THE SUBJECT EXPERT COMMITTEES

GUIDANCE DOCUMENT

CENTRAL DRUGS STANDARD CONTROL ORGANIZATION

DIRECTORATE GENERAL OF HEALTH SERVICES

MINISTRY OF HEALTH & FAMILY WELFARE

GOVT. OF INDIA

Contents

1. Introduction:

A robust evaluation process is critical for the most effective and efficient review of all applications. The review process involves evaluation of the applications relating to early clinical development phase, evaluation of safety, efficacy, quality data and other related information for approval of new drug or biological drug product, investigational medical device as well as applications relating to the assessment of safety/ efficacy of such products in post marketing phase.

Different categories of applications include applications on Investigational New Drug (IND), New Drug, Subsequent New drug, Fixed Dose Combination, rDNA Derived Products, Vaccines, Global Clinical Trial, Bioavailability & Bioequivalence (BA/BE) study, permission for Investigational Medical Devices (IMD) & clinical study on IMD, etc. which are received and processed in various divisions of CDSCO.

The application of a specific category may be for different purpose like Conduct of clinical trial, BA/BE studies, Marketing Authorization, approval of post approval changes/package inserts, Phase IV clinical trial protocol approval and data review, PMS data review, approval of clinical trial protocol amendments, etc.

1.1 Introduction to Subject Expert Committee (SEC):

The SEC experts examine and advice Drugs Controller General (India) (DGCI) on the proposals related to new drugs, clinical trials, new Investigational medical devices for regulatory approvals in the country. The SEC experts evaluate animal study, pre-clinical & clinical data along with the study protocol to undertake clinical trials to determine safety, efficacy and rationality of new drugs, Investigational medical devices.

The SECs are indispensable in the CDSCO's evaluation process due to their specialized expertise, independent perspective and commitment to quality assurance. These committees address complex scientific and regulatory challenges, fostering informed decision-making. By operating transparently and consistently across applications, SECs bolster public trust while safeguarding public health and promoting innovation in the healthcare sector.

The SECs of multiple therapeutic areas are in place viz. Oncology & Hematology, Cardiology & Nephrology, Neurology & Psychiatry, Endocrinology & Metabolism, Vaccine, Antimicrobials & Antiviral, Dermatology & Allergy, Ophthalmology, Pulmonary, etc. to advice CDSCO in evaluation of multiple categories of applications received and processed in various divisions of CDSCO.

Application of specific category are received and processed in the respective division for taking decision for forwarding the proposal to respective SEC. Depending on the nature of the product, category and purpose of application, the requirements, prescribed timelines for processing and priority may differ.

The SEC gives recommendations to CDSCO which are advisory in nature. CDSCO takes final decision under the applicable regulatory provisions considering all aspects including the recommendations of the SECs.

1.1.1 SEC Composition:

The Subject Expert Committee (SEC) comprises eminent experts drawn from different organizations such as Research Institute, Regulatory Bodies, Medical Colleges & Hospitals and other eminent institutions/organizations. These members possess a diverse range of expertise in fields like pharmacology, clinical research, statistics, epidemiology, medical devices, regulatory affairs, ethics and other related fields.

From the given panel of experts, subject expert committee (SECs) in various therapeutic areas are constituted comprising 8 experts (1 Pharmacologist and 7 specialists) drawing the names of the experts from the respective panels. In case any expert fails to attend the SEC meeting the another available expert from the same panel is invited to attend the meeting for evaluation of clinical trial and new drug/Investigational medical device application. A minimum of four members including one pharmacologist should be present to meet the quorum requirements.

1.1.2 Selection Criteria for SEC Members:

- **Expertise:** A proven track record (a minimum 10 publications in their domain/expertise) in the field of clinical trials/drug development is essential and a citation-to-publication ratio of at least 2:1 (20 citations per 10 publications) is required to ensure high-impact academic and research credentials.
- **Independence:** Affiliation with government, autonomous institutions, or academia is preferred to minimize potential conflicts of interest.
- **Term Limits:** Members serve a term of 3 years with the possibility of renewal to balance continuity with fresh perspectives.
- **Confidentiality:** Strict adherence to confidentiality protocols is mandatory to safeguard sensitive information.
- **Removal of expert:** Members who do not actively participate in meetings shall be subject to removal, with regular monitoring of their participation.

By adhering to these principles, the SECs are assured to be composed of highly qualified and impartial experts capable of providing rigorous evaluations of applications.

2. SEC review process:

2.1 Overview of the process:

- **Application Submission:** Applicants submit electronic applications to CDSCO through the Sugam portal/ MD Online with required documentation.
- **Document Evaluation:** CDSCO assesses the completeness and compliance of the application.
- **SEC Referral:** If required, the application is referred to the relevant SEC for expert evaluation.
- **Expert Review:** The SEC members examine the application, considering factors like safety, efficacy, quality, rationality and risk-benefit ratio.
- **SEC Meeting Notification:** Meeting will be notified to all the concerned with minimum 5 days in advance
- **SEC Meeting:** The SEC meets to discuss the application, ask questions to the applicant, and deliberate on the data presented.
- **SEC Meeting Quorum**: A minimum of four members including one pharmacologist should be present to meet the quorum requirements. In case of vaccines, quorum should include pediatrician and immunologist.
- **Recommendation:** The SEC will provide recommendations with its basis to CDSCO, which may include approval, rejection, or conditional approval along with specific requirements or further deliberation with additional data and the rationale for the recommendation.
- **CDSCO Decision:** CDSCO will take the final decision based on the SEC's recommendation and other regulatory considerations.

2.1.2 Applications Not Requiring SEC Review:

While most applications of new drugs, biological products, and new investigational medical devices necessitate SEC evaluation, certain categories may not require SEC intervention. These typically involve:

- **Routine Post-Approval Changes:** Minor modifications in product label, packaging, or Changes in quality information often do not necessitate SEC review. Minor queries raised in SEC, can be responded through online portal without re-deliberation
- **Administrative Changes:** Changes in company ownership, address, or contact information do not require SEC approval.
- **Minor CT/BA-BE protocol approval:** Minor changes which do not affect the quality and safety in CT/BA-BE protocols may not require SEC approval for an example: Change in study sites, change in sponsor address, extension of validity of NOC, extension of shelf life during the conduct of trial, change in ethics committee, etc.
- **Discontinuation or Withdrawal of Clinical trials:** Discontinuing or withdrawing a clinical trial may not require SEC review unless there is a concern about a clinical trial rights/safety of the trial participants/subject.

3. Bio wavier & CT waiver:

The drugs falling under BCS classification I & III may be exempted for BE study and as per the rules 101 of NDCT Rules 2019 for considering waiver of local clinical trial for approval of new drugs under chapter X, the countries namely; USA, UK, Japan, Australia, Canada and EU are hereby specified for following categories of new drugs:

a. Orphan drugs for rare disease.
b. Gene and Cellular therapy products.
c. New drugs used in pandemic situation.
d. New drugs used for special defense purpose.
e. New drugs having significant therapeutic advance over the current standard care.

4. Recommendation and Communication:

Following the applicant's presentation and Q&A, committee members engage in comprehensive deliberations, considering all presented information and raised questions. A final recommendation with clear justification should be made before the end of the meeting. Any reconsideration of a SEC decision requires prior notification and involvement of the relevant SEC members. The final recommendation for each application would be like:

- Recommended for Approval
- Recommended for Approval with minor changes (requiring no further SEC review)
- Recommended for Approval with major changes (requiring SEC re-evaluation)
- Recommended for Rejection.
- Further deliberation with additional data.

5. Re-deliberation of proposal:

In cases of re-deliberation, proper justification must be provided along with new data generated/published that was not available during the previous deliberation, to concern technical division. Ideally, the same SEC members participate in both the initial and subsequent reviews.

6. Technical Committee:

The cases rejected by the SEC shall, in case the applicant feels aggrieved, be placed before the Technical Committee for its consideration. Where the Technical Committee decides, for reasons to be recoded in writing to overrule the SEC, the decision of the Technical Committee shall be Final.

7. Roles & Responsibilities of the applicant:

The applicants play a crucial role in the SEC evaluation process. Their responsibilities include:

1. Submission of the briefing material along with one page summary and slides/presentation should be provided by the applicants and must be clear, concise and focused on the specific issues to be discussed by the SEC. The applicant should avoid including irrelevant or promotional information. The respective division of CDSCO should review and finalize this material which is to be forwarded to the SEC experts 5 days in advance, along with the presentation from applicant.

The briefing material should encompass the following key elements:

- A comprehensive overview of the product, including its mechanism of action or function with details of claims, indication, dosage and administration, adverse effects, contra indications, precaution and warning if any.
- Summarized non-clinical and clinical safety and efficacy data.
- A summary of adverse drug reaction data.
- A detailed analysis of safety and/or efficacy data relevant to the proposal.
- Complete clinical trial or BA/BE study protocols, including statistical justification for sample size.
- Proposed package inserts information, such as indications, dosage, administration, warnings, and precautions, etc. as per rules.
- Justification for any waivers (e.g., local clinical trial, BA/BE study).
- Regulatory status of the product in other countries, including approvals and package inserts.
- Previous SEC observations or recommendations (if applicable).
- A copy of the applicant's presentation slides with not more than 20-25 Slides.
- Relevant regulatory provisions and guidance documents.
- Pertinent published literature.

2. Submission of detailed information including preclinical, clinical, manufacturing, and quality data.

3. The application shall be submitted as per NDCT Rules 2019 and fees specified in sixth schedule.

7.1 Communication and Interaction:

- **Effective Communication:** Maintaining open and transparent communication with CDSCO throughout the application evaluation process.
- **Query Resolution:** Providing timely responses to queries on request of CDSCO based on SEC recommendation.
- **SEC Presentation:** Preparing and delivering clear and concise presentations during SEC meetings.

7.2 Data Integrity and Transparency:

- **Data Accuracy:** Ensuring the accuracy, reliability, and integrity of all submitted data.

- **Data Availability:** Providing access to original data for verification upon request.
- **Ethical Conduct:** Adhering to ethical principles in application submission, interaction and communication with CDSCO.

7.3 Post-Approval Compliance:

- **Adherence to Regulations:** Complying with post-approval requirements including pharmacovigilance, labeling and advertising regulations.
- **Continuous Monitoring:** Implementing systems for monitoring product safety and efficacy in post-market scenario.
- **Regulatory Updates:** Staying informed about regulatory changes and implementing necessary modifications.

8. Roles and Responsibilities of SEC members:

The SEC play a pivotal role in ensuring robust, scientific and ethical evaluation of the application in accordance with regulatory provisions and applicable guidelines.

8.1 Core Responsibilities:

- **Scientific Evaluation**: Conduct rigorous and comprehensive assessments of applications for clinical trials, new drugs, and medical devices. This involves evaluating the safety, efficacy and risk-benefit profile as well as the clinical study design, methodology, statistical analysis, and ethical considerations. Additionally, ensure the scientific validity and reliability of the data by reviewing proposals in accordance with both international and local guidelines and regulatory requirements.
- **Guidance and Support:** Provide expert advice to applicants on protocol and data generation in accordance with regulatory provisions and applicable guidelines to enhance the quality of clinical trials and applications.
- **Consistency:** Maintain standardized evaluation criteria across different therapeutic areas and fairness and predictability in the review process. **The interaction of the SEC members with the applicants during their presentation should be focused on addressing the questions relevant to the proposal.**

8.2 Specific Responsibilities:

- **Application Review:** Meticulously examining submitted proposals, assessing the scientific soundness, feasibility, and ethical acceptability of proposed clinical trial protocols.
- **Risk-Benefit Assessment:** Evaluating the potential benefits and risks of the product based on available evidence.
- **Compliance Evaluation:** Providing recommendation and advice to CDSCO for ensuring adherence in accordance with regulatory provisions and applicable guidelines.
- **Expert Opinion:** Providing expert opinions on complex scientific and technical issues.
- **Questioning Applicants:** Asking pertinent questions to clarify doubts and seek additional information during SEC meetings.

- **Consensus Building:** Participating in discussions and reaching consensus on recommendations.
- **Confidentiality:** Maintaining confidentiality of all information related to the application.
- **Conflict of Interest Management:** Declaring any potential conflicts of interest and recusing oneself from discussions if necessary.
- **Continuing Education:** Keeping abreast of the latest scientific advancements and regulatory updates.

8.2 Decision-Making and Communication:

- **Decision Making**: SEC should reach scientifically sound decisions based on consensus among committee members. Subsequent SECs cannot overrule the previous decision unless there is a strong reason to do that. CDSCO may also take the conflicting recommendations to the Technical Committee for a final decision.
- **Timely Review**: Adhere to specified timelines (within seven days) for Finalization of the recommendations from Experts to expedite approval process and application reviews.
- **Communication**: Provide recommendation and advise for maintaining open communication with applicants through response mechanism, providing clear feedback and addressing their inquiries.
- The SEC should follow the previous decision/ recommendations made in previous meetings and focus on current applications.
- All members should contribute to discussion and decision making.

The SEC's recommendation to grant a clinical trial waiver should be explicit, stated as either "Yes" or "No," and supported by a detailed justification. This justification must be formally documented. The waiver should comply with the provisions of the NDCT Rules, 2019/Medical Devices Rules 2017, while ensuring that the interests of all relevant parties are appropriately addressed.

Once clinical trial parameters like objective, design, eligibility criteria, safety and efficacy assessment criteria, etc. are decided for a specific drug product, they should remain consistent for subsequent applicants conducting similar studies to maintain data comparability and regulatory efficiency unless scientifically justified.

Topics unrelated to the product's safety, efficacy, or quality, such as pricing, should not be addressed during committee deliberations.

9. Preparing the Minutes of the Meeting:

The minutes should be prepared on the same day and after approval by SEC**,** the final minutes should be shared with the stakeholder within 7 working days of the meeting.

10. Roles and Responsibilities of the CDSCO moderator:

The moderators play a critical role in streamlining the discussion facilitating effective and productive SEC meetings.

Their primary responsibilities include:

- **Meeting Facilitation:** Guiding discussions, ensuring all members contribute, maintaining order, and adhering to the meeting agenda. The moderator should give advance briefings to experts before meetings or during the start of an actual meeting so that the discussion can start from where it ended in the first meeting of the same committee.
- **Issue Resolution:** Clarifying ambiguities, mediating disagreements and summarizing key points and decisions.
- **Stakeholder Coordination:** Liaising with relevant stakeholders as needed to ensure smooth meeting operations.
- **Expert Contribution:** Actively participating in discussions, sharing expertise, and encouraging diverse perspectives and ensure the regulatory compliance of applications.
- **Performance Enhancement:** Contributing to process improvements through focused assignments, detailed feedback and development of structured meeting materials.
- **Quality Assurance:** Striving to enhance review quality, optimize expert resource utilization, and generate actionable recommendations.

10.1 Other Responsibilities of the CDSCO moderator:

1. The respective division will also prepare the broad questions to be placed before the committee for deliberation. The questions should be proper, balanced and based on the proposal of the applicant and the relevant regulatory provisions.

2. The questions on each proposal shall be prepared by the respective divisions in advance with the approval of the concerned DDC(I)/JDC(I). A set of such questions as samples are enclosed as annexure for guidance to various divisions of CDSCO.

3. The briefing material and the questions on each proposal shall be shared with the members of the SEC and the Coordination Cell at least 5 days before the scheduled meeting of the SEC.

4. The questions shall also be shared with the respective applicant before the meeting so that they can prepare themselves to present their proposal before the committee in a proper, balanced and transparent manner for ensuring effective performance of the committee and the applicant.

5. Once specific agenda for SEC meeting is prepared by the respective division and forwarded to the Coordination Cell, the same will be then compiled and forwarded by the Coordination Cell to the members of the respective SEC and DCGI before the meeting.

6. The meeting notice/ invitation letter containing the list of proposals to be deliberated shall be prepared and issued by the SEC Coordination Cell to the expert members and concerned applicants for attending the meeting.

11. Voting Mechanism:

Subject Expert Committee may use a voting mechanism to determine their recommendations on regulatory issues.

- **Open Voting:** Committee members cast their votes openly, usually by a show of hands or electronic voting, etc.
- **Question-Based Voting:** Members vote on specific questions related to the topic under discussion.
- **Recommendation-Based Voting:** Members vote on the overall recommendation or approval of a product or application.
- **Advisory Role:** The majority of the experts will prevail in decision-making. The CDSCO ultimately makes the final decision, but the committee's vote is highly influential.

12. Broad Questions:

(for ensuring effective, balanced and proper interaction between the committee members and the applicants in SEC meeting/FAQ):

1. What efficacy data are necessary to evaluate the drug for the treatment of...?

2. What safety data are necessary to evaluate the risk of the drug when used for the indication…?

3. If you do not find the data adequate to support the indication, describe the data that would be necessary to support this indication?

4. Whether active comparator arms should be included for efficacy assessment in the clinical trial?

5. Whether placebo-controlled trial is adequate to evaluate the efficacy?

6. Whether active comparator arms should be included in the clinical trial for the indication…?

7. Whether placebo-controlled trial is adequate for safety assessment?

8. Does the data presented support approval of the new drug vaccine/ medical device / new indication/ dosage form /strength/ modified release form/pack size, etc. of the drug?

9. Does the data presented support approval of the proposed clinical trial/ BA-BE study/ global clinical trial/Phase IV clinical trial/ Active PMS study?

10. Based on the available safety data, whether the safety profile of the drug and based on the available data, the benefits to the patients outweigh the risks of the drug when approved for the indications?

11. Whether the benefits of the drug outweigh the risk for the indication ..… supporting approval of the drug?

12. Does the data from the local clinical trial, taken together with non-clinical and clinical data available from other countries, approval/marketing status in other countries, as presented by the applicant, provide evidence of efficacy of the drug for the treatment of …?

13. Does the data from the local clinical trial, taken together with the non–clinical and clinical data available from other countries as presented by the applicant, provide evidence of safety of the drug for the treatment of...?

14. Whether the nonclinical and clinical data from other countries, approval and marketing status of the drug in other countries, support the request of the applicant for waiver of local clinical trial/ BA-BE study/ Phase IV clinical trial under the relevant regulatory provisions and guidelines?

15. Do you recommend approval of the new drug / devices/ vaccine…?

16. Please deliberate if the data are adequate to support the proposed change in the indication from … to …?

17. Does the data from the non-clinical and clinical data available from other countries and other information on approval of the drug from other countries as presented by the applicant, support the use of the drug of all the doses and formulation for the treatment of …… with local clinical trial waiver?

18. Whether, the non-clinical and clinical data submitted/ presented provide evidence for safety of the trial subjects to be included as per the global clinical trial clinical trial protocol?

19. Whether, the non-clinical data submitted/ presented provide support for safety of the patients proposed to be included in the global clinical trial?

20. Whether, the clinical data submitted/ presented provide adequate support for the proposed global clinical trial to be conducted in India?

21. Whether, the non-clinical and clinical data submitted/ presented provide evidence for approval of the proposed global clinical trial protocol?

22. Whether, the proposed design of the clinical trial will ensure assessment of safety and efficacy of the new drug / vaccine/devices/….. for its approval in the country?

23. Whether the non-clinical and clinical data submitted/ presented provide adequate evidence for safety of the trial subjects to be included as per the clinical trial protocol?

24. Whether the data submitted/ presented support the rationality and usefulness of the new drug /FDC?

25. Whether rationality, PK/PD interaction, dosage compatibility data are adequate for considering the proposed clinical development of the FDC?

Additional Guiding Questions for SEC evaluation of application

Core Efficacy and Safety Assessment

1. Is the presented efficacy data sufficient to support the drug's intended indication?
2. Does the safety data adequately assess the drug's risk profile for the intended indication?
3. If data is insufficient, what additional information is required?
4. Is a placebo-controlled or active comparator trial necessary for efficacy evaluation?
5. Is a placebo-controlled trial sufficient for safety assessment?

Clinical Trial Design and Conduct

5. Does the presented data support the proposed clinical trial design (e.g., phase, endpoints, sample size)?
6. Is a local clinical trial, BA/BE study, or Phase IV trial necessary based on available data?
7. Does the data from other countries support the waiver of a local clinical trial?
8. Is the proposed global clinical trial design scientifically sound and ethical?
9. Does the data support the safety of trial subjects and patients in the proposed clinical trials?

Drug Approval and FDC Evaluation

10. Does the overall data support drug approval for the indicated use?
11. Does the data support the proposed change in indication?
12. Does the data support the use of all proposed doses and formulations?
13. Is the data sufficient to support the rationality and usefulness of the proposed fixed-dose combination (FDC)?

14. Are the pharmacokinetic (PK) and pharmacodynamics (PD) interaction data adequate for FDC development?

Investigational Medical Device

15. Does the clinical data generate on the device supports the claim of the device?

16. Whether the device is approved by the National Regulatory Authority of either the United Kingdom or the United States of America or Australia or Canada or Japan and it has been marketed for at least two years in that country?

17. Any Clinical data published in peer-reviewed journal and data relevant in the behavior and performance in the Indian population?

13. List of Annexures:

13.1 Important URL

13.1.1 Check list for applicants
13.1.2 SEC recommendation link
13.1.3 Waiver Order for Local Clinical Trials – Specified Countries (Rule 101)
13.1.4 Presentation Guidelines

Guidelines for PowerPoint Presentations for SEC Approval

In order to ensure uniformity, clarity, and effective communication during application review by the Subject Expert Committee (SEC), the following guidelines are issued for the preparation of PowerPoint Presentations (PPTs).

1. General Principles

- **Clarity**: Each slide must convey a clear, singular information relevant to SEC evaluation.
- **Conciseness**: Content should be brief, factual, and limited to essential information.
- **Professionalism**: Language and formatting must reflect professional standards.
- **Compliance-Oriented**: Content must directly address statutory and regulatory provisions.

2. Suggested Presentation Structure

Presentations must be **specific to the purpose of the SEC review**, typically emphasizing:

- Product overview including mechanism of action, claims, indications, dosage, administration, adverse effects, contraindications, and warnings.
- Summary of non-clinical and clinical safety/efficacy data, including adverse drug reactions.
- Detailed analysis supporting safety and/or efficacy relevant to the proposal.
- Complete clinical trial or BA/BE protocols with sample size justification.
- Proposed package insert as per regulatory norms.
- Justification for requested waivers (e.g., local trials or BA/BE studies).
- Regulatory status in other countries, including approvals and inserts.
- Previous SEC feedback (if applicable).
- Relevant regulatory provisions, guidance documents, and published literature.

Avoid content that falls outside the scope of SEC evaluation (e.g., commercial plans, marketing strategies, or manufacturing logistics unless directly related to clinical implications).

3. Design and Formatting

- **Slide Limit**: Around 20–25 slides is recommended to comprehensively cover the key points while keeping the presentation time-efficient.
- **Consistency**: Use a uniform template with sufficient white space.
- **Typography**: Sans-serif fonts (Arial/Calibri), minimum sizes: Title (36 pt), Headings (30 pt), Body (20 pt).
- **Text Density**: Prefer “Rule of Six” – max 6 lines/slide, 6 words/line.
- **Color Scheme**: Use 2–4 professional colors with high contrast.
- **Visuals**: Use relevant, high-resolution images, maps, and clean data charts.

4. Final Review

- **Proofreading**: Ensure slides are free from grammatical and factual errors.
- **Data Accuracy**: All information must be verified and evidence-based and correct.
- **Regulatory Alignment**: Ensure the presentation directly supports the SEC appraisal process.

** End of the document **