



BOARD OF DIRECTORS

**President**

Christine L. Mummery  
*Leiden, Netherlands*

**President Elect**

Melissa H. Little  
*Melbourne, Australia*

**Vice President**

Haifan Lin

*New Haven, CT USA*

**Clerk**

Amander T. Clark  
*Los Angeles, CA USA*

**Treasurer**

Kenneth S. Zaret  
*Philadelphia, PA USA*

**Immediate Past President**

Deepak Srivastava  
*San Francisco, CA USA*

**Directors**

Roger A. Barker  
*Cambridge, UK*

Marianne E. Bronner  
*Pasadena, CA USA*

Fiona Doetsch  
*Basel, Switzerland*

Valentina Greco  
*New Haven, CT USA*

Konrad Hochedlinger  
*Boston, MA USA*

Jürgen Knoblich  
*Vienna, Austria*

Arnold R. Kriegstein  
*San Francisco, CA USA*

Jane S. Lebkowski  
*Portola Valley, CA USA*

Urban Lendahl  
*Stockholm, Sweden*

Charles E. Murry  
*Seattle, WA USA*

Martin F. Pera  
*Bar Harbor, ME USA*

Lygia da Veiga Pereira

*São Paulo, Brazil*

Hans R. Schöler  
*Munster, Germany*

Takanori Takebe  
*Yokohama, Japan*

Joanna Wysocka  
*Stanford, CA USA*

Douglas A. Melton, Ex Officio  
*Cambridge, MA USA*

Leonard I. Zon, Ex Officio  
*Boston, MA USA*

Nancy Witty  
*Chief Executive Officer*

31 December 2020

Assistant Director Frank Chan  
Drug Office  
Department of Health  
Rm 1856, 18/F  
Wu Chung House  
213 Queen's Road East  
Wanchai, Hong Kong

Dear Mr. Chan,

On behalf of the International Society for Stem Cell Research (ISSCR), I write to share our comments on the draft Guidance for Cell and Tissue Products (those not classified as Advanced Therapy Products). The ISSCR is the leading professional organization of stem cell researchers and represents more than 4,000 members from around the world, including Hong Kong. Our members are scientists, clinicians, ethicists, and educators dedicated to the responsible advancement of stem cell research and its translation to the clinic. We support the crucial role of regulators in overseeing the development of new products and urge you to revise the guidance to clarify the classification of stem cell-based therapies as advanced therapy products.

The ISSCR condemns the premature commercialization of unproven cell therapies, which has resulted in patients being [blinded](#), [paralyzed](#), and [infected with dangerous pathogens](#). In many countries, unscrupulous businesses marketing these unproven cell therapies have abused ambiguous definitions for substantial/minimal manipulation and homologous use to claim they are not subject to oversight. Regulators around the world need to adopt harmonized product definitions to protect public health and to prevent the premature commercialization of stem cell-based products.

We appreciate that Hong Kong enacted the "Pharmacy and Poisons (Amendment) Ordinance 2020" because it broadly defined stem cell-based interventions as Advanced Therapy Products—requiring well-regulated clinical trials to demonstrate safety and efficacy prior to marketing. However, we are concerned that the

Promoting excellence in stem cell science and applications to human health.

definition of substantial manipulation and homologous use in the 2020 ordinance and the draft Guidelines for Cell and Tissue Products is too ambiguous and may be abused. We encourage you to include examples in the guidance to clearly explain the definition for substantial manipulation and homologous use since they are pivotal to delineate whether products are regulated as advanced therapies.

The examples provided by the U.S. Food and Drug Administration's guidance on [Minimal Manipulation and Homologous Use](#), the Australian Therapeutic Goods Administration's [autologous cell regulations](#), and the European Medicines Agency's [reflection paper on the classification of advanced therapy medicinal products](#) were crucial to explain the definitions for substantial/minimal manipulation and homologous/non-homologous use. Examples regarding adipose tissue are particularly important, as it is often used as a source of mesenchymal stromal cells, which is one of the cell types most commonly used by clinics marketing unproven cell therapies. Specifically, we urge you to include an example that clarifies that the processing of adipose tissue to isolate the stromal vascular fraction is considered substantial manipulation (see FDA's example 14-1). Similarly, we encourage you to include an example to explain that the transplantation of adipose tissue to non-fat tissue sites or the use of adipose tissue as a treatment for osteoarthritis or other musculoskeletal conditions are non-homologous uses (see FDA example 19-6 and EMA section 2.2.4 a).

Thank you for considering our recommendations on the draft Guidance for Cell and Tissue Products. If the ISSCR can clarify any of these views or be of assistance to you as you, please contact Eric Anthony, ISSCR's Director of Policy at [eanthony@isscr.org](mailto:eanthony@isscr.org).

Sincerely,

A handwritten signature in cursive script, appearing to read "Christine Mummery", with a horizontal line extending to the right from the end of the signature.

Christine Mummery  
President, ISSCR