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COMPREHENSIVE GUIDE OF PROTOCOL TO COMPLIANCE CLINICAL TRIAL REGULATIONS BY CDSCO AND DCGI IN INDIA

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ABSTRACT

The CDSCO, under the aegis of the DCGI, is responsible for formulating and implementing regulatory guidelines that govern clinical trial administration and the marketing authorization of new medications, medical devices, and biologics. These regulations are designed to safeguard the Trial participants' rights and well-being participants, ensure the trial validity results, and maintain public trust in the research process. Compliance with CDSCO and DCGI regulations is essential for sponsors, investigators, ethics committees, and all stakeholders involved in clinical research. This review article aims to provide a comprehensive overview of the protocol compliance requirements outlined by CDSCO and DCGI for conducting India clinical trials and information about Report any severe adverse events that occur during the clinical trial, formulae for determining the amount of compensation in the event of clinical trial injury, Regulatory pathway for product registration and SEC review process. By delving into the key regulatory aspects, procedural guidelines, and recent updates, this review intends to serve as a valuable resource for researchers, sponsors, regulatory authorities, and other professionals engaged in clinical research activities.

Keywords: - Clinical Trial, CDSCO and DCGI, Safety, Efficacy and Wellbeing of subject, SEC Review process, ADR, Product registration pathway

INTRODUCTION:

Clinical trials allow us to assess the efficacy of a drug or medical treatment., surgery, X-ray intervention, behavioural A strategy for intervention or preventive health care. These tests can be done on multiple Participants can range from healthy volunteers in a phase 1 drug trial to patients in the case of medical or surgical interventions. These trials are carried out in order to determine the efficacy of interventions and to practise evidence-based medicine. Patient safety and outcomes are improved by evidence-based practise, which promotes good public health **[1]**.

Randomized controlled clinical trials play an important role in informing clinical trial staff, sponsors, and investigators about the effectiveness, comparability, and safety of treatments in evidence-based medicine. A clinical trial's information is usually only useful if the trial is well designed and successful. To minimise confounding factors and biases, clearly articulated research questions and appropriate definitions of eligible study participants, outcomes, and structures are required **[2]**.

REGULATIONS OF NEW DRUGS AND CLINICAL TRIALS:

Prior to March 19, 2019, new drugs and clinical trials were governed by Part X-A of the Drugs and Cosmetics Rules, 1945, and Schedule Y to the Rules. They are now governed by the New Drugs and Clinical Trials Rules 2019, which the government issued on March 19, 2019. The new rules include a number of provisions aimed at encouraging scientific and ethical clinical research, as well as the development and approval of new drugs. Response time for new medication applications is 90 days or less **[3]**. There is a provision for expedited approval with a post-marketing trial requirement. There is a provision for the Sponsor to request Expedited Review. In the case of modified or new claims and NDDS, the non-clinical and clinical data requirements may be reduced or waived.

Animal toxicity studies can be planned, designed, and carried out in accordance with ICH Guidelines, with fewer animals used in accordance with the 3R (reduce/refine/replace) principles. Meetings before and after submission.

REPORT ANY SEVERE ADVERSE EVENTS THAT OCCUR DURING THE CLINICAL TRIAL:

A serious adverse event (SAE) is a medical event that occurs during a clinical trial and is related to one or more of the following: death, inpatient hospitalisation (if the study was conducted on an outpatient basis), hospitalisation prolongation (if the study was conducted on an inpatient basis), persistent or significant disability or incapacity, a congenital anomaly or birth defect, or other life-threatening events.

For reporting SAEs, the following timelines are provided: The investigator must notify the DCGI (for regulatory research), the sponsor, and the IEC within 24 hours of the occurrence of any SAE. The IEC should be the only party notified for academic investigations. If this is not possible, the DCGI should be notified, along with the report, of the delay in reporting the SAE **[4]**.

Table 1: Timeline For Serious Adverse Event Reporting

S. No.	Submitted by	Timeline (as of the time of writing) occurrence of SAE)	Reporting to
1	Investigator	Within 24 hours (initial report)	Sponsor, chairman of IEC, DCGI
2	Investigator and Sponsor	14 calendar days (analyzed report)	Chairman of IEC, Head of Institution, DCGI
3	Sponsor and Chairman of IEC	30 days (analyzed report and Recommendation on financial compensation)	DCGI
4	DCGI	The investigator's, sponsors, and ethics committee's reports.	Expert Committee
5	Expert Committee	within 60 days of the report's receipt (Recommendation and quantum of compensation).	DCGI

Send the SAE report to DCGI after thorough analysis. Furthermore, within 14 calendar days of the incident, send to the Chairman of the IEC and the Head of the institution where the trial was held. IEC should submit its report on the SAE to the DCGI within 30 calendar days of the event. This report should include a thorough analysis as well as opinion on any financial compensation that the sponsor or his agent should provide.

FORMULAE FOR DETERMINING THE AMOUNT OF COMPENSATION IN THE EVENT OF CLINICAL TRIAL INJURY [5]

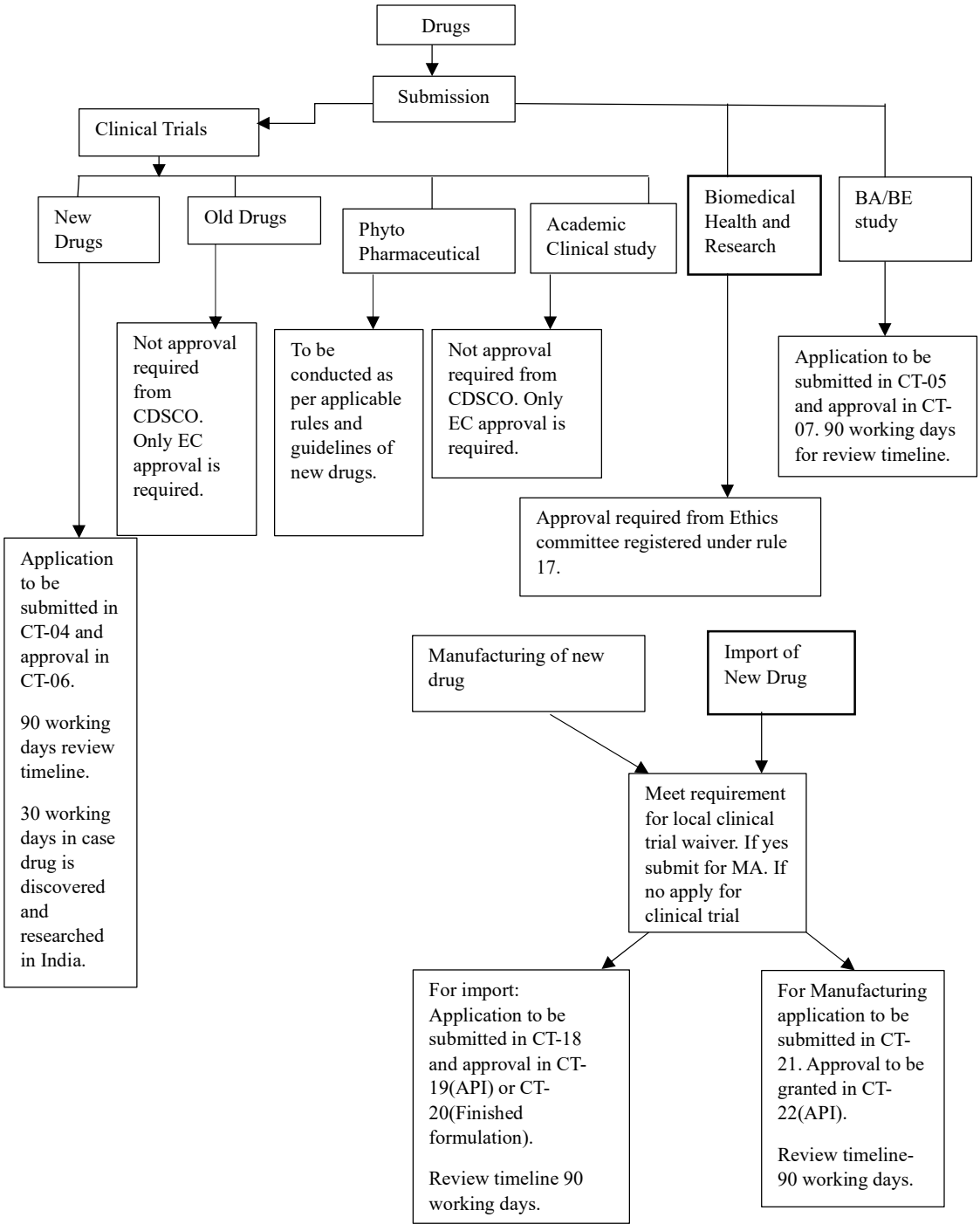
The following is how death benefits are calculated: B F R/99.37, where B is an 8 lakhs base sum, F is an age factor based on the Workmen Compensation Act, and R is a risk factor that takes into account the severity, duration, and co-morbidities of the condition. Compensation for permanent disability: (C D 90)/(100 100), where 'C' is the amount of compensation that would have been awarded to the nominee in the event of the participant's death and 'D' is the percentage of disability of the subject.

Compensation for an SAE that results in a life-threatening illness is 2 x W x N, where W is the unskilled worker's daily minimum wage (in Delhi) and N is the number of hospital days. Compensation for a congenital abnormality or birth defect: Medical attention will be made available for as long as necessary, and a one-time payment will be invested in the form of a fixed deposit will yield interest each month that is equal to half of Delhi's minimum salary for unskilled workers.

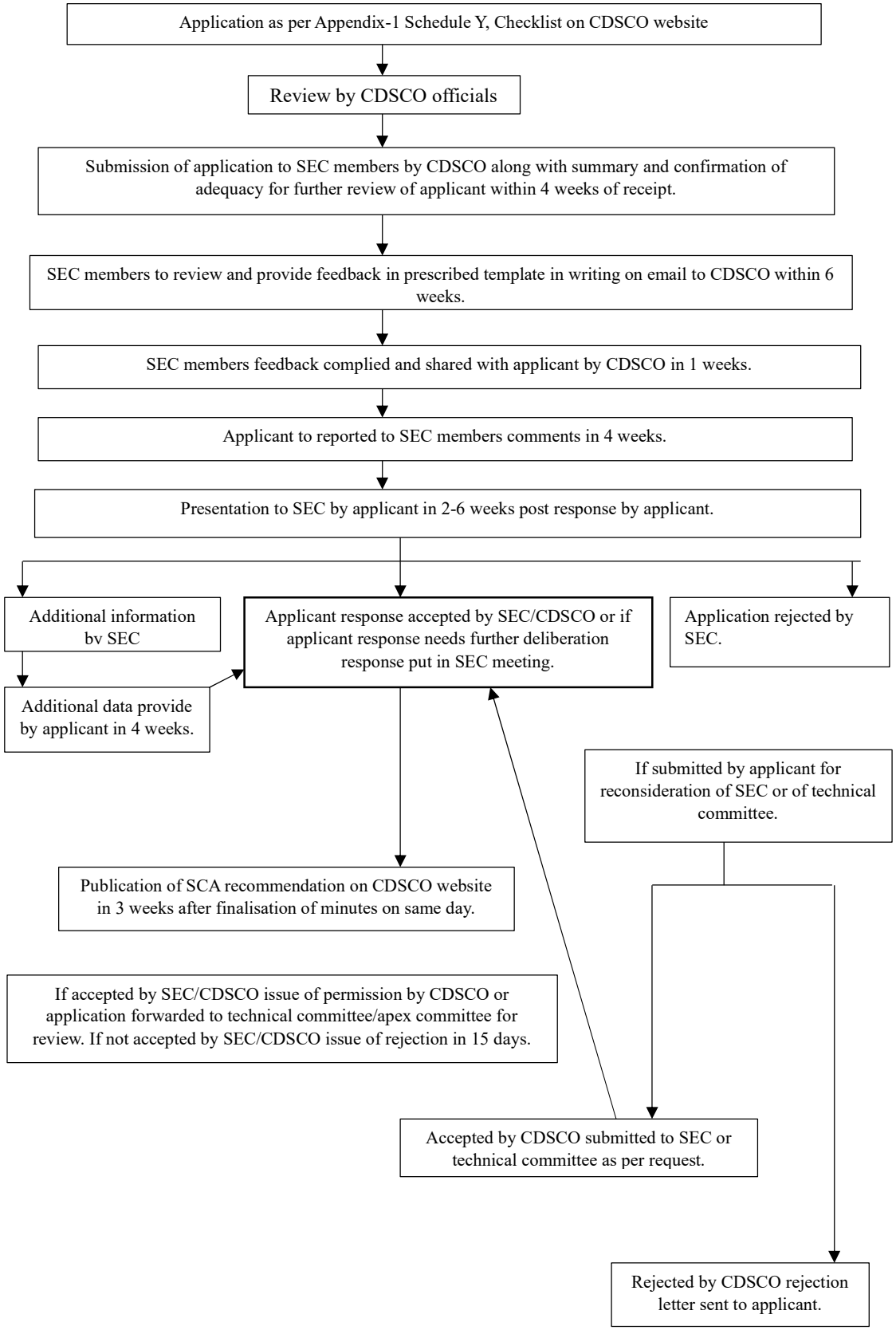
Regarding SAEs and compensation: Some institutions, in addition to the IEC, have an SAE subcommittee that meets frequently to study and assess SAEs. This would be a nice

committee to form for institutions without one. Since investigator-initiated (academic) studies and those pharmaceutical industry-sponsored both carry the risk of clinical trial-related harm or death, institutional budgetary provisions must be made for the adverse event medical management (AEs), serious adverse events (SAEs), as well as insurance coverage for trial participants.

REGULATORY PATHWAY FOR PRODUCT REGISTRATION [6, 7]



SEC REVIEW PROCESS [8-11]



GLOBAL AND NATIONAL SCENARIO

In 2021, the market for clinical trials in India was estimated. to be worth USD 1.93 billion, as well as from 2022 to 2030, it is expected to rise at a CAGR of 8.2%. The main reasons anticipated to drive the market are the increasing prevalence and variation of diseases, the globalization of clinical trials, the use of new clinical research technology, and the growth of outsourcing-promoting research and development **[12]**.

India is populated with 1.3 billion individuals with varying genetic backgrounds and a large treatment-naïve patient pool for the development of therapeutics on a range of disease conditions. Furthermore, the economic, environmental, and ecological variations in the 28 states and 8 union territories present the most diverse disease profile. Apart from this, the cost of carrying out clinical trials in India is nearly 40-70% less when compared to that in Europe or the U.S. Thus, the cost efficiency, along with skill sets and ease of doing business, is anticipated to fuel the market growth **[13]**.

The market for clinical trials was estimated to be worth USD 49.8 billion globally in 2022, and between 2023 and 2030, it is projected to increase at a compound annual growth rate (CAGR) of 5.8%. However, the COVID-19 pandemic in 2020 hampered business expansion. A strategic partnership was established in 2020 between Parexel and Synairgen plc to carry out a Phase III trial of an IFN-beta (interferon-beta) medication for COVID-19 patients. It is anticipated that CROs' strategic efforts will reduce obstacles and accelerate market expansion. As a result, the market is anticipated to expand due to elements including the globalization of clinical trials, the quick advancement of technology, and the growing need for CROs to carry out research projects **[14]**.

REGULATORY AUTHORITY REQUIREMENTS

The medicines Controller General of India (DC), who's responsible for overseeing the Central medicines Standard Control Organization (CDSCO), is needed to admit the Hdbk- Clinical trial, IND- 32, and IND- 35 documents as part of the blessing process for investigational new medicines (INDs). The specific process may vary depending on the type of operation, study phase, stage in the medicine development process, and study ideal. The ensuing lists give information that may be necessary (Note Not all particulars listed over will be set up in every regulation source due to lapping and unique rudiments). Form CT- 04 is an operation form for clinical trials that includes the following information the guarantor's name(also known as the aspirant), the guarantor's nature/ constitution and contact details, the contact details for the clinical trials point, the contact information for the person responsible for compensation payment, if applicable, the correspondence address, details of any new or investigational

medicines(including remedial class, lozenge form, composition, and suggestions), the clinical trial phase, the protocol number with date, and the names of the ethics commission(EC) and investigators **[15]**.

Table 2: Forms Under Clinical Trial Regulations In India

S. No.	Form	Description
1	122-A	Request for New Drug Import Permission
2	122-B	Application for permission to manufacture a New Drug that is notlisted in Schedules C and C. (1)
3	122-D	Permission to import or produce afixed dose combination
4	122-DA	Application for Clinical Trial Permission for a New Drug/Investigational New Drug
5	122-DB	Permission / Approval suspension or cancellation.
6	Form-44	Application for approval to import or manufacture a New Drug or to conducta clinical trial.
7	Form-44-1A	Application for the Importation orProduction of a New Drug or an Investigational New Drug.
8	Form 44 1B	Permission to Import or Produce a New Drug or an Investigational NewDrug for Export.
9	Form 44-3A	Application for conduct ClinicalStudies (Phase II to IV).
10	Form 44-3B	Application for Clinical Trials (PhaseI).
11	Form 44-3C	Application for conduct of ClinicalTrials (Bioequivalence Studies andBioavailability Studies)
13	Form CT-06	Serious Adverse Event (SAE) or Unexpected Serious Adverse Event(USAE) Report (USAE).
14	Form CT-04	Application for approval to import or manufacture a new drug for commercial sale, or to conduct clinical trials
15	Form CT-03	Request for approval to import or manufacture a new drug or investigational new drug for clinical trials.

Table 3: Fees Under Clinical Trial Regulations In India

S. No.	Rule	Subject	FEES
1	21	Request for permission toconduct a clinical trial 1) Phase-I 2) Phase- II 3) Phase -II 4) Phase -IV	 1)3,00,000 2)2,00,000 3)2,00,000 4)2,00,000
2	22	Application for permission to conduct a clinical trial is being reconsidered.	50,000
3	33	Permission to conduct a bioavailability or bioequivalence study.	2,00,000
4	34	Application for permission toconduct a bioavailability or bioequivalence study is being reconsidered.	50,000
5	45	Bioavailability and bioequivalence study centreregistration application	5,00,000
6	47	Application for bioavailabilityand bioequivalence study centre registration is being reconsidered.	1,00,000
7	52	Permission to produce new orinvestigational drugs for clinical trials, bioavailabilitystudies, or bioequivalence studies	5000 per product
8	53	Reconsideration of a new or investigational drug manufacturing application for clinical trials, bioavailability, or bioequivalence studies.	2000 per product
9	59	Application for approval to manufacture an unapprovedactive pharmaceutical ingredient for the developmentof a formulation for testing, analysis, clinical trials.	5000 per product
10	80	Request for approval to manufacture a new drug (Finished Formulation) for sale or distribution.	5,00,000
11	80	Application for permission tomanufacture new drug	5,00,000
12	80	Request for approval to manufacture a new drug	5,00,000

CONCLUSION

In conclusion, the landscape of clinical trial regulation in India has undergone significant transformation over the years, reflecting the country's commitment to ensuring the highest standards of patient safety, ethical conduct, and scientific rigor. The regulatory framework established by authorities such as the Central Drugs Standard Control Organization (CDSCO) and the Drug Controller General of India (DCGI) plays a pivotal role in shaping Clinical trials must be conducted within the country. India's clinical trial regulations serve as a cornerstone in the nation's pursuit of scientific excellence and improved healthcare outcomes. By upholding the principles of patient protection, ethical conduct, and scientific integrity, India is poised to make significant contributions to the global landscape of clinical research and drug development. As the nation moves forward, a steadfast commitment to refining and enhancing clinical trial regulations will be crucial in realizing the full potential of medical innovation for the benefit of both of its residents and of the larger international community.

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