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

The International Society for Stem Cell Research (ISSCR) is pleased to have the opportunity to provide comments on the Therapeutic Goods Administration's (TGA) public consultation on the regulation of autologous cell and tissue products.

The ISSCR is the leading professional organization of stem cell scientists, representing more than 3,600 members in Australia and over 60 other countries. Earlier this year, the ISSCR released an updated set of guidelines for stem cell research. This document, the Guidelines for Stem Cell Research and Clinical Translation, which updated 2006 and 2008 versions, provides guidance for the conduct of stem cell research under five basic principles: integrity of the research process, patient welfare, respect for research subjects, transparency, and social justice.

For this reason, we strongly support Option Four in version 3.0 of the TGA Consultation. We believe that this is the only one of the four options presented in version 3.0 that would meet the standards of the 2016 ISSCR Guidelines.

Option Four would place strict limitations on the direct advertisement of cell-based therapies and products that involve more than minimal manipulation of a patient's cells.

Throughout our history, the ISSCR has spoken out against "clinics" that offer unproven autologous cell-based therapies to patients who are urgently in search of relief from ailments currently without medically accepted treatments. These clinics, which operate in regulatory grey zones, charge patients large amounts of money for questionable treatments. The unproven therapies sold by some clinics have harmed patients, and are often highly questionable based on our understanding of the science.

This problem, sometimes referred to as stem cell tourism, does not necessarily depend on patients leaving their home countries and traveling abroad. However, the ease of international travel to nations with permissive medical regulatory systems makes it easier for patients to access to unproven treatments.

In addition, advertising, including internet-based advertising, has also made it possible for rogue clinics to reach out to would-be clients around the world.

Option Four would increase protections for patients who receive treatments using stem cells and tissue-based products that are more than minimally manipulated.

The ISSCR's Guidelines (Section 3.1) express the concern that even the most basic manipulation of cells "introduces additional risk of contamination with pathogens and prolonged passage in cell culture carries the potential for genomic and epigenetic instabilities that could lead to altered cell function or malignancy."

The increased protections in Option Four would be in line with Guidelines Recommendation 3.1.2.1, which calls for quality control in manufacturing, especially for extensively manipulated stem cells intended for use in the clinic. The protections would also adhere to Recommendation 3.1.2.2 which says that the level of oversight of processing should be proportional to the risk associated with the manipulation.

Furthermore, Guidelines Recommendation 3.4.1 stipulated that unproven stem cell-based interventions should only be provided outside of the context of a formal clinical trial if highly restrictive provisions are met including:

- Provision is limited to a small number of patients
- There is a strong scientific rationale, including pre-clinical evidence of efficacy and safety
- Full characterization of the types of cell being transplanted and their processing
- Explanation of why the proposed cell-based intervention should be attempted as compared to existing treatments.
- Peer-review by experts with no vested interest in the proposed procedure
- The patient is not eligible for an existing cell-based trial
- An action plan for adverse events exists
- There is a commitment to report the results of the intervention to the scientific and medical communities
- There is institutional support and accountability
- Personnel involved in the intervention have appropriate qualifications
- There is a commitment to move to a clinical trial in a timely manner after experience on a few patients

The over-riding principle of the ISSCR Guidelines is that therapies should only be sold to patients after safety and efficacy have been established in regulated clinical trials, with institutional oversight, peer-review, and systematic reporting of results.