Ministry of Health & Family Welfare
Government of India

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Ministry of Health, Labour and Welfare
Japan Ministry of Health, Labour and Welfare
(JMHLW)

5th India-Japan Medical Products Regulatory Symposium

(Through WEBEX, 21st & 22nd Dec. 2021)

Latest trend of clinical trial requirements (India)

Presented By

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CENTRAL DRUGS STANDARD CONTROL ORGANIZATION
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Regulations of New Drugs and Clinical Trials

- Before, 19.03.2019, new drugs and clinical trials were regulated under Part X-A of the Drugs and Cosmetics Rules,1945 and Schedule Y to the Rules.
- Now they are regulated under the New Drugs and Clinical Trials Rules, 2019, notified by the Govt on 19.03.2019.
- The new rules contains various provisions for promoting scientific and ethical clinical research as well as development and approval of new drugs.

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Approval of New Drugs - Salient features:-

- Disposal of New drug applications by within a period of 90 working days.
- Provision for Accelerated approval with condition of requirement of Post Marketing Trial
- Provision for application by Sponsor for Expedited Review
- In case of modified or new claims and NDDS, the non clinical and clinical data requirement may be relaxed, omitted under certain conditions.
- The animal toxicity studies may be planned, designed and conducted as per ICH Guidelines with reduced use of animals in accordance with the 3R (reduce/refine/replace) principles.
- Pre-submission and Post-submission meeting.

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Challenges in conduct of Clinical Trials in health emergency situation

- Sponsors should assess the situation and take appropriate decision, in consultation with Investigator and Ethics committee to ensure rights, safety and well being of the trial subjects, as well as integrity of the clinical data
- Complete records of the procedures followed including the reason for such amendments/deviations etc. should be maintained.
- In case of on-going clinical trials, the sponsor in co-ordination with the investigator and the respective Ethics committee should decide whether to continue the trial or otherwise, in interest of the trial subject.
- Communications between sponsor, Investigator and Ethics committee required for implementation of such amendments/deviations/modifications may be made through email or any other electronic mode.

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Compensation & Medical Management in case of CT
Medical Management and compensation

➢In case of an injury , the sponsor, shall provide free medical management as long as required or till such time it is established that the injury is not related to the CT, whichever is earlier.

➢If the death or the injury is related to CT, the compensation is payable as per the formula specified in the Schedule to the Rules.

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Emergency use of Unapproved or Investigational drugs-.....1

Import of unapproved new drug by Govt. hospitals

- Chapter XI of the ND & CT Rules, 2019 provides for import of unapproved new drug but approved for marketing in the country of origin for treatment of patients by Government Hospitals under a license.
- Government hospital may import new drug for treatment of their patients suffering from-

  a) Serious/ life threatening disease
  b) disease causing serious permanent disability
  c) disease for which there is unmet medical need.

- Legal undertaking stating that unapproved new drug shall be used for the treatment of the patient for the disease is required.

Emergency use of Unapproved or Investigational drugs-.....2

- Manufacture of unapproved new drug but under clinical trial
- Any medical officer of a Government hospital may prescribe in special circumstances, a new drug which is under clinical trial for patients suffering from serious or life threatening disease for which there is no satisfactory therapy available in the country.
- Such new drug may be approved to be manufactured by a manufacturer in limited quantity
- Application should be accompanied with copy of recommendation of EC and consent from the patient/Legal heirs.
- Manufacturing permission may be granted generally for the purpose upto a quantity not exceeding 100 doses /patient

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Compassionate use of unapproved new drug (Draft rules).....1

- As such no provision for compassionate use of unapproved new drug at present.
- Draft rules (G.S.R. 354(E)) has been published by Govt. on 05.06.2020
- Provision under the rules for import of unapproved new drug

- A medical officer of a any hospital/ institution may import new drug for compassionate use for treatment of patients suffering from-
- life threatening disease
- disease causing serious permanent disability
- disease requiring therapy for unmet medical need

- It is applicable for New Drugs which are not approved in the country, but under Phase-III clinical trial in the country or in any other country,
- An application duly certified by the Medical Superintendent of the hospital or Head of the institution is required.
- Import license may be granted for 100 doses per patients.

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Compassionate use of unapproved new drug (Draft rules).....2

Provision for manufacture of new drug

- Any medical officer of a hospital/ institution may prescribe a new drug for compassionate use for treatment of patients suffering from-
  - a) serious /life threatening disease or
  - b) disease causing serious permanent disability
  - c) disease requiring therapy for unmet medical need.
- It is applicable for --

  new drugs not approved in the country, but under Phase-III clinical trial in the country or in any other country.
- Informed consent and EC approval are required.
- Permission for manufacturing the new drug may be granted for 100 doses per patient.

Fast-tracking approval of new drugs in special situations…….1

- Provisions under ND & CT Rules, 2019 for **relaxation, abbreviation, omission or deferment of data** including local clinical trial data for approval of a new drug.

Accelerated Approval

- Accelerated approval process may be allowed to a new drug for-
  - Serious / life-threatening diseases
  - Rare diseases
  - Diseases of special relevance to Indian health scenario,
  - For disease for which there is unmet medical need
  - Disaster or special defence use

Fast-tracking approval of new drug in special situation.....2

Accelerated approval process

- Accelerated approval may be allowed for a new drug for a disease taking into account -
  - severity, rarity or prevalence of the disease
  - availability or lack of alternative treatments,
  - there is a prima facie case of the product being of meaningful therapeutic benefit over the existing treatment.

Fast-tracking approval of new drugs …….3

Accelerated approval process

- Surrogate endpoints may be considered rather than standard outcome measures such as survival or disease progression, which are reasonably likely to predict clinical benefit.
- In case of remarkable efficacy, marketing approval may be based on Phase II clinical trial data.
- Accelerated Approval may also be granted to a new drug intended for serious/ life threatening disease, disease of special relevance to India and Unmet medical need.
- Phase IV CT may be required to validate the anticipated clinical benefit.

Fast-tracking approval of new drug in special situations ……4

Expeditious review process

- Applicable for a situation where the evidence for clinical safety and efficacy have been established even if the drug has not completed the all or normal clinical trial phases
- In such case following conditions need to be satisfied-
  a) serious or life threatening or rare disease or condition;
  b) if approved, the drug would provide a significant advantage in terms of safety or efficacy
  c) there is substantial reduction of a treatment-limiting adverse reaction and enhancement of patient compliance that is expected to lead to an improvement in serious outcomes
- It is also applicable for new drug developed for disaster or defence use where new intervention has been developed and where real life clinical trial may not be possible.
- It is also applicable for approval of an orphan drug.
- **During COVID-19 pandemic situation adaptive clinical trial design and fast track approval process were used for approval of vaccines and new drugs.**

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Fast tracking approval of approved drugs for new claims

Expeditious review process

- The requirements of data depends on nature and regulatory status of the drug for the new claim.
- Usually, the requirement of animal pharmacological and toxicological data and clinical data are determined on case by case basis
- Consideration is given to the type of new claim as well as mechanism of action, pathopysiology of the disease and clinical data already generated in the approved claim.
- The requirements may be abbreviated or relaxed or omitted under following conditions:

(a) the drug is already approved and marketed in other country for the proposed new claim;

(b) clinical data supporting the benefit-risk ratio in favour of the drug in the proposed new claim is available;

(c) the clinical trial doesn't involve a route of administration, dose, patient population that significantly increases the risk associated with the use of the drug.

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Review Process

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- On receipt of application, the CDSCO reviews & verifies that the information is as per the checklist.
- If the application is incomplete, same is communicated to the applicant.
- Thereafter, CDSCO prepare a summary statement and refer the proposal to the subject experts for review.
- CMC data is reviewed completely by CDSCO.
- Decision on non-clinical and clinical data is taken in consultation with the respective subject expert committee (SEC).
- Final decision on the proposal is taken considering the recommendation of the SEC after complete review of CMC data, non-clinical data, clinical data, regulatory status in other countries, etc.
- In case of disagreement, with the recommendation of SEC, the applicant can request for deliberation in the Technical Committee chaired by the DGHS.

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Thank You

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