



THE AUSTRALASIAN COLLEGE OF DERMATOLOGISTS

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**Biological Science Section
Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606**

Dear Sir/Madam,

On behalf of The Australasian College of Dermatologists, thank you for the opportunity to comment on the Therapeutic Goods Administration's *Regulation of autologous cell and tissue products* consultation paper.

The Australasian College of Dermatologists is the leading authority in Australia for dermatology, providing information, advocacy and advice to individuals, communities, government and other health stakeholders concerning dermatological practice in Australia. Our focus is the delivery of efficient and effective dermatological specialty health services and work to improve outcomes for the skin health of individuals and whole communities.

The College has considered the issues raised in the consultation paper with respect to their impact on the practice of College Fellows and on the speciality of dermatology more broadly. Responses to consultation questions relevant to the College and its members are provided in the attached document.

Thank you for your consideration in this matter.

Please contact Dr Haley Bennett at haley@dermcoll.edu.au should you have any further questions relating to this submission.

Kind regards,

A handwritten signature in black ink, appearing to read 'AS'.

Dr Andrew Satchell
Honorary Secretary
The Australasian College of Dermatologists

Overview

The Therapeutic Goods Administration has released the *Regulation of autologous cell and tissue products* consultation paper in response to stakeholder feedback obtained during the initial consultation phase in 2015.

Currently, the use of autologous cells and tissues are regulated as medical practice and are excluded from regulation as therapeutic goods; while in many cases this continues to be a safe and effective approach, concerns were raised during consultation that certain procedures may have the potential for increased risk. As medical and scientific advancement continues, notably within the field of stem cell research, newly-emerging procedures offered to consumers may lack robust evidence of clinical efficacy and safety. Identifying the most appropriate regulatory body to provide oversight is a considerable challenge due to the current TGA definitions of autologous cells and tissues and a lack of clarity around the responsibility of enforcing compliance to advertising regulations.

The Australasian College of Dermatologists is cognisant of the regulatory challenges facing the TGA, AHPRA and other bodies such as the ACCC. The College is supportive in principle of the Minister's consideration of amending current regulatory frameworks as a pre-emptive approach to safeguard future patient safety. However there are concerns that certain options put forward in the consultation paper may result in creating an additional and unnecessary layer of complexity in regulation with respect to commonplace and novel procedures performed by specialist dermatologists, as well as a further blurring of boundaries between various regulatory bodies. These concerns are outlined below in response to relevant discussion questions selected from TGA's consultation paper.

2. Do you support the proposed approach? Please provide reasons to support this view or not.

The College agrees with the "approach" referred to in this question – the clarification that any regulatory change will apply to autologous cells and tissues generally, and will not be limited to stem cells. The College also supports the development of clear and consistent terminology when referring to stem cells to minimise further public confusion.

4. Please provide your views regarding the proposal to retain the concept of a 'single course of treatment'. Do you consider the storage of autologous cells and tissues as part of a single course of treatment carry risks of such a nature that should require TGA regulatory oversight? Please provide reasons to support this view, or not.

The College is supportive of retaining the concept of a single course of treatment, rather than a single procedure. Storage should remain the responsibility of the medical practitioner performing the procedure and should be carried out according to established protocols relevant to that procedure; for example, freezing and storage of fat products using Cytori Fat Banking (-190°C with bar coding of each vial). There is no compelling evidence to suggest that TGA oversight would reduce risks related to storage.

5. Do you agree that it is unnecessary to distinguish homologous and non-homologous use in the context of the exclusion (i.e. where the product is also for autologous use, under the supervision of a medical/dental practitioner, as part of a single course of treatment)? Why?

The College agrees that this distinction is unnecessary. According to the current definition of homologous use, the cell or tissue product performs the same basic function in the recipient; the definition is applied independently of whether the recipient is the same as the donor (autologous) or

different from the donor (allogeneic). For the purposes of the current exclusion, autologous use is specified and the issue of the cell or tissue product's intended purpose – i.e. whether it performs the same basic function as in its site of origin – will rest with how 'minimal manipulation' is defined.

6. Are any other cell and tissue products currently in use that:

- a) are currently covered by the TG Order; and
- b) form part of established medical practice; and
- c) would be more than minimally manipulated (and therefore would be subject to regulation under Options 3 or 4)?

Options 3 and 4 may impact on hospitals utilising the two types of products (identified above) that involve more than minimal manipulation but are also part of established medical practice. The TGA seeks the views from organisations (and others) on the impacts of this.

The College has concerns relating to proposed changes to the definition of 'minimal manipulation'. These changes may subject certain established procedures currently covered by the TG Order to regulation under Options 3 or 4. Procedures involving non-cultured cells, such as non-cultured epidermal cell grafting for the treatment of vitiligo or autologous fat grafting – as well as those utilising a culturing process to select and enrich specific cell populations such as melanocytes – may both be subject to regulation under the proposed definition. These issues are discussed further in Question 11. Furthermore, there is a lack of clarity regarding regulation of cell and tissue products in which the manufacturing procedure is covered as a medical device under TG regulation, such as ReCell.

The College is reluctant to support a role for the TGA in deciding those products which are to be considered established medical practice, based on the information provided in this consultation paper. There is inadequate discussion of proposed governance processes and the level of evidence required to support a claim of established practice; it is felt that this is beyond the scope of the TGA as a regulatory authority. Requirements of evidence of this type may also impact patient access to non-TGA approved therapeutic options which may have proven efficacy as evidenced by peer review publications but where large clinical trial data does not exist, for example, due to the rarity of the condition.

8. Given that advertising a service will still be possible what is your opinion on advertising of autologous cell and tissue products and the impact (including financial impact) of this option [option 2] on those practitioners currently advertising these products to consumers?

As autologous tissues are excluded as therapeutic goods, there is no TGA regulation on advertising of that good or service. Given this, advertising of autologous cell products should be sufficiently covered by AHPRA's regulation of advertising regulated health services under Section 133 of the National Law (i.e. banning of advertising of a health service that makes misleading claims; offers an inducement; uses testimonials; creates unreasonable expectations of beneficial treatment, or encourages the indiscriminate or unnecessary use of a service). In this case, it should remain the ethical responsibility of the practitioner to refrain from advertising procedures that are experimental or have insufficient evidence of benefit, and explain the risk-benefit profile to consumers on an individual basis. Concurrently, it remains the responsibility of AHPRA to enforce these regulations and act upon instances of non-compliance when consumer complaints are received.

Option 2, 3 and 4 propose excluding autologous cell and tissue products from TGA regulation on the condition that advertising to consumers is prohibited. While College concedes that protection of

consumers is paramount, there are concerns that this may lead to a duplication of regulatory effort by TGA and AHPRA – in the event where a service with unproven efficacy is advertised, both of these regulatory bodies would be required to take action. There is no doubt that external regulation of advertising is required, particularly the face of emerging technologies and their impact on expanding the range of therapeutic options. However there are concerns that using the threat of additional regulation as a disincentive for direct-to-consumer advertising may not be an appropriate approach; this is regarded as an ethical issue better suited to medical boards.

9. and 10. What is the impact of this option [Options 3 and 4] on practitioners currently manufacturing and using these cells and tissues? Does this option address the issues? Please provide the reasons why it does or does not.

Options 3 and 4 introduce the distinction of ‘more than minimally manipulated’, in which the final cell or tissue product is considered with respect to processing and subsequent alterations to biological, physiological or structural properties. Option 3 contains intermediary regulations which may present a level of unnecessary confusion and administrative burden, as outlined in the discussion paper. Option 4 is a much cleaner approach, whereby all autologous cell and tissue products which have been more than minimally manipulated would not be excluded under the TG Order. This may allow for greater degree of consumer protection, capturing new processing methodologies that involve a higher level of technical complexity, as well as providing the benefit of an existing mechanism for adverse event data collection. The College would support the exclusion of therapies that are a part of established medical practice, pending further information on decision-making processes as previously discussed.

11. Please provide your views on the proposed new definition of minimal manipulation.

As suggested in Question 6, there are concerns relating to the proposed new definition of minimal manipulation and the potential impact on certain dermatological therapies involving autologous cells.

It is stated in the discussion paper that the TGA “*considers that enzymatic digestion or physical disruption of a tissue (e.g. adipose tissue) when the aim is to dissociate cell-cell contacts constitutes more than minimal manipulation. Enzymatic digestion of adipose tissue to produce ‘vascular stromal fractions’ or adipose-derived ‘mesenchymal stem cells’ would be considered beyond minimal manipulation as it is likely that the process to isolate the cells would result in changes to their properties, e.g. activation state or surface molecule expression, which could significantly impact the cells characteristics or functions.*”

Several uses of autologous cells in procedures such as non-cultured epidermal cell or fat grafting involve trypsin degradation and manual cell separation to isolate cells of interest. While it is acknowledged that cell surface molecules would be transiently affected by dissolution of cell-cell contacts, once re-introduced *in vivo*, cells will re-establish expression and activation of cell surface molecules and adapt in accordance to their adopted microenvironment. Permanent alterations to cells at an intrinsic functional level are unlikely in this context.

According to the current definition in the Biologicals Framework, a Class 3 Biological is one which is “prepared using more complex methods, such as enzymatic dissociation, that have potential to alter the cells or tissue, but these methods do not change the biological properties of the product...” This definition acknowledges that a process such as trypsinisation may not necessarily alter key cellular characteristics. It is unclear why this distinction is not permitted under the proposed new definition of minimal manipulation. The College is concerned that this revision will result in overregulation of procedures with existing evidence of efficacy and safety.

12. Do you support the proposed changes to the classification criteria as set out in the proposed new definitions (to rely on the new definition of minimal manipulation and, as a result, to redefine Classes 3 and 4)?

Do you support redefining of the current Class 4 as proposed above?

What are the implications of this approach for your organisation?

As outlined in previous question, there are concerns around the proposed new definition of minimal manipulation. However should the changes to definitions proceed, then the College would support consistency in classifications across the Biologicals Framework.