GUIDANCE DOCUMENT ON PROCEDURES TO BE FOLLOWED FOR EVALUATION OF APPLICATIONS BY THE SUBJECT EXPERT COMMITTEES

DRAFT GUIDANCE

This guidance document is for feedback purposes only. Comments suggestions, if any, may please be submitted to the office of Drugs Controller General India within thirty days

CENTRAL DRUGS STANDARD CONTROL ORGANIZATION
DIRECTORATE GENERAL OF HEALTH SERVICES
MINISTRY OF HEALTH & FAMILY WELFARE
GOVT. OF INDIA

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BACKGROUND

A robust evaluation process is critical for 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 and efficacy and quality data and other related information for approval of new drug or biological drug product, 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 Product, vaccines, Global Clinical Trial, Bioavailability & Bioequivalence (BA/BE) study, New Medical Devices, etc. which are received and processed in different divisions of CDSCO.

SUBJECT EXPERT COMMITTEE (SEC)

Subject Expert Committees (SECs) of multiple therapeutic areas are in place viz. Oncology & Hematology, Cardiology & Nephrology, Neurology & Psychiatry, Endocrinology & Metabolism, 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.

The SECs gives recommendation 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.

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.

Depending on the nature of the product, category and purpose of application, the requirements, prescribed timelines for processing and priority may differ.

Applications of a specific category are received and processed in the respective division for taking decision for forwarding the proposal to the respective SEC.

Similarly, for a proposal which has already been deliberated in any SEC and the SEC has sought additional data/ information or has not recommended for approval and subsequently, in response, the applicant has submitted further data/ information/clarification, the response of the firm is again examined by the respective division for taking decision to refer the proposal again to the expert committee for re-deliberation.

Once such decision is taken, the proposal is forwarded to Expert Committee Coordination Cell of CDSCO for deliberation or re-deliberation in the SEC meeting.

PROCEDURES TO BE FOLLOWED BY ALL CONCERNED FOR EFFICIENT VALUATION OF THE APPLICATIONS

In order to address the various challenges raised by the stakeholders including the committee members and have a robust evaluation process ensuring proper, balanced, consistent and transparent interaction with the applicants and deliberation by the expert members for evaluation of various proposals of new drugs, clinical trials, new medical devices etc. as mentioned above, following procedures shall be followed by the all concerned.

Briefing material

i. The respective division will prepare the briefing material of each of such proposals to be deliberated by the SEC which will be based on input from the applicant / information available in the application, available literature and the regulatory requirements and guidelines.

ii. The applicant will submit the briefing material to the concerned division of CDSCO, based on which the final briefing material to be provided to the SEC, will be prepared by the respective division.

iii. Depending on the categories of applications, the content of the briefing material may vary. The contents of the briefing materials on a particular proposal may also differ from meeting to meeting and the type and amount of information included will depend on the specific issues to be discussed.

iv. In general, it should contain the summary of the non-clinical and clinical data of safety and efficacy, regulatory status of the product, clinical trial, BA/BE study protocol, details of claims /indication, dosage and administration, adverse effects, contra indications, precaution and warning, if any, required to be the maintained during use of the product, detailed justification for waiver of local clinical trial. BA-BE study, as applicable etc. alongwith the presentation slides as provided by the applicant and the details of the questions required to be discussed /deliberated during the meeting.

v. The briefing material should emphasize the meeting’s focus based on the application.

vi. It is important that the briefing materials include only information related to the issue being discussed by the committee. Statements or suggestions that could be viewed as misleading or promotional are inappropriate for inclusion in the briefing materials. In addition, statements or language that are irrelevant, or

intemperate are inappropriate for inclusion in briefing materials and should be avoided.

vii. In general, the briefing material for the SEC should contain the following: -

- A general description of the product including mechanism of action /functions of the product;
- Summaries of non-clinical safety and efficacy data;
- Summaries of clinical safety and efficacy data;
- Summaries of adverse drug reaction data;
- Written discussion or analysis of safety and /or efficacy data relevant to the proposal;
- Clinical trial / BA-BE study protocols or summaries of protocols including statistical justification for sample size;
- Information that is proposed to be included in the package insert such as indications and usage, dosage and administration, and safety information such as warnings and precautions; etc;
- Justification for local clinical trial / BA-BE study waiver, as applicable,
- Details about the regulatory status of the new drug/ devices in other countries including the copy of approvals, as available from key countries, package insert circulated in other countries;
- Earlier observations / recommendations of SEC in re-deliberation case;
- Copy of the applicant's slides to be presented at the committee meeting;
- Relevant regulatory provisions as per the New Drugs and Clinical Trials Rules, 2019, Medical Devices Rules, 2017, as the case may be, and applicable guidance documents;
- Literature references including the copy of the relevant published literature;

Broad Questions for deliberation

i. 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.

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

iii. The briefing material and the questions on each proposal shall be shared with the members of the SEC and the Coordination Cell well in advance before the scheduled meeting of the SEC.

iv. 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.

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

vi. 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.

Presentation and interaction of the SEC members with the applicant

i. During the meeting, the applicant will make their presentation before the SEC focusing on the questions already forwarded to them in advance.

ii. The interaction of the SEC members with the applicant during their presentation shall be focused to address the questions raised on the proposal.

iii. For effective performance of a committee meeting following aspects needs to be ensured by all concerned:

- Clear and scientifically valid proper, balanced and transparent presentations of proposals by the applicants
- The committee hears from the applicants regarding the relevant proper, balanced, scientific/ regulatory aspects of the proposals.
- The tone of the committee interaction with the applicant as well as deliberations by the committee is set properly.
- Balance adherence to the agenda.
- Committee discussion and deliberation time is protected.
- Assurance of sufficient coverage of relevant issues.

Recommendation of the SEC

After the presentation and interaction of the SEC members with the applicant, the SEC members will deliberate the proposal with involvement of all the members present in the meeting.in light of the question placed before them and provide recommendation on the proposal with reason on the same day. deliberation

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Broad Questions for ensuring effective, balanced and proper interaction between the committee members and the applicants in SEC meeting

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

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

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

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

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

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

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

VIII. Do the data presented support approval of the new drug vaccine/ medical device / new indication/ dosage form /strength/ modified release form/ NDDS/pack size of the drug?

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

X. 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?

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

XII. Do 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 ……?

XIII. Do 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 ……?

XIV. 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?

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

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

XVII. Do 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?

XVIII. 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?

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

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

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

XXII. 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?

XXIII. 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?

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

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