



**Submission to the Therapeutic Goods Administration's  
Public Consultation – *Regulation of autologous cell and  
tissue products and proposed consequential changes to  
the classification of biologicals***

**5 October 2016**

**A/Prof Megan Munsie, Ph.D.**

Head, Education, Ethics, Law & Community Awareness Unit  
University of Melbourne  
Stem Cells Australia

**Professor Martin F Pera, Ph.D.**

Professor of Stem Cell Science  
University of Melbourne  
Walter and Eliza Hall Institute of Medical Research  
Florey Neuroscience Institutes  
Program Leader, Stem Cells Australia

Correspondence to MM at [megan.munsie@unimelb.edu.au](mailto:megan.munsie@unimelb.edu.au)

## Executive Summary

We welcome the opportunity to contribute to the TGA 2016 public consultation on the regulation of autologous cell and tissue products.

We believe that there is an urgent need for greater regulation of autologous cell-based interventions in Australia and we strongly recommend that the Therapeutic Goods Administration (TGA) remove from the Excluded Goods Order autologous cell therapies that are subject to more than minimal manipulation and intended for other than homologous use.

Almost all cell therapy remains experimental, and as such carries known and unknown risks which merit careful consideration and regulatory oversight, in order to protect the Australian public and overseas visitors from harm, and to ensure genuine efforts to translate promising stem cell research into clinical benefit are not stymied.

We support the proposed change in definition of minimal manipulation and modifications to the *Therapeutic Goods Order No. 1 of 2011* (the Order) whereby more than minimally manipulated autologous cell and tissue products would be regulated as biologicals under the *Therapeutic Goods Act* (Option 4). We would also recommend that the TGA incorporate a proviso regarding non-homologous use into Option 4 to remove any ambiguity regarding when an autologous cell or tissue product should be excluded from TGA oversight.

We recognize that under the current regulatory scheme, agencies apart from the TGA provide, in principle, oversight of autologous cell and tissue therapies. However, we believe the unbridled growth of Australian providers and clinics marketing unproven 'stem cell' treatments that we have observed and reported over the last five years clearly illustrates the current deficiencies in the Australian regulatory framework (which can only address transgressions of standards *post hoc*) and the challenge of enforcing those regulations that are in place.

The possibility of harm – physical, psychological and financial – to those who pursue unproven autologous interventions is real. The recent NSW Coroners Court findings<sup>1</sup>, relating to the death of a woman following complications from a unfounded autologous cell intervention for her dementia, highlight the reality of the situation and the need for “legal protection against the exploitation of severely and chronically ill people by purveyors of scientifically dubious ‘therapies’”.

We need a proactive and coordinated approach across the responsible Australian agencies rather than the current *ad hoc* measures only triggered by consumer or practitioner complaint after the fact and usually only limited to an individual practitioner.

We continue to reject the claims that all use of autologous cells represents medical practice rather than provision of Therapeutic Goods, and that greater regulatory oversight by TGA will inhibit medical innovation or delay the introduction of promising new cell-based interventions into clinical trial.

Responsible translation of stem cell research into clinical application in Australia and around the globe must be underpinned by scientific evidence. Failure to apply rigorous standards to the introduction of unproven treatments has opened the door in Australia to a growth in unethical, exploitative, and potentially hazardous practices. Immediate action is required by TGA and other Australian regulators to curb this activity.

---

<sup>1</sup> NSW Coroners Court Findings – Inquest into the death of Sheila Drysdale (15 July 2016); <http://www.coroners.justice.nsw.gov.au/Documents/Findings%20Drysdale.pdf>

## **Who we are**

This submission has been lodged in our capacity as Program Leader (M.F.P.) and Director of Ethics, Education, Law, and Community Awareness Unit (M.M.) for Stem Cells Australia, the Australian Research Council Special Research Initiative in Stem Cell Science. We, and our colleagues in Stem Cells Australia, are internationally regarded authorities in stem cell science, regenerative medicine, and public policy matters related thereto. Ethics, education and public policy are indeed important aspects of the Stem Cells Australia mission, as mandated by our Funding Agreement with the Australian Research Council. In fulfilling our public outreach mission, we frequently receive and respond to enquiries regarding stem cell research and availability of possible therapies<sup>2</sup>.

In terms of expertise, M.F.P is Professor of Stem Cell Sciences at The University of Melbourne, the Florey Institute of Neuroscience and Mental Health, and the Walter and Eliza Hall Institute for Medical Research. He serves as Program Leader for Stem Cells Australia, the Australian Research Council Special Research Initiative in Stem Cell Science. His research interests include the cell biology of human pluripotent stem cells, early human development, and germ cell tumours. Pera was among a small number of researchers who pioneered the isolation and characterisation of pluripotent stem cells from human germ cell tumours of the testis, work that provided an important framework for the development of human embryonic stem cells. His laboratory at Monash University was the second in the world to isolate embryonic stem cells from the human blastocyst, and the first to describe their differentiation into somatic cells in vitro. He has provided extensive advice to state, national and international regulatory authorities on the scientific background to human embryonic stem cell research.

M.M. is a researcher based in the Department of Anatomy and Neuroscience at The University of Melbourne where she combines her extensive technical expertise in stem cell science with an understanding of the complex ethical, social and regulatory issues associated with stem cells in research and in the clinic. Munsie is a member of several multi-disciplinary international research teams exploring the regulations of, and community expectation in, stem cell therapy. In particular, she has investigated community attitudes in relation to unproven stem cell treatments offered abroad and in Australia. She is a co-author of the recently published International Society for Stem Cell Research (ISSCR) Guidelines For Stem Cell Research and Clinical Translation, a member of ISSCR Ethics Committee, the previous Chair of the ISSCR Taskforce On Public Education; and Chair of the Australasian Society for Stem Cell Research's Policy, Ethics and Translation sub-committee.

---

<sup>2</sup> Stem Cells Australia has responded to more than 1,800 enquires since late 2011.

## Our submission

In this submission we address the specific questions raised in Chapter 2 and Chapter 3 (Part A) of the TGA 2016 Discussion Paper and provide an analysis of each of the four regulatory options canvassed. We also address the extent of the problems arising out of the current regulatory framework, and provide comment about terminology and process involved in the proposed regulatory reform.

**We call on TGA to take immediate action to provide more effective oversight of this issue so that the Australian public and overseas visitors are protected from harm, and to ensure genuine efforts to translate promising stem cell research into clinical benefit are not stymied. We believe Option 4, when coupled with the new definition of minimal manipulation, and subject to provisions relating to homologous use<sup>3</sup>, would enable this objective.**

Furthermore, a **proactive and coordinated approach across all responsible Australian agencies should be implemented** to avoid the current *ad hoc* regulatory measures which are only triggered by consumer, their family or practitioner complaint after the fact and usually only limited to an individual practitioner.

## Response to specific questions raised in the discussion paper

### 1. Does Chapter 2 (Part B) adequately describe ‘the problem’?

As stated in our 2015 submission to the TGA public consultation on the regulation of autologous stem cell therapies<sup>4</sup>, we have long been concerned about the provision of unnecessary and unproven autologous interventions marketed as ‘stem cell treatments’ by Australian practitioners and/or clinics that has been enabled by the broad exclusion of autologous cells and tissues from TGA oversight<sup>5</sup>.

While Chapter 2, Part B of the 2016 TGA Consultation Paper provides an adequate summary the extent of the problem, there a several additional points that we believe require further clarification and consideration.

### Quantification of the problem

As stated in our 2015 submission to TGA, the current regulatory framework – in particular the blanket exemption of all autologous cell therapies from TGA oversight – has manifestly failed as a mechanism to foster development of novel and innovative cell and tissue therapies, and has instead encouraged the proliferation of clinics marketing unproven and unfounded treatments to the public, in the absence of any sound evidence supporting their safety or efficacy.

The last five years have seen an exponential growth in clinics and individual doctors providing unproven and unfounded autologous interventions. We have documented the growth of this sector from two providers in 2011 to over 40 at 14 clinics in 2014<sup>6</sup>. A recent study of the global distribution of businesses marketing ‘stem cell’ interventions showed that Australia had the fifth highest number of clinics, whether ranked per country or per capita, with 19 practices identified<sup>7</sup>. We deem the actual

---

<sup>3</sup>TGA definition of ‘Homologous use’: The repair, reconstruction, replacement, or supplementation of a recipient’s cells or tissues with a biological that performs the same basic function in the recipient as in the donor.

<sup>4</sup> Munsie & Pera (2015) Available via <http://www.stemcellsaustralia.edu.au/AboutUs/Document-Library/SCA-Documentation.aspx>

<sup>5</sup> Pera & Munsie (2012) Submission to the NHMRC Public Consultation – Stem Cell Treatments [<http://www.stemcellsaustralia.edu.au/AboutUs/Document-Library.aspx>; Munsie & Hyun (2014) A question of ethics: Selling autologous stem cell therapies flaunts professional standards. *Stem Cell Research* 13, 647–653.

<sup>6</sup> Munsie & Pera (2014) Regulatory loophole enables unproven autologous cell therapies to thrive in Australia. *Stem Cells Dev* 23 (Suppl 1):34-8.

<sup>7</sup> Berger et al (2016) Global distribution of businesses marketing stem cell-based interventions. *Cell Stem Cell* 9(2):158-162.

number to be likely more than twice that figure, according to websites we have identified during a recent audit or have had reported to us by members of the public.

With no formal monitoring mechanism in place, it remains impossible to accurately quantitate the extent of the 'industry', the number of Australian and overseas patients 'treated' and the extent of adverse events (or for that matter, benefit). However, there is sufficient evidence to lead the NSW Coroners Court to describe the current state of affairs as bearing "the troubling hallmarks of 'quack' medicine: desperate patients, pseudo-science and large amounts of money being charged for unproven therapies"<sup>1</sup>.

### ***Extensive ex vivo manipulation and high risk procedures allowed under current exclusion***

While it is often difficult to ascertain from publically available information exactly how the cells are prepared, we are aware of a range of autologous interventions marketed by Australian clinics and individual practitioners from the administration of resuspended adipose-derived stromal vascular fraction<sup>8</sup> (SVF) administered via intra-articular injection for various musculoskeletal conditions; to intravenous (IV) delivery of a variety of cellular products. These include cultured mesenchymal stromal cells derived from lipoaspirates, to cells from blood that have been extensively manipulated.

For example, one company<sup>9</sup> claims to obtain blood cells from patients and, through an *in vitro* procedure where the cells are expanded and converted to what they term multi-lineage potential cells (implied to be 'pluripotent' cells) over a period of around five days. The cells are then administered to the patient via intravenous, intra-articular or dermal injections. From information on the company's website, or information provided to prospective patients by representative of a company claiming to be the local outlet<sup>10</sup>, it is implied that:

- the treatment available for a wide range of conditions and has shown benefit and is safe,
- the company have treated over 300 patients including many from abroad,
- the cost is routinely \$100,000 AUD but the fee can be discounted under certain circumstances, and
- two Australian doctors are involved (although neither have specialist credentials in the many areas of medicine for which the treatment has been promoted).

To our knowledge no preclinical data concerning the treatment protocol/technology provided by this company has been published in a peer-reviewed journal, and the treatment is not being offered in the context of a registered clinical trial nor has it to our knowledge been the subject of one. As described, such *ex vivo* manipulation of blood cells to enhance their differentiation potential (if indeed this is actually achieved as advertised) would considerably increase the potential safety hazards of this autologous therapy, particularly as it appears there is no attempt to direct differentiation of the cells prior to administration, nor any acknowledgement of the need to monitor patients or provide for their follow-up care.

Such extreme manipulation should require the highest level of manufacturing oversight by the TGA (i.e. Class 4) but due to the current Excluded Goods Order the company's activities fall outside the remit of the TGA.

We first raised our concerns about a company operating on the same premises, and with similar if not identical technology, with the TGA and several other agencies in

---

<sup>8</sup> **SVF** is a heterogeneous mixture of cells derived from adipose tissue or liposuction aspirates following collagenase digestion or other mechanical disruption and centrifugation. Pelleted cells include stromal cells, vascular endothelial, leucocytes and erythrocytes with adipocytes assumed to be separated and discarded in the supernatant during preparation.

<sup>9</sup> www.asctreatment.com

<sup>10</sup> Autologous Stem Cell Research Organisation Pty. Ltd. ACN 613283800

late December 2014, and yet the company continues to advertise and market these services and presumably treat Australian and overseas patients.

We have also expressed concerns to regulators over a Victorian cosmetic clinic that was offering IV and intrathecal injection of autologous liposuction derived cells for numerous conditions including dementia and other neurological disorders. While the cells in this same day procedure may have been subject to minimal *ex vivo* manipulation, the route of administration is clearly of concern as it leads to significantly elevated risks associated with the intervention. The risks of such an intervention are particularly troubling, since as in the Drysdale case, it is quite unlikely that the cells would provide any therapeutic benefit for patients with these conditions. Although we raised this issue with relevant Australian authorities in June 2015, attracting some media interest and concern<sup>11</sup>, it was not until a second media enquiry some 13 months later that the clinic withdrew the promotional material from their website<sup>12</sup>.

### **Marketing tactics and challenge of triggering an investigation**

We and others have long been concerned about direct to consumer advertising and the false and misleading claims made by Australian providers and clinics<sup>13</sup>. While we recognize that TGA has limited scope to intervene under the *Therapeutic Goods Act* (due to the current broad exclusion), we have been frustrated by the lack of action by the Australian Health Practitioners Regulatory Agency (AHPRA), state regulatory bodies and the Australian Competition and Consumer Commission (ACCC).

As scientists it is not our role to undertake investigations into the operations of providers of unproven treatments. However due to our position as a leading source of authoritative opinion on stem cell research, many Australian patients and/or their family members, friends or doctors contact us for information about stem cell research, and in doing so inform us of dubious practices. We have an obligation to bring such concerning practices to the attention of the appropriate authorities. While we have done so on many occasions, and arguably are one of the stakeholders that triggered the current and previous TGA public consultations on this matter, in reality we have seen little effective action to curb these exploitative activities. Rather we have observed an unfettered expansion of Australian clinics and providers of autologous cell interventions.

In part this lack of action by the authorities is due to a lack of formal complaints by individuals involved to trigger investigations. Although we frequently encourage patients and their families who speak to us to contact appropriate authorities (e.g., ACCC, TGA, AHPRA or state regulators), few appear to take action. This is not due to a lack of a justifiable grievance, but is we believe a consequence of a number of factors that inhibit victims from taking their complaints forward to regulatory authorities.

To illustrate this point we have included three case studies in the attached Appendix to this submission. These cases demonstrate the challenge of relying on consumer driven complaints as a marker of unacceptable or unsatisfactory practices on the part of Australian cell therapy providers. Central to two of these cases was the high regard in which the provider of the unproven and unfounded intervention was held by those involved. The current direct-to-consumer advertising, coupled with lack of independent ethical or peer oversight of these private commercial practices, means

---

<sup>11</sup> McArthur (2015) Rogue clinics furore *Herald Sun* (7 July); Editorial (2015) Stemming bad practice *Herald Sun* (7 July).

<sup>12</sup> See ABC Radio National Background Briefing (2016) Selling stem cell promise (aired 17 July; <http://www.abc.net.au/radionational/programs/backgroundbriefing/2016-07-17/7621838>)

<sup>13</sup> Munsie & Pera (2014) Regulatory loophole enables unproven autologous cell therapies to thrive in Australia. *Stem Cells Dev* 23 (Suppl 1):34-8; McLean et al (2014) The emergence and popularization of autologous somatic cellular therapies in Australia: therapeutic innovation or regulatory failure? *J Law Med* 22(1):65-89; Berger et al (2016) Global distribution of businesses marketing stem cell-based interventions. *Cell Stem Cell* 9(2):158-162.

that the inherent conflict of interest at play (given the same doctor who sells the treatment also oversees the consent process) is left unchallenged.

Indeed research on stem cell tourism documented that many Australians who have traveled overseas for unproven stem cell interventions are not dissatisfied, even though they may not have experienced the health benefits that they had hoped for<sup>14</sup>. The opportunity to do something, and in particular find a doctor who was prepared to help them, was seen as highly beneficial. Clearly, patients and their family are in a vulnerable situation where they are grateful for access to any form of treatment, however dubious it may be.

In the absence of regulatory oversight in Australia, patients or indeed even their physicians have little or no basis on which to reach an informed opinion on autologous cell therapies. The precise nature of the intervention and its supposed therapeutic outcome is often vague, there is often no scientific evidence beforehand to support claims of safety or efficacy, no objective outcome measures are in place to assess possible therapeutic effects, and there is no provision for monitoring adverse events.

Other significant factors restrict the reporting of complaints: the patients are facing chronic health problems, they often are suffering substantial pain and disability, and they may simply lack the energy or resources to lodge a formal complaint.

### **Additional international guidelines**

Since our 2015 submission, the ISSCR has published a revised version of their Guidelines For Stem Cell Research And Clinical Translation<sup>15</sup>. These guidelines were updated to in part address the ongoing marketing of unproven interventions alleged to involve stem cells. Specifically, the 2016 ISSCR guidelines state that the application of stem cell-based interventions “outside of formal research settings should be evidence-based, subject to independent expert review, and serve patients’ best interests”. Furthermore, they emphasise that it should be considered “a breach of professional medical ethics to market and provide stem cell-based interventions to a large patient population prior to rigorous and independent expert review of safety and efficacy”. Current practice in Australia is in breach of these guidelines, and also those recently published by the International Cell Therapy Society<sup>16</sup>, as noted in the 2016 TGA consultation paper.

The positions of the leading international scientific bodies on unproven cell therapies are consistent and unequivocal. It is time we take notice of these views, and act to bring Australia into alignment with other jurisdictions and recommendations of leading international learned scientific and research organisations.

### **Risk to Australian industry**

As stated in our 2015 submission, it is not just individual medical practitioners who are seeking to meet the demand for ‘stem cell’ treatments from Australian and overseas patients. It appears that overseas companies are moving to Australia to take advantage of our more lenient regulatory environment. At least one of these companies appears to be offering remedies that rely on extensively manipulated cells that would be considered to carry the highest level of risk under the Biologicals Framework if the autologous exclusion was not in place.

---

<sup>14</sup> Petersen et al. (2014) Therapeutic journeys: the hopeful travails of stem cell tourists. *Social Health Illn.* 36(5):670-85; Seear et al. (2010) Hopeful Journeys: Experiences of Stem Cell Treatments Offered Outside Australia.

[[http://www.industry.gov.au/industry/IndustrySectors/nanotechnology/Publications/Documents/Hopeful\\_Journeys\\_Stem\\_Cell\\_Treatment.pdf](http://www.industry.gov.au/industry/IndustrySectors/nanotechnology/Publications/Documents/Hopeful_Journeys_Stem_Cell_Treatment.pdf)]

<sup>15</sup> Available via <http://www.isscr.org/home/publications/2016-guidelines>

<sup>16</sup> Dominici et al. (2015) Positioning a Scientific Community on Unproven Cellular Therapies: The 2015 International Society for Cellular Therapy Perspective *Cytotherapy* 17: 1663-1666.

There is of course genuine clinical research of the highest standard being conducted in Australia, and the environment that Australia provides for legitimate clinical trials attracts significant outside investment. If the current expansion of clinics marketing unproven cell therapies is allowed to continue unchecked, there is substantial reputational risk to our biomedical enterprise in this emerging sector, which many consider will become the fourth pillar of healthcare, along with drugs, devices, and biologicals.

At present there appears to be little barrier to opening a 'stem cell' business in Australia, and we risk becoming a safe harbour for unscrupulous providers of cell therapies. It is important to note that, far from encouraging the introduction of innovative breakthroughs, the current regulatory framework has fostered the unfettered propagation of unfounded therapies that are most often derivatives of similarly dubious interventions, available wherever providers can operate free of regulatory constraint<sup>17</sup>.

## **2. Assessment of proposed regulatory options**

We believe the only option that will adequately curb the growth of Australian commercial clinics and health practitioners providing unproven autologous stem cell interventions would be a **modified version of Option 4** together with a proposed change in the definition of minimal manipulation. To remove ambiguity and to make the regulation of autologous cellular products consistent with those from allogeneic sources, we would also urge the TGA to incorporate 'homologous use' into Option 4.

None of the other options will limit the hazards associated with the expansion of clinics offering unproven and unfounded cell therapies. Option 1 is essentially the status quo with risk of further expansion and is clearly unacceptable. Option 2 merely bars direct advertising of products to consumers. Though such a ban would be a step forward, it is predictable that this restriction will be easily circumvented, by providers advertising medical services (outside of TGA authority) instead of specific products, or by marketing to other clinicians, such as those clinics operating under a franchise model do presently. Option 3 captures procedures involving more than minimal manipulation but does not address the issue of non-homologous use, and describes a complex, bespoke solution that raises substantial challenge in terms of enforcement (as noted in the TGA Consultation Paper). As we have indicated above, procedures involving minimal manipulation but non-homologous use carry risks associated with introduction of cell products into heterotopic sites, where their presence may lead to obstruction or occlusion of vital tissues, inappropriate physiological activity, or formation of abnormal growths. Importantly Options 1-3 are powerless to prevent the provision of unproven autologous cell therapies for conditions in which they are most unlikely to prove beneficial, such as the administration of adipose cells to treat advanced dementia. Even a minimal level of risk is not justified in such a scenario.

We have outlined below our views regarding key terms and regulatory options canvassed in the 2016 TGA consultation paper.

### **2.1 Term definitions**

#### **Human cells and tissue products for autologous use**

We welcome the position taken in the current consultation paper were the issue is more broadly autologous human cells and tissues rather than 'stem cells'. Although frequently advertised as 'stem cells', it is unclear whether many of the interventions on offer actually contain stem cells in the administered product as the cellular content of the preparation is not often defined and certainly not independently verified by

---

<sup>17</sup> Turner & Knoepfler (2016) Selling stem cells in the USA: Assessing the direct-to-consumer industry. *Cell Stem Cells* 19(2):154-7; Berger et al. (2016) Global distribution of businesses marketing stem cell-based interventions. *Cell Stem Cell* 9(2):158-162.

accredited laboratories. Furthermore, while some clinics may describe their products in more general terms such as SVF and not specifically state that 'stem cells' are administered, the fact that the clinic has 'stem cells' in its title provides their clients with an expectation that they are accessing state-of-the-art stem cell-based interventions.

With any cellular therapeutic, proper risk assessment and risk control must consider the provenance of the cells used in the preparation, the steps in the manufacture of the product, its mode of administration, and its intended use. There are no scientific or medical grounds to exempt therapeutics derived from autologous 'stem cells' from these considerations.

### ***Under the supervision of medical/dental practitioner***

While we recognise that the exclusion needs to be broadened to dental practitioners so that autologous cells and tissues currently used in a number of recognised dental procedures are not unduly restricted by changes to the Excluded Goods Order, we warn that in the absence of much stricter regulation of autologous cell therapy, the inclusion of dental practitioners in the revised orders could actually exacerbate the current problem.

We are aware of at least one Australian dentist who has previously offered autologous 'stem cell' infusions from peripheral blood as part of their dental care and now appears to promote 'regenerative dentistry'<sup>18</sup>. Furthermore, by expanding the exclusion to dentists, it is possible that such a change will herald a new 'tooth bank' industry in Australia. So called tooth banks promote a service to parents that comprises storage of stem cells derived from their child's deciduous teeth<sup>19</sup>. Although providers draw a comparison with cord blood banks, in fact there are no established clinical applications of stem cells from deciduous teeth unlike cord blood. Therefore, many experts feel these banks are exploiting parental concerns for their child's future health.

### ***Single course of treatment***

We are aware that several of the Australian providers of autologous 'stem cell' interventions offer to bank the patient's cells for future administration. In addition to the risks associated with the unwarranted and inappropriate use of 'fresh' autologous cells, the addition of banking and subsequent thawing and administration of cells raises another level of concern.

These additional services could lead to unjustified additional charges to patients. More importantly, in the absence of regulatory standards and inspection and audit procedures, poorly controlled cryopreservation and banking practices may lead to contamination of the product with adventitious agents or toxins, loss of cell viability, or mislabeling and administration of the product to the wrong individual. Furthermore, as described in case study 2 in the Appendix, patients whose cells have been banked often feel under additional pressure to complete therapies, even if they are having second thoughts. We recently have also spoken to a patient who contacted us after she received a call from a clinic that she had previously visited for SVF treatment for a chronic illness. She was told that unless she was able to get to the clinic (from interstate) and the money to pay the additional fee, her cells would be discarded. Although she felt that the original IV infusion of SVF had not provided the hoped for benefit, she did not want to "miss out" on a possible chance. There was also an element of pressure given the clinic representative implied that there had

---

<sup>18</sup> From correspondence with patient and on the clinic's then Facebook page: <https://www.facebook.com/2nRichHolisticWellnessandVitalityCentre/info>. Current website states that regenerative dentistry uses concentrated growth factors (CGF) derived from your own blood. [http://www.laserandholisticdental.com/about/dental-treatments/#regenerative\\_dentistry](http://www.laserandholisticdental.com/about/dental-treatments/#regenerative_dentistry). It is unclear what evidence underpins this claim.

<sup>19</sup> Overseas companies are already offering to collect and store children's teeth in order to "save your child's stem cells for the future" eg. <http://www.store-a-tooth.com>.

been a change in the “laws” that meant that the cells had to be either used or discarded and she had limited time to make a decision. While this is admittedly an anecdotal report, it illustrates the unchecked business model and opportunity for exploitation currently enabled by the Australian regulations. Why should the fact that the cells are intended for autologous use preclude due diligence and independent oversight from authorities?

### ***Human cell and tissue products that form part of established medical practice***

We are aware of the following recognised medical interventions that use autologous cells and tissue and which should continue to be excluded under 4q of the Excluded Goods Order. We would suggest that these uses would fulfill the criteria of minimal manipulation and homologous use, and/or established medical procedures:

- i. skin grafts inclusive of sprayed and/or cultured skin;
- ii. skull flaps;
- iii. vascular conduits;
- iv. transplantation of pancreatic islet cells;
- v. bone grafts;
- vi. blood to seal CSF leaks and re-infused during surgery;
- vii. cosmetic/reconstructive procedures utilising skin, bone and fat transfer.

### ***Mechanisms for implementing options***

Given the ambiguity over the last five years, any change that will provide greater legal certainty is to be encouraged. We would therefore support the TGA changing the mechanism by which certain ‘goods’ are excluded under the *Therapeutic Goods Act* making it a Ministerial Order.

## **2.2 Assessment of proposed Options**

We believe the only option that will adequately curb the growth of Australian commercial clinics and health practitioners providing unproven autologous cell-based interventions would be Option 4 together with a proposed change in the definition of minimal manipulation. Furthermore, to remove ambiguity and to make the regulation of autologous cellular products consistent with those from allogeneic sources, we would also urge the TGA to incorporate ‘homologous use<sup>20</sup>’ into Option 4. We have provided a more detailed assessment of each option below.

We also note that there is likely to be a direct financial impact on providers if any option beyond Option 1 is adopted by TGA. We do not wish to impose any unwarranted financial barrier for Australian companies and health practitioners conducting legitimate clinical research in an effort to ascertain the safety and efficacy of novel autologous cell-based interventions, and there is room for discourse around reviewing and expediting the approval process for these therapies. However, we do not believe that costs associated with compliance or regulatory review should justify delaying or reducing the much needed measures to protect Australian patients and overseas visitors from unproven, unnecessary procedures and the risks thereof.

While there is much discussion internationally about mechanisms to accelerate novel cell therapy product development through changes to regulatory approval processes, there is no suggestion that abandoning such regulation altogether (essentially the status quo for autologous cell products in Australia) is the answer to the current challenges. The mere promise of investment by entrepreneurial health practitioners or businesses should not justify unregulated provision of unproven and unfounded cell therapies, which as we have noted above, are in general devoid of innovation, lacking in scientific basis, and of dubious benefit to patients.

---

<sup>20</sup> TGA definition of ‘Homologous use’: The repair, reconstruction, replacement, or supplementation of a recipient’s cells or tissues with a biological that performs the same basic function in the recipient as in the donor.

**Option 1: Status quo and extend to dental practitioners**

**UNACCEPTABLE.** This option would allow unfettered growth of an Australian industry providing non-evidence based, unnecessary medical procedures that risk patient physical and psychological health. Rather than address the ‘problem’ as described in Chapter 2 (Part B) of this consultation paper, this option is likely to further exacerbate it by allowing dental practitioners to engage in provision of inappropriate cell therapies. As we have seen over the last five years, standards required by AHPRA, ACCC and relevant state or territory agencies have not impeded the growth of the sector. Furthermore, any action by regulators is only triggered after the event, impacts solely on the individual practitioner or company involved, and usually requires those involved to make a direct complaint (which as we have outlined earlier may often not occur due to a complex range of reasons).

**Option 2: Maintains existing exclusion, but extends to dental practitioners and blocks direct-to-consumer advertising of ‘products’**

**UNACCEPTABLE.** While we welcome any move to restrict advertising of unproven interventions, we are concerned that this change alone would have minimal impact on reducing the potential exposure of patients and their family and friends to information about unproven treatments. The ban would relate only to autologous cell-based ‘products’ and not to promotion of any services by clinics or health practitioners (such as stem cell treatments or regenerative or “rejuvenative” therapy), which are outside of the scope of the TGA. While such services are already subject to oversight from AHPRA and ACCC, this has not proved to be a barrier to business for Australian clinics. For example, in the NSW Coroners Court Report into the death of Sheila Drysdale, it is noted that the patient’s husband first became aware of Macquarie Stem Cells after hearing a radio advertisement in 2013. Several Australian clinics have also featured on TV and radio programs<sup>21</sup> where the Australian medical practitioners have touted health benefits in the absence of support by recognised evidence. We agree that advertising material may be provided through routes that are difficult for the TGA to monitor, such as via brochures and signage, and we would also point out that many patients considering unproven treatments abroad rely on word-of-mouth endorsement from past patients<sup>22</sup>. A ban on advertising of products alone will not curb the growth of these practices.

**Option 3: Maintains existing exclusion, but extends to dental practitioners, blocks advertising of ‘products’ for minimal manipulated but increased ‘intermediate level of regulation’ for products that involve more than minimal manipulation reflecting level of potential risk**

**UNACCEPTABLE:** We do not support the complex, ‘bespoke’ solution. There is no sound justification for regulating more than minimally manipulated autologous biologicals in a different way to how allogeneic products are regulated under the *Therapeutic Goods Act*. While each of the five separate requirements proposed in this option may partially address risks associated with advertising, notification, manufacturing and reporting, we echo the concerns raised by TGA in relation to the potential challenges of enforcement. This option will lead to further ambiguity particularly around adverse event reporting. If goods are not listed on the ARTG or subject to requirements for clinical trials prior to approval, there is no requirement to define expected adverse events and therefore no clear trigger to report such events to TGA. Furthermore, this option assumes the medical or dental practitioner has

<sup>21</sup> 2GB Afternoons with Luke Grant featuring interview with Dr Ralph Bright, Macquarie Stem Cells (and response to caller enquiries about stem cell treatment; 14 April 2014); Controversial treatment to ease the pain of osteoarthritis *A Current Affair* (29 August 2014)

<http://aca.ninemsn.com.au/article/8898361/controversial-treatment-to-ease-the-pain-of-osteoarthritis-sufferers>; Arthritis Stem Cell Treatment *Today Tonight* (24 June 2013)

<http://www.todaytonightadelaide.com.au/stories/arthritis-stem-cell-treatment>

<sup>22</sup> Petersen et al. (2014) Therapeutic journeys: the hopeful travails of stem cell tourists *Social Health Illn.* 36(5):670-85.

systems in place to allow for careful monitoring and reporting of adverse events; few of the clinics currently in operation would appear to engage in these activities.

**Option 4: Maintains existing exclusion, and extends to dental practitioners, but only where autologous products are not advertised directly to consumers and not more than minimally manipulated**

**ACCEPTABLE WITH FURTHER AMENDMENT:** This is the only option that provides sufficient safeguards to address risks associated with unproven autologous cell-based interventions. To avoid ambiguity and to bring the Australian regulations into alignment with international best practice, we would also suggest that the TGA amends Option 4 with the addition of 'and for homologous use' as outline below:

**Excluded Goods Order 4g:**

**Human cell and tissue products:**

- a. for autologous use, under the supervision of a medical/dental practitioner, as part of a single course of treatment, would be excluded from TGA regulation only if the product is:
  - i. not advertised directly to consumers; ~~and~~
  - ii. not more than minimally manipulated; **and**
  - iii. **for homologous use.**
- b. that are more than minimally manipulated or otherwise do not meet the exclusion criteria (i.e. not for autologous use, not under the supervision of a medical/dental practitioner, **not for homologous use**, not part of a single course of treatment or advertised) would be regulated under the TG Act in the same way as any other biological in the applicable class.

### **2.3 Revised definition of minimal manipulation**

We support the proposed modification of the definition of minimal manipulation in the classification of biological but suggest that without the inclusion of 'homologous use' into the revised wording of the Excluded Goods Order the current regulatory problem will not be fully addressed. While we agree that how the cells are processed needs to be linked to the intended clinical function of the product, it may be difficult to demonstrate that the biological characteristics, physical function or structural properties have been altered relative to the intended use. We suggest that to avoid ambiguity, and fully address the current problem, TGA consider adding 'homologous' to the Excluded Goods Order as outlined above.

### **3. Recommendation**

We call on **TGA to take immediate action to provide more effective oversight of this issue** so that the Australian public and overseas visitors are protected from harm, and to ensure genuine efforts to translate promising stem cell research into clinical benefit are not stymied. **We believe Option 4, when coupled with the new definition of minimal manipulation, and subject to provisions relating to homologous use, would enable this objective.**

Furthermore, **a proactive and coordinated approach across all responsible Australian agencies should be implemented** to avoid the current *ad hoc* regulatory measures which are only triggered by consumer, their family or practitioner complaint after the fact and usually only limited to an individual practitioner.

The positions of the leading international scientific bodies on unproven cell therapies are consistent and unequivocal. **It is time we take notice of these views, and act to bring Australia into alignment with other jurisdictions** and recommendations of leading international learned scientific and research organisations.

## APPENDIX

The following cases illustrate different reasons why formal complaints were not made to Australian authorities after what can only be described as less than satisfactory experiences.

### CASE STUDY 1:

The unfortunate death of Sheila Drysdale in 2013, following complications of the liposuction procedure used to obtain the autologous cells for her dementia treatment, has recently been extensively reviewed by NSW Deputy State Coroner HCB Dillion<sup>23</sup>. As outlined in his findings, the death was due to a “cluster of errors” of which the question of informed consent was “particularly complex, ambiguous and disconcerting”.

Due to her condition, Mrs Drysdale lacked the capacity to provide consent, which was therefore provided by her husband on her behalf. Understandably, Mr Drysdale was desperate to find a treatment to help his wife. According to an ABC Radio National *Background Briefing* report<sup>24</sup>, Mr Drysdale emailed the doctor thanking him for agreeing to try and help “which is gratefully accepted on the basis of no guarantees of success” prior to the procedure. Despite the dire outcome following the questionable intervention, the Coroner’s Report notes that Mr Drysdale “bears him [the doctor who performed the intervention] no ill-will”. Further commenting to *Background Briefing* that “Had Sheila survived that night and not bled to death, we may have seen something very positive”.

This case highlights the complex patient/guardian-doctor relationship that may make lodging a formal complaint to authorities unlikely.

### CASE STUDY 2:

As part of a sociological study of stem cell tourism<sup>25</sup> - which captured the experience of Australians who sought, or contemplated seeking, experimental stem cell interventions at home or abroad - one patient described her unsatisfactory experience regarding receiving autologous stem cell treatment for a chronic condition.

Her dissatisfaction stemmed from:

- a belief that she had not been effectively anaesthetised during liposuction procedures to extract stem cells from fat, reporting experiencing extreme pain;
- frustration that the treating doctor (a cosmetic surgeon) refused to stop the procedure in spite of repeated requests;
- lack of information about the liposuction procedure including that it may be painful;
- concern that stem cells were not administered correctly into sites of injury, and
- lack of information/consent about the storage of her ‘stem cells’ for future use and the associated costs (around \$2,000) with having a procedure to have the cells subsequently administered.

---

<sup>23</sup> NSW Coroners Court Findings – Inquest into the death of Sheila Drysdale (15 July 2016; <http://www.coroners.justice.nsw.gov.au/Documents/Findings%20Drysdale.pdf>)

<sup>24</sup> ABC Radio National Background Briefing (2016) Selling stem cell promise (aired 17 July; <http://www.abc.net.au/radionational/programs/backgroundbriefing/2016-07-17/7621838>).

<sup>25</sup> Australian Research Council funded project High Hopes, high risks?: A sociology study of stem cell tourism [<http://artsonline.monash.edu.au/research-showcase/high-hopes-high-risk-a-sociological-study-of-stem-cell-tourism/>]

However, when reflecting on this experience, the patient remained supportive of her treating doctor and did not seek to lodge a formal complaint. She specifically mentioned that she was thankful as the doctor provided the treatment at a lower rate than other patients, as he knew she had difficulty paying (reducing fee from \$10,000 to around \$3,000). She also didn't want to jeopardise future treatment and/or her relationship with the doctor.

A full report of this case is included in *Stem cell tourism and the political economy of hope*<sup>26</sup> (Petersen et al.; Palgrave Macmillan *in press*).

### **CASE STUDY 3:**

Stem Cells Australia was recently approached by a family who were concerned about the aggressive and they believed in appropriate marketing practices associated with an Australian clinic.

In this case, the patient had identified a clinic offering stem cell treatment in Queensland via an internet search and then made contact with a representative before electing to visit the clinic ahead of making a final decision about treatment. The patient suffered from multiple medical complaints, the most troubling being severe pain relating to longstanding musculoskeletal conditions.

Following their visit, where they discovered the company representative used an alias, the patient and his wife were bombarded with emails that:

- make undocumented claims regarding the potential benefits (and safety) of the unproven treatment;
- offer significant discounts on the therapy then threatening to withdraw the offer if full or part payment were not forthcoming;
- suggested to the patient that he would be missing a unique opportunity to reverse his condition unless he immediately availed himself of the treatment;
- provided no information on possible risks of the treatment or the possibility that it might fail to yield any benefit, and
- made repeated demands for down payment prior to provision of medical services.

The patient was told that the treatment was usually \$100,000 (which is what overseas clients apparently pay) but available for him for a short time for \$44,000.

In addition to seeking clarification about whether stem cells were a proven treatment for this condition, the family were initially intent on lodging a formal complaint and contacting journalists to raise awareness about these concerning practices so that others would not be subjected to such harassment and potentially to financial loss.

With the family's permission Stem Cells Australia lodged a formal complaint to various authorities<sup>27</sup>, including ACCC, about the false and misleading marketing practices in which this company and its representatives appeared to be engaged in.

However, once this was achieved, and media alerted, the family decided not to formally proceed with a complaint nor participate in any media coverage<sup>28</sup>. Understandably they wanted to concentrate on supporting the patient, who was not doing well, and also to avoid any further engagement with the Company or its representatives.

---

<sup>26</sup> MM is one of the co-authors of this book.

<sup>27</sup> Lodged with ACCC and Office of Queensland Health Ombudsman on 1 September 2016. AHPRA and TGA were also formally involved of this disturbing example.

<sup>28</sup> This case was the focus of an ABC 730 story by Louise Milligan *Would you buy stem cell treatment from this man?* [aired 21 September 2016; <http://www.abc.net.au/news/2016-09-21/stem-cell-marketer-referred-to-police-over/7866526>]