DRAFT POLICY FOR APPROVAL OF NEW DRUGS

CENTRAL DRUGS STANDARD CONTROL ORGANIZATION

DIRECTORATE GENERAL OF HEALTH SERVICES

MINISTRY OF HEALTH & FAMILY WELFARE

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INTRODUCTION

1. A number of communicable as well as non-communicable diseases place heavy burdens in terms of morbidity and mortality, and economic losses, onto the populations and health systems of the country.

2. In order to address the disease burden, it is of paramount importance that safe and effective new drugs are developed and available for prevention and treatment of various diseases.

3. It is absolutely necessary to evaluate the safety and efficacy of any new drug before it is approved for manufacture or import and marketing in the country,

4. Clinical studies of new drug or investigation new drug are conducted to provide information that can ultimately improve access to safe and effective products with meaningful impact on patients, while protecting those participating in the studies.

5. Clear policy on regulatory requirements, system and procedures is critical for efficient development and approval of new drug through generation of adequate non-clinical and clinical data and their evaluation in transparent and scientific manner for assessment of safety and effectiveness of the new drug.

6. Such policy will not only enhance the public assurance that any new drug approved for marketing is safe and effective, but also facilitate and encourage the development of new drug in the country.

BACKGROUND

1. Import or manufacture for sale of drugs are regulated under Drugs and Cosmetics Act, 1940 and Drugs Rules, 1945 and New Drugs and Clinical Trials Rules, 2019.
2. Detailed requirements and guidelines for conduct of nonclinical and clinical studies and approval of new drug are specified in SECOND SCHEDULE of New Drugs and Clinical Trials Rules, 2019.

3. As per the rules, for manufacture or import of new drugs, the manufacturers/ importer are required to obtain manufacturing/ import permission from CDSCO under the New Drugs and Clinical Trials Rules, 2019 before Licencing the product under the Drugs Rules,1945.
4. Robust system for evaluation of applications of clinical trial and new drug which contains data of Chemistry, Manufacture, Control (CMC), non-clinical data, and clinical data and other regulatory information is critical to ensure safety and effectiveness of new drugs.
5. One of the recommendations of a committee constituted by the Ministry of H &F.W. for reforming the drug regulatory system in India is that there should be Policy on new drug approval.
6. Accordingly, this document has been prepared to provide policy on approval new drugs in the country.

POLICY ON NEW DRUG APPLICATION:

1. The content of New Drug Application (NDA) should be designed by the sponsor to answer general question as follows:
    i. Does the new drug provide a clinical benefit?
    ii. Is the associated risk outweighing the benefits for the proposed indication?
    iii. Can the product be manufactured ensuring quality and batch to batch consistency?
2. There should be a system that before an NDA is submitted to the CDSCO, the applicant should discuss with CDSCO wherein the applicant may present summary of the clinical, CMC, Pre-clinical, Clinical and any other information the applicant considers relevant.
3. Such discussion to help the reviewers becomes acquainted with the information to be included in the NDA.
4. In case the sponsor intends to seek exemption of local clinical trial, clear request for the same should be made in the NDA alongwith rationale and justification and the relevant regulatory provision, under which the exemption is sought.
5. Similarly, in case the sponsor intends to seek approval under Accelerated approval process or expeditious review process. clear request for the same

should be made in the NDA alongwith rationale and justification and the relevant regulatory provision, under which the exemption is sought.

6. However, accelerated approval should be used for a drug that represent significant advances over existing treatment or in case there is an unmet medical need for the indication for which the drug is intended, orphan drug for rare disease etc. in accordance with the provision prescribed under Second Schedule of ND&CT Rules, 2019.
7. ND & CT rules recognize the consideration of surrogate endpoints for approval of new drugs in certain situation where, the approval of a new drug may be based on the clinical data generated considering surrogate end-point rather than using standard outcome measures such as survival or disease progression which are reasonably likely to predict clinical benefit, or a clinical end point.
8. Surrogate endpoint may be acceptable if there is a strong indication that they will result in subject benefit.
9. Surrogate endpoint may not be acceptable if there are only causally related to clinical outcome.
10. As provided in the rules, surrogate marker should be considered as an interim data point and further clinical data should be generated following the approval of the new drug based on surrogate marker consideration that must unequivocally support the patients benefit.
11. Upon receipt of NDA the CDSCO should review the application to determine its completeness within timeline to be prescribed within which CDSCO either accepts the filing or sent its back to the applicant mentioning grounds for rejection.
12. After the NDA is accepted the various section of the application should undergo concurrent review. The non-clinical and chemical data should be reviewed in consultation with subject expert committee as per the standard procedures.
13. With the increasing globalization of drug development, it has also become important that data from global clinical trials (GCTs) can be accepted as the primary source of evidence to support marketing approval of new drug.
14. CDSCO recognize the global clinical trial data for considering the marketing approval of New drug under the provisions of the New Drugs and Clinical Trials Rules,2019.
15. However, detailed guidance documents should be prepared providing the requirements and adequacy of global clinical data that can be considered for

approval of any new drug in the country in both the cases where India was one of the participating countries in the global clinical trial or in cases where India was not a participating country.

16. The sponsor intending to submit NDA to CDSCO for marketing of new drug after successful generation of clinical trial data, should also plan and design GCTs considering the regulatory requirement as per the New Drugs and Clinical Trials Rules,201 and the applicable guidelines with the aim of increasing the acceptability of GCTs in regulatory submissions.
17. When easily co-relatable deficiencies are found during review the CDSCO should notify the applicant within the prescribed timelines and the applicant should send the additional information as soon as possible.
18. Based on the medical and scientific review the proposed package insert of the drug product should be reviewed in consultation with SEC.
19. Considering the recommendation of SEC and review, CDSCO will take decision for approval of the drug or otherwise in accordance with the ND&CT Rules, 2019.
20. The opinion/recommendations of SEC are not binding for CDSCO, however, CDSCO may override the opinion of SEC with details of the reason to be recorded in writing.
21. New Drug Application for submission to CDSCO should be prepared meticulously with well indexed, comprehensive and readable documents.
22. It is the responsibility of the applicant to submit data that satisfy the requirements as per the ND&CT Rules 2019 for review and approval of safe and effective drug products.
23. The NDA should include a cover letter that cite any relevant correspondence or meeting by date and topic along with a summary which should be presented in a comprehensive way. The most important formation about the drug product and the conclusion that can be drawn from the presentation.
24. The summary should contain a summary of each technical section, a discussion of the benefit and risk of a drug, a discussion of non-Indian marketing history of the drug and a copy of proposed package insert.
25. In case of a decision to approve a new drug, CDSCO should prepare a Summary Basis of Approval for the drug. The summary should contain the summary of CMC, non-clinical and clinical data and other relevant information based on which the drug is being consider for approval.

26. Because each therapeutic and diagnostic situation is different the amount of the data that must be submitted with each applicant should be adequate and in accordance with the rules and applicable guidelines.
27. The new drug application should be submitted to CDSCO when the sponsor is convinced and satisfied that the safety and efficacy of drug product has been established to the degree required as per the ND&CT Rules, 2019 to permit appropriate use by medical professional for prevention or alleviation of human suffering.

POLICY ON POST-APPROVAL STUDIES

1. Post-approval studies may be required to provide additional information on the efficacy, safety, and use of the drug in populations more diverse than included in the clinical trials conducted prior to approval of the new drug in accordance with the provisions of the rules.
2. Necessary guidance documents should o be developed to provide the extent of requirements of such studies depending on the nature of the new drug, rarity and severity, unmet medical need, etc. for the disease for which the drug is indicated and the overall data that was available at the time of approval.

PRESENTATION AND SUBMISSION OF APPLICATION

1. In order to make regulatory review process as efficient for CDSCO as possible, the submission of applications for approval of clinical trials and new drugs to CDSCO ensuring conciseness, correctness, consistency and clarity.
2. A clear well-presented submission facilitates the evaluation process in a timely manner, whereas, a difficult-to-evaluation submission will require more time to correct the deficiencies before actual evaluation can proceed leading to delay in taking final decision on the application.
3. Thus, in order to evaluate the applications of new drugs and clinical trials applications under the ND &CT rules should be submitted in CTD format only.

INDUSTRY AND CDSCO COMMUNICATION

1. CDSCO needs to work collaboratively and cooperatively with Industry, academia and others to promote new drug development and to expedite the review process

and making the safe and effective new drugs available at the earliest to address various disease burden in the country.

2. CDSCO should be dedicated to ensure that all persons involved in the new drug development have the regulatory information including the regulatory requirements, process needed to research, develop, review, market and distribute the drug safely and effectively in the country.
3. To enhance the communication aspects, CDSCO should ensure that the industry representatives, and other stakeholders have easy and open access to all the relevant regulatory information and are educated about the drug regulatory requirements, process involved in new drug development.
4. Similarly, CDSCO meetings including Pre-submission/ Post–submission/SEC meetings should be held as per the laid down procedures efficiently to facilitate the development of safe and effective new drugs in the country.

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