5215 Old Orchard Rd, Suite 270
Skokie, IL 60077 USA
Tel: +1-224-592-5700
Fax: +1-224-365-0004
isscr@isscr.org
www.isscr.org

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Jiao Hong
Director
National Medical Products Administration
No.2 Building Xuanwumenxi Lu
Xicheng Qu, Beijing 100053

Re: ISSCR comments regarding the Management of Clinical Research and Transformation Applications for Somatic Cell Therapy (Draft for Comment)

Dear Director Jiao Hong,

On behalf of the International Society for Stem Cell Research (ISSCR), I write to share our comments regarding China's draft regulations for the Management of Clinical Research and Transformation Applications for Somatic Cell Therapy. The ISSCR is the leading professional organization of stem cell scientists, representing more than 4,000 members in China and around the world. Our members are scientists, clinicians, ethicists, and educators dedicated to the responsible advancement of stem cell research and its translation to the clinic.

China's investments in stem cell research have the potential to transform the field of regenerative medicine and yield new therapies for major public health problems. While the ISSCR is excited about the progress in China and the possibilities it creates for global leadership, our experience in other countries shows that it is critical to test the safety and effectiveness of new therapies before they are marketed to patients.

We are deeply concerned that China's newly proposed regulations will provide incentives for hospitals to market unsafe and ineffective interventions directly to consumers. This has the potential to harm the people of China, undermine public health and discredit the international standing of the Chinese regenerative medicine community.

We urge you to rescind these draft regulations and limit the use of stem cell-based interventions to well-regulated clinical trials and products approved by the National Medical Products Administration after the completion of clinical trials demonstrating safety and effectiveness.

Safety and Efficacy Testing Before Marketing

The limited safety and efficacy testing proposed in Article 10 of China's draft regulations is not adequate. It does not meet international standards, including the ISSCR Guidelines for Stem Cell Research and Clinical Translation. These draft regulations allow certain hospitals to provide unproven, complex, and speculative cell therapy products to any patient with a disease that is life-threatening or that affects the quality of life. By allowing clinical research to

occur without adequate scientific or regulatory review, the draft regulations have the potential to disseminate unsafe and ineffective therapies, jeopardize public health, and undermine China's leadership in the field of regenerative medicine.

A recent analysis of the impact of unproven cell therapies identified scores of cases in which patients experienced acute or chronic complications, including death. Regulators around the world, including the US Food and Drug Administration, the Australian Therapeutic Goods Administration, and Health Canada, are now strengthening regulations to curb the marketing of unproven cell therapies. We encourage you to harmonize China's regulations with other international regulators, as the current draft regulations are a significant departure from international standards.

Publication of Pre-Clinical Studies and Clinical Results

The timely exchange of accurate scientific information in internationally recognized journals is essential for the advancement of the stem cell field. The ISSCR Guidelines (Recommendation 3.2.4.1) encourage the publication of pre-clinical studies to enable independent peer review of the science, including the relevant scientific basis and confirmatory studies. The ISSCR Guidelines (Recommendation 3.3.6.3) also recommend the publication of all clinical results, whether positive, negative, or inclusive, to advance scientific understanding and to inform other clinical investigations.

In other countries, the failure to publish systematic analyses of patient outcomes allowed the sale of unproven therapies to flourish, facilitating the ability of unscrupulous clinics to profit from the marketing of therapies that do not benefit patients.

Rigorous Regulatory Review

While rigorously tested stem cell therapies have great potential to treat a wide range of serious conditions, much clinical research is needed before these therapies can be used safety and effectively. The regulatory review process must be designed to ensure this. Accordingly, the ISSCR Guidelines (Recommendation 3.5.1) urge national governments to "maintain rigorous review pathways to ensure that stem cell-based products conform to the highest standards of evidence-based medicine."

As written, the draft regulations delegate too much of the regulatory oversight responsibility to provincial health authorities that may have varying levels of expertise and commitment to rigor. We applaud the fact that draft regulations require the timely reporting of adverse events but are concerned that the reporting of such events is limited to provincial regulators. The oversight and review process is better administered jointly by competent local institutional review boards and the National Medical Products Administration to ensure a consistent national standard.

Transparency and Standards of Informed Consent

Stem cell-based interventions are complex procedures and that are associated with unique risks. It is essential that patients be adequately informed about the nature of the treatment and the potential risks through a thorough and transparent informed consent process.

Inadequate informed consent has the potential to facilitate the dissemination of fake therapies that harm the people of China.

In March, we commented on China's draft New Biomedical Technology Application Management Regulations and offered several recommendations for improving the informed consent process for new biomedical technologies. We remain concerned about the informed consent process for clinical research in China:

- Clinicians and researchers should disclose the fact that many stem cell-based interventions cannot be removed after they have been administered to patients (Recommendation 3.3.2.6 of the ISSCR Guidelines).
- The potential benefits of unproven products must not be overstated by researchers or misunderstood by patients (Recommendation 3.3.3.1 of the ISSCR Guidelines). This has been a major problem in countries that lack adequate regulation, or that fail to enforce their regulations.
- Patients should be informed about the clinical alternatives that exist for their disease or condition (Recommendation 4.3 of the ISSCR Guidelines).

We are very concerned that the integrity of the Chinese health care system will be jeopardized if the proposed regulations, as currently drafted, are finalized and implemented. They will undermine the integrity of the science and the clinical trials, complicate the development of safe and effective new therapies, and put patients at risk. We urge you to protect China's investment in stem cell research and the field of regenerative medicine by rescinding these proposed regulations.

China has the opportunity to lead the world in the development of regenerative medicine by creating a regulatory regime that ensures therapies are proven to be safe and effective in clinical trials before being marketed to patients. We believe that the draft regulations will attract unscrupulous actors to China, pose unnecessary risks to patients in China, and undermine China's historic investment in regenerative medicine.

Thank you for considering our concerns. Without significant revisions to the draft guidelines, as mentioned in this letter, the ISSCR will oppose the implementation of the regulations for the Management of Clinical Research and Transformation Applications for Somatic Cell Therapy. If the ISSCR can clarify any of these views, or be of assistance, please contact Eric Anthony, ISSCR's Director of Policy at eanthony@isscr.org.

Sincerely,

Doug Melton

Douglas A. Melton, PhD
President, ISSCR
Xander University Professor, Harvard University
Co-Director, Harvard Stem Cell Institute