Central Drugs Standard Control Organization
Directorate General of Health Services
Ministry of Health and Family Welfare
Government of India

New Drugs Division

Frequently Asked Questions (FAQs) on Approval of new Phytopharmaceutical Drugs

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Notice:

The replies to the FAQs are aimed only for creating public awareness about new phytopharmaceutical drugs regulations by CDSCO and are not meant to be used for legal or professional purposes. The readers are advised to refer to the statutory provisions of Drugs and Cosmetics Act & Rules and respective Guidelines / Clarifications issued by CDSCO from time to time for all their professional needs

FREQUENTLY ASKED QUESTIONS (FAQs) ON APPROVAL OF NEW PHYTOPHARMACEUTICAL DRUGS

1. What is a phytopharmaceutical drug?

"Phytopharmaceutical drug" includes purified and standard fraction with defined minimum four bio-active or phyto-chemical compound (qualitatively and quantitatively assessed) of an extract of a medicinal plant or its part, for internal or external use of human beings or animals for diagnosis, treatment, mitigation or prevention of any disease or disorder but does not include administration by parenteral route as specified in Rule 2 (eb) of the Drugs & Cosmetics (D&C) Rules, 1945.

2. When a phytopharmaceutical drug is considered as new drug?

As defined in the Rule 122E of D&C Rules, a phytopharmaceutical drug which has not been used in the country to any significant extent under the conditions prescribed, recommended or suggested in the labeling thereof and has not been recognised as effective and safe by the licensing authority mentioned under Rule 21 of D&C Rules for the proposed claims is considered as a new drug.

3. How does phytopharmaceutical drug differ from ayurvedic, siddha or unani (ASU) under Section 3 (a) & (h) of Drugs & Cosmetic Act 1940?

Ayurvedic, Siddha or Unani drugs include all medicines intended for internal or external use for or in the diagnosis, treatment, mitigation or prevention of (disease or disorder in human beings or animals, and manufactured) exclusively in accordance with the formulae described in, the authoritative books of ayurvedic, siddha and unani tibb systems of medicine specified in the first Schedule. However, phytopharmaceutical drugs are fraction of crude extract and are distinctly differentiated by being purified and standardized.

4. The definition demands "with defined minimum four bio-active / phyto chemical compounds (qualitatively & quantitatively assessed)". Should four bio-active / phyto chemical compounds need to be assessed qualitatively & quantitatively?

Minimum four compounds shall be identified as bio-active / phyto chemical compounds. It is ideally if all of them are bio active, hence the condition of identification of minimum four compounds from fraction is non-negotiable. The number of compounds with bio activity may be considered on case to case basis, based on the justification submitted by the applicant. However the applicant should specify the limits of the bio-active / phyto chemical compounds for maintaining batch to batch consistency.

5. Does a new phytopharmaceutical drug undergo clinical trial in India?

The data requirements have been specified in the *Appendix IB* of Schedule Y of D&C Rules.

(i) Clinical trials for phytopharmaceutical drugs to be conducted as per applicable rules and guidelines for new drugs.

(ii) For all phytopharmaceutical drugs data from phase I (to determine maximum tolerated dose and associated toxicities) and the protocols shall be submitted prior to performing the studies.

(iii) Data of results of dose finding studies performed and the protocols shall be submitted prior to performing the studies.

Provided that in the case of phytopharmaceutical drug already marketed for more than five years or where there is adequate published evidence regarding the safety of the phytopharmaceutical drug, the studies may be abbreviated, modified or relaxed.

6. How and where to apply for grant of permission to import or manufacture new phytopharmaceutical drug (as new drug) in the country for sale or to undertake clinical trial?

Applications for grant of permission to import or manufacture new phytopharmaceutical drug are to be made in Form 44 prescribed in D&C Rule to Drugs Controller General (India), Central Drugs Standard Control Organization, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India, FDA Bhawan, ITO, Kotla Road, New Delhi -110002. Applicant shall submit all the documents specified under *Appendix IB* of Schedule Y of D&C Rules. (Checklist for submission is available on CDSCO website).

Applications as per checklist can be mailed by Post to Drugs Controller General (India), (Address as specified above).

7. New drug applications are currently required to be filed online to DCG(I) Office. Whether online submission of applications for phytopharmaceutical drugs is available?

Work on providing access and necessary data entry for filing phytopharmaceutical application online is ongoing and will be made possible in due course of time. In the meantime interested stakeholders may file hard copy applications along with suitable covering letter to CDSCO. Such applications would be received and acknowledged by CDSCO after pre- screening as per the checklist.

8. What are the fees to be paid along with the application for grant of permission to import / manufacture of new phytopharmaceutical drug?

(i) Application for grant of permission to import new phytopharmaceutical drug (Form 44) - Rs 50,000/-.

(ii) Application for grant of permission to manufacture new phytopharmaceutical drug (Form 44) - Rs 50,000/- .

9. What are the fees to be paid along with the application for grant of permission to conduct clinical trial for new phytopharmaceutical drug?

(i) Clinical trial Phase-I application (Form 44) - Rs 50,000/-

(ii) Clinical trial Phase-II application (Form 44) - Rs 25,000/-

(iii) Clinical trial Phase-III application (Form 44) - Rs 25,000/-

However, as specified under Rule 122DA (2) (c), no fees shall be required to be paid along with the application by Central Government or State Government Institutes involved in clinical research for conducing trials for academic or research purpose

(iv) Application for import of new phytopharmaceutical drug for purpose of examination, test or analysis (Form 12) - Rs 100/- for single drug and additional fee of Rs 50/- for each additional drug.

10. Where and how to deposit the specified fees for the application?

The fees shall be paid through a Challan in the Bank of Baroda, Kasturba Gandhi Marg, New Delhi-110001 or any other branch or branches of Bank of Baroda, or any other bank, as notified, from time to time by the Central Government, to be credited under the Head of Account "0210-Medical and Public Health, 04-Public Health, 104-Fees and Fines". Following are the additional banks notified by the Govt. where fees can be deposited.

1. Bank of Baroda, Law Garden Branch, Bank of Baroda Towers, Ellis Bridge, Ahmedabad-380006.
2. Bank of Baroda, Plot No 8/3/2014/17, Annapurna Nilayam, B.K. Guda, S.R Nagar, Hyderabad Nagar 500038.
3. Bank of Baroda, Raj Nagar Branch, Raj Nagar, Ghaziabad-201002, Uttar Pradesh.
4. Bank of Baroda Tardeo Branch, Everest Building, D.J Dadaji Road, Tardeo, Mumbai 400034.
5. Bank of Baroda, India Exchange Branch, 4, India Exchange Place, Kolkata-700001.
6. Bank of Baroda, Chennai Main Branch, 70, Rajaji Salai, Chennai-600001.
7. Bank of Baroda. SCO-212, Sector-40-D, Chandigarh-160036.
8. Bank of Baroda, Gandhinagar Branch, Fole Market, Gandhinagar, Jammu, Jammu Tawi.
9. Bank of Baroda, Vasco-Da-Gama Branch, P.O.-144, Swatantra Path, Vasco-Da-Gama, Goa-403802.
10. Bank of Baroda, Malleswaram Branch, 74, Seventh Cross, Malleswaram, Bangalore.

11. What are the conventional preclinical study & safety document required to be submitted alongwith application for phytopharmaceutical drug?

Based on disease, nature of phytopharmaceutical drug and duration of treatment the applicant may submit as much as available documents to establish safety and efficacy of the phytopharmaceutical drug as specified under *Appendix IB* of Schedule Y of D&C Rules.

12. Whether parenteral formulation of phytopharmaceutical drugs can be considered for market authorization in India?

No. As per the definition specified under Rule 2 (eb) of the D & C Rules the parenteral dosage form of phytopharmaceutical drugs cannot be considered for market authorization.

13. Can phytopharmaceutical drug be sold as without prescription or is it prescription drug?

CDSCO would specify this aspect, whether any phytopharmaceutical drug for which marketing authorization is issued need to be sold only against prescription of a R.M.P. / specialist / or it can be sold without prescription.

14. What are the current GMP requirements to manufacture phytopharmaceutical drugs?

GMP requirements for manufacture of drugs are prescribed in the Schedule M of the D & C Rules. However, presently, there is no specific GMP guidelines finalised for Phytopharmaceutical drugs. The GMP requirements would depend on the ingredients and the stage of processing. It may be recognized that a common GMP requirements across the chain - raw herb (cultivation / collection / drying / minimal processing / storage and transport): processing of botanical (grinding / extraction / fractionation steps / other unit operations like spry drying, tray drying etc / packing and storage in bulk): formulation (compatibility with excipients / dosage form selected for product formulation / various steps involved in the production etc) should be implemented.

It is expected that this area will be further developed in the future and currently applicants would need to adopt such procedures and documentation that would prevent contamination, degradation and protect the quality and integrity of the final phytopharmaceutical product.

15. What shall be the Pharmacopoeial standard of Phytopharmaceuticals?

Currently no phytopharmaceutical drug has been approved by the CDSCO as a new drug meeting the definition of phytopharmaceutical drug. As and when CDSCO will approve a phytopharmaceutical drug the aspect of including a monograph in IP would be considered keeping in mind various other factors.

16. What shall be the quality standard of raw material used for Phytopharmaceuticals, IP or USP etc.?

The applicant will need to provide adequate information including specifications and test methods for raw botanical, processed botanical forming the phytopharmaceutical and the formulation of the phytopharmaceutical as prescribed in *Appendix IB* of Schedule Y of the D&C Rules. The applicant should adopt monograph for any of these parameters as per the general standards prescribed in IP. If not prescribed in IP but included in the official Pharmacopoeia of any other country, same may be followed.

17. Samples of new drugs normally go through a step of checking the specification and test method for the new drug in one of the central drug-testing laboratories. Would a similar step is involved for a phytopharmaceutical drug for quality?

Yes. In fact the applicant is required to send adequate quantity of phytopharmaceutical, phytopharmaceutical formulation / product along with adequate quantities of all the identified bio-active / phyto chemical compounds to the laboratories when demanded by the CDSCO for testing.

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***Note*: Any suggestions to this document may be communicated to *email*: dci@cdsco.nic.in**