File No: BIO/CT/20/000051

Government of India

Directorate General of Health Services

Central Drugs Standard Control Organization

(Biological Division)

FDA Bhawan, Kotla Road
New Delhi 110 002

To,

JSS Medical Research India Pvt. Ltd.
Plot 12/2, 6th Floor, Vatika Mindscapes Tower- B,
Sarai Khwaja Metro Station, NH-2 Mathura Road,
Sector 27 D, Faridabad, Haryana- 121003, India

Subject: Application for grant of clinical trial permission to conduct "A Multi-center, Randomized Controlled, Phase III Study to evaluate the Clinical Outcomes and Safety of Tocilizumab along with Standard of Care in Patients with Cytokine Release Syndrome associated with COVID-19 infection, Protocol Number –Protocol Number: TCZ/ COVID-19/01/2020, Version: 2.0, Dated: 05/MAY/ 2020" under the D&C Act and Rules thereunder-Regarding

Ref: Your application no. BIO/CT04/FF/2020/19487 dated 24-APR-2020
Sir,

Please refer to your application no. BIO/CT04/FF/2020/19487 dated 24-APR-2020, received by this office on the above subject. Please find enclosed herewith permission to conduct Phase III clinical trial in Form CT-06 under the New Drugs and Clinical Trials Rules, 2019 along with the details of new drug and clinical trial sites.

Please acknowledge receipt of the same

Yours faithfully,

VENUGOPAL GIRDHARILAL SOMANI

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

File No: BIO/CT/20/000051

Government of India

Directorate General of Health Services

Central Drugs Standard Control Organization

(Biological Division)

FORM CT-06

(See rules 22, 25, 26, 29 and 30)

Permission to conduct clinical trial of new drug or investigational new drug

The Central Licensing Authority hereby permits to JSS Medical Research India Pvt. Ltd. Plot 12/2, 6th Floor, Vatika Mindscapes Tower- B, Sarai Khwaja Metro Station, NH-2 Mathura Road, Sector 27 D, Faridabad, Haryana- 121003, India to conduct clinical trial of the new drug or investigational new drug as per Protocol No.: ACZ/COVID-19/01/2020, Version: 2.0, Dated: 05/MAY/ 2020 in the below mentioned clinical trial sites.-

Details of new drug or investigational new drug:	
Name of the new drug or investigational new drug:	Tocilizumab
Therapeutic class:	Interleukin 6 receptor monoclonal antibody
Dosage form:	Concentrate solution for infusion
Composition:	Each vial of 4 ml/ 10 ml/20 ml/ Contains: Tocilizumab =20.0000 mg/ml In House Specification Active, Polysorbate 80 =0.5000 mg/ml U.S.P.,E.P.,J.P. Inactive, Sucrose =50.0000 mg/ml U.S.P.,E.P.,J.P. Inactive, Disodium phosphate dodecahydrate =0.0000 q.s. U.S.P.,E.P.,J.P. Inactive, Sodium dihydrogen phosphate dihydrate =0.0000 q.s. U.S.P.,E.P.,J.P. Inactive , Total volume adjusted with WFI = q.s. U.S.P.,E.P.,J.P. Inactive
Indications:	Patients with Cytokine Release Syndrome associated with COVID-19 infection

Details of clinical trial sites-

S.No.	Name and Address of Clinical Trial Site	Ethics Committee details	Name of Principal Investigator
1	Apollo Speciality Hospitals-Vanagaram, Plot No 64,Vanagaram- Ambattur Road,Ayanambakkam, Kilayanambakkam, Chennai-600095, Tamil Nadu, India	Institutional Ethics Committee-Clinical Studies Apollo Hospitals Enterprises Limited No-21 Greams Lane off Greams Road, Chennai, Tamil Nadu - 600006, India EC Reg No. ECR/37/Inst/TN/2013/RR-19	Dr. D. Suresh Kumar

2	Apollo Hospitals,Road Number 72,Opposite Bharatiya VidyaBhavan School, Jubilee Hills,Hyderabad- 500096, Telangana, India	Institutional Ethics Committee- Clinical Studies, Apollo Hospitals Enterprise Limited Apollo Research andInnovations, Jubilee HillsApollo Health City, Hyderabad Shaikpet, Telangana - 500033 India EC Reg No. ECR/38/Inst/AP/2013/RR-19	Dr. Suneetha Narreddy
3	Indraprastha Apollo Hospitals, Sarita Vihar, Delhi – Mathura Road, New Delhi – 110076, India	Institutional Ethics Committee – Clinical Studies, Indraprastha Apollo Hospitals Delhi Mathura Road, SaritaVihar, New Delhi – 110076, India EC Reg No. ECR/5/Inst/ DL/2013/RR-19	Dr. Rajesh Chawla
4	Fortis Hospitals Limited,Mulund Goregaon Link Road, Bhandup- West, Mumbai-400078, Maharashtra, India	Institutional Ethics Committee, Fortis Hospitals Limited 101, Mulund Goregaon Link Road, Bhandup-West Mumbai-400078, Maharashtra, India EC Reg No. ECR/531/Inst/MH/2014/RR19	Dr Rahul Anil Pandit
5	P.D. Hinduja Hospital and Medical Research Centre,Veer Savarkar Marg, Mahim West, Mumbai – 400016, Maharashtra, India	Institutional Ethics committee, P D Hinduja Hospital & Medical Research Centre, 913, 9th Floor, Research Department, Lalitha Girdhar Building T H Katariya Marg, Mahim Mumbai, West, Mumbai, Maharashtra EC Reg No. ECR/61/Inst/MH/2013/RR-19	Dr. Lancelot Pinto
6	Fortis Memorial Research Institute, Sector - 44, Opposite HUDA City Centre Gurgaon, Haryana - 122002, India	Institutional Ethics Committee, Fortis Memorial Research Institute, Sector-44 Gurugram, Haryana - 122002 India. EC Reg No. ECR/223/Inst/HR/2013/RR-19	Dr. Manoj Kumar Goel
7	Nayati Medicity, NH 2, Mathura- 281001, Uttar Pradesh, India	Nayati Multi Super Speciality Hospital Institutional Ethics Committee, Department of Academic and Research Development Room No- 4527, 4th Floor, Behind Sawaria gas station, NH2 Agra Bypass Road, Mathura- 281003, Uttar Pradesh, India. E EC Reg No. CR/1050/Inst/UP/2018	Dr. Vipul Mishra
8	Medanta-The Medicity, Sector-38, Gurugram, Haryana-122001, India	Medanta Institutional Ethics Committee, Medanta- The Medicity Sector- 38, Gurugram, Haryana – 122001, India EC Reg No. ECR/282/Inst/HR/2013/RR-20	Dr. Sushila Kataria
9	B J Medical College and Sassoon General Hospitals, Jai Prakash Narain Road, Pune, Maharashtra - 411001 India	IEC of B.J.G.M.C and Sassoon General Hospital, B.J.G.M.C and Sassoon General Hospital, Sassoon Road Station Road,Pune, Maharashtra - 411001India EC Reg No. ECR/280/Inst/Maha/2013/RR-19	Dr. Shashikala A Sangle

10	Artemis Hospital, Sector 51, Gurugram, Haryana – 122001, India	Artemis Health Sciences IEC Artemis Hospital Sector-51 Gurugram Haryana - 122001 India ECR/53/Inst/HR/2013/RR-19	Dr. Reshma Tewari

Conditions of permission for conduct of clinical trial—
The permission granted by the Central Licensing Authority to conduct clinical trial under this Chapter shall be subject to following conditions, namely:—
(I) Clinical trial at each site shall be initiated after approval of the clinical trial protocol and other related documents by the Ethics Committee of that site, registered with the Central Licensing Authority under rule 8;
(II) Where a clinical trial site does not have its own Ethics Committee, clinical trial at that site may be initiated after obtaining approval of the protocol from the Ethics Committee of another trial site; or an independent Ethics Committee for clinical trial constituted in accordance with the provisions of rule 7: Provided that the approving Ethics Committee for clinical trial shall in such case be responsible for the study at the trial site or the centre, as the case may be: Provided further that the approving Ethics Committee and the clinical trial site or the bioavailability and bioequivalence centre, as the case may be, shall be located within the same city or within a radius of 50 kms of the clinical trial site;
(III) In case an ethics committee of a clinical trial site rejects the approval of the protocol, the details of the same shall be submitted to the Central Licensing Authority prior to seeking approval of another Ethics Committee for the protocol for conduct of the clinical trial at the same site;
(IV) The Central Licensing Authority shall be informed about the approval granted by the Ethics Committee within a period of fifteen working days of the grant of such approval;
(V) Clinical trial shall be registered with the Clinical Trial Registry of India maintained by the Indian Council of Medical Research before enrolling the first subject for the trial;
(VI) Clinical trial shall be conducted in accordance with the approved clinical trial protocol and other related documents and as per requirements of Good Clinical Practices Guidelines and the provisions of these rules;
(VII) Status of enrolment of the trial subjects shall be submitted to the Central Licensing Authority on quarterly basis or as appropriate as per the duration of treatment in accordance with the approved clinical trial protocol, whichever is earlier;
(VIII) Six monthly status report of each clinical trial, as to whether it is ongoing, completed or terminated, shall be submitted to the Central Licensing Authority electronically in the SUGAM portal;
(IX) In case of termination of any clinical trial the detailed reasons for such termination shall be communicated to the Central Licensing Authority within thirty working days of such termination;
(X) Any report of serious adverse event occurring during clinical trial to a subject of clinical trial, shall, after due analysis, be forwarded to the Central Licensing Authority, the chairperson of the Ethics Committee and the institute where the trial has been conducted within fourteen days of its occurrence as per Table 5 of the Third Schedule and in compliance with the procedures as specified in Chapter VI;
(XI) In case of injury during clinical trial to the subject of such trial, complete medical management and compensation shall be provided in accordance with Chapter VI and details of compensation provided in such cases shall be intimated to the Central Licensing Authority within thirty working days of the receipt of order issued by Central Licensing Authority in accordance with the provisions of the said Chapter;
(XII) In case of clinical trial related death or permanent disability of any subject of such trial during the trial, compensation shall be provided in accordance with Chapter VI and details of compensation provided in such cases shall be intimated to the Central Licensing Authority within thirty working days of receipt of the order issued by the Central Licensing Authority in accordance with the provisions of the said Chapter;

(XIII) The premises of the sponsor including his representatives and clinical trial sites, shall be open for inspection by officers of the Central Licensing Authority who may be accompanied by officers of the State Licensing Authority or outside experts as authorised by the Central Licensing Authority, to verify compliance of the requirements of these rules and Good Clinical Practices Guidelines, to inspect, search and seize any record, result, document, investigational product, related to clinical trial and furnish reply to query raised by the said officer in relation to clinical trial;

(XIV) Where the new drug or investigational new drug is found to be useful in clinical development, the sponsor shall submit an application to the Central Licensing Authority for permission to import or manufacture for sale or for distribution of new drug in India, in accordance with Chapter X of these rules, unless otherwise justified;

(XV) The laboratory owned by any person or a company or any other legal entity and utilised by that person to whom permission for clinical trial has been granted used for research and development, shall be deemed to be registered with the Central Licensing Authority and may be used for test or analysis of any drug for and on behalf of Central Licensing Authority;

(XVI) The Central Licensing Authority may, if considered necessary, impose any other condition in writing with justification, in respect of specific clinical trials, regarding the objective, design, subject population, subject eligibility, assessment, conduct and treatment of such specific clinical trial;

(XVII) The sponsor and the investigator shall maintain the data integrity of the data generated during clinical trial.

(XVIII) 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.

Yours faithfully,

VENUGOPAL GIRDHARILAL SOMANI

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Date: 2020.05.08 17:55:09 +05'30'

(Dr. V. G. Somani)
Drugs Controller General (I)
Central Licensing Authority

Place: New Delhi
Date: 08-MAY-2020