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F. No 12-44/14-DC
Directorate General of Health Services
Office of Drugs Controller General (India)
(New Drug Division)

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FDA Bhawan,
Kotla Road, New Delhi
Dated: 10-01-2018

To

Dr. C. Padmapriyadarsini,
National Institute for Research in Tuberculosis,
ICMR (Indian Council of Medical Research)
No. 01, Mayor, Sathyamoorthy Road,
Chetpet, Chennai – 600 031.

Subject: Permission to Conduct a Stage II, Open Label, Non-Randomized, Two stage, Dose –Finding study of Verapamil [IR] Tablet Formulation in Adult Tuberculosis Patients in Continuation Phase of Anti- Tuberculosis Treatment (Stage-I) - regarding.

Reference: Your letter no. NIRT/DIR/Verapamil/DCGI/Re/2017 dated 10-01-2018 24.07.2017 on the subject mentioned above.

CT NOC No. CT/ND/111/2017

Madam,

This Directorate has no objection to your conducting the subject mentioned clinical trial as per the provisions of Drugs & Cosmetics Rules under supervision of the following investigator and as per the protocol version no. 3.2 dated 10.11.2017.

Sr. No.	Investigator & Trial site	Ethics Committee Name/Registration Number
1.	Dr. C. Padmapriyadarsini National Institute for Research in Tuberculosis, (ICMR) No. 01, Mayor, Sathyamoorthy Road, Chetpet, Chennai – 600 031.	Institutional Ethics Committee-NIRT National Institute for Research in Tuberculosis, (ICMR) No. 01, Mayor, Sathyamoorthy Road, Chetpet, Chennai – 600 031. **ECR/135/Inst/TN/2013**
2.	Dr. Rohit Sarin, Director National Institute of TB & Respiratory Diseases, Sri Aurobindo Marg, New Delhi – 110 030	Institutional Ethics Committee-NITRD National Institute of TB & Respiratory Diseases(NITRED) , Sri Aurobindo Marg, New Delhi – 110 030. **ECR/315/Inst/DL/2013**

Kindly note that the clinical trial permission is subject to the following conditions:

a) Clinical trial shall be conducted in compliance with the approved protocols, requirements of Schedule Y, Good Clinical Practice Guidelines issued by this Directorate and other applicable regulations.

b) Approval of Institutional Ethics Committee duly registered with CDSCO (under Rule 122DD of Drugs & Cosmetics Rules) should be obtained and submitted to this Directorate before initiation of the study.

c) Clinical trials shall be registered at Clinical trials Registry of India before enrolling the first patient for the study.

d) Annual status report of each clinical trial, as to whether it is ongoing, completed or terminated, shall be submitted to the Licensing Authority, and in case of termination of any clinical trial the detailed reasons for the same shall be communicated to the said Licensing Authority.

e) Any report of serious adverse event occurring during clinical trial study to the subject, after due analysis, shall be forwarded within ten days of its occurrence as per Appendix XI and in compliance with the procedures prescribed in Schedule Y.

f) In case of an injury or death during the study to the subjects, the applicant shall provide complete medical management and compensation in the case of trial related injury or death in accordance with rule 122 DAB and the procedures prescribed under Schedule Y, and the details of compensation provided in such cases shall be intimated to the Licensing Authority within thirty days of the receipt of the order of the said authority.

g) The premises of Sponsor including their employees, subsidiaries and branches, their agents, contractors and sub-contractors and clinical trial study sites shall be open to inspection by the officers authorized by the Central Drugs Standard Control Organization, who may be accompanied by an officer of the State Drug Control Authority concerned, to verify compliance to the requirements of Schedule Y, Good Clinical Practices guidelines for conduct of clinical trial in India and other applicable regulations.

h) The Sponsor including their employees, subsidiaries and branches, their agents, contractors and sub-contractors and clinical trial study sites and the Investigator shall allow officers authorized by the Central Drugs Standard Control Organization, who may be accompanied by an officer of the State Drug Control Authority concerned, to enter with or without prior notice, any premises of Sponsor including their employees, subsidiaries and branches, their agents, contractors and sub-contractors and clinical trial sites to inspect, search and seize any record, data, document, books, investigational drugs, etc. Related to clinical trial and provide adequate replies to any queries raised by the inspecting authority in relation to the conduct of clinical trial.

i) Clinical trial shall be conducted only at those sites which are institutes/hospitals having adequate emergency facilities and duly registered Institutional Ethics committees.

j) The sponsor shall ensure that the number of clinical trials an investigator can undertake should be commensurate with the nature of the trial, facility available with the Investigator etc. However, under no circumstances the number of trials to be conducted by an Investigator should be more than three at a time.

k) The details of payment/honorarium/financial support/fees paid by the Sponsor to the Investigator(s) for conducting the study shall be made available to this directorate before initiation of each of the trial sites.

l) In addition to the requirement of obtaining written informed consent, audio - visual recording of the informed consent process of each trial subject, including the procedure of providing information to the subject and his/her understanding on such consent is required to be done while adhering to the principles of confidentiality. Such audio-visual recording and related documentation shall be preserved. This is applicable to the new subjects to be enrolled in all clinical trials including Global Clinical Trials. All the sponsor/ Investigators /Institutes/Organizations and other stake holders involved in conduct of clinical trials in the country are required to adhere to this requirement of audio-visual recording of informed consent process of trial subjects.

m) The formulations intended to be used in the clinical trial shall be manufactured under GMP conditions.

n) Target AUC &Cmax of Verapamil should be less than the levels achieved with maximum tolerated dose of the drug.

o) The exclusion criteria should be modified to exclude patient with systolic blood pressure of less than 100 and/or pulse rate of less than 60.

p) Detailed rescue plan particularly related to the cardiovascular complications should be included.

q) After every dose data of respective group should be reviewed by the DSMB before proceeding to the next dose.

r) Stage-II study report shall be submitted to office of DCG (I).

Yours faithfully,

(Dr. G.N Singh)
Drugs Controller General (India)