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Updates of Regulations & Recent trends in Regenerative medicinal products in India

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Outline of Presentation

- Legal Provisions
- Stem cell derived Products
- Guidance for Industry
- Licensing Procedure
  - Pathway for indigenous manufacturers
  - Pathway for Importers
- Clinical Trial requirements
- Accelerated approval process

Legal Provisions

- Regenerative medicinal products (RMPs) like stem cell derived products, gene therapeutic products & Xenografts are regulated as Drugs under New Drugs and Clinical trial Rules, 2019.

- New Drugs means:- any drug which is not yet approved by central licensing authority under Drugs and Cosmetics Act 1940.

- As per Rule 2(1)(w)(v) of NDCT Rules, 2019, "new drug" definition includes a vaccine, r-DNA derived product, living modified organism, monoclonal anti-body, stem cell derived product, gene therapeutic product or xenografts, intended to be used as drug;

Legal Provisions

- Rules for requirement to import & manufacture of new drug in India are specified under Chapter X of New Drugs and Clinical Trial Rules 2019.
- Rules for requirement to conduct Clinical trial in India are specified under Chapter V Part A of New Drugs and Clinical trial Rules 2019.
- CMC data, pre-clinical, clinical trial data on safety & efficacy data is required to be submitted for approval of Regenerative Medicinal Products.
- Data is evaluated by SEC committee as defined in the Rules.

Stem cell derived Products

The clarification of the Stem cell derived product is:-

'Stem Cell Derived Product' *means a drug which has been derived from processed stem cells and which has been processed by means of substantial or more than minimal manipulation with the objective of propagation and / or differentiation of a cell or tissue, cell activation and production of a cell-line which includes pharmaceutical or chemical or enzymatic treatment, altering a biological characteristic, combining with a non-cellular component, manipulation by genetic engineering including gene editing & gene modification'.*

Stem cell derived Products

For this purpose:

(i) Substantial or more than minimal manipulation means ex-vivo alteration in the cell population (T-Cell depletion, cancer cell depletion), expansion, which is expected to result in alteration of function.

(ii) The isolation of tissue, washing, centrifugation, suspension in acceptable medium, cutting, grinding, shaping, disintegration of tissue, separation of cells, isolation of a specific cell, treatment with antibiotics, sterilization by washing or gamma irradiation, freezing, thawing and such similar procedures, regarded as minimal manipulations and are not considered as processing by means of substantial or more than minimal manipulation.

(iii) Stem cells removed from an individual for implantation of such cells only into the same individual for use during the same surgical procedure should not undergo processing steps beyond rinsing, cleaning or sizing and these steps shall not be considered as processing."

Further, the cell based products and tissue based products which have been processed by means of substantial or more than minimal manipulation as per criteria mentioned above are also covered under the New Drugs and Clinical Trials Rules 2019.

Guidance for Industry

- ✓ Submission of clinical trial application for Evaluating Safety and Efficacy.
- ✓ Requirements for permission of New Drugs Approval
- ✓ Post Approval Change in biological products
- ✓ Preparation of the Quality Information for Drugs submission for New Drugs Approval.

Licensing Procedure

- **Indigenously manufacturers:** The applicant is required to obtain market authorization from CLA in Form CT-23 before obtaining manufacturing license in Form 28 from State Licensing Authority (SLA).

- **Importers:** The applicant is required to obtain market authorization from CLA in CT-20 before obtaining Registration Certificate in Form 41 and import license in Form 10.

Pathway for indigenous manufacturers

Application in Form CT-10 to obtain permission in Form CT-11 for test & analysis or clinical trial from CDSCO

Application in Form 30 to obtain License in Form 29 to Manufacture test batches for test and Analysis from the SLA

Pre clinical studies as per NDCT Rules, 2019

Application for conducting clinical trial study in Form CT-04

Presentation by applicant

Review of Application in consultation with subject Experts and grant of permission in Form CT-06

Submission of Clinical Study Report along with application in Form CT-21 for MA

Presentation by applicant

Permission issued in Form CT-23 for Market Authorization after consultation with subject experts

Manufacturing License in Form 28 by SLA

Pathway for Importers

Application for clinical trial study in Form CT-04 along with Application to Import of finished formulation for Test and Analysis in Form CT-16

Review of Application in consultation with Subject Experts and issuance of permission in Form CT-06 to conduct clinical trial along with Permission to Import of finished formulation for Test and Analysis in Form CT-17

Presentation by applicant

Submission of Clinical Study Report along with Application in Form CT-18 for Grant of Market Authorization

Presentation by applicant

Grant of Market Authorization Permission in Form CT-20 after consultation with Subject Experts

Registration Certificate in Form 41 & Import license in Form 10 by CLA

Clinical Trial requirement prior marketing approval

- For New Drug products including biologicals discovered in India, clinical trial is required to be conducted right from Phase I.

- For New Drugs including biologicals approved outside India, Phase III studies need to be carried out to generate evidence of efficacy and safety of the drug in Indian patients when used as recommended in the prescribing information.

- Approval of new drugs is also considered based on clinical trial conducted in adequate number of Indian patients as a part of global clinical trial and the drug is also approved in other countries.

Clinical Trial Requirement Relaxation

- As per second Schedule of New Drug and Clinical trial 2019, For new drug substances discovered or developed in countries other than India, Phase I data should be submitted along with the application.
- After submission of Phase I data generated outside India to the Central Licensing Authority, permission may be granted to repeat Phase I trials or to conduct Phase II trials and subsequently Phase III trial concurrently with other global trials for that drug.
- For a drug going to be introduced for the first time in the country, Phase III trial may be required to be conducted in India before permission to market the drug is granted unless otherwise exempted.

Accelerated Approval Process

- Accelerated approval process may be allowed to a new drug for a disease or condition, taking into account its severity, rarity, or prevalence and the availability or lack of alternative treatments, provided that there is a prima facie case of the product being of meaningful therapeutic benefit over the existing treatment.
- If the remarkable efficacy is observed in the Phase II clinical trial of investigational new drug for the unmet medical needs of serious and life threatening diseases in the country, it may be considered for grant of marketing approval. In such cases, additional post licensure studies may be required to be conducted to generate the data to further verify and describe the clinical benefits.

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Thank You

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