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Government of India
Ministry of Health & Family Welfare

NOTICE

Comprehensive regulatory protocol for the stem cell research in human participants in Autism Spectrum Disorder

Introduction

This document provides a comprehensive protocol explaining the regulatory regime governing the use of stem cells in research and clinical trials relating to Autism Spectrum Disorder (ASD). Stem cell therapy for ASD is permissible only in the context of research, as part of an approved clinical trial. There are two regulatory pathways for stem cell research based on the level of stem cell manipulation. The levels of manipulation of stem cells into minimal or more than minimal manipulation have been described in the MoHFW directions issued under Section 33P, dated 9 February 2021. For research studies involving administration of minimally manipulated stem cells, research is regulated by DHR and for those involving administration of substantial or more than minimally manipulated stem cells, research is regulated by CDSCO. In addition, all stem cell research shall be required to comply with ICMR National ethical guidelines for biomedical and health research involving human participants.

Regulatory Framework

A. Research involving minimally manipulated stem cells:

- Where stem cells have undergone minimal manipulation, the research is regulated by the National Stem Cell Research Regulation Committee (NSRC). The Principal Investigator (PI) shall first submit the research proposal for

scientific review followed by ethical review. Stem cell research involving administration of minimally manipulated stem cells requires a prior scientific review at the institution where the research is proposed. Every institution/ clinical establishment conducting stem cell research must therefore, constitute a Scientific Review Committee (SRC), which could be an institutional scientific committee or an independent expert group, responsible for the scientific review of stem cell research proposals. The SRC must function independently of the Ethics Committee. Its composition must include subject matter expertise relevant to the proposals under review, along with at least two members with stem cell expertise and at least one member with statistical or methodological expertise.

- In case, an institution is unable to constitute a SRC with the requisite expertise, the scientific review may be undertaken by a scientific committee at another institution, or the institution must engage external scientific reviewers with documented competence in stem cell biology and clinical research. The review must be documented and its conclusions communicated formally to the Ethics Committee (EC). The EC reviewing stem cell proposals must be actively registered with DHR. The EC shall ensure that appropriate scientific review has been done and shall, in addition, also co-opt two stem cell experts (at least one external) to evaluate the proposal. EC shall forward only those proposals that are found appropriate, to the NSRC for final vetting.
- NSRC shall consider the recommendations of the Ethics Committee (EC) and assess whether the proposal has undergone appropriate scientific and ethical review in accordance with applicable requirements and falls within the mandate of the NSRC. The EC shall retain responsibility for ensuring that scientific and ethics review of the proposed study has been completed. It shall also look at the adequacy of safeguards in place for the protection of rights, safety, and well-being of participants. NSRC shall not undertake a parallel scientific or ethical review of the proposal.

- The NSRC shall review the proposal and communicate its decision back to the EC within ninety working days. The EC shall subsequently communicate the final decision to the Principal Investigator.

B. Clinical trial involving substantial or more than minimally manipulated stem cells to be used as Drug:

- Where stem cells intended to be used as "Drug" for the treatment of ASD and which have undergone more than minimal manipulation, the product is classified as a "New drug or Investigational New drug" as defined in New Drugs and Clinical Trials Rules, 2019 (NDCT Rules, 2019), as the case may be and must follow the regulatory clinical trial route through CDSCO as per the requirements of NDCT Rules, 2019.
- The applicant shall submit the clinical trial application accompanied with the information and documents as specified under NDCT Rules, 2019 for regulatory review through online SUGAM portal.
- The established procedures under NDCT Rules, 2019, and other applicable regulatory requirements are required to be followed.
- The regulatory review timelines may be 30 (if discovered and developed in India) or 90 working days (discovered and developed outside India).
- CDSCO grants permission, if satisfied, that the requirements of NDCT Rules, 2019 have been complied with, with certain conditions specified under Rule 25 of NDCT Rules, including that clinical trial at each site shall be initiated after approval of the clinical trial protocol and other related documents by the Ethics Committee of that site, registered with the Central Licencing Authority under rule 8 and also the CDSCO shall be informed about the approval granted by the Ethics Committee within a period of fifteen working days of the grant of such approval.

FLOWCHART: PROTOCOL WITH THE DUTIES AND OBLIGATIONS OF CONCERNED STAKEHOLDERS

Below is a step-by-step flowchart with the duties and obligations of the stakeholders involved in the regulatory framework for stem cell research in human participants that applies to autism spectrum disorders:

