F. No. 12-01/21-DC(Pt-15)
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(New Drugs Division)

FDA Bhawan, Kotla Road
New Delhi- 110002
Dated: 23/7/2021

CIRCULAR

Subject: Clarification if change in a) polymorphs/crystalline/amorphous/solvates/ hydrate etc (b) Salt and (c) Derivative/analogue/ester etc of already approved active substance to be considered as new drug if main active moiety (Active Pharmaceutical Ingredient-API) is same? -Reg.

Representation has been received seeking clarification, if already approved drugs with change in

(a) Polymorphs/crystalline/amorphous/solvates/hydrate etc,
(b) Salt, and
(c) Derivative/ analogue/ester etc are manufactured using the new manufacturing process, will be considered as old drug or new drug.

It is clarified that change in (a) (b) & (c) of already approved active substance may lead to change in drugs specification and may influence on;

- Physicochemical properties particle size, hygroscopicity, solubility, density, flowability and compatibility etc.
- Dissolution, bioavailability and bioequivalence.
- Manufacturing of drug substance/drug product.
- Stability of drug substance/drug product.

Hence, change in (a) (b) & (c) of already approved active substance may require validation of manufacturing process, stability studies, additional clinical and non-clinical studies, Bioavailability/Bioequivalence studies, to demonstrate its safety and efficacy.

Therefore, any new (a) (b) & (c) of already approved active substance is considered as new drug. However, applications of such new drug may be processed considering following: -

I. In case (a) (b) & (c) of already approved active substance is significantly affecting physicochemical properties, manufacturing process, stability, safety and efficacy and Bioavailability/Bioequivalence etc. the new drug will be processed as new active substance and requirements will be same as for any new active substance as prescribed in New Drugs and Clinical Trials Rules, 2019.

II. In case of any (a) (b) & (c) of already approved active substance, if there is no significant effect on physicochemical properties, manufacturing process, stability, safety and efficacy and Bioavailability/Bioequivalence etc. the new drug will be processed as subsequent new drug of already approved new drug and requirements will be same as for new claim for any on already approved new drug, as prescribed in New Drugs and Clinical Trials Rules, 2019.

Accordingly, applicant should submit application as per the requirement prescribed in the New Drugs and Clinical Trials Rules, 2019.

(Dr. V. G. Somani)
Drugs Controller General (India)

To,

1. All States/UTs Drug Controllers.
2. All Zonal/Subzonal/Port Offices of CDSCO.

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All stakeholders through CDSCO website.