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4 September 2020

Professor Guido Rasi
Executive Director
European Medicines Agency
Domenico Scarlattilaan 6
1083 HS Amsterdam
The Netherlands

Dear Professor Rasi,

On behalf of the International Society for Stem Cell Research (ISSCR), I write to share our comments on the European Medicines Agencies Network Strategy to 2025. The ISSCR is the leading professional organization of stem cell researchers and represents more than 4,000 members in Europe 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. We support the crucial role of EMA and national regulators in overseeing the development of new products and offer a few recommendations to ensure that new products are proven safe and effective before being marketed to patients.

Conditional Authorization of New Products

The conditional authorization of new products can provide patients with early access to innovative treatments, but it must be carefully balanced with protecting the public health by requiring robust and sound clinical safety and efficacy data before products are authorized and ensuring proper post-market surveillance. Robust surveillance and oversight are essential to confirm the efficacy of conditionally authorized products, identify adverse events, and quickly remove products from the market if they are found to be unsafe or ineffective. Surveillance systems that can monitor and track outcomes for years are crucial for stem cell-based treatments and other regenerative medicines where the treatment's effects may last for the patient's life. Regulators must ensure long-term follow-up for stem cell-based treatments because certain types of stem cells are capable of migration after transplantation and may result in off-target effects and unintended integration.

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

We appreciate that the draft strategy recognizes the post-approval challenges posed by the conditional authorization of products and urge the EMA to emphasize the importance of robust post-market surveillance systems to track outcomes and hold developers accountable for completing the clinical safety and efficacy studies to confirm the benefit and safety profile of conditionally authorized products.

Sustainability of the Network and Operational Excellence

The surge of cell and gene therapy products and other regenerative medicines in clinical trials and other stages of development is straining the capacity of regulatory agencies around the world. According to the Alliance for Regenerative Medicine's annual report, there are 260 active cell and gene therapy clinical trials in Europe, a 20% increase since 2018. Regulatory agencies are also being strained by unscrupulous businesses seeking to capitalize on the hope and excitement around these products. As we mentioned in our [24 June 2020 letter](#), these businesses sell products whose safety and effectiveness have not been demonstrated in clinical trials. Moreover, many such products lack a scientific rationale for why they would be expected to provide any benefit to patients. Many of the cell-based interventions provided by these businesses require authorization from EMA or national regulators and should be carefully reviewed by regulators before being marketed to patients. We urge you to highlight the enforcement challenges in the Network Strategy to 2025 and the need to dedicate resources to coordinated enforcement activities to prevent the premature commercialization of stem cell-based products and other regenerative medicines.

Consistent Rules Across the European Union

The unscrupulous businesses seeking to capitalize on the premature commercialization of stem cells often take advantage of inconsistent regulatory oversight across regions. We have observed these businesses move across borders to evade oversight while continuing to advertise their products to the same markets. The EMA and the national regulatory authorities should ensure this does not occur in Europe by harmonizing the enforcement of the EU's regulations across member nations. The regulations for what types of products are classified as ATMPs are quite clear and broadly include all cell and tissue products that have been "substantially manipulated" or are "not intended to be used for the same essential function or functions" ([EC No 1394/2007, Chapter 1, Article 2, \(c\)](#)). The EMA's Committee for Advanced Therapies (CAT) further explained the definition of ATMPs in the [reflection paper on the classification of advanced therapy medicinal products](#) that included clear guidance on substantial manipulation and non-homologous use. The CAT has also released multiple product classifications that illustrate that many of the unscrupulous businesses are marketing stem cell-based products that should be regulated as ATMPs. We appreciate that the draft network strategy acknowledges the lack of consistency across the EU for how some products are regulated, and we encourage the EMA to prioritize the consistent application of the regulations and enforcement to prevent the premature commercialization of stem cell-based products and other regenerative medicines.

Thank you for considering our concerns regarding the European Medicines Agencies Network Strategy to 2025. 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,

A handwritten signature in black ink, appearing to read "Christine Mummery", with a long horizontal flourish extending to the right.

Christine Mummery
President, ISSCR