File No: BIO/CT/18/000064

Government of India

Directorate General of Health Services

Central Drugs Standard Control Organization

(Biological Division)

To,

M/s. Reliance Life Sciences Pvt. Ltd.,
Dhirubhai Ambani Life Sciences Center, R-282 TTC Area of MIDC,
Thane -Belapur Road, Rabale Navi Mumbai Maharashtra (India) - 400701

Subject: Permission for conducting a Phase III clinical trial titled "Prospective, multi-center, randomized, double-blind, two-arm, parallel group, active control, comparative clinical study to evaluate efficacy and safety of R-TPR-047 / Tysabri in patients with relapsing multiple sclerosis".

Reference:- Your Application No. BIO/Form44/FF/2018/10095 dated 21-AUG-2018 on the subject mentioned above for Phase III clinical trial of Natalizumab.

Sir,

This Directorate has no objection to your conducting subject mentioned study under the provisions of Drugs and Cosmetics Rules 122-DA and 122-DAC, under the supervision of the investigators mentioned below as per Protocol No.: RLS/MS/2018/02; Version 2.0, Dated: 11 Dec 2018 submitted to this Directorate.

S.No.	Name of Investigator	Clinical Trial Site Address	Name and Address of the Ethics Committee
1	Dr. Usha Kant Misra	Sanjay Gandhi Post Graduate Institute of Medical Science, Department of Neurology, SGPGI, Rae Barelli Road, Lucknow, U.P.	Institutional Ethics Committee, Sanjay Gandhi Post Graduate Institute of Medical Sciences Bioethics Cell, Room No. 205, 1st Floor, administrative Block, Raebareli Road, Lucknow,UP-226014 Regist .No. ECR/16//Inst/UP/2013/RR-16
2	Dr. PK Sethi	Sir Ganga Ram Hospital, Old Rajender Nagar, New Delhi Central - Delhi	Sir Ganga Ram Hospital Ethics Committee, Room No. 1496. IV Floor, Old Building, Old Rajinder nagar, New Delhi. Regist .No. ECR/20/Inst/DL/2013/RR-16
3	Dr. R Suresh Kumar	Amrita Institute of Medical Sciences and Research Centre, AIMS Neurology Department, Ponekkara, P. O Kochi, Ernakulam, Kerala	Institutional Ethics Committee, Amrita Institute of medical Sciences and Research Centre Ponekkara Kochi Kerala Regist .No. ECR/129/Inst/KL/2013/RR-16
4	Dr. Rajiv Anand	Dr. B.L. Kapur Memorial Hospital, Pusa Road, New Delhi -110005	Dr. B. L Kapur Memorial Hospital Ethics Committee, Academic Affairs Research and Continuing Education AARCE Dr. B. L Kapur Memorial Hospital Pusa Road, New Delhi Regist.No.ECR/3/BLK/Inst/DL/2013/RR-16
5	Dr.Dheeraj Khurana	Post Graduate Institute of Medical Education & Research (PGIMER), Department of Neurology, Sector 12, block A, Chandigarh, Punjab	Institutional Ethics committee, Post Graduate Institute of medical Education and Research Room No. 6006 6th Floor PN Chuttani bloack Chandigarh-160012 Regist .No. ECR/25/Inst/CH/2013/RR-16

Licensing Authority as defined in clause (b) of Rule 21, issue permission for conduct of clinical trial, subject to the following conditions further, namely:- (a) Clinical trial shall be conducted in compliance with the approved protocols, requirements of Schedule Y annexed to these rules, Good Clinical Practice Guidelines for conduct of clinical trials in India and other applicable regulations;

(b) Approval of the Ethics Committee shall be obtained before initiation of the study;

(c) Clinical trial 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 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 clinical trial to the subject of the clinical trial 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 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 trials in India and other applicable regulations;

(h) The Sponsor including their employees, subsidiaries and branches, their agents, contractors and sub-contractors and clinical trial sites and the investigator shall allow officers authorized by the Central Drug 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 trials and provide adequate replies to any queries raised by the inspecting authority in relation to the conduct of clinical trial;

(I)Submit complete report of clinical trials as per the approved protocol from the individual investigator duly signed by him along with his observations/remarks on the drug.

(j) Indicating the date of commencement and conclusion of the clinical trial at each center (in case the study is multicentric).

(k) The bulk drug to be used in the manufacturing of finished formulation intended to be used in the clinical trial and clinical trail batches of finished formulation shall be manufactured under GMP conditions using validated procedure and shall have ongoing stability programme.

(l) If the clinical trial batches are different from that of the primary batches for which data have been submitted, stability report for clinical trial batches are to be submitted as per Appendix IX of Schedule Y of Drugs and Cosmetic Rules for Drug substance and formulation along with Clinical study report.

It may kindly be noted that merely granting permission to conduct clinical trials with the drug does not convey or imply that based on the clinical trial data generated with the drug, permission to market this drug in the country will automatically be granted to you.

It is informed that all the amendments to Rule 122DAA, inclusion of Rule 122DAB, compensation matters etc. that are appended to the Drugs & Cosmetics Act & Rule, vide GSR 53 (E) dated 30.01.2013 and in Part X-A, after Rule 122DAB, Rule 122 DAC vide GSR 63 (E) dated 01.02.2013 are mandatory and binding.

Yours faithfully,

S ESWARA REDDY

Digitally signed by S ESWARA REDDY
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Date: 2019.02.04 14:34:32 +05'30'

(Dr. S. Eswara Reddy)
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