

The emergence and popularisation of autologous somatic cellular therapies in Australia: Therapeutic innovation or regulatory failure?

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Private stem cell clinics throughout Australia are providing autologous stem cell therapies for a range of chronic and debilitating illnesses despite the lack of published literature to support the clinical application of these therapies. The Therapeutic Goods Administration has excluded autologous stem cell therapies from its regulatory domain leaving such therapies to be regulated by the same mechanisms that regulate research, such as the National Health and Medical Research Council Research Ethics Guidelines, and clinical practice, such as the Australian Health Practitioner Regulation Agency. However, the provision of these stem cell therapies does not follow the established pathways for legitimate medical advance – therapeutic innovation or research. The current regulatory framework is failing to achieve its aims of protecting vulnerable patients and ensuring the proper conduct of medical practitioners in the private stem cell industry.

INTRODUCTION

Across Australia there are an increasing number of private medical practices offering autologous stem cell therapies for a range of chronic diseases. As yet there is no peer-reviewed scientific evidence to support the majority of these clinical applications outside of bone marrow transplantation. These clinics offer the unproven cellular therapies under the guise of “innovative” or “experimental” therapies to patients suffering from chronic illnesses – patients who are often desperate and vulnerable.

This article examines the regulation of autologous cellular therapies within the Australian context. It begins by reviewing the scientific basis for regenerative medicine and autologous cellular therapies, including the different definitions of stem cells. The current clinical application of stem cell therapies, and the evidence upon which this is based, is then reviewed. The article then describes the existence and growth of private autologous stem cell clinics operating across Australia and the marketing of these cellular therapies directly to the consumer via websites and television appearances. It provides an overview of the regulatory framework of cell and tissue products in Australia, looking at therapeutic goods law, professional discipline, the law of negligence, consumer protection law, and the regulation of advertising and research regulation, and describes how in each of these areas there are significant concerns about the current practice of private stem cell therapy in Australia.

The article concludes with suggestions for both regulatory change and increased enforcement, on the grounds that if the Australian private stem cell industry is allowed to continue with its current practices, there are significant risks to the community, to the ethical integrity of the medical profession and to public trust in medical research.

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THE SCIENTIFIC BASIS OF STEM CELL THERAPY

Stem cells are defined functionally as cells that have the capacity to self-renew. This means that a stem cell has the capacity to generate one daughter cell that is also a stem cell, as well as the ability to generate another “daughter cell” that produces differentiated cells.¹

The three key concepts that define a stem cell are:²

1. clonality, or the ability of the stem cells to generate daughter cells that are identical to the mother stem cells;
2. unlimited replication capacity (or for at least the lifetime of the animal); and
3. potency, or the capacity of a stem cell to produce a defined set of cellular progeny which are differentiated cells.³

Stem cell science is rapidly emergent and stem cells have been organised according to categories such as potency, source or derivation and their immunophenotype. It is important to note, however, that each of these categories is problematic and it is likely that none of these categories are currently adequate to categorise the variability of stem cells fully.

Stem cells can also be characterised according to their physiological properties. A *totipotent* cell has the potential to generate all the cells and tissues to form an entire conceptus and thus give rise to a new individual unaided.⁴ *Pluripotent* cells can give rise to cells of all tissue types of an organism but cannot develop into an entire organism.⁵ Pluripotent cells are derived from the inner cell mass of the blastocyst and rely on the outer layer of the blastocyst to provide the supporting structures such as the placenta to survive.⁶ For example, embryonic stem cells and induced pluripotent cells are pluripotent. A *multipotent* cell can generate multiple types of differentiated cells.⁷ Differentiated cells have distinct cellular morphology and gene expression patterns.⁸ For example, haematopoietic stem cells are multipotent as they can give rise to all of the blood cells lineages and mesenchymal stem cells which have the capacity to differentiate into cells of all the connective tissue lineages including bone, fat, cartilage and muscle.⁹ *Unipotent* stem cells are stem cells that are capable of differentiating along one cellular line and are the equivalent of a progenitor cell. Examples of unipotent cells include satellite cells found in muscle or myeloblasts in bone marrow that can only differentiate into granulocytes (that is, only the myeloid lineage of blood cells) such as neutrophils, basophils or eosinophils.¹⁰

The concept of plasticity is also important in the definition of stem cells. Plasticity refers to the notion that cellular differentiation is not permanent but is flexible and reversible.¹¹ Experiments have shown that differentiated cells under the appropriate conditions can be returned to their most primal state.¹²

¹ Smith AG, “Embryo-derived Stem Cells: Of Mice and Men” (2001) 17 *Annu Rev Cell Dev Biol* 435; Melton D and Cowan C, “Stemness” in Lanza R (ed), *Handbook of Stem Cells* (Elsevier Academic Press, 2004) p xxv

² Melton and Cowan, n 1, p xxv.

³ Weissman IL, Anderson DJ and Gage F, “Stem and Progenitor Cells: Origins, Phenotypes, Lineage Commitments, and Transdifferentiations” (2001) 17 *Annu Rev Cell Dev Biol* 387.

⁴ Kelly EB, *Stem Cells* (Greenwood Publishing Group Inc, USA, 2007) pp 6-7.

⁵ Kelly, n 4, pp 6-7.

⁶ Kelly, n 4, pp 6-7.

⁷ Melton and Cowan, n 1, pp xxiii-xxix.

⁸ Melton and Cowan, n 1, pp xxiii-xxix.

⁹ Lee MW, Jang IK, Yoo KH, Sung KW and Koo HH, “Stem and Progenitor Cells in Human Umbilical Cord Blood” (2010) 92 *Int J Hematol* 45 at 46; Barry FP and Murphy JM, “Mesenchymal Stem Cells: Clinical Applications and Biological Characterization” (2004) 36 *Int J Biochem Cell Biol* 568.

¹⁰ Melton and Cowan, n 1, pp xxiii-xxix; Kelly, n 4, pp 6-7.

¹¹ Melton and Cowan, n 1, pp xxv-xxx.

¹² Melton and Cowan, n 1, pp xxv-xxx.

Stem cells are also classified according to their source. The three main sources of stem cells are the embryo, the umbilical cord and adult tissues (such as bone marrow and fat). Each source contains different stem cells and may contain a combination of different stem cells.

The embryo is the main source of the totipotent human embryonic stem cell. Umbilical cord blood is a rich source of a wide variety of multipotent stem cells including haematopoietic and mesenchymal stem cells, as well as other stem cells such as embryonic-like stem cells.¹³ Many adult tissues contain stem cells, including bone marrow, peripheral blood, fat tissue, brains, hearts, kidneys, lungs and intestines. The adult stem cell is an unspecialised and undifferentiated cell but can differentiate to yield all the specialised cell types of the tissue from which they originate only,¹⁴ and so has limited potential for differentiation.¹⁵ Bone marrow contains at least two types of multipotent stem cells: haematopoietic stem cells and mesenchymal stem cells. The most common and preferred source of mesenchymal stem cells for current use in clinical trials is bone marrow.¹⁶ The heart contains a reservoir of cardiac and progenitor cells.¹⁷ Neural stem cells are self-renewing multipotent populations present in the developing and adult mammalian central nervous system that can generate the neurons and glial cells for the developing brain and account for the limited regenerative potential of the adult brain.¹⁸ The intestinal epithelium is the most rapidly self-renewing “solid” tissue in the human body, its ability to self-renew is a function of multipotent stem cells residing at the basis of intestinal crypts.¹⁹

Recently, somatic cellular reprogramming has produced the induced pluripotent stem cell (iPS cells) via insertion of particular genes into adult somatic cells to cause them to revert to an “embryonic cell-like” state.²⁰

In sum, stem cells are defined according to a three-tiered functional definition of clonality, immortality and potency. The problem with this form of classification is that it is highly inconsistent and a function of the currently limited technological capacity and scientific understanding of stem cells. Using the source of stem cells as the basis for classification is also problematic as more than one type of stem cell can be found in a single source. For example, umbilical cord blood contains a plethora of distinct stem cells, while bone marrow contains both haematopoietic stem cells and mesenchymal stem cells.

THE CLINICAL APPLICATION OF STEM CELLS

Research surrounding the clinical application of stem cells is burgeoning. While stem cell therapy holds much promise for the future treatment of diseases, stem cell therapies are the standard treatment in only a limited number of conditions. Early phase clinical trials are currently being undertaken to test the clinical efficacy of stem cell therapy for many diseases.

Embryonic stem cells

The clinical use of human Embryonic Stem Cells (hESCs) has been hampered by controversy surrounding the source of hESCs for clinical trials. In 2012, the first reports of safety and tolerability

¹³ Lee et al, n 9 at 48.

¹⁴ Kelly, n 4, pp 6-7.

¹⁵ Melton and Cowan, n 1, p xxiv.

¹⁶ Minguell JJ, Allers C and Lasala GP, “Mesenchymal Stem Cells and the Treatment of Conditions and Diseases: The Less Glittering Side of a Conspicuous Stem Cell for Basic Research” (2013) 22 *Stem Cells Dev* 193 at 193.

¹⁷ Barile L, Messina E, Giacomello A and Marbán E, “Endogenous Cardiac Stem Cells” (2007) 50 *Prog Cardiovasc Dis* 31; Beltrami AP, Barlucchi L, Torella D, Baker M, Limana F and Chimenti S et al, “Adult Cardiac Stem Cells Are Multipotent and Support Myocardial Regeneration” (2003) 114 *Cell* 763.

¹⁸ Conti L and Cattaneo E, “Neural Stem Cell Systems: Physiological Players or In Vitro Entities?” (2010) 11 *Nat Rev Neurosci* 176 at 176.

¹⁹ Tesori V, Puglisi MA, Lattanzi W, Gasbarrini GB and Gasbarrini A, “Update on Small Intestinal Stem Cells” (2013) 19 *World J Gastroenterol* 4672.

²⁰ Stein GS, Borowski M, Luong MX, Shi MJ, Smith KP and Vazquez P (eds), *Human Stem Cell Technology and Biology: A Research Guide and Laboratory Manual* (Wiley, Hoboken, 2011).

of human embryonic stem cells for the treatment of two patients were published. Both patients had retinal pathology and suggested apparent short-term safety, tolerability and perhaps efficacy of this treatment in humans.²¹

iPS

iPS cells have widely been viewed as a preferred alternative to embryonic stem cells, for both scientific and moral reasons. From a scientific standpoint, the virtually unlimited supply of adult somatic cells from which iPS cells are produced provides a significant advantage over relying upon discarded embryos and limited donor oocytes to create embryonic stem cell lines.²²

Umbilical cord stem cells

Umbilical cord blood is a safe and easily utilised source of haematopoietic stem cells. Umbilical cord blood is particularly advantageous as a source of haematopoietic stem cells when transplantation is urgent or a donor cannot be found.²³ During the past 25 years, over 30,000 umbilical cord blood transplantations have been carried out.²⁴

There are 120 ongoing registered clinical trials involving stem cells derived from umbilical cord blood for a wide range of clinical disorders.²⁵ The use of an autologous infusion of umbilical cord blood to improve the neurodevelopmental function of children between one and six years with cerebral palsy is currently in phase II.²⁶ A recent Korean trial suggests that some improvement was observed following umbilical cord stem cell therapy from donors in children with cerebral palsy.²⁷

Adult stem cells

Haematopoietic stem cell transplantation is an established form of treatment for many diseases, as listed in Table 1.²⁸ The outcomes of haematopoietic stem cell transplantation vary according to the type and stage of each disease, the source of the stem cells to be transplanted and the degree of human leukocyte antigen (HLA) mismatch.²⁹

TABLE 1 Diseases commonly treated with haematopoietic stem cell transplantation

	Autologous transplantation	Allogeneic transplantation
Cancer	Multiple Myeloma	Acute myeloid leukaemia
	Non-Hodgkin’s Lymphoma	Acute lymphoblastic leukaemia
	Hodgkin’s disease	Chronic myeloid leukaemia
	Acute myeloid leukaemia	Myelodysplastic syndromes

²¹ Schwartz SD, Hubschman J, Heilwell G, Franco-Cardenas V, Pan CK, Ostrick RM and Mickunas E et al, “Embryonic Stem Cell Trials for Macular Degeneration: A Preliminary Report” (2012) 379 *The Lancet* 713.

²² Fung RF and Kerridge IH, “Uncertain Translation, Uncertain Benefit and Uncertain Risk: Ethical Challenges Facing First-in-Human Trials of Induced Pluripotent Stem (iPS) Cells” (2013) 27 *Bioethics* 89.

²³ Copelan EA, “Hematopoietic Stem-Cell Transplantation” (2006) 354 *N Engl J Med* 1813.

²⁴ Ballen KK, Gluckman E and Broxmeyer HE, “Umbilical Cord Blood Transplantation: The First 25 Years and Beyond” (2013) 122 *Blood* 491.

²⁵ ClinicalTrials.gov was searched on 4 April 2014: <http://www.clinicaltrial.gov>. A search using the search term “umbilical cord blood stem cell” was conducted, excluding studies with unknown status and including only open studies.

²⁶ See NCT01147653, “A Randomised Study of Autologous Umbilical Cord Blood Reinfusion in Children with Cerebral Palsy”. See also National Stem Cell Foundation of Australia and Stem Cells Australia, *The Australian Stem Cell Handbook – What You Should Know About Stem Cell Therapies: Now and Into the Future* (2013).

²⁷ National Stem Cell Foundation of Australia and Stem Cells Australia, n 26.

²⁸ Copelan, n 23 at 1814. Table 1 has been adapted from information in Copelan at 1814.

²⁹ Copelan, n 23 at 1822.

TABLE 1 *continued*

	Autologous transplantation	Allogeneic transplantation
	Neuroblastoma	Myeloproliferative disorders
	Ovarian Cancer	Non-Hodgkin's lymphoma
	Germ-cell tumours	Hodgkin's Disease
		Chronic lymphocytic leukaemia
		Multiple myeloma
		Juvenile chronic myeloid leukaemia
Other diseases	Autoimmune disorders	Aplastic anaemia
	Amyloidosis	Paroxysmal nocturnal haemoglobinuria
		Fanconi's Anaemia
		Diamond Blackfan Anaemia
		Thalassemia major
		Sickle cell anaemia
		Severe combined immunodeficiency
		Wiskott-Aldrich syndrome
		Inborn errors of metabolism

Of the adult stem cells, mesenchymal stem cells have considerable clinical potential due to their ability for self-renewal and pluripotency, allowing commitment, differentiation and maturation into specific phenotypes under the control of intrinsic cell signalling mechanisms.³⁰ Mesenchymal stem cells are attractive because of their ability to provide trophic support to other cells, to slow down degenerative processes and to secrete biochemical substances (such as growth factors, cytokines, neurotransmitters, and extracellular matrix components) that may influence tissue repair, tissue growth and both local and systemic cellular immunological reactions.³¹

Internationally, hundreds of clinical trials are investigating the application of adult stem cells for a wide range of diseases. Most of these are early Phase I or Phase II trials to determine the safety and efficacy of stem cells in the treatment of different diseases.³² These preliminary trials include the use of stem cells to improve heart function,³³ vision,³⁴ stroke,³⁵ peripheral arterial disease,³⁶ amyotrophic

³⁰ Minguell et al, n 16 at 193.

³¹ Minguell et al, n 16 at 193.

³² Minguell et al, n 16 at 194.

³³ Jeevanantham V, Butler M, Saad A, Abdel-Latif A, Zuba-Surma EK and Dawn B, "Adult Bone Marrow Cell Therapy Improves Survival and Induces Long-term Improvement in Cardiac Parameters: A Systematic Review and Meta-analysis" (2012) 126 *Circulation* 551.

³⁴ National Stem Cell Foundation of Australia and Stem Cells Australia, n 26, p 16.

³⁵ Boncoraglio GB, Bersano A, Candelise L, Reynolds BA and Parati EA, "Stem Cell Transplantation for Ischemic Stroke" (2010) 8 *Cochrane Database Syst Rev* CD007231.

³⁶ Bura A, Planat-Benard V, Bourin P, Silvestre JS, Gross F and Grolleau JL et al, "Phase I Trial: The Use of Autologous Cultured Adipose-derived Stroma/Stem Cells to Treat Patients with Non-revascularizable Critical Limb Ischemia" (2014) 16 *Cytotherapy* 245.

lateral sclerosis,³⁷ diabetes,³⁸ multiple sclerosis,³⁹ and spinal cord injury.⁴⁰ While there is limited high-level evidence to support any applications of autologous stem cell therapy other than those listed in Table 1, there is some early evidence of clinical efficacy in a limited range of conditions.

A recently published non-randomised pilot study (both Phase I and II) carried out in Korea recruited 18 patients who received intra-articular injections of autologous adipose-derived mesenchymal stem cells for osteoarthritis.⁴¹ Over six months follow-up the nine patients who received a high dose of mesenchymal stem cells had improvements in pain scales, reduction on MRI of cartilage defect, regeneration of cartilage on arthroscopy and histological evaluation particularly in areas of most damage over the medial and femoral condyles.⁴² There are a number of limitations to this study including that it lacked a control group which the authors comment “would be necessary for clinical application”; had a brief six month follow-up of patients; required eight months of rehabilitation including limitation upon weight-bearing on the affected joint, which may have allowed for native regeneration of articular cartilage; and the WOMAC score relied upon may be an inappropriate tool to evaluate intra-articular injection of stem cells.⁴³

TABLE 2 Levels of evidence that currently support stem cell therapy interventions for different diseases

Level of evidence	Disease/intervention
I	Diseases listed in Table 1 Adjuvant stem cell therapy will improve left ventricular function following acute myocardial infarction
II	–
III	Autologous stem cell therapy for osteoarthritis
IV	Spinal cord injury, peripheral arterial disease and acute myeloid leukaemia
None	Cerebral palsy, blindness, autism, muscular dystrophy, headache and asthma

The current level of evidence available to support stem cell therapy for different diseases is listed in Table 2.⁴⁴ There is also Level I evidence that autologous haematopoietic stem cell therapy has no statistically significant improvement in long-term stroke outcomes. Importantly, there are no randomised, double-blinded, multicentre clinical trials of sufficient statistical power to generate generalisable clinical data that the efficacy of these new applications for adult stem cell therapies is greater than the currently available standard practice.⁴⁵

³⁷ Thomsen GM, Gowing G, Svendsen S and Svendsen CD, “The Past, Present and Future of Stem Cell Clinical Trials for ALS” (2014) *Exp Neurol* (forthcoming).

³⁸ National Stem Cell Foundation of Australia and Stem Cells Australia, n 26, p 18.

³⁹ Lau D, Ogbogu U, Taylor B, Stafinski T, Menon D and Caulfield T, “Stem Cell Clinics Online: The Direct-to-Consumer Portrayal of Stem Cell Medicine” (2008) 3 *Cell Stem Cell* 591.

⁴⁰ National Stem Cell Foundation of Australia and Stem Cells Australia, n 26, p 16.

⁴¹ Jo CH, Lee Yg, Shin WH, Kim H, Chai JW, Jeong EC and Kim JE et al, “Intra-articular Injection of Mesenchymal Stem Cells for the Treatment of Osteoarthritis of the Knee: A Proof-of-concept Clinical Trial” (2014) 32 *Stem Cells* 1254.

⁴² Jo et al, n 41 at 1255-1257.

⁴³ Jo et al, n 41 at 1259-1262.

⁴⁴ Levels of evidence are set out in National Health and Medical Research Council, *NHMRC Additional Levels of Evidence and Grades for Recommendations for Developers of Guidelines: Stage 2 Consultation* (2008), http://www.nhmrc.gov.au/files_nhmrc/file/guidelines/stage_2_consultation_levels_and_grades.pdf.

⁴⁵ Sipp D, “The Uregulated Commercialization of Stem Cell Treatments: A Global Perspective” (2011) 5 *Front Med* 348 at 348.

Studies of the safety of all forms of stem cell therapies are critical as malignant transformation is a risk with any cellular therapy.⁴⁶ This risk is higher with less differentiated stem cells such as embryonic stem cells and iPS cell therapy.⁴⁷ This was illustrated when a patient with ataxia telangiectasia developed a multifocal brain tumour after travelling overseas to receive neural stem cell “therapy” from an unlicensed clinic.⁴⁸ In this case the brain tumour was shown to have derived from the donor cells.⁴⁹ Reassuringly, the risk of tumour formation with autologous adult somatic stem cells appears extremely low.⁵⁰

PRIVATE CLINICS AND STEM CELL THERAPIES IN AUSTRALIA

Despite the lack of evidence for the efficacy of stem cell therapies, there are an increasing number of private clinics operating across Australia providing autologous stem cell therapies for a wide range of diseases. Eighteen private clinics and three private companies were identified as offer stem cell therapies across Australia. A number of features common to these clinics are a cause for major ethical, legal and clinical concern.

A lack of scientific support for clinical applications

The majority of these private clinics do not provide published scientific data to support their clinical activities. Only Macquarie Stem Cells references a publication – this being a “pilot study” of six patients treated with stem cells for joint disease published in the *Journal of Cosmetic Surgery and Medicine*.⁵¹ The results state that all patients “showed significant improvement most marked in the first month and plateauing after four months”. However, there is no statistical analysis to support the significance of the observations. The publication also fails to indicate whether there was human ethics approval to conduct the research and the article lacks a declaration of conflicts of interest. It is also noteworthy that the *Journal of Cosmetic Surgery and Medicine* is not indexed by Medline; however, the journal’s homepage does state that it is peer-reviewed.⁵²

A lack of evidence of research participation

A number of stem cell clinics state that they are conducting research in the area of stem cells without providing evidence of publications, affiliated universities or active registered trials. For example, a doctor at the Lakeside Sports Centre claims to be conducting a double-blind randomised control trial comparing hyaluronic acid to adipose-derived stem cells for the treatment of osteoarthritis of the knee. This study was registered with the Australian and New Zealand Clinical Trials Registry on 15 March 2011. However, the current status of the trial states that it is not yet recruiting, even though three years have passed.⁵³ Lakeside also states it has designed a prospective case series of 60 patients who will be treated “as if in a trial” and followed with pain scales and MRIs and the results will be published. It is unclear whether this case series has progressed and to date there is no evidence that this has been published.⁵⁴

⁴⁶ Prockop DJ, Brenner M, Fibbe WE, Horwitz E, Le Blanc K and Phinney DG et al, “Defining the Risks of Mesenchymal Stromal Cell Therapy” (2010) 12 *Cytotherapy* 576.

⁴⁷ Prockop et al, n 46 at 576; Ren G, Chen X, Dong F, Li W, Ren X and Zhang Y et al, “Concise Review: Mesenchymal Stem Cells and Translational Medicine: Emerging Issues” (2012) 1 *Stem Cells Transl Med* 51.

⁴⁸ Amariglio N, Hirshberg A, Scheithauer BW, Cohen Y, Loewenthal R and Trakhtenbrot L et al, “Donor-derived Brain Tumor Following Neural Stem Cell Transplantation in an Ataxia Telangiectasia Patient” (2009) 6 *PLoS Med*.

⁴⁹ Amariglio et al, n 48 at 223.

⁵⁰ Lalu MM, McIntyre L, Pugliese C, Fergusson D, Winston BW, Marshall JC and Granton J et al, “Safety of Cell Therapy with Mesenchymal Stromal Cells (SafeCell): A Systematic Review and Meta-analysis of Clinical Trials” (2012) 7 *PLoS One* 7(10).

⁵¹ Bright R, “Adipose Derived Stromal Cells to Treat Joint Disease” (2010) 5 *Journal of Cosmetic Surgery and Medicine* 62.

⁵² *Journal of Cosmetic Surgery*, “Advice to Authors” (as at 21 June 2014), <http://www.jcsmonline.com/advice-authors.html>.

⁵³ See Trial ID ACTRN12611000274976, “Adipose Derived Stem Cells in Patients with Knee Osteoarthritis: A Randomized Controlled Trial Evaluating Pain, Function and Cartilage Repair”.

⁵⁴ PubMed was searched on 21 June 2014: <http://www.ncbi.nlm.nih.gov/pubmed>. An author search on “Bates” and a keyword search on “Osteoarthritis” was conducted.

Stem Cell Solutions states on its website that it is part of a “research effort” to compile long-term data. However, no trial appears to be registered on the Australian and New Zealand Clinical Trials Registry.⁵⁵ It is also unclear for what purposes Stem Cell Solutions is collecting this data, whether it is for peer-reviewed publication or for publication internally on its website and provided to patients.

Regeneus, a stem cell company, is sponsoring a 40-patient randomised controlled Phase II clinical trial at Royal North Shore Hospital, Sydney. The results of this trial have not been published in a peer-reviewed journal. However, the interim report states that a peer-reviewed paper will be submitted for publication in due course.⁵⁶

Problematic inclusion and exclusion criteria

The inclusion and exclusion criteria listed by some private clinics for stem cell therapies are extremely vague. For example, Stem Cell Solutions requires patients to be “reasonably well” and “have a little bit of fat”. Stem Cell Solutions excludes from stem cell therapy patients who are undergoing cancer treatment, who are pregnant and who have bleeding disorders.⁵⁷

Previously, Macquarie Stem Cells listed cancer as one of the conditions that could be effectively treated with autologous (non-haematopoietic) stem cells. However, this claim has been rescinded with Doctor Ralph Bright, a doctor at Macquarie, admitting that this was a “big mistake”. Cancer is now listed as a relative contra-indication.⁵⁸ At Sydney Sports Medicine Specialists the inclusion criteria for being eligible for treatment with stem cells is Grade 2, Grade 3 and early Grade 4 osteoarthritis, mechanical impairment, and “quality of life being affected and pain on most days”.⁵⁹ The other clinics do not list either inclusion or exclusion criteria.

Worrying use of testimonials

Some private stem cell clinics have been using patient and doctor narratives and testimonials to market and sell stem cell therapies on their websites, television and radio. The websites and media appearances selectively use positive patient testimonials to promote stem cell therapies.

For example, a doctor from Macquarie Stem Cells has made a number of television appearances to discuss the use of autologous stem cell therapies for osteoarthritis.⁶⁰ In all of these interviews, the doctor discussed his experience of successful stem cell treatments that he had provided at Macquarie. For example, the doctor stated that what he has found for osteoarthritis is that “one injection is enough to take away the symptoms and stop the pain and stiffness”.⁶¹ As well, patients who have had successful treatments appear on the show to discuss their personal experience of stem cell therapy. For example, one successful recipient of stem cell treatment commented the therapy “brought life back to me, it’s fantastic”.⁶²

⁵⁵ The Australia and New Zealand Clinical Trials Registry (ANZCTR) was searched on 21 June 2014: <http://www.anzctr.org.au>. An advanced search on the search terms “stem cells” AND “Johnston” was conducted.

⁵⁶ Regeneus Ltd, *OSCARS (Osteoarthritis Stem Cell Advanced Research Study) Interim Report: A Randomised Double-blind, Placebo-controlled Trial of the Efficacy and Safety of Autologous Non-expanded Adipose-derived Stem Cells in the Treatment of Knee Osteoarthritis* (2013).

⁵⁷ Stem Cell Solutions, “Suitable Candidates” (as at 27 August 2014), <http://www.stemcellsolutions.com.au/stem-cell-treatment-candidate>.

⁵⁸ Aubusson K, “Stem Cell Doctor Hits Out at Critics”, *Australian Doctor* (22 January 2014).

⁵⁹ Sydney Sports Medicine Specialists, “Fat Derived Stem Cell Injections” (as at 21 June 2014), <http://www.sportsdoc.com.au/fat-derived-stem-cell-injections.html>.

⁶⁰ Garner P, “Stem Cells to Treat Osteoarthritis”, *Today Tonight* (19 October 2012), <http://au.news.yahoo.com/today-tonight/latest/article/-/15166678/stem-cells-to-treat-osteoarthritis>; Wellings H, “Arthritis Stem Cell Therapy”, *Today Tonight* (10 December 2013), <http://au.news.yahoo.com/today-tonight/celebrity/article/-/20249412/arthritis-stem-cell-therapy>; “Osteoarthritis Relief?”, *Nine MSN* (18 March 2013), <http://aca.ninemsn.com.au/article/8628233/osteoarthritis-relief>; Willing E, “Geoff Lawson Trials Stem Cell Cure”, *A Current Affair* (6 December 2013), <http://aca.ninemsn.com.au/article/8767292/geoff-lawson-trials-stem-cell-cure>

⁶¹ Gardner, n 60.

⁶² Gardner, n 60.

Another example comes from the Lakeside clinic, which detailed the results of the first four patients it treated with adipose-derived autologous stem cell therapy on its website. The first patient was also featured in a segment on 6.30 with George Negus.⁶³

A further example comes from Norwood Day Surgery, where one of its doctors appeared on *Today Tonight Adelaide*. During this segment, two of his patients appeared on the show to detail their treatment with stem cell therapy and how it had improved pain symptoms and mobility of affected joints.⁶⁴

Another doctor from Stem Cell Assisted Arthroscopic Surgery uses its website to present the stories of three patients who underwent stem cell therapy. The patients are claimed to be a professional triathlete, a former professional rugby player and a recreational jogger. Some of the comments stated by the patients include “Dr Sam and his little Stem Cells are amazing. I would do it all again in a heartbeat”.⁶⁵ The MasterDerm Clinic also uses before and after photos to illustrate the success of stem cell therapy for facial rejuvenation.⁶⁶

Private stem cell clinics have also tapped into the power of celebrity to sell stem cell therapies to the wider community. Macquarie Stem Cells gave free stem cell therapy to former Australian Test Bowler Geoff Lawson who stated he was “very happy” with this treatment. The late Charlotte Dawson, a model and presenter, who almost lost her career due to bilateral knee injury, was given stem cell therapy by Macquarie. This was featured on *Today Tonight*. A doctor from Macquarie stated on the program that Charlotte Dawson’s treatment had been “life-changing”⁶⁷ and “she will be back to normal”.⁶⁸ Two days later, Charlotte Dawson appeared on a panel show on Channel 7, called *The Daily Edition*, where she discussed the benefits of her stem cell therapy.⁶⁹

The Sydney Sports Medicine Specialists’ website references a 2012 article in *The Daily Telegraph* which reported that stem cell therapy “saved” rugby league player, Anthony Tupou, from retirement.⁷⁰ Following stem cell therapy, Anthony Tupou was described by his coach as “stronger, more powerful than ever”.⁷¹

Unsupported claims

Claims regarding the efficacy and results of stem cell therapies are presented on the websites of these private clinics without providing any supporting evidence from peer-reviewed literature. For example, the Macquarie website claims that stromal vascular fraction therapy can decrease the amount of inflammation in psoriasis sufferers by “regulating the genes which become upset because of an overreaction of T-cells in the skin and joints”.⁷²

Stem Cell Solutions claims that over 85% of patients treated showed a significant improvement of between 50 to 100% in pain and mobility of the joint. Approximately 15% of patients treated are

⁶³ As reported on the Lakeside Clinic Facebook page on 21 June 2014, https://www.facebook.com/permalink.php?story_fbid=237923836257090&id=175313305814990.

⁶⁴ Polkinghorne L, “Arthritis Stem Cell Treatment”, *Today Tonight Adelaide* (24 June 2013).

⁶⁵ Stem Cell Assisted Arthroscopic Surgery, “Patient Stories” (as at 15 June 2014), <http://scaas.com.au/patient-stories>.

⁶⁶ Master Derm Cosmetic and Anti-ageing Clinic, “Stem Cell Therapy” (as at 21 June 2014), http://www.masterderm.net.au/stem_cell%20therapy.html.

⁶⁷ Wellings, n 60 at 00:02:12.

⁶⁸ Wellings, n 60 at 00:02:15.

⁶⁹ “Charlotte’s Battle”, *The Daily Edition* (12 December 2013), <http://au.tv.yahoo.com/the-daily-edition/video/watch/20286742/charlottes-battle>.

⁷⁰ Otto T, “Stem Cell Injections Resurrect Cronulla Shark Anthony Tupou’s Career”, *The Daily Telegraph* (29 February 2012).

⁷¹ Otto, n 70.

⁷² Macquarie Stem Cells, “There’s Still a Misconception about Stem Cell Therapy” (1 August 2013), <http://www.macquariestemcells.com/media-centre/why-theres-still-a-debate-around-stem-cells>.

described as non-responders – experiencing improvement of less than 20% over three months.⁷³ Stem Cell Solutions also describes stem cell therapy as “safe and biocompatible”⁷⁴ and a “validated treatment” for a range of conditions, including joint pain and osteoarthritis.⁷⁵ Norwood Day Surgery, likewise, claims that “stem cell therapy has a safety record demonstrated in both humans and animals for many years. At this time it appears to be very safe and highly effective.”⁷⁶

The Sydney Sports Medicine Specialists’ website claims 80% of patients treated showed significant improvement between 50 to 100% in pain and mobility of the joint and a 60% decrease in pain scores in the first two weeks after treatment.⁷⁷ Brisbane Regeneration on its homepage comments that “with our extensive stromal cell treatment you will no longer have to rely on pills to ease your pain. Stromal cell therapy involves regenerating damaged tissue at the source of the affected area which will restore function and improve your quality of life.”⁷⁸

Regeneus claims that at 12 months post-treatment, 69.4% of HiQCell treated patients responded with a 30% or greater reduction in pain. The Regeneus website states that, “this treatment is, in every respect, conventional, science-based medicine”.⁷⁹

The Me Clinic website states that “our own Research and Development has shown that Stem Cell Therapy has the capacity to slow down the ageing process as well as reducing the impact and effects of ageing and the associated diseases and illnesses”.⁸⁰ Dr Chan, from the Victorian Cosmetic Institute, states that combining platelets with stem cells from fat improves the longevity of the treatment to 10 or more years.⁸¹

The high cost of stem cell therapies

The cost of stem cell therapy for osteoarthritis is substantial, considering that these treatments, which for a single stem cell infusion at \$9,000, are still to be proven effective. These clinics include Macquarie Stem Cells, Stem Cell Solutions, Norwood Day Surgery, Sydney Sports Medicine Specialists, SCAAS, Hip and Knees Clinic @ Sydney Olympic Park. Additionally, Stem Cell Solutions, Macquarie, Norwood and Brisbane Regeneration offer or recommend payment plans for patients for up to a cost of \$70,000 and over 84 months duration.

AUSTRALIAN REGULATION OF STEM CELL THERAPIES

In Australia three separate schemes operate to regulate the provision of therapeutic goods and services, the regulation of health professionals and the regulation of medical research. First, the Therapeutic Goods Administration (TGA) oversees the regulation of therapeutic goods including prescription, non-prescription and complementary medicines and medical devices. In particular, the TGA regulates blood and cell products, including stem cells, through a regulatory scheme called the Biologicals Framework. Secondly, 14 different health professions are regulated under the national regulatory scheme coordinated by the Australian Health Practitioner Regulation Agency (AHPRA). Thirdly, the

⁷³ Stem Cell Solutions, “Osteoarthritis Patient Treatment Information” (10 June 2012), <http://www.stemcellsolutions.com.au/wp-content/uploads/2012/12/Osteoarthritis-Treatment.pdf>.

⁷⁴ Stem Cell Solutions, “Stem Cells Used to Alleviate Pain from Osteoarthritis in Hip” (3 September 2013), <http://www.stemcellsolutions.com.au/media/stem-cells-used-alleviate-pain-osteoarthritis-hip>.

⁷⁵ Stem Cell Solutions, “5 Benefits to Treating your Osteoarthritis with Stem Cell Therapy” (30 May 2013), <http://www.stemcellsolutions.com.au/media/5-benefits-to-treating-your-osteoarthritis-with-stem-cell-therapy>.

⁷⁶ Norwood Day Surgery, “Osteoarthritis Treatment Options” (as at 21 June 2014), <http://www.norwooddaysurgery.com.au/osteoarthritis-treatment-options>.

⁷⁷ Sydney Sports Medicine Specialists, “Fat Derived Stem Cell Injections – Who Can Benefit from Stem Cells” (as at 27 August 2014), <http://www.sportsdoc.com.au/fat-derived-stem-cell-injections.html>.

⁷⁸ Brisbane Regeneration (as at 17 May 2014), <http://www.brisbaneregeneration.com.au>.

⁷⁹ HiQCell, “FAQs” (as at 21 June 2014), <http://www.imaginelessjointpain.com.au/faqs>.

⁸⁰ The Me Clinic, “Stem Cell Therapy” (as at 13 June 2014), <http://www.meclinic.com/sydney/face/anti-ageing-procedures/stem-cell-therapy.html>.

⁸¹ Demasi M, “Skin Deep”, *Catalyst* (7 November 2013), <http://www.abc.net.au/catalyst/skindeep>.

National Health and Medical Research Council (NHMRC) is responsible for regulating medical research to ensure the integrity and quality of medical research in Australia.

Regulation of therapeutic goods

The *Therapeutic Goods Act 1989* (Cth) defines a “therapeutic good” to include any good which is represented in any way to be for therapeutic use, or for use as an ingredient or component in the manufacture of therapeutic goods or for use as a container for a therapeutic good.⁸² The TGA is responsible for ensuring that therapeutic goods available for supply in Australia are safe and fit for their intended purpose.⁸³ The TGA regulates a wide range of medicines, both prescription and “over the counter”; medical devices; and products used in the diagnosis of various diseases or conditions, such as blood tests and vaccines, blood products and other biologics.⁸⁴ The TGA also regulates the manufacturing and advertising of the products it regulates.⁸⁵

Regulation of medicine by the TGA under the *Therapeutic Goods Act* involves classifying each medicine based on the level of risk and implementing regulatory control for the manufacturing processes of medicines. The level of TGA regulatory control increases with the level of risk the medicine can pose. Medicines that are classified into the high-risk category, including prescription medicines and some non-prescription medicines, are evaluated for quality, safety and efficacy. In contrast, medicines that are classified into the low-risk category are evaluated for quality and safety only. Low-risk medications are available over the counter. Once medications are made readily available, they are subject to continued monitoring by the TGA including adverse event reporting.⁸⁶

Biologicals regulation

The Biologicals Regulatory Framework came into effect in May 2011 to regulate human cell and tissue-based products as a distinct group of therapeutic goods called “biologicals”.⁸⁷ Biologicals are regulated under a separate framework due to the unique nature of the risk they carry such as disease transmission or other unforeseen biological reactions.⁸⁸ Products that are classified as biological can also be regulated as therapeutic goods under the *Therapeutic Goods Act*, rather than as biologicals. The Act also permits some biologicals to be classified as “excluded goods” so that they are taken out of the biological regulation altogether.

The definition of a “biological” is twofold.⁸⁹ First, a biological is a “thing” that either comprises, contains, or is derived from, human cells or human tissues.⁹⁰ Secondly, a biological must be represented for use in the treatment or prevention of a disease, ailment, defect or injury; or process of making a medical diagnosis; or influencing a physiological process in persons; or testing the susceptibility of persons to a disease or ailment; or in the replacement or modification of parts of the anatomy in persons. Stem cells fall under the definition of a “biological” as a human cell that is used in the treatment of a disease.

The Biologicals Regulatory Framework includes a risk-based classification system which adopts a documented risk-management approach during the life of the product. Therapeutic Goods Orders

⁸² *Therapeutic Goods Act 1989* (Cth), s 3 – definition of “therapeutic goods” at subs (a).

⁸³ Therapeutic Goods Administration, *What the TGA Regulates* (last updated 5 March 2014), <http://www.tga.gov.au/about/tga-regulates-what.htm>.

⁸⁴ Therapeutic Goods Administration, n 83.

⁸⁵ Therapeutic Goods Administration, n 83.

⁸⁶ Therapeutic Goods Administration, n 83.

⁸⁷ Therapeutic Goods Administration, *The Therapeutic Goods Administration’s Risk Management Approach to the Regulation of Therapeutic Goods* (Department of Health and Ageing, Canberra, 2011) p 29.

⁸⁸ Therapeutic Goods Administration, n 87, p 29.

⁸⁹ *Therapeutic Goods Act 1989* (Cth), s 32A.

⁹⁰ Anything that is specified in a legislative instrument can also be defined as a biological: *Therapeutic Goods Act 1989* (Cth), s 32A.

detail the containing standards that apply to specific biologicals. A *Code of Good Manufacturing Practice for Blood and Tissue* and a comprehensive post-market surveillance and adverse event reporting program is also employed.⁹¹

The Biologicals Regulatory Framework allows four classes of biological based on a risk assessment. Risks that are assessed relate to the methods of preparation and processing of the products during their manufacture and whether their intended use is the same as their biological function.⁹² Class 2 biologicals are those that have had minimal manipulation, which includes antibiotic treatment, filtration, mixing with a cryopreservative and freezing. If any process in the manufacture of the stem cells includes processes such as in vitro expansion of cells, cell isolation procedures and cell selection, all of which are greater than “minimal manipulation”, the biological will be classified as at least Class 3. If the biological has a different phenotype than the donor, or was manipulated to differentiate into a phenotype, then the biochemical, physiological or immunological property of the cells have changed and they are classified as Class 4. Cells can be classed as either Class 3 or Class 4 if they are for non-homologous use – mesenchymal stem cells from bone marrow used in myocardial ischaemia (heart attack) are Class 3 but if these stem cells are differentiated into skeletal muscle and are thus phenotypically different then they are Class 4.

The *Therapeutic Goods (Things that are not Biologicals) Determination No 1 of 2011* (TGD 1) specifies a range of biological products that are not regulated as biological and are instead regulated as therapeutic goods. The two main examples are haematopoietic progenitor cells and umbilical cord blood.⁹³

As stated above, it is possible for the regulation to exclude goods from the operation of the *Act*. The *Therapeutic Goods (Excluded Goods) Order No 1 of 2011* (TGO 1) specifies a range of products that would fall within the definition of a biological and the definition of therapeutic goods. TGO 1 excludes human tissue and cells that are:

- collected from a patient who is under the clinical care and treatment of a registered medical practitioner; and
- manufactured by that medical practitioner, or by a person or persons under the professional supervision of that medical practitioner, for therapeutic application in a single treatment and in a course of single treatment of that patient by the same medical practitioner, or by a person or persons under the professional supervision of the same medical practitioner.⁹⁴

The TGA has produced a guidance document for the interpretation of the exempted items listed in the TGO 1. For the s 4(q) exclusion to apply, the human cells or tissue for autologous use must be provided by a single medical practitioner to a single patient for a single clinical indication.⁹⁵ However, a single clinical indication does not exclude more than one dose or administration of human cells or tissues to treat that one indication such that patients with chronic conditions could receive autologous cellular therapy over years to treat one condition.⁹⁶ A medical practitioner also has to assure ongoing responsibility for clinical care during the treatment for s 4(q) to apply.⁹⁷

Under s 4(q), the human cells and tissues must be manufactured by that medical practitioner or under the professional supervision of that medical practitioner. However, the guidance document states that the fact that the products used for the treatment of a patient are not directly manufactured by the

⁹¹ Therapeutic Goods Administration, n 87, p 29.

⁹² Therapeutic Goods Administration, *Australian Regulatory Guidelines for Biologicals (ARGB)* (Department of Health and Ageing, Canberra, 2011).

⁹³ Therapeutic Goods Administration, *Excluded Goods Order No 1 of 2011: Guideline for Items 4(o), 4(p), 4(q) and 4(r)* (Department of Health and Ageing, Canberra, 2013) p 5.

⁹⁴ *Therapeutic Goods (Excluded Goods) Order No 1 of 2011*, s 4(q)

⁹⁵ Therapeutic Goods Administration, n 93, pp 6-7.

⁹⁶ Therapeutic Goods Administration, n 93, p 7.

⁹⁷ Therapeutic Goods Administration, n 93, p 7.

treating medical practitioner does not exclude the application of s 4(q).⁹⁸ The term “professional supervision” requires that the medical practitioner is party to all manufacturing steps that are performed in a formal governance arrangement with the person undertaking the manufacturing, including input into the protocols and quality systems used in the manufacturing processes.⁹⁹ To illustrate, pancreatic tissue may be collected by a surgeon in collaboration with an endocrinologist for the processing of islet cells in a laboratory. Following processing, the islet cells are given to the same patient as an autologous transplantation. The collection, processing and infusion remain under the professional supervision of the endocrinologist caring for the patient.¹⁰⁰ If the processing, storage or infusion or implantation of the human cells or tissue is undertaken by a person, organisation or other third party on behalf of a medical practitioner where there is no specified relationship with the agent or agency that meets the requirements for professional supervision, then the exemption would not apply.

The guidance document suggests that there must be a formal arrangement between the clinician and the person “manufacturing” the cell product and the clinician must have contributed to the protocols and quality assurance of the manufacturing process.¹⁰¹ The meaning of “specified relationship” depends on the “manufacturing” process of the cell product, and according to the TGA the concept of “manufacturing” is complicated. As mentioned above, the stratification of biologicals also depends on the meaning of “manufacturing” of a cell product and over 10 pages of explanatory examples are devoted to clarifying what level of manipulation determines the classification of specific biologicals.¹⁰²

Fresh viable human haematopoietic progenitor cells for direct donor-to-host transplantation are also excluded from regulation as either therapeutic goods or biologicals, under s 4(p) of the TGO 1, if they are for the purpose of haematopoietic reconstitution, such as bone marrow cells and cord blood.¹⁰³ The exclusion in s 4(p) is also unclear with regards to what constitutes “fresh” and “direct.” Specifically, it is unclear as to whether “fresh” implies certain time constraints on the use of cells or excludes freezing or cryopreservation in the use of these cells. As well, there is no indication as to what the meaning of “direct” is and whether it requires identification of a specific host at the time the tissue is donated.

The guidance document makes the comment that treating medical practitioners “should be mindful of adherence to professional standards when using products that have not been evaluated for safety and efficacy by the TGA”, including considerations of whether the treatment is “necessary and safe and whether its efficacy is supported by credible clinical evidence”.¹⁰⁴ Importantly, this statement does not contribute to the interpretation and implementation of s 4(o), (p), (q) and (r) and does not refer specifically to the relevant professional standards.

PROFESSIONAL DISCIPLINE OF STEM CELL PRACTITIONERS

In Australia, there is a single national registration and accreditation system known as the National Registration and Accreditation Scheme for the Health Professions. Since July 2012, this regulatory scheme covers 14 health professions including medical practitioners. This legislative scheme establishes AHPRA as the national agency to implement and administer the *Health Practitioner Regulation National Law Act 2009*, as in force in each State and Territory (the National Law).

The National Law is the principal piece of legislation regulating medical practitioners. One of the stated purposes of the National Law is “to provide for the protection of the public by ensuring that

⁹⁸ Therapeutic Goods Administration, n 93, p 7.

⁹⁹ Therapeutic Goods Administration, n 93, p 7.

¹⁰⁰ Therapeutic Goods Administration, n 93, p 7.

¹⁰¹ Therapeutic Goods Administration, n 93, p 7.

¹⁰² Therapeutic Goods Administration, *Blood Tissue and Biologicals* (Department of Health and Ageing, Canberra, 2011) pp 24-34.

¹⁰³ *Therapeutic Goods (Excluded Goods) Order No 1 of 2011*.

¹⁰⁴ Therapeutic Goods Administration, n 93, p 7.

only health practitioners who are suitably trained and qualified to practise in a competent and ethical manner are registered”.¹⁰⁵ This objective recognises that effective regulation of the health profession must be able to appropriately limit entry, monitor performance and restrict practice in order to protect the public from those doctors who put the public at risk.¹⁰⁶

AHPRA manages the 14 national boards of health professionals across Australia, including the Medical Board of Australia. The Medical Board of Australia develops standards, codes and guidelines for the medical profession as well as investigating notifications and complaints against medical practitioners. In the Code of Conduct, the Medical Board of Australia sets out the expectations of registered doctors in terms of working with patients, in teams within the hospital system and undertaking research.

AHPRA, on behalf of the national boards, manages investigations into professional conduct and performance of health professionals. AHPRA and the national boards have three broad options when resolving complaints: decide that no further action is required as there is no risk to public safety; or take immediate action such as to caution the practitioner, impose conditions on registration, refer the matter to the appropriate State-based body such as the New South Wales Health Care Complaints Commission (HCCC), constitute a health panel to hear the matter, or refer to the appropriate tribunal such as the New South Wales Civil and Administrative Tribunal; or request more information.

Unlike other States and Territories, New South Wales has “a co-regulatory” scheme where all complaints to AHPRA or the national boards in New South Wales must refer notifications to the New South Wales HCCC or professional councils in New South Wales for investigation.¹⁰⁷ The HCCC and professional councils deal with issues about professional performance, health and competence including fitness to practise, while the national boards deal with registration and accreditation issues. A similar framework has been introduced in Queensland under the *Health Ombudsman Act 2013* (Qld).

There are multiple avenues available for health consumers to make a notification or complaint to either the federal AHPRA or the relevant State bodies (such as the HCCC or the Medical Council of New South Wales) regarding health practitioners. Healthcare professionals also have mandatory notification obligations. Under s 141 of the National Law, health practitioners must report to AHPRA any “notifiable conduct”. Most relevantly to the present discussion, s 140 of the National Law defines “notifiable conduct” to include circumstances where the practitioner has “placed the public at risk of harm because the practitioner has practised the profession in a way that constitutes a significant departure from accepted professional standards.”

The statutory bodies under the National Law have a range of powers with which to investigate matters further if required, such as health or performance assessments or information from employees or family members. The primary purpose of disciplinary proceedings is the protection of the public and not the punishment of wrongdoing.¹⁰⁸ Alternatively, immediate action can be taken by these bodies. They have a number of avenues at their disposal with which to resolve or escalate the matter accordingly, such as cancellation of medical registration or referral to a tribunal.

As of January 2014, AHPRA had received at least one notification of a doctor using unproven stem cell therapy but did not provide any further details.¹⁰⁹ The Medical Board of Australia has commented that use of unproven stem cell therapy could constitute unprofessional conduct if the stem cell therapies were excessive, unnecessary or otherwise not required for the person’s wellbeing.¹¹⁰ In Queensland, a doctor was found guilty of unsatisfactory professional conduct, had his registration cancelled and was prevented from reapplying for registration for three years, for offering stem therapy

¹⁰⁵ *Health Practitioner Regulation National Law Act 2009*, s 2(a).

¹⁰⁶ Elkin K, “Medical Practitioner Regulation: Is it All About Protecting the Public?” (2014) 21 JLM 682 at 684.

¹⁰⁷ Kerridge I, Lowe M and Stewart C, *Ethics and Law for the Health Professions* (4th ed, Federation Press, 2013) p 170.

¹⁰⁸ Kerridge et al, n 107, p 172.

¹⁰⁹ Aubusson, n 58.

¹¹⁰ Aubusson, n 58.

for adhesive arachnoiditis.¹¹¹ Other health practitioners such as chiropractors¹¹² and Chinese medicine practitioners¹¹³ have also been disciplined for offering or inappropriately promoting stem cell-related therapies.

Another issue for professional discipline relates to the offering of financial loans and investment schemes to patients by private stem cell clinics. Many clinics offer financial plans for patients wishing to have stem cell therapy. This might also be considered to be in breach of the code of conduct provisions that prohibit such arrangements.¹¹⁴

A third concern is the lack of disclosure of financial conflicts of interest. The failure to disclose a pecuniary interest may constitute unsatisfactory professional conduct under the National Law.¹¹⁵ Doctors working in these clinics should disclose their pecuniary interests in the provision of stem cell therapies to their patients. Patients should also be told of alternative therapies. Such disclosure is potentially of great significance as where there is a conflict of interest the medical practitioner has a duty to resolve the conflict in the best interests of the patient.¹¹⁶

A further concern relates to scope of practice. Doctors should not practice outside their area of expertise. This is particularly salient with regards to autologous cellular therapies as many of the practitioners are prescribing and administering stem cell therapies for an extensive range of diseases across disciplines within medicine in which they lack advanced training. A number of cosmetic surgeons are treating patients with osteoarthritis, asthma, multiple sclerosis, stroke and motor neurone disease. While it may be claimed that these practitioners are simply providing a “technical” service, it is also arguable that treating such patients is so far removed from the practice of a cosmetic surgeon that it could be unethical or constitute unsatisfactory professional conduct.¹¹⁷

The description of those who administer these therapies as “stem cell physicians” is also arguably misleading as there is no specialist registration category for this qualification and most medical practitioners working in these clinics are trained in other fields, such as a cosmetic surgeon. If it is judged that this constitutes a misrepresentation of the qualifications of the practitioner working in these clinics then this may arguably contravene the code of conduct.¹¹⁸

NEGLIGENCE AND STEM CELL PRACTITIONERS

It is generally accepted that health professionals owe a duty of care to their patients.¹¹⁹ A breach of the standard of care owed to patients that causes damage may form the basis of a civil action in medical negligence.¹²⁰ The damage caused to the patient needs to be a result of the breach of the standard of care owed by the health professional.¹²¹ Since the Ipp reforms, a professional can defend such an allegation by establishing that he or she acted in a manner that was widely accepted in Australia by peer professional opinion as competent professional practice. The fact that there are differing peer professional opinions concerning the practice does not prevent any of those opinions being relied on. Nor does the peer professional have to be universally accepted. The only exception is where the peer professional opinion being relied on was *irrational* (in New South Wales, Queensland, South

¹¹¹ *Medical Board of Queensland v Tarvydas* [2010] QCAT 246.

¹¹² *Chiropractic Board of Australia v Hooper (Review and Regulation)* [2013] VCAT 878.

¹¹³ *Chinese Medicine Registration Board of Victoria v Ghaffurian (Occupational and Business Regulation)* [2012] VCAT 478.

¹¹⁴ Medical Board of Australia, *Good Medical Practice: A Code of Conduct for Doctors in Australia* (2014), s 8.12.

¹¹⁵ *Health Practitioner Regulation National Law Act 2009*, s 139B(1)(i); Medical Board of Australia, n 114, s 8.11.

¹¹⁶ Medical Board of Australia, n 114, s 8.11.

¹¹⁷ *Health Practitioner Regulation National Law Act 2009*, s 139B(1)(l).

¹¹⁸ Medical Board of Australia, n 114, s 8.9

¹¹⁹ Kerridge et al, n 107, p 198.

¹²⁰ Kerridge et al, n 107, p 212.

¹²¹ Kerridge et al, n 107, p 216.

Australia, Tasmania), *unreasonable* (in Victoria) or was *so unreasonable that no reasonable health professional would have adopted it* (in Western Australia).¹²²

When one applies the current standard of care test to the practices of private stem cell clinics, there immediately is an issue of whether such practices would be able to satisfy the requirements of competent professional practice. Therefore it would be very difficult to argue that the practice of private stem cell clinics was “widely accepted in Australia” by peer professional opinion.

Even more alarming is the question of whether such practices could satisfy the duty to provide material information about the risks of treatment, as required under *Rogers v Whitaker*.¹²³ The doctrine of *Rogers v Whitaker* requires health professionals to provide information concerning both the objective risks of treatment (which would ordinarily be provided to patients), and the subjective risks of treatment (which are risks that may have special significance for an individual patient). The Ipp reforms did not change these requirements. Instead, the common law was preserved in all jurisdictions (barring the Australian Capital Territory and the Northern Territory).¹²⁴ In Queensland and Tasmania, the *Rogers* principle was placed into the legislation.¹²⁵ In Victoria, s 50 of the *Wrongs Act 1958* (Vic) states that:

A person (the defendant) who owes a duty of care to another person (the plaintiff) to give a warning or other information to the plaintiff in respect of a risk or other matter, satisfies that duty of care if the defendant takes reasonable care in giving that warning or other information.

Given the lack of evidence concerning the benefits and risks of stem cell therapy, it is hard to envisage how a practitioner could provide advice in line with the doctrine of *Rogers*, except in the most perfunctory and basic way.

Serious cases of negligence can also give rise to professional discipline proceedings where the negligence amounts to professional misconduct.¹²⁶ As mentioned above, negligence can also be the grounds of mandatory notifications for conduct that has placed the public at risk because the conduct is a significant departure from accepted professional standards.¹²⁷ Where negligence causes the death of a patient it is possible that the healthcare provider might be prosecuted for criminal negligence.¹²⁸ The negligence required for criminal negligence must be gross negligence as evidenced by such disregard for the life and safety of others as to deserve punishment.¹²⁹

CONSUMER PROTECTION LAW AND STEM CELL PRACTICE

Patients may be protected by consumer law if they are misled or deceived into believing certain treatments are safe or effective when they are not.¹³⁰ Under Australian consumer law, corporations are prohibited from engaging in misleading or deceptive conduct during trade or commerce.¹³¹ Patients can complain to the Australian Competition and Consumer Commission (ACCC) about businesses

¹²² *Civil Liability Act 2002* (NSW), s 50; *Civil Liability Act 2003* (Qld), s 22; *Civil Liability Act 1936* (SA), s 41; *Civil Liability Act 2002* (Tas), s 22; *Wrongs Act 1958* (Vic), s 59; *Civil Liability Act 2002* (WA), s 5PB.

¹²³ *Rogers v Whitaker* (1992) 175 CLR 479.

¹²⁴ *Civil Liability Act 2002* (NSW), s 5P; *Civil Liability Act 2003* (Qld), s 22; *Civil Liability Act 1936* (SA), s 41; *Civil Liability Act 2002* (Tas), s 22; *Wrongs Act 1958* (Vic), s 60; *Civil Liability Act 2002* (WA), s 5PB.

¹²⁵ Both the *Civil Liability Act 2003* (Qld), s 21, and the *Civil Liability Act 2002* (Tas), s 21, state that a doctor does not breach a duty to warn of a risk unless the doctor fails to provide: (a) information that a reasonable person in the patient’s position would, in the circumstances, require to enable the person to make a reasonably informed decision about whether to undergo the treatment or follow the advice; and (b) information that the doctor knows or ought reasonably to know the patient wants to be given before making the decision about whether to undergo the treatment or follow the advice.

¹²⁶ Kerridge et al, n 107, p 227.

¹²⁷ *Health Practitioner Regulation National Law Act 2009*, ss 140, 141.

¹²⁸ Kerridge et al, n 107, p 229.

¹²⁹ Kerridge et al, n 107, p 229.

¹³⁰ National Health and Medical Research Council, *Stem Cell Treatments – A Quick Guide for Medical Practitioners* (2013).

¹³¹ *Competition and Consumer Act 2010* (Cth), s 29(1).

involved in the delivery of their health care that has made a false or misleading claim. For example, if the business predicts the health benefits of a therapeutic device or health product but has no evidence that such health benefits can be attained.¹³² Private practitioners often practise as a small business and so are vulnerable to complaints against them under consumer law as patients pay the incorporated business for the advice of the practitioner.

ADVERTISING REGULATION

In addition to consumer law, advertising of health services is also regulated by the National Law and the AHPRA *Guidelines for Advertising Regulated Health Services*. Under the Guidelines, advertising includes promotion through public communications including television, radio, internet, electronic and social media.¹³³

Under the National Law, a “regulated health service” is a service provided by, or usually provided by, a health practitioner.¹³⁴ A person or business must not advertise a regulated health service in a way that is false, misleading or deceptive; uses testimonials or purported testimonials about the service or business; or creates an unreasonable expectation of beneficial treatment.¹³⁵

Included in the concept of misleading or deceptive conduct under the Guidelines and the National Law is the use of words, letters or titles that may mislead or deceive a health consumer into thinking that the provider of a health service is more qualified or more competent, for example using the phrase “stem cell physician”, when there is no specialist registration category for that specialty.¹³⁶ The National Law also prohibits health care providers from using specialist titles unless they are registered under the National Law in that specialty or from claiming they are a specialist health practitioner when they are not a registered health practitioner.¹³⁷ Alternatively, advertising a health benefit of a regulated health service when there is no proof that such benefits can be obtained may also constitute misleading or deceptive advertising.¹³⁸

The National Law does not define “testimonial”, so it is taken to have its ordinary meaning, including the use of patient stories to promote a regulated health service or selectively publishing patient comments on a business website.¹³⁹ A practitioner is required to take steps to remove a testimonial associated with his or her health service once he or she becomes aware of the testimonial.¹⁴⁰ The creation of an unreasonable expectation of benefit may occur through the provision of incomplete or biased information, or failing to disclose health risks.¹⁴¹ The use of scientific information in advertising should be from a reputable peer-reviewed source.¹⁴²

If one examines the practice of private stem cell clinics in light of these regulatory requirements a number of problems are immediately apparent. The inclusion of patient testimonials and claims of data from “clinical studies” by some Australian clinics is contrary to the *Australian Code for the*

¹³² Australian Competition and Consumer Commission, “False or Misleading Claims” (as at 4 March 2014), <http://www.accc.gov.au/consumers/misleading-claims-advertising/false-or-misleading-claims>.

¹³³ Australian Health Practitioner Regulation Agency, *Guidelines for Advertising Regulated Health Services* (2014).

¹³⁴ *Health Practitioner Regulation National Law Act 2009*, s 133(4)

¹³⁵ *Health Practitioner Regulation National Law Act 2009*, s 133(1)(a), (c) and (d); see also Australian Health Practitioner Regulation Agency, n 133, ss 6.2.1, 6.2.3, 6.2.4

¹³⁶ Australian Health Practitioner Regulation Agency, n 133, s 7.3.

¹³⁷ *Health Practitioner Regulation National Law Act 2009*, ss 113, 115, 118.

¹³⁸ Australian Health Practitioner Regulation Agency, n 133, s 6.2.1; Australian Competition and Consumer Commission, n 132.

¹³⁹ Australian Health Practitioner Regulation Agency, n 133, s 6.2.3.

¹⁴⁰ Australian Health Practitioner Regulation Agency, n 133, s 6.2.3.

¹⁴¹ Australian Health Practitioner Regulation Agency, n 133, s 6.2.4.

¹⁴² Australian Health Practitioner Regulation Agency, n 133, s 7.6.

*Responsible Conduct of Research*¹⁴³ and the *National Statement on Ethical Conduct in Human Research*,¹⁴⁴ which requires that human subject research be approved by a Human Research Ethics Committee.¹⁴⁵

The use of unsupported claims and patient testimonials on the websites of autologous stem cell clinics is also in violation of the AHRPA Advertising Guidelines and may constitute misleading and deceptive conduct under the National Law, the AHPRA Advertising Guidelines and consumer law.¹⁴⁶ For example, claims of 80% efficacy of intra-articular autologous stem cell therapy for osteoarthritis made by some clinics¹⁴⁷ appear to be in breach. Likewise, the claims made by another clinic that its technique of simultaneous intra-articular injection and intravenous injection “has been found to almost double the effectiveness of the procedure”¹⁴⁸ in patients with osteoarthritis, without provision of any supporting information, is both misleading and creates an unreasonable expectation of beneficial treatment. Similarly, the claim made by one clinic that treatment “appears 100% safe”¹⁴⁹ also creates an unreasonable expectation of beneficial treatment¹⁵⁰ and is patently false as all medical interventions are associated with risks, including infection, allergic reaction, immune system rejection and even the small possibility of malignancy (as has been reported with stem cell therapies).¹⁵¹

The use of patient testimonials by private clinics is prohibited under the National Law and the Advertising Guidelines.¹⁵² Some clinics publish selected positive patient testimonials and media reports, not supported by evidence, and fail to publish more reliable information from the NHMRC and the International Society for Stem Cell Research (ISSCR).¹⁵³

RESEARCH REGULATION AND STEM CELL THERAPY

The NHMRC is an independent statutory body within the Commonwealth Department of Health’s portfolio. The legislative basis of the NHMRC is the *National Health and Medical Research Act 1992* (Cth) and the *National Health and Medical Research Council Regulations 2006* (Cth).

The *Australian Code for the Responsible Conduct of Research* guides researchers and institutions in responsible practices and establishes the parameters of responsible research including management of data, supervision of trainees, publication of research, peer review, authorship, collaboration and conflicts of interest.¹⁵⁴ Research misconduct is comprised of a breach of the Code of Conduct; intent

¹⁴³ National Health and Medical Research Council and Australian Research Council, *Australian Code for the Responsible Conduct of Research* (2007), s 1.8.

¹⁴⁴ National Health and Medical Research Council and the Australian Research Council, *National Statement on Ethical Conduct in Human Research* (2007), ss 3.2.3, 5.1.6.

¹⁴⁵ National Health and Medical Research Council and the Australian Research Council, n 144, s 3.3.

¹⁴⁶ *Health Practitioner Regulation National Law Act 2009*, s 133(a); Australian Health Practitioner Regulation Agency, n 133, s 6.2.1; *Competition and Consumer Act 2010* (Cth), s 29(1).

¹⁴⁷ Macquarie Stem Cells, “What is Your Success Rate?” (as at 27 August 2014), <http://www.macquariestemcells.com/specials/faqs/what-is-the-stem-cell-therapy-success-rate>; Norwood Day Surgery, “The Stem Cell Therapy Procedure” (as at 27 August 2014), <http://www.norwooddaysurgery.com.au/stem-cell-therapy-procedure>; Stem Cell Solutions, “Osteoarthritis Patient Treatment Information” (10 June 2012), <http://www.stemcellsolutions.com.au/wp-content/uploads/2012/12/Osteoarthritis-Treatment.pdf>.

¹⁴⁸ Macquarie Stem Cells, “The Stem Cell Therapy Procedure” (as at 21 June 2014), <http://www.macquariestemcells.com/stem-cell-therapy-treatment>.

¹⁴⁹ Stem Cell Solutions, “Stem Cell Information Sheet” (10 June 2012) p 3 (adverse effects), <http://www.stemcellsolutions.com.au/wp-content/uploads/2012/12/stem-cell-information.pdf>.

¹⁵⁰ Australian Health Practitioner Regulation Agency, n 133, s 6.2.4.

¹⁵¹ Medical Board of Australia, n 114.

¹⁵² *Health Practitioner Regulation National Law Act 2009*, s 133(1)(c); Australian Health Practitioner Regulation Agency, n 133, s 6.2.3; Medical Board of Australia, n 114, s 8.6.4.

¹⁵³ Lau et al, n 39; National Health and Medical Research Council, n 130.

¹⁵⁴ National Health and Medical Research Council and Australian Research Council, n 143, s 1.

and deliberation, recklessness or gross and persistent negligence; and serious consequences, such as false information on the public record, or adverse effects on research participants, animals or the environment.¹⁵⁵

The *National Statement on Ethical Conduct in Human Research* promotes ethical human research by clarifying the responsibilities of institutions and researchers for ethical design, conduct and dissemination of results of human research and review bodies in the ethical review of research. In conjunction with the Code of Conduct, any protocol for human research needs to be approved by a human research ethics committee in accordance with the National Statement, as well as disclosing any actual or potential conflicts of interest to the human research ethics committee.

STEM CELL CLINICS: MEDICAL INNOVATION OR RESEARCH?

Standard medical therapies gain acceptance through two different pathways, either rigorous evaluation through research or through innovation developed in the course of clinical practice. The distinction between research and innovative therapies is important as they attract different regulatory frameworks.

The NHMRC defines research as a “systematic investigation to establish facts, principles or knowledge and a study of some matter with the objective of obtaining or confirming knowledge”.¹⁵⁶

Innovative therapy is born out of the overlap between the intent to benefit a patient and the dissatisfaction with standard therapy as well as professional creativity.¹⁵⁷ There are two central aspects to the definition of innovative therapies: first, the departure from standard medical therapy and secondly, that the therapy has not been validated by reliable research methods or there is not enough available evidence to support the safety and efficiency of the therapy required for acceptance or approval from peers and regulatory bodies.¹⁵⁸

The intention is useful to delineate research from innovative therapies. There are two goals in clinical research: the generation of new information (knowledge) that can be used to treat future patients; and to treat those patients enrolled in the study. Thus, unlike standard clinical care where the primary aim is the optimal treatment of the patient, in research, the treatment of the patient is not the sole purpose.¹⁵⁹ In contrast, innovative therapies are primarily offered to benefit patients and any new knowledge gained from use of the therapy in the clinical setting is secondary.¹⁶⁰ However, distinguishing innovative therapy from research on the basis of the primary intention to optimise patient management is problematic as innovative therapies may be used to support pilot studies and further research in the future.¹⁶¹ Nevertheless, it seems true that innovative therapy is individualised whereas research may involve the same treatment in a patient population to create a body of information which can be generalised to treat future patients.¹⁶²

Innovative therapy is part of medical care and sits within that therapeutic paradigm where oversight is provided by the physician-patient relationship as well as post-hoc review processes including as disciplinary proceedings or tort law remedies for medical negligence.¹⁶³ This regulatory system is retrospective and not triggered prior to the delivery of the therapy to the patient. In contrast,

¹⁵⁵ National Health and Medical Research Council and Australian Research Council, n 143, s 10.1.

¹⁵⁶ National Health and Medical Research Council and the Australian Research Council, *National Statement on Ethical Conduct in Human Research* (1999) p 6.

¹⁵⁷ Taylor PL, “Overseeing Innovative Therapy without Mistaking It for Research: A Function-Based Model Based on Old Truths, New Capacities, and Lessons from Stem Cells” (2010) 38 J Law Med Ethics 286 at 289.

¹⁵⁸ Taylor, n 157; Chan TE, “Legal and Regulatory Responses to Innovative Treatment” (2013) 21 Med Law Rev 92; Cowan D, “Innovative Therapy Versus Experimentation” (1986) 21 Tort & Ins LJ 619.

¹⁵⁹ Chan, n 158 at 153.

¹⁶⁰ Chan, n 158 at 94.

¹⁶¹ Chan, n 158 at 102.

¹⁶² Chan, n 158 at 127.

¹⁶³ Chan, n 158 at 93; Taylor, n 157 at 289.

research is prospectively regulated by, for example, institutional review boards, research ethics committees, and peer-review dependent funding before any patients receive a new therapy.¹⁶⁴

It is clear, however, that innovative therapies are legitimate tools for advancing the body of medical knowledge.¹⁶⁵ Innovative therapy in clinical practice can be used as the foundation from which to develop more formal testing such as clinical trials.¹⁶⁶ The knowledge gleaned from innovative therapies may contribute to the clinical trial process by producing standardised procedures and more specific inclusion and exclusion criteria.¹⁶⁷ Innovative therapies are also subject to less regulatory oversight, which allows for rapid advancement of new medical therapies.

Many surgical procedures considered routine today were introduced through the pathway of innovation with little regulatory oversight rather than through the pathway of research.¹⁶⁸ For example, laparoscopic surgical techniques, endovascular arterial repair and cardiac transplants were introduced through innovation in standard practice.¹⁶⁹ The introduction of new, innovative surgical procedures is not integrated into any regulatory framework as these procedures fall outside the ambit of major regulatory bodies such as the TGA.¹⁷⁰

But innovative therapy may create a potential conflict between the patient's best interest and the personal, professional and financial interests of the physician.¹⁷¹ Innovative therapy is of increasing concern where market forces influence the health care system.¹⁷² A direct conflict of interest arises where the physician has a vested financial interest in demonstrating the success of the innovative therapy due to, for example, a financial stake in the intellectual property connected to the innovative therapy.¹⁷³ Such potential for abuse of innovative therapies suggests that greater regulatory oversight is necessary to protect patients and the community.

Regulation of innovative therapies is also necessary to protect against harm to patients and harm to the reputation of the medical profession.¹⁷⁴ Regulation of innovative therapies needs to be able to balance "protecting vulnerable patients from unknown risks and suboptimal treatment" with the "need for preserving a healthy amount of flexibility in clinical practice to encourage innovation, and the practical competencies and resources of the research ethics oversight system".¹⁷⁵ A system that overregulates could stifle advancement and it would be left to the slow and cumbersome research pathway.¹⁷⁶

Research and innovative therapies both pose common regulatory difficulties due to the risks to patients that stem from the lack of knowledge, lack of proficiency, uncertainty regarding clinical application and the potential for bias due to the ambitions of the physician or investigator.¹⁷⁷

¹⁶⁴ Chan, n 158 at 97.

¹⁶⁵ Cowan, n 158 at 620.

¹⁶⁶ Healey P and Samanta J, "When Does the 'Learning Curve' of Innovative Interventions Become Questionable Practice?" (2008) 36 *Eur J Endovasc Surg* 253.

¹⁶⁷ Hyun I, "Allowing Innovative Stem Cell-based Therapies Outside of Clinical Trials: Ethical and Policy Challenges" (2010) 38 *J Law Med Ethics* 277.

¹⁶⁸ Healey and Samanta, n 166 at 254; Hyun, n 167 at 280.

¹⁶⁹ Healey and Samanta, n 166 at 254; Hyun, n 167 at 280-281; Strasberg S and Ludbrook P, "Who Oversees Innovative Practice? Is There a Structure that Meets the Monitoring Needs of New Techniques?" (2003) 196 *J Am Coll Surg* 938.

¹⁷⁰ Barkun JS et al, "Evaluation and Stages of Surgical Innovations" (2009) 374 *The Lancet* 1089.

¹⁷¹ Chan, n 158 at 109; Lewens T, "Distinguishing Treatment from Research: A Functional Approach" (2006) 32 *J Med Ethics* 424.

¹⁷² Chan, n 158 at 93.

¹⁷³ Taylor, n 157 at 291; Chan, n 158 at 118.

¹⁷⁴ Healey and Samanta, n 166 at 255.

¹⁷⁵ Chan, n 158 at 108.

¹⁷⁶ Healey and Samanta, n 166 at 254.

¹⁷⁷ Taylor, n 157 at 296.

The ICSSR supports innovative stem cell therapies and provides a series of recommendations to clinicians implementing innovative stem cell therapies. The ISSCR recommends that innovative therapies be carried out to a small number of patients with a written plan including the scientific rationale and justification for the procedure, characterisation of the cells, description of how the cells are administered and formal follow-up of patients. Such innovative therapies should be supported by clinical and administrative leadership, be carried out by appropriately qualified personnel, ensure patients give voluntary informed consent, provide an action plan for adverse events, appropriate insurance and the commitment of scientists to disseminate their findings to contribute to generalisable knowledge.¹⁷⁸

The ICSSR task force expressed its concern about stem cell clinics, operating in unregulated jurisdictions,¹⁷⁹ offering hyped but unproven stem cell therapies to desperate and vulnerable patients. The ISSCR condemns the use of unproven stem cell therapies to a large series of patients outside of a clinical trial, particularly when patients are charged for such services.¹⁸⁰

The ISSCR criteria can be used to distinguish legitimate attempts at medical innovation of stem cell therapies from problematic abuses of stem cell innovation. There are two types of unproven stem cell therapies. The first are without scientific rationale and efficacy and potentially have serious side-effects that have not been demonstrated in animal studies. The second have a scientific rationale with efficacy and have a lack of serious side-effects demonstrated in animal models but clinical safety has not been established.¹⁸¹ The first category is professionally and ethically irresponsible whereas the second category is a valid attempt at medical innovation. Legitimate medical innovation of stem cell therapies is where there is a scientific rationale and efficacy and absence of side-effects has been demonstrated in animal models but has not been established clinically.¹⁸² Following clarification of scientific rationale, the therapy is then subject to peer review, progresses to clinical use in a limited number of patients and is then tested in clinical trials where possible.

Examination of the Australian private stem cell industry in light of this discussion raises serious concerns about both the practice and regulation of the emerging stem cell industry. Providing an “experimental” treatment to hundreds of patients is, in many respects, a departure from both innovation and research – which are the established forms of medical advancement.¹⁸³ Innovative therapies are generally provided to a small number of patients with very specific needs – many of who may have no other alternatives.¹⁸⁴ The fact that many patients who are administered autologous stem cell therapies in private clinics receive a schedule of repeated infusions, may experience no clear benefit and often go into great personal debt raises questions as to whether these clinics are really concerned with innovation or are simply well-organised commercial enterprises offering lucrative treatments.¹⁸⁵

There are also a number of reasons why the services offered by Australian stem cell clinics cannot properly be regarded as research. For the most part, there is rarely (if ever) evidence of an identifiable research question or hypothesis being tested by the medical professionals at these clinics, no evidence of approvals by research ethics committees to conduct research on human subjects and no apparent emphasis on the responsible dissemination of research findings through publication. Instead, these

¹⁷⁸ International Society for Stem Cell Research (ISSCR), *Guidelines for the Clinical Translation of Stem Cells* (2008), Recommendation 34, pp 15-16.

¹⁷⁹ Taylor PL, Barker RA, Blume KG, Cattaneo E, Colman A, and Deng H et al, “Patients Beware: Commercialized Stem Cell Treatments on the Web” (2010) 7 *Cell Stem Cell* 43.

¹⁸⁰ International Society for Stem Cell Research, n 178, p 5.

¹⁸¹ Hyun, n 167 at 281.

¹⁸² Lindvall O and Hyun I, “Medical Innovation Versus Stem Cell Tourism” (2009) 324 *Science* 1664.

¹⁸³ Taylor et al, n 179 at 48.

¹⁸⁴ Taylor et al, n 179 at 44; International Society for Stem Cell Research, n 178, p 15; Lindvall and Hyun, n 182 at 1664.

¹⁸⁵ Lindvall and Hyun, n 182; Qiu J, “Trading on Hope” (2009) 27 *Nat Biotechnol* 790.

clinics widely advertise “positive” clinical outcomes of interventions that have not been established in high-level clinical trials nor even established scientifically within their own patient populations.

CONCLUSIONS: A STORY OF REGULATORY FAILURE?

It is difficult not to conclude that the current regulatory framework is failing to achieve its goals of ensuring proper conduct of practitioners in the private stem cell industry. Moreover the regulators who have the power to police breaches of practice, including AHPRA, the ACCC and the HCCC have not yet engaged with this industry in any widespread fashion. The TGA also appears to have been reluctant to manage this area of practice, perhaps on the assumption that other regulators would do so.¹⁸⁶ The NHMRC is clearly aware of the problems – having released *Stem Cell Treatments – A Quick Guide for Medical Practitioners* (to warn of the dangers of unproven medical therapies).¹⁸⁷ Nevertheless, there appears a real unwillingness to hold the medical professionals in these clinics to account, both at the level of professional discipline and at the government level, through meaningful and enforceable regulation.¹⁸⁸

TGA’s specific exclusion of autologous stem cell therapies for single indications is tantamount to a regulatory failure. Autologous stem cell therapies can effectively escape the whole edifice of therapeutic goods regulation because of this exclusion. This leaves private stem cell practice to be regulated by the same mechanisms that regulate clinical practice, namely, health care complaints under the National Law, common law actions for medical negligence and consumer protection mechanisms.

Allowing the continued provision of unproven autologous stem cell therapies (outside of ethically approved clinical trials) is deeply problematic.¹⁸⁹ This article has shown that these therapies rest on unsubstantiated and misleading claims of clinical efficacy and may expose patients to small but uncertain risks due to the lack of safety data. Moreover, the treated patients risk being excluded from participation in clinical trials due to the unknown effects of unproven stem cell therapies.¹⁹⁰ This is a further risk for desperate patients who are seeking the latest advances in medicine and it may lead to delays in patients having access to proven beneficial therapies.¹⁹¹

The current advertising and provision of these therapies undermines the integrity of the medical profession.¹⁹² Current practices appear to breach a significant number of professional codes. The treatments also have the potential to take advantage of vulnerable patients who are exposed not only to unknown medical risk but also significant financial burdens. Such behaviour could very well erode the public perception of the medical profession.¹⁹³

The disciplinary system needs to respond in a manner that shows the regulation of health practitioners is effective to protect the public.¹⁹⁴ Failing to act to restrict the prescription of autologous stem cell therapies outside of clinical trials could also potentially discredit the entire promising field of stem cell medicine, impede the progress of legitimate clinical translation of stem cell therapies¹⁹⁵ and threaten Australia’s reputation of producing high-quality biomedical research.¹⁹⁶

¹⁸⁶ Tuch BE and Wall DM, “Self-regulation of Autologous Cell Therapies” (2014) 200 Med J Aust 196.

¹⁸⁷ National Health and Medical Research Council, n 130.

¹⁸⁸ Tuch and Wall, n 186 at 196; Elkin, n 106 at 692.

¹⁸⁹ Qiu, n 185; Lau et al, n 39; Zarzeczny A, Rachul C, Nisbet M and Caulfield T, “Stem Cell Clinics in the News” (2010) 28 Nat Biotechnol 1243.

¹⁹⁰ Qiu, n 185 at 792.

¹⁹¹ Qiu, n 185 at 792.

¹⁹² Chan, n 158 at 121.

¹⁹³ Elkin, n 106 at 693.

¹⁹⁴ Elkin, n 106 at 684.

¹⁹⁵ Taylor et al, n 179 at 48.

¹⁹⁶ Sipp, n 45 at 352

Greater oversight of autologous stem cell therapies in Australia is therefore required. While there may be some apprehension about regulating stem cell therapies on the grounds that this may stifle innovation or research and impair medical progress, careful regulation would avoid this problem (see summary of recommendations in Box 1).

BOX 1: Summary of recommendations

Recommendations

Bring autologous cellular therapies within the jurisdiction of the TGA and the Biologicals Regulatory Framework.
Educate health and medical practitioners.
Educate health consumers.
Enforce breaches of advertising standards.
Create a register of innovative therapies to enable assessment of innovative stem cell therapies prior to their clinical use.
Enforce professional standards through AHPRA, the HCCC in New South Wales and the Health Ombudsman in Queensland.

One alternative would be to bring autologous stem cell therapies within the jurisdiction of the TGA, thereby allowing use of the existing framework for the regulation of biologicals. If autologous stem cell therapies were to be included as a therapeutic good, they would also be subject to more stringent advertising standards by the TGA and ensure that there was adequate evidence to support clinical application. In particular, this would require reporting of any adverse events that do not have to be reported under the current framework for autologous stem cell therapies.

Another approach would be to enhance the education of health professionals about the evidence for, risks and costs of autologous stem cell therapies. (In this regard, it is worth noting that the NHMRC has already taken steps to increase information available to medical practitioners with the release of its guide to stem cell treatments.)¹⁹⁷ But while education of health practitioners is important, it is clearly inadequate, partly because these stem cell therapies are not refundable through Medicare and so do not cover patients who are referred to clinics by their usual medical practitioner or specialist, and partly because patients often self-refer, meaning that they often lack a sophisticated understanding of the risks and benefits of such therapies and have not had an opportunity to discuss the treatments with their usual carers.

Education and information should, therefore, also be targeted at consumers and patients to empower them to take responsibility for their health choices. Importantly, this should be communicated not only through “established” or traditional means of health communication, such as health departments and the NHMRC, but also through the print and online media, entertainment programs and social media. Whether any form of health education will reduce the appeal of these therapies is open to debate, as reports in the media warning of the dangers of unproven stem cell therapies appear to have had no impact upon the continued growth of stem cell clinics in Australia and internationally.¹⁹⁸ Nevertheless, media organisations that take advertising dollars from the private stem cell industry have an ethical duty to ensure that such advertising is not misleading and deceptive.

Enforcing the prohibition on unsubstantiated claims on websites and media appearances to sell stem cell therapies through consumer protection law and advertising regulation may also reduce misconceptions about the current efficacy of stem cell therapies. So far little seems to have been done to police this area and it may take a number of years to undo the already positive media coverage that currently surrounds stem cell therapies.¹⁹⁹

Another option would be to create a register of innovative stem cell therapies. Such a register might provide a mechanism for the comprehensive evaluation of new stem cell therapies prior to their translation into clinical practice, prevent the treatment of hundreds of patients without adequate

¹⁹⁷ National Health and Medical Research Council, n 130.

¹⁹⁸ National Health and Medical Research Council, “NHMRC Warns of the Risks Associated with Unproven Stem Cell Therapies in Australia and Overseas”, Media Release (19 December 2013); Aubusson, n 58.

¹⁹⁹ Zarzeczny et al, n 189 at 1245.

oversight, ensure the long-term follow-up of patients and enable the differentiation of legitimate from illegitimate innovation. This could be structured along the same lines of the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) established by the Royal Australasian College of Surgeons and funded by the Department of Health. This Register has been created to properly assess emerging surgical technologies and techniques.²⁰⁰ At the very least, a register would allow transparent scrutiny of the innovative medical technologies and interventions and facilitate informed public and professional debate about its merits.

Ultimately, the medical profession itself must take some responsibility for the probity and integrity of the profession and for ensuring that practices are not clinically and ethically questionable. While the most preferable means for ensuring this is respectful professional discourse and considered self-reflection, ultimately harder regulatory measures, including enforcement of codes of conduct and reporting to regulatory and professional authorities, such as APHRA, are necessary.

This article has shown that Australian regulators need to police these standards more thoroughly. If these standards are not policed there is a danger that they will become meaningless and serve only to undermine the integrity of the medical profession.

Ensuring accountability through appropriate regulatory mechanisms and effective enforcement are fundamental to the success of the health professional regulatory system and the removal of “dangerous” doctors not only protects the public but ensures trust in the medical profession and is an effective deterrent.²⁰¹

The New South Wales Stem Cell Network is currently in the process of developing a code of conduct for autologous somatic stem cell therapies, in conjunction with representatives of some of the clinics mentioned above, based on the Medicines Australia model that provides for self-regulation of the pharmaceutical industry (or at least companies that submit to self-regulation through Medicines Australia).²⁰² This code of conduct has four goals: practise evidence-based medicine; ensure fully informed consent is obtained; ensure that internationally accepted standards are adhered to in the manufacture of autologous cell products; and follow the AHPRA advertising standards.²⁰³

While laudable and ambitious, it is unclear how effective such a model of voluntary self-regulation would be. Some might argue that where this model has been used in the pharmaceutical industry it has functioned primarily to give a veneer of moral respectability and has had a limited impact in preventing and punishing some of the most egregious promotional and marketing activities.

It is unlikely that a voluntary code would genuinely achieve its aims. First, it is not possible for clinics to practise evidence-based medicine at present because there is no current evidence base for their treatments. Secondly, if these clinics were to adhere to AHPRA advertising standards then it is clear that they would need to overhaul their websites fundamentally – removing testimonials and suggestions of efficacy or clinical benefit, and declaring pecuniary and non-pecuniary interests. Thirdly, if they were to properly comply with each of the ethical and legal factors necessary for consent to be valid – then they would need to:

- acknowledge the limits of their clinical expertise;
- require interaction with experts in the diseases faced by the patients who seek their services;
- provide clear information to their patients about financial conflicts of interest; and
- consider how these therapies are currently not supported by high-level evidence of benefit and that long-term safety data is not yet available.

Given the lucrative nature of stem cell therapies such self-limiting behaviour is unlikely.

²⁰⁰ Royal Australasian College of Surgeons, “ASERNIP-S”, <http://www.surgeons.org/for-health-professionals/audits-and-surgical-research/asernip-s>; Maddern G, Boulton M, Ahern E and Babidge W, “ASERNIP-S: International Trend Setting” (2008) 78 ANZ J Surg 853; Chan, n 158 at fn 173.

²⁰¹ Elkin, n 106 at 691.

²⁰² Tuch and Wall, n 186 at 196.

²⁰³ Tuch and Wall, n 186 at 196.

Stem cell research and regenerative medicine hold great promise and have driven enormous volumes of research and medical innovation. But in the rush to replicate the extraordinary success of haematopoietic transplant and to establish new therapeutic alternatives for many diseases for which few effective treatments currently exist, the integrity of medical research and the medical profession should not be put at risk. Nor should the best interests of patients who are often vulnerable and desperate be put at risk. It is time that the problems of the private stem cell therapy industry in Australia were taken seriously.