Regulations and Guidelines specific to Ethics: Schedule Y & CDSCO-GCP

Dr. K. Bangarurajan
Deputy Drugs Controller (India)
CDSCO West Zone Mumbai
VISION

To protect and promote public health in India
MISSION

To safeguard and enhance the public health by assuring the safety, efficacy and quality of drugs, cosmetics and medical devices.
Drugs is in concurrent list of Indian Constitution

It is governed by both Central And State Governments under the Drugs & Cosmetics Act, 1940
Legal Enactments to Regulate Import, Manufacture & Sale of Drugs

- Drugs & Cosmetics Act, 1940
- Drugs & Magic Remedies (Objectionable Advertisements Act, 1954)
- Drugs & Cosmetics Rules, 1945 made under the Act
- Drug Price Control Order (DPCO) 2013
Functions of CDSCO

- Approval of New Drugs and Clinical Trials
- Import Registration and Licensing
- Licensing of Blood Banks, LVPs, Vaccines, r-DNA products & some Medical Devices
- Amendment to Drugs & Cosmetics Act and Rules
- Banning of Drugs and Cosmetics
- Grant of Test License, Personal License, NOCs for Export
- Testing of Drugs
Functions of State Licensing Authorities

- Licensing of Manufacturing Site for Drugs including API and Finished Formulation
- Licensing of Establishment for sale or distribution of Drugs
- Approval of Drug Testing Laboratories
- Monitoring of Quality of Drugs and Cosmetics marketed in the Country
- Investigation and prosecution in respect of contravention of legal provision
- Recall of sub-standard drugs
# India-Well defined Drug Regulatory System

## Government of India

<table>
<thead>
<tr>
<th>Ministry of Health &amp; Family welfare</th>
<th>Ministry of Chemicals &amp; fertilizers</th>
<th>Ministry of Commerce</th>
<th>Ministry of science &amp; Technology</th>
<th>Ministry of Environment</th>
</tr>
</thead>
<tbody>
<tr>
<td>DGHS</td>
<td>Department of Pharmaceuticals</td>
<td>Patent Office</td>
<td>DBT</td>
<td>Environmental clearance to the manufacturing sites</td>
</tr>
<tr>
<td>CDSCO</td>
<td>NPPA</td>
<td>Controller General of patents</td>
<td>CSIR Labs</td>
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<tr>
<td>DCGI</td>
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</tbody>
</table>

- Enforcement & GMP audit Div
- Quality Control Division-CDTL
- Registration Div
- New Drugs Div.
- Pharmacovigilance
- Trainings
CDSCO – Geographical location Zonal/Sub-Zonal Offices (10)

- CDSCO North Zone (Ghaziabad)
- CDSCO West Zone (Mumbai)
- CDSCO South Zone (Chennai)
- CDSCO East Zone (Kolkata)
- CDSCO Zone (Ahmedabad)
- CDSCO Zone (Hyderabad)
- CDSCO Sub Zone (Bangaluru)
- CDSCO Sub Zone (Chandigarh)
- CDSCO Sub Zone (Jammu)
- CDSCO Sub Zone (Goa)

Port Offices /Airports : 11, Laboratories : 08

Proposed SubZonal offices (2): Guwahati, Indore
Proposed Port Office at Vishakhatapnam
# Approval of Clinical Trials, Import & Manufacture of New Drugs

## Requirements and Guidelines - Schedule Y

<table>
<thead>
<tr>
<th>Rule 122 A</th>
<th>Permission to import new drug</th>
</tr>
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<tbody>
<tr>
<td>Rule 122 B</td>
<td>Permission to manufacture new drug</td>
</tr>
<tr>
<td>Rule 122 DAA</td>
<td>Definition of Clinical trials</td>
</tr>
<tr>
<td>Rule 122 E</td>
<td>Definition of New Drugs*</td>
</tr>
</tbody>
</table>

### Definition of New Drugs*:
- New substance having therapeutic indication
- Modified or new claims, new route of administration for already approved drug
- Fixed Dose Combination
Legal Provisions for regulation of Clinical Trials

Requirements and Guidelines - Schedule Y

Rule 122 DA: Permission to conduct clinical trial

Rule 122 DAA: Definition of Clinical trials

Rule 122 DAB: Compensation in case of trial related injury or death

Rule 122 DAC: Conditions of Clinical Trial permission & Inspection

Rule 122 DD: Registration of Ethics Committee

Rule 122 E: Definition of New Drugs

GCP Guidelines, 2001
Concerns in Clinical Trials

• Ethics Committee Review
• Informed Consent of subject
• Compensation for participation
• Compensation for accidental injury
• Review of Clinical Trial Applications
• Monitoring of Clinical Trials
• Analysis of SAEs
Recent Amendments in Drugs & Cosmetics Rules

- **Amendment vide G.S.R. 53(E) dated 30-01-2013** –
  - analysis of SAEs,
  - provisions for payment of compensation,
  - expansion of responsibilities of Investigator, Sponsor and EC,
  - amendment in ICD.

- **Amendment vide G.S.R. 63(E) dated 01-02-2013**
  - conditions for conduct of CT,
  - authority for CT inspections
  - actions in case of non-compliance

- **Amendments vide G.S.R No. 72(E) Dated 08.02.13** –
  - requirements and guidelines for registration of Ethics Committee
Ethics Committee

• Composition of Ethics Committee:
  – At least 07 members
    • Chairperson (from outside the Institution)
    • Member Secretary
  – Other members for quorum of Ethics Committee with at least 5 members as follows:

1. Basic Medical Scientist
2. Clinician
3. Legal Expert
4. Social Scientist / representative of Non-Governmental Voluntary Agency/ Philosopher / Ethicist / Theologian
5. Lay person from the community
Responsibilities of Ethics Committees

• To review and accord its approval to a trial protocol
• Revoke its approval granted
• Give opinion on financial compensation in case of SAE
• Review of the trial study progress reports periodically furnished by Investigator
• Review of internal audit reports furnished by sponsor & by visiting study sites
• Adequacy of documentation for ensuring privacy, confidentiality and justice.
• To evaluate possible risks and expected benefits to the subjects
Registration of EC - Requirements

- Name and Address of EC
- Authority under which EC constituted
- Membership requirements
- Terms of reference
- Procedures for resignation, replacement
- Biodata of all members and supporting staff
- All SOPs
- Prevention of conflict of interest
- Training policy
- Audit report, if any
- Undertaking by the Committee
Records to be maintained – NLT 5 years

- Constitution and Composition
- Curriculum of vitae of all members
- All SOPs
- National and international guidelines.
- Copies of protocols, CRF, IB etc
- All correspondences made with members
- Agenda and Minutes of all meetings
- Copies of decisions communicated
- Records of all notifications issued
- Reports of study.
Amendment in Patient Information Sheet/ ICF

• Essential elements of ICF have been amended to include statements that
  – in the event of injury, free medical management as long as required
  – in case of CT related injury or death, financial compensation

• The Format of ICF have been amended to include:
  – Address,
  – Qualification and Occupation
  – Annual income of the subject and Name & address of his nominee

• Mandatory for Investigator to hand over a copy of duly filled ICD to the subject or his/her attendant
Expansion of Responsibilities of EC

• The report of **SAE of death**, after due analysis along with its opinion on the financial compensation, if any, shall be forwarded within **twenty one** calendar days to:
  - Chairman of the independent Expert Committee
  - Copy to DCG(I)

• The report of **SAE other than death**, after due analysis along with its opinion on the financial compensation, if any, shall be forwarded within **21** calendar days
  - DCG(I)
Ethics Committee:

- No EC shall review and accord its approval to a clinical trial protocol without prior registration with DCG (I)
- An application for registration of EC is required to be made to DCG(I) as per Appendix VIII of Schedule Y
- EC shall approve the CT and conduct periodic review as per the provisions of Schedule Y and the GCP Guidelines and other applicable regulations
Ethics Committee:

- In the case of any SAE, the EC shall analyse and forward its opinion as per procedures specified under Appendix XII of Schedule Y.
- CDSCO can inspect the facilities, records, documents, etc. of EC.
- The registration of an EC shall be valid for a period of three years.
- If the EC fails to comply with any of the conditions of registration, DCG(I) may suspend or cancel the registration.
Expansion of Responsibility of Investigators

• The report of SAE other than death, after due analysis shall be forwarded within ten calendar days to:
  - Chairman of the EC,
  - DCG(I)
  - Head of the Institution where the trial has been conducted.

• The Investigator shall provide information through informed consent process to the subject about
  - Essential elements of the clinical trial as per Appendix-V
  - Right to claim compensation in case of trial related injury or death
  - Right to contact the applicant for the purpose of making claims in the case of trial related injury or death
Expansion of Responsibility of Sponsor

- The report of SAE of death, after due analysis shall be forwarded within **ten** calendar days to:
  - **Chairman of the EC**
  - Chairman of the independent Expert Committee with a copy to DCG(I)
  - Head of the Institution where the trial has been conducted.

- In case of clinical trial related injury or death compensation to be paid within **thirty** days of order of DCG(I)
Investigator (within 24hrs of occurrence)

Sponsor / Investigator (within 10 calendar days after analysis of SAE)

In case of Death

Head of Institution

Chairman Expert Committee (Recommendation in 30 days)

Chairman Ethics Committee (within 21 calendar days after due analysis)

DCG(I)* (order within 3 months of occurrence)

*SIf required DCG(I) can constitute Expert Committee in cases of SAE other than death

Sponsor / Applicant Payment of Compensation within 30 days of Order
• **Formula on Quantum of Compensation**
  
  \[ \text{Compensation} = \frac{\text{B} \times \text{F} \times \text{R}}{99.37} \]

  - \( \text{B} \) = Base Amount (8 lakhs)
  - \( \text{F} \) = Factor depending on age (Workmen Compensation Act)
  - \( \text{R} \) = Risk Factor (severity & seriousness, co-morbidities etc 0.5-4.0)

<table>
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<tr>
<th>Sr No</th>
<th>Age</th>
<th>( \text{F} ) (factor)</th>
<th>Compensation amount (in Rupees lakhs)</th>
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<td>( \text{R} = 4 )</td>
<td>( \text{R} = 3 )</td>
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<td>Healthy volunteers</td>
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STATE WISE LIST OF ETHICS COMMITTEE REGISTERED (Total 737)

- Andhra Pradesh : 80
- Assam : 03
- Bihar : 04
- Chattisgarh : 01
- Delhi : 48
- Goa : 04
- Gujarat : 86
- Haryana : 09
- Himachal Pradesh : 02
- Jammu & Kashmir : 01
- Karnataka : 75
- Kerala : 40
- Madhya Pradesh : 09
STATE WISE LIST OF ETHICS COMMITTEE REGISTERED

- Maharashtra : 178
- Mizoram : 01
- Orissa : 10
- Puducherry : 04
- Punjab : 14
- Rajasthan : 24
- Sikkim : 02
- Tamilnadu : 70
- Uttarakhand : 02
- Uttar Pradesh : 32
- West Bengal : 38
Conclusion

- Clear understating of Mandate & Regulations
- Training to all members
- Accreditation/Registration of Members
- Integrity of approvals
- Audit of CT sites
- Taking action against violators
Thank You