Diary No: 11181
Date: 02.04.18

F. No 12-66/12-DC
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
FDA Bhawan, New Delhi – 110002 (India)
New Drugs Division

Tele No.011-23236965
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FDA Bhavan ,Kotla road
NewDelhi.
Dated : 17.01.2019

To
M/s Sanofi-Syntholabo(i) Pvt.Ltd.
Sanofi House, CT Survey No. 117-B,
L&T Business Park, Saki Vihar Road,
Powai Mumbai – 400072

Subject: Phase IV clinical study of Teriflunomide Tablets 14 mg.

CT NOC No.CT/ND/72/2018

Reference: Your application diary no 11181 dated 02.04.2018 on the subject mentioned above.

Sir,

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 No: TERIFL08918484, Version 1.1, dated 04.12.2018 submitted to this Directorate.

S.No	Investigator and Trial site	Ethics Committee Name and Registration Number
1.	**Dr. A.K Meena** MD,DM(Neurology) Nizam's Institute of Medical Sciences Nizam's Institute of Medical sciences Millenium Block, Room No. 110, Panjgutta Hyderabad, Telangana, India – 500082. Department ofChhatrapati Sahuji Ma Lucknow, 226003, Uttar Pradesh, India	**ECR/303/Inst/AP/2013/RR-16** NIMS Ethics Committee Nizams Institute of Medical Sciences,Punjgutta,Hyderbad 500082, Andhra Pradesh, India
2.	Dr.Dhiraj Khurana MD,DM(Neurology) Postgraduate Institute of Medical	**ECR/25/Inst/CH/2013/RR-16** Postgraduate Institute of Medical Education & Research, Chandigarh

	Education & Research(PGIMER),Chandigarh Postgraduate Institute of Medical Education & Research (PGIMER), Chandigarh	– Institutional Ethics Committee Postgraduate Institute of Medical Education and research, Room No. 6006, Sixth floor, Pn Chuttani Block, Chandigarh – 160012.
3.	**Dr. Manjari Tripathi** MD,DM(Neurology) All India Institute of Medical Scineces Room No. 705, 7th Floor, C.N. Centre, AIIMS, Ansari Nagar, New Delhi - 110029	**ECR/538/Inst/DL/2013/RR-17** All India Institute of Medical Sciences Institute Ethics Committee All India Institute Of Medical Sciences, Room No. 102,1st Floor, Old O.T. Block, Ansari Nagar, New Delhi-110029, India
4.	**Dr. JD Mukherjee** MD, DM (Neurology) West Block, Ground Floor, Press Enclave Road, Mandir Marg, Saket, New Delhi 110017 Delhi	**ECR/110/Inst/DL/2013/RR-16** Max Healthcare Ethics committee Max Super Specialty Hospital, 6th Floor 2, Press Enclave Road, Saket, New Delhi- 110017, India
5.	**Dr. Ish Anand** MD, DNB (Neurology) Sir Ganga Ram Hospital Room No. 1412, 4th Floor, Old Building Sir Ganga Ram Hospital , Sir Ganga Ram Hospital Marg, Rajinder Nagar,New Delhi-110060	**ECR/20/Inst/DL/2013/RR- 16** Sir Ganga Ram Hospital Ethics Committee Room No 1496, 4th Floor, Old Building, Old Rajinder Nagar, New Delhi-110060
6.	**Dr. Pahari Ghosh** MD, DM (Neurology) Sri Aurobindo Seva Kendra Room No. 114A, 1st Floor OPD, Sri Aurobindo Seva Kendra 1H, Gariahat road (South), Jodhpur Park, Kolkata-700068	**ECR/317/Aurobindo/Inst/WB/2013** Institutional Ethics Committee Sri Aurobindo Seva Kendra, 1 H, Gaiahat Road (South), Jodhpur Park, Kolkata- 700 068
7.	**Dr. Sumit Singh** MD, DM (Neurology) Artemis Health Institute Clinical Research Room, Ground Floor, Artemis Hospital Sector 51, Gurgaon-122001,	ECR/53/Inst/HR/2013/RR-16 Artemis Health Sciences Institutional Ethics Committee Artemis Health Institute, Sector- 51, Gurgaon-122001, Haryana

	Haryana	
8.	**Dr. Thomas Mathew** MD, DM (Neurology) St. Johns's Medical College Hospital Department of Neurology, St. Johns's Medical College Hospital Sarjapur road, Bangalore-560034	**ECR/238/Inst/KA/2013/RR-16** Institutional Ethics Committee St. John's Medical College St. John's Medical College, Room No. 116, Next To Cardinal Gracias Hall, Ground Floor, Old College Building, Ban Galore -560034
9.	**Dr. Hardeep Singh Malhotra** MBBS, MD, DM (Neurology), Department of Neurology, King George's Medical University Department of Neurology, King George's Medical University (Earlier ChhatrapatiSahujiMaharaj Medical University), Lucknow, 226003, Uttar Pradesh, India	Institutional Ethics Committee, Office of Research Cell, Administrative Block, King George's Medical University, Lucknow – 226003, U.P., India. **ECR/262/Inst/UP/2013/RR-16**
10.	**Dr. ManojGulhane** D.M Neurology HCG Manavata Cancer Centre Behind Shivang Auto, Mumbai Naka, Nashik 422001, Maharashtra, India	Manavata Clinical Research Institute Ethics Committee (MCRI EC), Curie Manavata Cancer Centre, Opp. Mahamarg Bus Stand, Mumbai Naka, Nashik – 422004, Maharashtra **ECR/500/Inst/MH/2013/RR-17**
11.	**Dr. R. Srinivasan** MBBS, MD, DM M.S Ramaiah Medical College and Hospital M.S Ramaiah Nagar, MSRIT Post, Bangalore - 560054	Ethics Committee M.S Ramaiah Medical College and Hospitals, M.S Ramaiah Medical College and Hospitals, MSR Nagar, MSRIT Post, Banagalore – 560054, Karnataka, India. **ECR/215/Inst/Ker/2013**
12.	**Dr. Rahul Kulkarni** MD (Medicine), DM, DNB (Neurology) DeenanathMangeshkar hospital and Research Centre DeenanathMangeshkar hospital and Research Centre SS Building, 2nd Floor, Neurology Research Department, Erandwane,	The Institutional Ethics Committee Deparmement OF resercch, 14th Floor, C Wing, Super Speciality Building Deenanath Mangeshkar Hospital & Reseach Centre, Off karve Road, Erandewane, Pune – 411004, Maharashta **ECR/15/Inst/Maha/2013/RR-16**

	Pune 411004	
13.	Dr. Sudhir Kothari MD (Medicine), DM, (Neurology) Poona Hospital and Research Centre Poona Hospital and Research Centre 27 L.B Shastri Road, Sadashiv Peth, Nera Alka Theatre, Pune – 411030, Maharashtra, India	Institutional Ethics Committee Poona Hospital and Research Centre 27, Sadashiv Peth, Near Alka Talkies, Pune – 411030, Maharashtra **ECR/327/Inst/MH/2013/RR-16**
14.	**Dr. Sudhir Kumar** MD (Medicine), DM, (Neurology),Apollo Hospitals, Jubilee Hills, Hyderabad 500096, Telangana, India	Institututional Ethics Committee - Apollo Hospitals (Apollo Health City), Jubilee Hills, Hyderabad – 500096 Telangana **ECR/38/Inst/AP/2013**
15.	**Dr. Suresh Kumar** MBBS, MD(Gen Medicine), DM (Neurology), Amrita Institute of Medical Sciences, Dept. of Neurology Amrita Institute of Medical Sciences AIMS Ponekkara P.O Kochi-682041	Institutional Ethics Committe Amrita Institute of Medical Scinences AIMS Ponekkara P.O. Kochi - 682041 **ECR/129/Inst/KL/2013/RR-16**

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 fourteen 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.

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, an audio-video recording of the informed consent process in case of vulnerable subjects in clinical trial of New Chemical Entity or New Molecular Entity including procedure of providing information to the subject and his understanding on such consent, shall be maintained by the investigator for record; provided that in case of clinical trial of anti-HIV and anti-leprosy drugs, only audio recording of the informed consent process of individual subject including the procedure of providing information to the subject and his understanding on such consent shall be maintained by the investigator for record, as per Government of India, Gazette Notification vide G. S. R. no. 611(E) dated 31.07.2015.

m) The formulation intended to be used in the clinical trial shall be manufactured under GMP conditions using validated procedures and shall have ongoing stability programme.

n) If the clinical trial batches are different from that of the primary batches for which data have been submitted, stability reports for clinical trial batches are to be submitted as per Appendix IX of schedule Y of drugs and Cosmetics Rules for Drug substances and formulation along with Clinical study Report.

o) Base line assessment of patients should include duration of disease, severity assessed using EDSS and list of drugs used prior to entry into this study

p) Secondary end points should include proportion of patients who remain relapse free, and proportion patients free of disability progression

q) Patinets should be assessed for adverse events, disability and any relapse every three months

Yours faithfully,

(Dr. S.Eswara Reddy)
Drugs Controller General (India)
And Licensing Authority