INTERNATIONAL SOCIETY FOR STEM CELL RESEARCH

31 December 2020

Emer Cooke
Executive Director
European Medicines Agency
Domenico Scarlattilaan 6
1083 HS Amsterdam
The Netherlands

Dear Director Cooke,

On behalf of the International Society for Stem Cell Research (ISSCR), I write to share our comments on the draft Guideline on Registry-based Studies (EMA/502388/2020). 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 in overseeing the development of safe and effective new products and the draft Guideline on Registry-based Studies. We encourage EMA to clarify the appropriate uses for patient registries to prevent them from being abused by businesses seeking to prematurely commercialize unproven stem cell-based interventions.

Pre-Authorization Studies Involving Patient Registries

The ISSCR supports the narrow use of patient registries in pre-authorization studies for evidence generation as described in the draft guidelines (lines 111 to 129). For many stem cell- and gene-based interventions, patient registries are useful tools for accelerating the development of products for rare diseases and other serious conditions. Disease history registries facilitate the development of products for conditions with small patient populations by providing a historical control to assess safety and efficacy. For similar reasons, registry-based historical controls are also useful for stem cell-based interventions involving invasive delivery procedures where a placebo or sham comparator is not feasible or ethical.

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However, we are concerned that unscrupulous businesses seeking to prematurely commercialize stem cell-based interventions may inappropriately use patient registries by submitting substandard outcome measures, such as low-quality, patient reported outcomes. These businesses have a history of citing anecdotal findings as evidence that their products are safe and effective, despite the scientific implausibility of their claims. Furthermore, these businesses have a track record of abusing government sponsored databases to appear legitimate and to promote their treatments to patients. We recommend defining who is eligible to enter data into the registry to the Data Quality Management section of the draft guidelines (lines 308 to 325) to prevent patient registries from being abused by these unscrupulous businesses. It will be critical to have mechanisms in place to remove from the registry products that are scientifically implausible or that a highly unlikely to provide a benefit to patients. Moreover, we recommend that registries not be used for evidence generation in the context of common conditions such as osteoarthritis, joint pain, stroke, or neurodegenerative diseases of aging.

Post-Approval Long-term Monitoring

Patient registries are crucial tools for monitoring long-term outcomes of stem cell-based therapies after they have been authorized for routine clinical use. Stem cell-based treatments are often impossible to remove and have the potential to persist for the lifetime of the patient, necessitating long-term monitoring for adverse events. Patient registries are also useful tools to confirm the safety and efficacy of products conditionally authorized using surrogate endpoints. This is particularly important for stem cell-based treatments with lengthy primary endpoints due to their potential lifelong and curative benefits. We appreciate that the draft guidance (lines 130 to 152) acknowledges the potential uses of registry-based studies for monitoring the long-term outcomes of Advanced Therapy Medicinal Products.

Thank you for considering our recommendations for the draft Guideline on Registry-based Studies (EMA/502388/2020). 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,

Christine Mummery
President, ISSCR