inventor	Applicant	Filing Date
		Presnell, Sharon C Sears, Rosalie Allen-Petersen, Brittany Langer, Ellen		
7.	EP3374495 Improved methods for tissue fabrication	Retting, Kelsey Nicole Nguyen, Deborah Lynn Greene Presnell, Sharon C King, Shelby Marie	Organovo, Inc	09/11/2016
8.	EP3496774 Three dimensional bioprinted tumor models for drug testing	Presnell, Sharon C King, Shelby Marie Nguyen, Deborah Lynn Greene Jo, Minji Pelz, Rosalie Sears Allen-Petersen, Brittany Langer, Ellen	Organovo, Inc Oregon Health and Science University	15/08/2017
9.	EP3519558 Use of engineered renal tissues in assays	King, Shelby Marie Nguyen, Deborah Lynn Greene Presnell, Sharon C	Organovo, Inc	28/09/2017
10.	EP3494213 Blood brain barrier model and methods of making and using the same	Wicks, Robert T Atala, Anthony Nzou, Goodwell Wicks, Elizabeth E	Wake Forest University Health Sciences	04/08/2017
11.	EP3362554 Multi-layer airway organoids and methods of making and using the same	Murphy, Sean V Atala, Anthony	Wake Forest University Health Sciences	14/10/2016
12.	EP2814529 Tissue engineering device and construction of vascularized dermis	Boland, Thomas	University of Texas Boland, Thomas	13/02/2013

S/No	Patent No/Title	Inventor	Applicant	Filing Date
13.	EP3310902 Continuously bioprinted multilayer tissue structure	Beyer, Simon Mohamed, Tamer Pan, Sheng Wadsworth, Sam	Aspect Biosystems Ltd	16/06/2015
14.	EP3471789 Bioprinted meniscus implant and methods of using same	Wadsworth, Sam Beyer, Simon Mohamed, Tamer Walus, Konrad	Aspect Biosystems Ltd	16/06/2017
15.	WO2019126600 Bioprinted meniscus implant and methods of using same	Wadsworth, Sam Beyer, Simon Mohamed, Tamer Walus, Konrad Kamal, Khan Mohammad Kapyla, Elli Hwang, Julia Ault, Joe	Aspect Biosystems Ltd DePuy Synthes Products Inc	20/12/2018
16.	EP3234108 Differentiation of pluripotent stem cells to form renal organoids	Takasato, Minoru Little, Melissa	University of Queensland	15/12/2015
17.	WO2019075397 Three-dimensional bioprinting of cardiac patch with anisotropic and perfusable architecture	Cui, Haitao Zhang, Lijie Huang, Yimin	George Washington University The United States of America, as represented by the Secretary Department of Health and Human Services	12/10/2018

S/No	Patent No/Title	Inventor	Applicant	Filing Date
18.	WO2019079424 Scaffold-free 3d bioprinting of porcine cells	Ekser, Burcin	Indiana University Research & Technology Corporation	17/10/2018
19.	WO2019106695 A 3d bioprinted scar tissue model	Ghosh, Sourabh Chawla, Shikha	Indian Institute of Technology, Delhi	30/11/2018
20.	WO2019122351 Tissue-specific human bioinks for the physiological 3d-bioprinting of human tissues for in vitro culture and transplantation	Frenguelli, Luca Martinez, Hector Gatenholm, Erik Mazza, Giuseppe	Cellink AB Engitix Ltd	21/12/2018
21.	EP3463822 Preparation and applications of rgd conjugated polysaccharide bioinks with or without fibrin for 3d bioprinting of human skin with novel printing head for use as model for testing cosmetics and for transplantation	Gatenholm, Paul	Cellink AB	03/06/2017
22.	EP3532117 Preparation and applications of 3d bioprinting bioinks for repair of bone defects, based on cellulose nanofibrils hydrogels with natural or synthetic calcium phosphate particles	Gatenholm, Paul Martinez, Hector Schetnno, Michela Gatenholm, Erik	Cellink AB	27/10/2017
23.	EP3233493 Cellulose nanofibrillar bioink for 3d bioprinting for cell culturing, tissue	Gatenholm, Paul	Cellink AB	18/12/2015

S/No	Patent No/Title	Inventor	Applicant	Filing Date
	engineering and regenerative medicine applications			
24.	EP3361986 Automated fabrication of layer-by-layer tissue engineered complex tubes	Acevedo, Juan Pablo Wilkens, Camila Khoury, Maroun Rivet, Christopher	Universidad de los Andes Cells for Cells S P A Acevedo, Juan Pablo Wilkens, Camila Khoury, Maroun Rivet, Christopher	14/10/2016

c) Search Terms

Search Terms	
Organovo	Sichuan Revotek Biotechnology Co., Ltd.
Koninklijke Philips	Psimedica Ltd
Wake Forest University	Dai Nippon Printing Co., Ltd.
Hewlett-Packard Company	Massachusetts Institute of Technology
The University of Texas System	Celgene Corporation
Medprin Regenerative Medical Technologies Co Ltd	Seiko Epson Corporation
Corning Incorporated	University of Utah
Aspect Biosystems	Regenovo Biotechnology Co., Ltd.
University of Queensland	Johnson & Johnson
SMR Patents S.a.r.l.	Cell* print* tissue*
Aspect Biosystems Ltd	Biofab*, bio-fab*, bio fab*
Bioprint AS	Bioprint*
Inventia Life Science	Rapid prototype*
Mammadov, Asad	Layer by layer
Zhejiang University	Biomanufact*
Shanghai University	Tissue engineer*
Northwestern Polytechnical University/ Northwestern University	Additive manufacturing
Agency for Science Technology and Research	

Appendix C: United States of America Patent Landscape Search Report

a) Granted Patents

S/No	Patent No/Title	Inventor	Applicant	Filing Date/Patent Date
1.	9,481,868 B28 Engineered renal tissues, arrays thereof, and methods of making the same	Nguyen, Deborah Lynn Greene King, Shelby Marie Presnell, Sharon C	Organovo, Inc	Filed 6/10/2015 Patent date 1/11/2016
2.	9,851,706 Artificial hollow biological tissue network and method for preparation thereof	Koc, Bahattin Kucukgul, Can Ozler, Saime Burce	Sabancı Üniversitesi	Filed 29/05/2015 Patent date 26/12/2017
3.	9,983,195 Engineered three-dimensional breast tissue, adipose tissue, and tumor disease model	King, Shelby Marie Nguyen, Deborah Lynn Greene Gorgen, Vivian A Shepherd, Benjamin R Presnell, Sharon C	Organovo, Inc	Filed 3/04/2015 Patent date 29/05/2018
4.	10,094,821 Engineered renal tissues, arrays thereof, and methods of making the same	Nguyen, Deborah Lynn Greene King, Shelby Marie Presnell, Sharon C	Organovo, Inc	Filed 8/09/2016 Patent date 9/10/2018
5.	9,222,932 Engineered liver tissues, arrays thereof, and methods of making the same	Shepherd, Benjamin R Robbins, Justin B Gorgen, Vivian A Presnell, Sharon C	Organovo, Inc	Filed 3/06/2014 Patent date 29/12/2015
6.	8,747,880 Engineered biological nerve graft, fabrication and application thereof	Forgacs, Gabor Colbert, Stephen H Hubbard, Bradley A	Forgacs, Gabor Colbert, Stephen H Hubbard, Bradley A	Filed 2/02/2011 Patent date 10/06/2014

S/No	Patent No/Title	Inventor	Applicant	Filing Date/Patent Date
		Marga, Francoise Christiansen, Dustin	Marga, Francoise Christiansen, Dustin Assignee: The Curators of the University of Missouri	
7.	8,143,055 Self-assembling multicellular bodies and methods of producing a three-dimensional biological structure using the same	Forgacs, Gabor Marga, Francoise Suzanne Norotte, Cyrille	Assignee: The Curators of the University of Missouri	Filed 24/06/2009 Patent date: 27/03/2012
8.	8,241,905 Self-assembling cell aggregates and methods of making engineered tissue using the same	Forgacs, Gabor Jakab, Karoly Neagu, Adrian Mironov, Vladimir	Assignee: The Curators of the University of Missouri MUSC Foundation for Research Development	Filed 24/02/2005 Patent date 14/08/2012
9.	10,195,644 Tissue engineering device and construction of vascularized dermis	Boland, Thomas	The Board of Regents of the University of Texas System	Filed 13/02/2013 Patent date 05/02/2019
10.	9,005,972 Inkjet printing of tissues and cells	Xu, Tao Yoo, James J Atala, Anthony Dice, Dennis	Wake Forest University Health Sciences	Filed 20/02/2014 Patent date 14/04/2015
11.	10,350,329 Graphene-based ink compositions for three-dimensional printing application	Shah, Ramille N Jakus, Adam E Hersam, Mark C Secor, Ethan B	Northwestern University	Filed 15/10/2015 Patent date 16/06/2019

b) Filed Applications

S/No	Patent No/Title	Inventor	Applicant	Filing Date
1.	20180196034 Engineered Three-Dimensional Breast Tissue, Adipose Tissue, and Tumor Disease Model	King, Shelby Marie Nguyen, Deborah Lynn Greene Gorgen, Vivian A Shepherd, Benjamin R Presnell, Sharon C Sears, Rosalie Allen-Petersen, Brittany Langer, Ellen	Organovo, Inc Oregon Health & Science University	05/03/2018
2.	20180265839 Improved Methods for Tissue Fabrication	Retting, Kelsey Nicole Nguyen, Deborah Lynn Greene Presnell, Sharon C King, Shelby Marie	Organovo, Inc	09/11/2016
3.	20180272035 Engineered Three-Dimensional Skin Tissues, Arrays Thereof, and Methods of Making the Same	Retting, Kelsey Nicole O'Neill, Colin M Nguyen, Deborah Lynn Greene Presnell, Sharon C Langer, Jessica Balooch, Guive Wu, Elizabeth Demaude, Julien	Organovo, Inc L'Oréal	05/11/2015
4.	20180313822 Engineered Tissues for in vitro Research Uses, Arrays Thereof, and Methods of Making the Same	Murphy, Keith Khatiwala, Chirag Dorfman, Scott Shepherd, Benjamin Presnell, Sharon Robbins, Justin	Organovo, Inc	09/07/2018

S/No	Patent No/Title	Inventor	Applicant	Filing Date
5.	20190032020 Differentiation of pluripotent stem cells to form renal organoids	Takasato, Minoru Little, Melissa	The University of Queensland	15/12/2015
6.	20190041381 Engineered Renal Tissues, Arrays Thereof, and Methods of Making the Same	Nguyen, Deborah Lynn Greene King, Shelby Marie Presnell, Sharon C	Organovo, Inc	08/10/2018
7.	20170023550 Engineered three-dimensional breast tissue, adipose tissue, and tumor disease model	King, Shelby Marie Nguyen, Deborah Lynn Greene Gorgen, Vivian A Shepherd, Benjamin R Presnell, Sharon C Sears, Rosalie Allen-Petersen, Brittany Langer, Ellen	Organovo, Inc Oregon Health and Science University	06/06/2014
8.	20170037349 Devices, systems, and methods for the fabrication of tissue utilizing UV cross-linking	Murphy, Keith Dorfman, Scott Law, Richard Jin Le, Vivian Anne	Organovo, Inc	20/10/2016
9.	20170131264 Engineered renal tissues, arrays thereof, and methods of making the same	Nguyen, Deborah Lynn Greene King, Shelby Marie Presnell, Sharon C	Organovo, Inc	08/09/2016
10.	20150282885 Engineered three-dimensional breast tissue, adipose tissue, and tumor disease model	King, Shelby Marie Nguyen, Deborah Lynn Greene Gorgen, Vivian A Shepherd, Benjamin R Presnell, Sharon C	Organovo, Inc	03/04/2015
11.	20150342720	Koc, Bahattin	Sabancı Üniversitesi	29/05/2015

S/No	Patent No/Title	Inventor	Applicant	Filing Date
	Artificial hollow biological tissue network and method for preparation thereof	Ku Ukgul, Can Ozler, Saime Burce		
12.	20160040132 Three-dimensional bioprinted pancreatic tumor model	Sears, Rosalie Allen-Petersen, Brittany Langer, Ellen	Sears, Rosalie Allen-Petersen, Brittany Langer, Ellen Assignee: Oregon Health and Science University	06/08/2015
13.	20160097039 Engineered renal tissues, arrays thereof, and methods of making the same	Nguyen, Deborah Lynn Greene King, Shelby Marie Presnell, Sharon C	Organovo, Inc	06/10/2015
14.	20160272946 Engineered liver tissues, arrays thereof, and methods of making the same	Shepherd, Benjamin R Robbins, Justin B Gorgen, Vivian A Presnell, Sharon C	Organovo, Inc	26/05/2016
15.	20130164339 Platform for engineered implantable tissues and organs and methods of making the same	Murphy, Keith Khatiwala, Chirag Dorfman, Scott Shepherd, Benjamin Presnell, Sharon	Murphy, Keith Khatiwala, Chirag Dorfman, Scott Shepherd, Benjamin Presnell, Sharon Assignee: Organovo, Inc	12/09/2012
16.	20130190210 Engineered tissues for in vitro research uses, arrays thereof, and methods of making the same	Murphy, Keith Khatiwala, Chirag Dorfman, Scott Shepherd, Benjamin Presnell, Sharon	Murphy, Keith Khatiwala, Chirag Dorfman, Scott Shepherd, Benjamin Presnell, Sharon	12/09/2012

S/No	Patent No/Title	Inventor	Applicant	Filing Date
		Robbins, Justin	Robbins, Justin Assignee: Organovo, Inc	
17.	20130345794 Multilayered vascular tubes	Khatiwala, Chirag Murphy, Keith Shepherd, Benjamin	Khatiwala, Chirag Murphy, Keith Shepherd, Benjamin Assignee: Organovo, Inc	16/03/2011
18.	20140093932 Devices, systems, and methods for the fabrication of tissue utilizing uv cross-linking	Murphy, Keith Dorfman, Scott Law, Richard Jin Le, Vivian Anne	Organovo, Inc	11/03/2013
19.	20140099709 Engineered three-dimensional connective tissue constructs and methods of making the same	Presnell, Sharon C Shepherd, Benjamin R Evinger III, Albert J	Organovo, Inc	13/03/2013
20.	20140274802 Engineered liver tissues, arrays thereof, and methods of making the same	Shepherd, Benjamin R Robbins, Justin B Gorgen, Vivian A Presnell, Sharon C	Organovo, Inc	15/03/2013
21.	20140287960 Engineered liver tissues, arrays thereof, and methods of making the same	Shepherd, Benjamin R Robbins, Justin B Gorgen, Vivian A Presnell, Sharon C	Organovo, Inc	03/06/2014
22.	20190194625	Wicks, Robert T Atala, Anthony Nzou, Goodwell	Wake Forest University Health Sciences	04/08/2017

S/No	Patent No/Title	Inventor	Applicant	Filing Date
	Blood brain barrier model and methods of making and using the same	Wicks, Elizabeth E		
23.	20190209738 Preparation and applications of modified cellulose nanofibrils with extracellular matrix components as 3d bioprinting bioinks to control cellular fate processes such as adhesion, proliferation and differentiation	Gatenholm, Paul	Gatenholm, Paul	09/06/2017
24.	20190119626 Scaffold-free 3d bioprinting of porcine cells	Ekser, Burcin	Indiana University Research and Technology Corporation	17/10/2018
25.	20190177688 Three-dimensional tissue	Lin, Waka Hasegawa, Aino Hemmi, Natsuko Izumi, Satoshi Shiomoto, Shusaku	Lin, Waka Hasegawa, Aino Hemmi, Natsuko Izumi, Satoshi Shiomoto, Shusaku	10/05/2017
26.	20190187128 Screen printing tissue models	Lavik, Erin Bernstein, Steve Day, Adam Ibarra, Bryan	University of Maryland, Baltimore County	27/07/2018
27.	20190076577 Composite medical grafts and methods of use and manufacture	Stevens, Peter J Stilwell, Reginald Southard, Matthew Samaniego, Adrian C Manuele, Charles	AlloSource	16/03/2017

S/No	Patent No/Title	Inventor	Applicant	Filing Date
28.	20190076578 In situ expansion of engineered devices for regeneration	Bhatia, Sangeeta N Stevens, Kelly R Chen, Christopher S	Massachusetts Institute of Technology Trustees of Boston University	07/10/2016
29.	20190030212 Vascularized biphasic tissue constructs	Zhang, Lijie G Cui, Haitao Zhu, Wei	The George Washington University	20/03/2018
30.	20190022279 Tunable porous 3d biodegradable, biocompatible polymer/nanomaterial scaffolds, and fabricating methods and applications of same	Alghazali, Karrer M Saini, Viney Nima, Zeid A Biris, Alexandru S Bourdo, Shawn E	Board of Trustees of the University of Arkansas	21/09/2018
31.	20190022283 Method of printing a tissue construct with embedded vasculature	Lewis, Jennifer A Kolesky, David B Skylar-Scott, Mark A Homan, Kimberly A Truby, Ryan L Gladman, Amelia Sydney	President and Fellows of Harvard College	26/09/2018
32.	20180273904 Spontaneously beating cardiac organoid constructs and integrated body-on-chip apparatus containing the same	Skardal, Aleksander	Wake Forest University Health Sciences	30/09/2016
33.	20180291350 Multi-layer airway organoids and methods of making and using the same	Murphy, Sean V Atala, Anthony	Wake Forest University Health Sciences	14/10/2016

S/No	Patent No/Title	Inventor	Applicant	Filing Date
34.	20180320141 Methods of producing in vitro liver constructs and uses thereof	Atala, Anthony Bishop, Colin Mead, Ivy	Wake Forest University Health Sciences	14/10/2016
35.	20180250434 Bone-tendon graft biomaterial, use as a medical device and method of making same	Ker, Dai Fei Elmer Yang, Yunzhi	The Board of Trustees of the Leland Stanford Junior University	02/03/2017
36.	20180110901 Tubular tissue construct and a method of printing	Lewis, Jennifer A Homan, Kimberly A Kolesky, David B Truby, Ryan L Skylar-Scott, Mark A	President and Fellows of Harvard College	04/05/2016
37.	20180171304 Continuously bioprinted multilayer tissue structure	Beyer, Simon Mohamed, Tamer Pan, Sheng Wadsworth, Sam	Aspect Biosystems Ltd	16/06/2016
38.	20180193528 Printable morphogenetic phase-specific chitosan-calcium-polyphosphate scaffold for bone repair	Muller, Werner Ernst Ludwig Georg Schroder, Heinrich-Christoph Wilhelm Friedrich Wang, Xiaohong	Muller, Werner Ernst Ludwig Georg	24/07/2015
39.	20170368743 Integrated organ and tissue printing methods, system and apparatus	Kang, Hyun-Wook Lee, Sang Jin Atala, Anthony Yoo, James J	Wake Forest University Health Sciences	09/08/2017
40.	20180021140 High speed 3d printing system for wound and tissue replacement	Angelini, Thomas Ettor Sawyer, Wallace Gregory Rowe, Kyle Gene Bhattacharjee, Tapomoy	MARQUEZ; Samantha M University of Florida Research Foundation, Inc	12/04/2016

S/No	Patent No/Title	Inventor	Applicant	Filing Date
		Fernandez-Nieves, Alberto Chang, Ya-Wen Marquez, Samantha M	Georgia Tech Research Corporation	
41.	20180030409 Methods of generating functional human tissue	Lewis, Jennifer A Skylar-Scott, Mark A Kolesky, David B Homan, Kimberly A Ng, Alex H M Church, George M	President and Fellows of Harvard College	03/03/2016
42.	20180037870 Three-dimensional structure for cardiac muscular tissue regeneration and manufacturing method therefor	Cho, Dong-Woo Jang, Jinah Park, Hun-Jun	T & R Biofab Co Ltd	25/03/2016
43.	20170319746 A method for building a structure containing living cells	Lutolf, Matthias Negro, Andrea	École Polytechnique Fédérale de Lausanne (EPFL)	12/12/2014
44.	20170348458 Graft scaffold for cartilage repair and process for making same	Kesti, Matti Zenobi-Wong, Marcy Muller, Michael	ETH Zurich	11/12/2015
45.	20170354763 Multi-layer skin substitute products and methods of making and using the same	Atala, Anthony Jeong, Gayoung Yoo, James J Lee, Sang Jin Seol, Young-Joon	Wake Forest University Health Sciences	11/01/2016
46.	20170216498 Compositions for cell-based three-dimensional printing	Kang, Yujian James Zuo, Xiao	Sichuan Revotek Co Ltd	14/04/2017

S/No	Patent No/Title	Inventor	Applicant	Filing Date
47.	20170281828 Three-dimensional bioprinted artificial cornea	Zhang, Kang Chen, Shaochen Qu, Xin Ouyang, Hong	The Regents of the University of California	24/09/2015
48.	20160243286 Tissue engineered devices and methods for making same	Collins, Scott Forrest Boland, Thomas Yanez, Maria	The Board of Regents of the University of Texas System	27/10/2014
49.	20160287756 Method of printing a tissue construct with embedded vasculature	Lewis, Jennifer A Kolesky, David B Skylar-Scott, Mark A Homan, Kimberly A Truby, Ryan L Gladman, Amelia Sydney	President and Fellows of Harvard College	04/11/2016
50.	20170107483 Method of producing in vitro testicular constructs and uses thereof	Pendergraft, Samuel Sadri-Ardekani, Hooman Atala, Anthony Bishop, Colin	Wake Forest University Health Sciences	14/10/2016
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S/No	Patent No/Title	Inventor	Applicant	Filing Date
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54.	20130172985 Crosslinked hydrogels and methods of making and using thereof	Prestwich, Glenn D Skardal, Aleksander Zhang, Jianxing	Prestwich, Glenn D Skardal, Aleksander Zhang, Jianxing Assignee: University of Utah Research Foundation	13/01/2011
55.	20150017140 Organoids comprising decellularized and repopulated placental vascular scaffold	Bhatia, Mohit B Hariri, Robert J Hofgartner, Wolfgang Wang, Jia-Lun Ye, Qian	Bhatia, Mohit B Hariri, Robert J Hofgartner, Wolfgang Wang, Jia-Lun Ye, Qian Assignee: Anthrogenesis Corporation	21/12/2012
56.	20150119994 Integrated organ and tissue printing methods, system and apparatus	Kang, Hyun-Wook Lee, Sang Jin Atala, Anthony Yoo, James J	Wake Forest University Health Sciences	03/09/2014
57.	20120089238 Integrated organ and tissue printing methods, system and apparatus	Kang, Hyun-Wook Lee, Sang Jin Atala, Anthony Yoo, James J	Unnamed	06/10/2011
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S/No	Patent No/Title	Inventor	Applicant	Filing Date
		Christiansen, Dustin		
59.	20170369851 Artificial ovary	Laronda, Monica M Rutz, Alexandra L Shah, Ramille N Woodruff, Teresa K	Northwestern University	28/01/2016
60.	20180055643 Three-dimensionally printed tissue engineering scaffolds for tissue regeneration	Castro, Nathan Jonathan Holmes, Benjamin Blair	Nanochon, LLC	07/082017

c) Search Terms

Search Terms
Organovo
Bioprint$
Organ printing
Biofab$
Bio-fab$
bio fabricate
bio fabrication
Organ engineering
Tissue printing
Tissue engineering
Three-dimensional printing + Organ
bio-print
organ print

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