GOVERNMENT OF INDIA
Directorate General of Health Services
Central Drugs Standard Control Organization
(Global Clinical Trial Division)
FDA Bhawan, Kotla Road, New Delhi-110002
Te No: 01123236965, Fax: 01123236971
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File No: CT/17/000037

To,

M/s. Baxalta Bioscience India Pvt. Ltd.,
6th Floor, Tower-C, Building No. 8,
DLF Cyber City, DLF Phase II,
Gurgaon - 122002, Haryana.

Subject: Clinical trial titled "Phase III, prospective, multi-center, open label study to investigate safety, immunogenicity, and hemostatic efficacy of PEGylated Factor VIII (BAX 855) in previously untreated patients (PUPs) < 6 years with severe hemophilia A (FVIII < 1%)."– regarding.

Reference: Your Application No. GCT/Form44/FF/2017/3324 (GCT/38/17) dated 16/May/17.

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 investigators mentioned below and as per the **Protocol No: 261203 Amendment No. 03 dated 26/Nov/2015** submitted to this Directorate.

1. Dr. Vijay Bahendrakumar Shah, Department of Pediatrics, Government Medical College and New Civil Hospital, Out Side Majuragate Ring Road, Surat-395002, Gujarat, India.
2. Dr. Kirankumar Chandulal Shah, Apple Hospital, Udhna Darwaja, Ring Road, Surat-395002, Gujarat, India.
3. Dr. Shashikant Janardan Apte, Sahyadri Speciality Hospital, 30 C, Erandwane, Karve Road, Pune-411004, Maharashtra, India.
4. Dr. Taksande Amar Mohanrao, Department of Paediatrics, Datta Meghe Institute of Medical Sciences (DU), Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha-442004, Maharashtra, India.
5. Dr. Apte Mohini Uday, Government Medical College & Hospital, Medical College Square Road, Nagpur-440003, Maharashtra, India.
6. Dr. Gupta Naresh Kumar, Department of Medicine Maulana Azad Medical College and Lok Nayak, Hospital, New Delhi, 110 002, Delhi, India.
7. Dr. Sharma Sujata Manojkumar, Department of Pediatrics, Lokmanya Tilak Municipal Medical College and General Hospital, Sion-Mumbai-400 022, Maharashtra, India.
8. Dr. Lohade Sunil Devichand, Department of Haematology, Sassoon General Hospital, Pune, Jayprakash Narayan Road, Pune Railway Station Near Pune-411001, Maharashtra, India.
9. Dr. Ross Cecil Reuben, St. Johns Medical College Hospital, Sarjapur Road, Bangalore, Karnataka-560034.
10. Dr. Prantar Chakrabarti, Haematology Department, Nil Ratan Sircar Medical College and Hospital, Centenary Building 4th Floor, 138-A.J.C. Bose Road Kolkata-700014, West Bengal, India.
11. Dr. Deepak Bansal, Advanced Pediatrics Center, Postgraduate Institute of Medical Education and Research, Chandigarh-160012, India.

12. Dr. Kasi Vishwanathan Thiagarajan, Department of Paediatric Haematology-Oncology, Meenakshi Mission Hospital and Research Centre, Lake Area, Melur Road, Madurai, 625107, Tamil Nadu, India.
13. Dr. Ajay Sharma, Sir Ganga Ram Hospital, Sir Ganga Ram Hospital Marg, Rajinder Nagar, New Delhi-110060, India.
14. Dr. Neeraj Sidharthan, Amrita Institute of Medical Sciences, AIMS Ponekkara, Cochin-682041, Kerala, India.
15. Dr. Alok Srivastava, Department of Haematology, Christian Medical college, Ida Scudder Road, Vellore-632004, Tamil Nadu, India.

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

a. **Subjects who continue to have inhibitors at the end of the proposed study should be provided adequate management free of cost including by-passing agents.**

b. 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.

c. Approval of the Ethics Committee shall be obtained before initiation of the study.

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

e. 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.

f. 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.

g. 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.

h. 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.

i. 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.

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

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. An audio-video recording of the informed consent process in case of vulnerable subjects in clinical trials 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.

m. 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.

Yours faithfully,

GYANENDRA NATH SINGH Digitally signed by GYANENDRA NATH SINGH Date: 2017.09.21 12:26:46 +05'30'

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