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14 June 2018

The Honourable Ginette Petitpas Taylor
Minister of Health
70 Colombine Driveway
Ottawa, ON K1A 0K9, Canada

Dear Minister Petitpas Taylor,

On behalf of the International Society for Stem Cell Research (ISSCR), the leading professional organization of stem cell scientists, I write to urge you to consider updating Health Canada's guidance regarding the regulation of Cell Therapy Products. The ISSCR represents more than 4,000 stem cell researchers around the world, including many in Canada. We were delighted to learn that Health Canada began reviewing the clinics affiliated with Cell Surgical Network, a group of clinics that have also drawn the attention of the US Food and Drug Administration for marketing unapproved therapies. We encourage you to modernize and align your regulation of cell therapies with the international community and assure patients that stem cell-based products in Canada are safe and effective.

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. The ISSCR urges Health Canada to consider the following recommendations to strengthen Health Canada's Cell Therapy Products guidance and harmonize it with the international community.

Autologous Products

We encourage Health Canada update the Guidance Document for Cell, Tissue and Organ Establishments - Safety of Human Cells, Tissues and Organs for Transplantation to clarify that non-homologous and more than minimally manipulated autologous cell products are regulated under the Food and Drug Regulations, requiring clinical trials to establish safety and efficacy. Even though Health Canada's intent to regulate these products as drugs is clearly defined through the Guidance Document: Preparation of Clinical Trial Applications for use of Cell Therapy Products in Humans, some clinics marketing unproven treatments as stem cell therapies use the autologous cell exclusion in the Cells, Tissues, and Organs guidance

to suggest that autologous stem cell therapies are not regulated by Health Canada. For example, INOVO Medical located in Ottawa claims that "Health Canada does not currently regulate cells that are for autologous use." We believe Health Canada can remedy this ambiguity by updating both guidance documents to clarify Health Canada's intent to regulate non-homologous and more than minimally manipulated autologous cell products as drugs.

Minimal Manipulation

While Health Canada's definition for minimal manipulation is comparable with other international regulators, including the US Food and Drug Administration (FDA), Health Canada's Cells, Tissues, and Organs guidance lacks important examples to clarify how products are classified. Over the last few months, the FDA and Australia's Therapeutic Goods Administration (TGA) released new guidance with specific examples to ensure that high-risk products are regulated as biologics. We recommend updating your guidance with specific examples to clarify and align your definition of minimal manipulation with the other global regulators. Examples regarding adipose tissue are particularly important, as adipose tissue is often used as a source for mesenchymal stromal cells (sometimes improperly referred to as mesenchymal stem cells), which is one of the cell types most commonly marketed by private businesses as an unproven "stem cell" intervention. We urge you to include an example that clarifies that the processing of adipose tissue by centrifugation and/or enzymatic digestion to isolate the "stromal vascular fraction" is considered substantial manipulation. This would harmonize your guidance with the FDA's guidance regarding minimal manipulation (example 14-1) and TGA's regulation of autologous human cell and tissue products (Adipose tissue example b). Finally, we urge Health Canada to provide these examples within the context of the Cell Therapy Products guidance to eliminate any ambiguity regarding the regulatory pathway for autologous cell-based products.

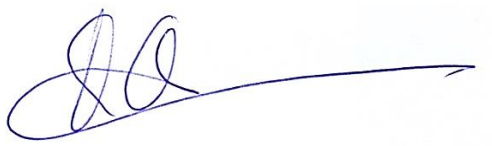
Homologous Use

We encourage you to update your guidance to include unambiguous examples of homologous and non-homologous use to illustrate how the non-homologous use of cells poses significant risks to patients and must be regulated as biologics. The uses of cell-based products as non-homologous treatments are complex, speculative and have been shown to have risk, including tumor growth and blindness. As a result, these products should be regulated as drugs or biologics with regulated clinical trials to establish their safety and efficacy. As with our recommendation regarding minimal manipulation, we recommend including specific examples regarding adipose tissue since it is commonly used by the clinics marketing unproven treatments as stem cell therapies. The FDA's guidelines for Minimal Manipulation and Homologous Use (Example 19-6) include four specific adipose tissue examples that explain the FDA's rationale for considering the transplantation of adipose tissue for breast reconstruction and other cosmetic uses a homologous use, while the use of adipose cells and tissue to treat neurological disorders or musculoskeletal conditions, for example, are considered non-homologous uses. Similarly, the TGA's autologous cell regulations and the

European Medicines Agency reflection paper on the classification of Advanced Therapy Products included adipose tissue examples to delineate homologous and non-homologous use.

Thank you for considering our recommendations to improve Health Canada's regulation of cellular therapies. If the ISSCR can be of further assistance to you as you consider this issue, please contact Eric Anthony, ISSCR's Director of Policy at eanthony@isscr.org.

Sincerely,



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