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16 March 2018

Dr. Rochelle Christian  
Assistant Secretary, Department of Health  
Scientific Evaluation Branch  
Therapeutic Goods Administration  
PO Box 100  
Woden ACT 2606, Australia

Dear Dr. Christian,

On behalf of the International Society for Stem Cell Research (ISSCR), the leading professional organization of stem cell scientists, I write to share our views regarding the regulation of autologous cell and tissue products in Australia. The ISSCR, which represents more than 4,000 members in Australia and more than 65 other countries, supports global efforts to improve the regulation of new stem cell therapies so that patients can be assured they are safe and effective.

The ISSCR welcomes the recent announcement from the Therapeutic Goods Administration (TGA) that the agency is updating its regulations for autologous cell and tissue products to ensure that these products are safe and effective. In 2016, the ISSCR submitted [comments to TGA](#) in support of placing strict limits on the marketing and sale of stem cell therapies until their safety and effectiveness have been established in regulated clinical trials. The ISSCR also released [Guidelines for Stem Cell Research and Clinical Translation](#) that condemn the premature commercialization of unproven stem cell therapies.

The ISSCR encourages the TGA to include specific definitions and concrete examples in the agency's new guidance documents for autologous cell and tissue products to ensure that stem cell therapies are regulated as biologicals. The ISSCR believes that these therapies should only be sold to patients after being tested in regulated clinical trials, with institutional oversight, peer-review, and systematic reporting of results.

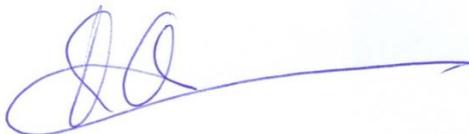
Countries around the world are now strengthening their regulation of cell and tissue products to rein in unscrupulous clinics marketing unproven therapies as stem cell treatments. These clinics often exploit common loopholes in cell and tissue regulations. Guidelines must be carefully drafted to allow common medical procedures like skin grafts and breast reconstructions to continue, while ensuring that complex and more speculative medical therapies are more stringently regulated as biological products.

In 2015, the European Medicines Agency (EMA) eliminated much of the ambiguity regarding the regulation of stem cell therapies in the EU when they adopted [new guidelines to clarify the classification of advanced therapy medicinal products](#) (ATMP). Under the new EMA guidelines, substantial manipulation was defined to include “enzymatic digestion of tissue to release cells,” which is a common practice used to isolate adipose-derived stromal cells that are often marketed by clinics as stem cell treatments. The definition of “non-homologous” was also clarified to include “adipose cells transplanted to other than fat tissue,” which draws an important distinction between the homologous use of adipose tissue to reconstruct the breast, for example, and the non-homologous use of adipose-derived stromal cells for stem cell therapies. These new guidelines clarify the classification of unproven stem cell therapies as ATMPs, requiring clinical trials to establish the safety and efficacy of products prior to marketing.

More recently, in November 2017, the United States Food and Drug Administration (FDA) finalized two new guidance documents that provide explicit criteria for determining how stem cell products are regulated, and closing loopholes commonly exploited by clinics marketing unproven therapies as stem cell treatments. The FDA’s new [guidance regarding same surgical procedures](#) clarified that processing adipose tissue to isolate cells (Example 7-2, stromal vascular fraction) would disqualify the process from the same surgical procedure exemption. Likewise, the FDA’s new [guidance regarding minimal manipulation](#) further clarified that the processing of adipose tissue to isolate cells as a stromal vascular fraction is also considered more than minimal manipulation (Example 14-1), resulting in these products being regulated as biologicals. Finally, the FDA strengthened its definition of homologous use (Example 19-6 b & c) to clarify that the use of adipose tissue for the regeneration of cartilage or tendons or the treatment of neurological disorders is not considered homologous use, requiring these products to be regulated as biologicals. Together, these specific examples create a regulatory framework for stem cell products that requires the safety and efficacy of products to be established before they are marketed and sold to patients.

Thank you for considering our views as you finalize the agency’s guidance for autologous cell and tissue products. If the ISSCR can be of further assistance to you as you move forward on this issue, please contact Eric Anthony, ISSCR’s Director of Policy at [eanthony@isscr.org](mailto:eanthony@isscr.org).

Sincerely,

A handwritten signature in blue ink, appearing to read 'Hans Clevers', with a long horizontal line extending to the right.

Hans Clevers, MD, PhD  
President, ISSCR  
Professor of Molecular Genetics at Hubrecht Institute  
Research Director at the Princess Maxima Center for Pediatric Oncology