File No: BIO/CT/24/000057
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(Biological Division)

From:

The Drugs Controller General, India
Directorate General of Health Services,

FDA Bhawan, Kotla Road,
New Delhi-110002
Dated: 17.09.2024

To,

M/s. Shilpa Biologicals Private
Limited, Plot No. 532-A, Belur Industrial Area,
Dharwad, Karnataka (India) - 580011

Subject: Application for grant of permission to conduct Phase IV clinical trial titled – "An Open label, Phase IV, Multi-Centric, Post-Marketing Study Evaluating the Safety and Efficacy of Adalimumab Manufactured by Shilpa Biologicals Private Limited in patients with active Rheumatoid Arthritis" vide protocol No. 24-AGCR-001, Version 3.0 dated 21.08.2024- Regarding

Ref.: Your Application No. BIO/CT04/FF/2024/43387 dated 22-May-2024

Sir,

With reference to your Application No.: BIO/CT04/FF/2024/43387 dated 22-May-2024, please find enclosed herewith the permission in Form CT-06 for conduct of subject clinical trial under the provisions of New Drugs and Clinical Trial Rules, 2019.

The permission granted by the Central Licensing Authority to conduct clinical trial under this Chapter shall be subject to following conditions, namely:

(I) The firm shall submit insurance certificate to CDSCO before initiation of the clinical study.
(II) 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;
(III) 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;

(IV) 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;
(V) 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;
(VI) 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;

(VII) 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;

(VIII) 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;

(IX) 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;

(X) 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;

(XI) 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;

(XII) 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;

(XIII) 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;

(XIV) 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 authorized 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;

(XV) The laboratory owned by any person or a company or any other legal entity and utilized 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) You are required to submit the clinical study report after completion of the study.

Yours faithfully,

RAJEEV SINGH RAGHUVANSHI

Digitally signed by RAJEEV SINGH RAGHUVANSHI
DN: c=IN, o=CENTRAL DRUGS STANDARD CONTROL ORGANISATION, ou=CENTRAL DRUGS STANDARD CONTROL ORGANISATION, 2.5.4.20=42d7189b1c0981bb5a263a4a73d025ff4b11b680a91f08773480400a43ee361b, postalCode=110002, st=Delhi, serialNumber=657f5e47d940985d8f03bdc902d0e1fe73cfa12a1a126

(Dr. Rajeev Singh Raghuvanshi)
Central Licensing Authority

File. No. BIO/CT/24/000057

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 M/s. Shilpa Biologicals Private Limited, Plot No. 532-A, Belur Industrial Area, Dharwad, Karnataka (India) – 580011 to conduct clinical trial of the new drug or investigational new drug trial titled as – “An Open label, Phase IV, Multi-Centric, Post-Marketing Study Evaluating the Safety and Efficacy of Adalimumab Manufactured by Shilpa Biologicals Private Limited in patients with active Rheumatoid Arthritis” vide Protocol No.:- 24-AGCR-001, Version 3.0 dated 21.08.2024 in the below mentioned clinical trial sites.

2. Details of new drug and clinical trial site [as per Annexure].

3. This permission is subject to the conditions prescribed in part A of Chapter V of the New Drugs and Clinical Trials Rules, 2019 under the Drugs and Cosmetics Act, 1940.

RAJEEV SINGH RAGHUVANSHI

Digitally signed by RAJEEV SINGH RAGHUVANSHI
DN: c=IN, o=CENTRAL DRUGS STANDARD CONTROL ORGANISATION, ou=CENTRAL DRUGS STANDARD CONTROL ORGANISATION, 2.5.4.20=42d7189b1c0981bb5a263a4a73d025ff4b11b680a91f08773480400a43ee361b, postalCode=110002, st=Delhi, serialNumber=657f5e47d940985d8f03bdc902d0e1fe73cfa12a1a126ea94fa5701124a19013, cn=RAJEEV SINGH RAGHUVANSHI
Date: 2024.09.17 [illegible]

Place: New Delhi
Date:17-Sept.-2024

(Dr. Rajeev Singh Raghuvanshi)

Central Licensing Authority

Annexure:

Details of new drug or investigational new drug:

<table>
<tr><td>Names of the new drug or investigational new drug:</td><td>Adalimumab 40 mg/0.4ml solution for Injection in single dose prefilled syringe (r-DNA origin)</td></tr>
<tr><td>Therapeutic class:</td><td>Immunosuppressant</td></tr>
<tr><td>Dosage form:</td><td>Single use prefilled syringe for subcutaneous injection.</td></tr>
<tr><td>Composition:</td><td>Each Pre-filled syringe contains:
<table>
<tr><th>Name of Ingredient</th><th>Function</th><th>Quantity/PFS
(40 mg/0.4 ml)</th></tr>
<tr><td>Adalimumab IH</td><td>Active Drug Substance</td><td>40 mg</td></tr>
<tr><td>Mannitol IP/BP/EP/USP</td><td>Tonicity</td><td>16.8 mg</td></tr>
<tr><td>Polysorbate 80 IP/BP/EP/USP</td><td>Surfactant</td><td>0.4 mg</td></tr>
<tr><td>Citric Acid
IP/BP/EP/USP</td><td>Buffering agent</td><td>0.4 mg</td></tr>
<tr><td>Sodium Hydroxide
IP/BP/EP/USP</td><td>pH adjustment</td><td>q.s.</td></tr>
<tr><td>Water for Injection
IP/BP/EP/USP</td><td>Vehicle</td><td>q.s.</td></tr>
</table></td></tr>
<tr><td>Indications:</td><td>Adalimumab is indicated for Rheumatoid Arthritis (RA) (in adults)
• Moderate to severe, active RA
• Severe, active and progressive RA</td></tr>
</table>

Details of clinical trial site:

S. No.	Name and Address of Clinical Trial Site	Ethics Committee Details	Name of Principal Investigator
1	Sheth Vadilal Sarabhai General Hospital Madalpur Gam, Paldi Road, Elish Bridge, Ahmedabad, Gujarat- 380006	Sangini Hospital Ethics Committee, Sangini Hospital Santorini Square, B/H Abhishree Complex Opp. Star Bazar Nr Jodhpur Cross Roads Satellite, Ahmedabad Gujarat - 380015 India EC Reg. No.: ECR/147/Inst/GJ/2013/RR-19	Dr Dhaiwat Shukla

2	Navneet Memorial Hospital "SUSHRUSHA" Opp Sardar Patel Seva Samaj Hall, In Lane, Opp. Navrangpura Tele Exchange, Navrangpura, Ahmedabad -380006	Ethics Committee of Navneet Memorial Hospital, Navneet Memorial Hospital Opp. Sardar Patel Seva Samaj Hall, Navrangpura Ahmedabad Gujarat - 380006 India EC Reg. No.: ECR/1866/Inst/GJ/2023	Dr Rutviz Mistry
3	Motilal Nehru National Institute of Technology Allahabad Prayagraj – 211004 (U.P.)	Institutional Ethic Committee Motilal Nehru Medical College, Allahabad-211001, U.P. EC Reg. No.: ECR/922/Inst/UP/2017/RR-22	Dr. Jitendra Shukla
4	Belagavi institute of Medical Sciences Belagavi, Dr B R Ambedkar Road, Belagavi, Karnataka 590001	Institutional Ethics Committee, Belagavi institute of Medical Sciences, Dr B R Ambedkar Road, Belagavi, Karnataka 590001 EC Reg. No.: ECR/801/Inst/KA/2016/RR-20	Dr Satish Nesari
5	GSVM Medical College, Kanpur Uttar Pradesh 208002	Ethics Committee GSVM Medical College, SWAROOP NAGAR, Kanpur Nagar Uttar Pradesh - 208002 India EC Reg. No.: ECR/680/Inst/UP/2014/RR-20	Dr. Rohit Nath