F. No. 04-01/2013-DC (Misc. 13-PSC) (Pt. II) (Sub Part-1)
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(FDC Division)

FDA Bhawan, Kotla Road,
New Delhi

Dated:
24 FEB 2025

To
All State/UT Drugs Controllers,

Subject:- Evaluation of certain pre 1988 permitted Fixed Dose Combinations (FDCs) de novo for manufacture for sale in the country without due approval from Central Licensing Authority -regarding.

Sir,

This is in continuation to this Directorate notice of even number dated 11.01.2024. As per this said letter, manufacturers who are already holding licenses from State Licensing Authorities for such FDCs before 01.10.2012 and did not apply to DCG (I) were required to submit their applications for Phase IV Clinical Trial protocol / Active Post Marketing Surveillance to this Directorate. The date for filing such applications expired on 11.07.2024 and already passed approximate 12 months from the date of above mentioned notice.

However, it is observed that most of the firms have not submitted their application to this Directorate. It has been decided that the manufacturers/stakeholders who were holding license prior to 01.10.2012 may submit their applications w.r.t category 'd' FDCs within 03 months from the date of issuance of this letter.

In view of above, without prejudice to legal validity of such product licenses, all the concerned manufacturers/stakeholders may be requested to submit their application within 03 months from the date of issuance of this letter, failing which appropriate regulatory action will be recommended from CDSCO.

Yours faithfully

(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India)

Copy to:-

1. PS to JS(R), Ministry of Health and family Welfare, Nirman Bhawan, New Delhi
2. CDSCO Zonal and Sub-Zonal offices
3. Indian Drug/Pharmaceuticals Association Forum
4. Website of CDSCO

File No. 4-01/2013-DC (Misc. 13-PSC) (Pt. II) (Sub Part-1)
Govt. of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(FDC Division)

Dated: 11 JAN 2024

NOTICE

Subject: Evaluation of certain pre 1988 permitted Fixed Dose Combinations (FDCs) de novo for manufacture for sale in the country without due approval from Central Licensing Authority -regarding.

This is with reference to this office letter dated 15.01.2013 whereby all the State/UT Drugs Controllers were requested to ask the concerned manufacturers in their State to prove the safety and efficacy of FDCs within 18 months which were permitted by State Licensing Authorities without due approval from the office of DCG(I).

In continuation to Hon'ble Supreme Court order dated 15.12.2017 and 14.02.2019, Accordingly, Ministry of Health & Family Welfare vide order No. X11035/53/2014-DFQC (Part-IV) dated 02.02.2021 constituted an Expert Committee under the Chairmanship of Dr. M. S. Bhatia, Professor & Head, D/o Psychiatry, University College of Medical Sciences, New Delhi for examining certain pre-1988 FDCs denovo licensed for manufacturing for sale in the country without due approval from Central Licensing Authority.

The Expert Committee submitted its report accordingly on these 19 FDCs claimed to be pre-1988 after holding a series of meetings as well as by providing hearing to the stakeholders wherein, the Committee after detailed deliberation recommended for generation of data w.r.t. following 03 FDCs:-

Sr. No.	Name of FDC as per the public notice	Recommendations
1.	Paracetamol IP 500mg + Phenylephrine Hydrochloride IP 10mg + Caffeine Anhydrous IP 32mg tablets	The committee recommended for continued manufacturing and marketing of the FDC with the condition to generate safety and efficacy data by way of conducting Phase IV Clinical Trial. Accordingly, Phase IV Clinical Trial is required to be conducted to generate the data within time frame of one year.

2.	Caffeine Anhydrous IP + Paracetamol IP + Phenylephrine Hydrochloride IP + Chlorpheniramine Maleate IP (15mg + 500mg + 5mg + 2mg, 30mg + 500mg + 5mg + 2mg, 30mg + 500mg + 10mg + 2mg, 30mg + 500mg + 10mg + 4mg & 30mg + 650mg + 10mg + 2mg) tablets	The committee recommended for continued manufacturing and marketing of FDC with following conditions: a. FDC shall be sold by retail on the prescription of a R.M.P. only b. Package insert should also mention caution for patients suffering from cardiovascular diseases. c. Dose of Paracetamol in the FDC should be minimum 500mg The Committee also recommended to conduct a Randomized comparative, Phase IV Clinical Trial comparing the FDC with the individual ingredients present in the FDC. Accordingly, Phase IV Clinical Trial is required to be conducted to generate the data within time frame of one year.
3.	Paracetamol IP 250mg + Propyphenazone 150mg + Caffeine 30mg tablets	The committee recommended for continued manufacturing and marketing of the FDC for mild to moderate Headache with the conditions that: a. FDC shall not be taken more than 5 to 7 days b. FDC to be sold by retail on the prescription of a R.M.P. only". c. Further, the firm(s) shall conduct Active PMS study to generate safety and efficacy data on the FDC. Accordingly, Active Post Marketing Surveillance is required to be conducted to generate the data within time frame of one year.

With the approval of Ministry, it has been now decided to follow the pathway for clearance of such subsequent applications as under:-

1. Documents required in case of manufacturers already holding licenses from State Licensing Authority (SLA) before 01.10.2012 for the proposed FDCs shall at least contains:-
    a) Form CT-21 (duly filled, signed and stamped)
    b) Fees as specified in sixth schedule of New Drugs and Clinical Trials Rules 2019 through Bharatkosh.
    c) Name and composition of the FDC
    d) Product Permission issued by SLA
    e) Copy of Manufacturing license in Form 25/28

f) Phase IV trial protocol / commitment for conducting Active Post Marketing Surveillance study protocol, as the case may be.

2. Documents required in case of new manufacturers for the proposed FDCs shall at least contain:-
    a) Form CT-21 (duly filled, signed and stamped)
    b) Fees as specified in sixth schedule of New Drugs and Clinical Trials Rules 2019 through Bharatkosh.
    c) Name and composition of the FDC
    d) Product Permission issued by SLA in Form 29
    e) Copy of Manufacturing license in Form 25/28
    f) Stability studies data (06 months accelerated)
    g) Test Specifications of the FDC alongwith Method of Analysis
    h) Phase IV trial protocol / commitment for conducting Active Post Marketing Surveillance study protocol, as the case may be.

3. All the manufacturers who are already holding licenses from State Licensing Authorities for such FDCs before 01.10.2012 and did not apply to DCG (I) are required to submit their applications to this Directorate at the earliest but not later than 6 months, failing which their applications will not be considered and their licenses will be considered as without legal validity.
4. Manufacturers shall comply with the recommendation of the expert committee w.r.t. revision of the prescribing information/label.

In view of above, all concerned stakeholders are required to follow above procedure for clearance of such cases.

Yours faithfully,

(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India)

To:-
All State/UT Drugs Controllers/All Zonal/Sub Zonal offices of CDSCO.

Copy to:-
1. PPS to Secretary/AS(F&D)/JS(R), Ministry of Health and Family Welfare, Nirman Bhawan, New Delhi.
2. Indian Drug & Pharmaceuticals Associations/Website of CDSCO.