6th India-Japan
Medical Products Regulatory Symposium
(Through Zoom, 01st Feb 2023)

Updates of Regulations &
Recent trends in
Regenerative Medical Products in India

Mr. Sanjeev Kumar
Deputy Drugs Controller (India)
CDSCO, DGHS, MoHFW, Govt. of India

Legal Provisions

- Regenerative medicinal products (RMPs) like cell* or stem cell derived products, gene therapeutic products & Xenografts are regulated as Drugs under New Drugs and Clinical trial (NDCT) 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, cell or stem cell derived product, gene therapeutic product or xenografts, intended to be used as drug.

* the word "cell" was included vide notification GSR 14(E) dated 13.1.2022

Legal Provisions

- Requirement to import & manufacture of new drug in India are specified under Chapter X of New Drugs and Clinical Trial Rules 2019.
- 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 in consultation with Subject Expert committee (SEC) as defined in the Rules.

Cell or 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'.

Cell or 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 Trial Rules 2019.

Guidance for Industry

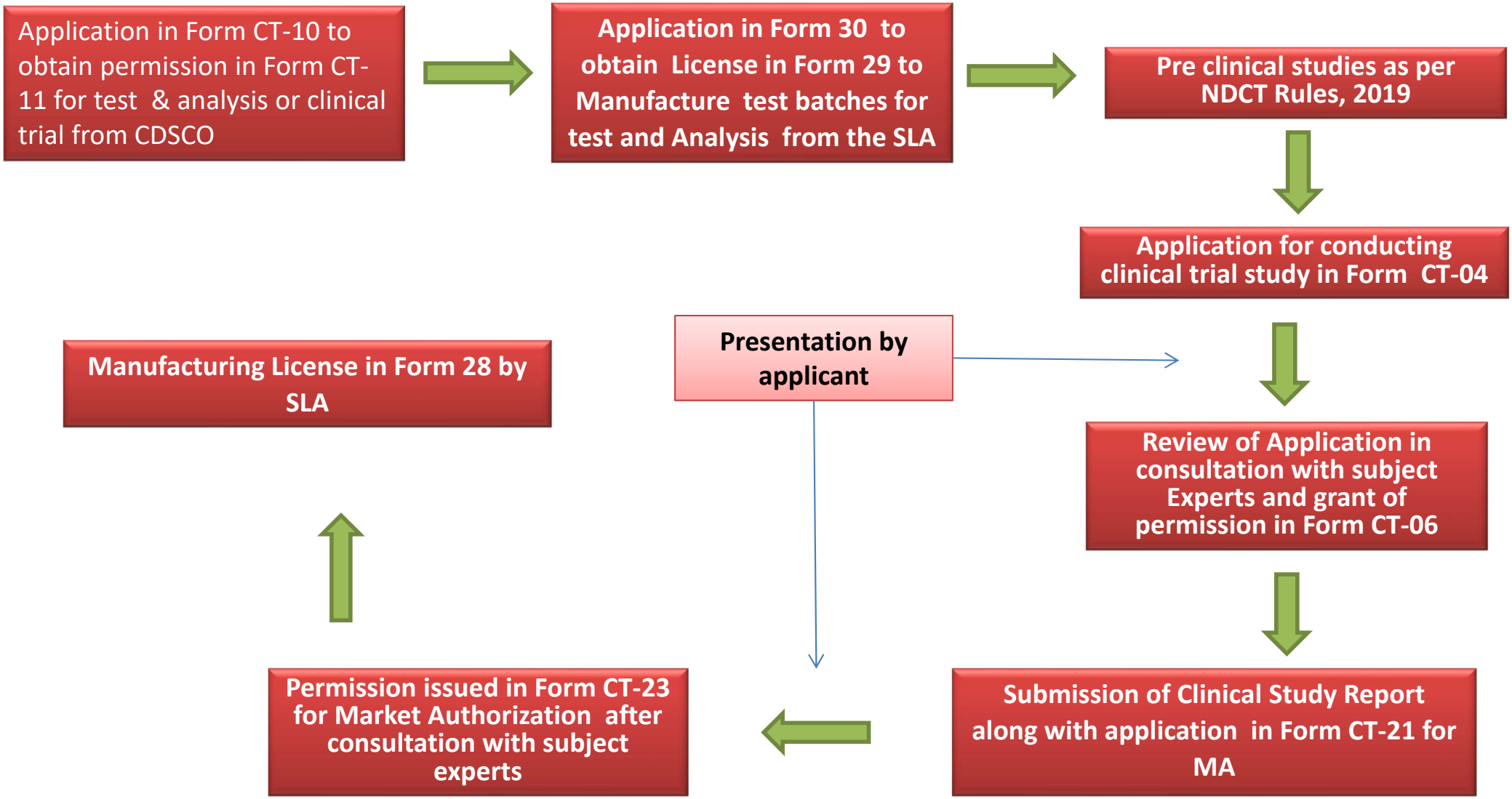
- Submission of clinical trial application for Evaluating Safety and Efficacy.
- Requirements for permission of New Drugs Approval
- Post Approval Change in biological products
- Preparation of the Quality Information for Drugs submission for New Drugs Approval.

Licensing Procedure

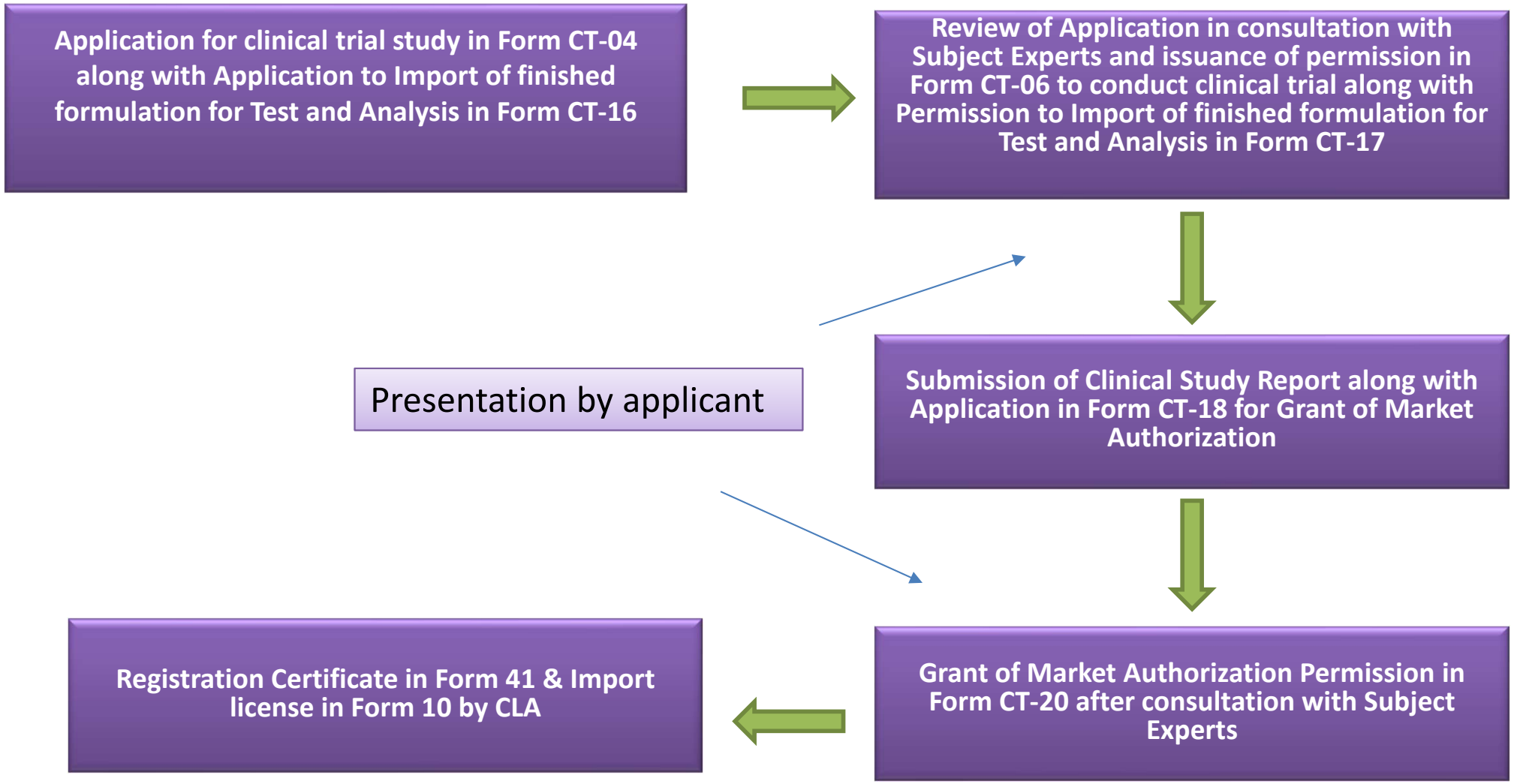
- **Indigenously manufacturers:** The applicant is required to obtain market authorization from CLA in Form CT-23 before obtaining manufacturing license in Form 28 from State Licensing Authority (SLA).

- **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



Pathway for Importers



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.

- 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

Clinical Trial Requirement

- 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.

- 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.

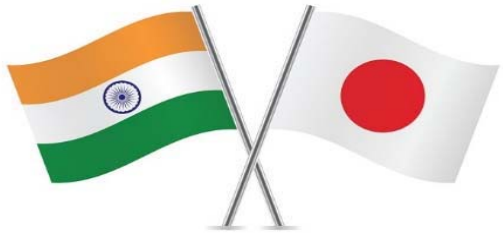
Deemed Approval Process

- To promote the research and development in India and to avoid regulatory delay, MoHFW has published amendment in New Drugs and Clinical trial Rules, 2019 vide G.S.R. 778(E) dated 14.10.2022 wherein if no communication has been received from the Central Licensing Authority within the period of ninety working days, then the permission shall be deemed to have been granted by the Central Licensing Authority for conducting the clinical trial.

Draft Notification regarding requirement of Pre-Clinical Studies

- MoHFW has published draft amendment in New Drugs and Clinical trial Rules, 2019 vide G.S.R. 835(E) dated 22.11.2022 wherein the Non-Clinical testing methods to assess the safety and efficacy of a new drug or investigational new drug may include the following:

1. Cell-based assay;
2. Organ chips and micro physiological systems;
3. Sophisticated computer modeling;
4. Other human biology-based test methods;
5. Animal studies.



Thank You