CLINICAL RESEARCH ETHICS COMMITTEE (CREC)

APPROVAL LETTER

20th April 2011

To,

Dr. R. Gursahani
P.D. Hinduja National Hospital and Medical Research Centre
Veer Savarkar Marg, Mahim,
Mumbai-400016, Maharashtra, India

Ref: Project No.618-11-RG Protocol no 1358 ‘A randomized, double-blind, placebo controlled, multi-center, parallel group study to evaluate the efficacy & safety of brivaracetam in subjects (≥16 to 80 years old) with partial onset seizures.’

Sub-Ethics Committee approval for the conduct of the referenced study at “P.D. Hinduja National Hospital and Medical Research Centre, Mumbai”, and approval of the study related documents.

Dear Dr. R. Gursahani,

Clinical Research Ethics Committee (CREC) reviewed and discussed your research proposal dated 21st March 2011 to conduct the research study entitled “A randomized, double-blind, placebo controlled, multi-center, parallel group study to evaluate the efficacy & safety of brivaracetam in subjects (≥16 to 80 years old) with partial onset seizures.” during the CREC meeting held on 1st April 2011
The following documents were reviewed and approved:

2. Investigator’s Brochure(IB); Version dated 29 Mar 2010
3. Informed Consent Forms,
   - India Specific ICF’s- English, Hindi, Marathi, Gujrati-version 1.3 dated 12 Nov 2010
   - India specific Assent form-English, Hindi, Marathi, Gujrati- Version 1.2 dated 29 Oct 2010
4. Informed consent forms translated certificates.
11. Investigator’s Undertaking signed & dated 29 October 2010
13. Investigator Curriculum Vitae- signed & dated 2 Dec 2010
14. Draft clinical trial agreement
CREC also acknowledged DCGI approval letter submitted on 18th April 2011.
At the Ethics Committee meeting held on 1\(^{st}\) April 2011 these documents were examined and discussed. After due consideration, the committee has decided to approve the submitted documents and the proposed methods for patient accrual.

The following members of Clinical Research Ethics Committee (CREC) were present at the meeting held on 1\(^{st}\) April 2011 Meeting room, 9\(^{th}\) Floor, S1 building, Hinduja Hospital, Mahim, Mumbai-400016

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<tr>
<th>Sr. No.</th>
<th>Name</th>
<th>Designation/ Occupation</th>
<th>Affiliation to Institute (Y/N)</th>
<th>Gender</th>
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<tr>
<td>1.</td>
<td>Dr. Atul Garud</td>
<td>Chairman</td>
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<td>2.</td>
<td>Dr. V. R. Joshi</td>
<td>Secretary</td>
<td>Yes</td>
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<td>3.</td>
<td>Dr. S. Iyer</td>
<td>Member</td>
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<td>4.</td>
<td>Mrs. Manisha Naik Dalal</td>
<td>Member</td>
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<td>5.</td>
<td>Dr. Urmila Thatte</td>
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<td>6.</td>
<td>Dr. A. Almeida</td>
<td>Member</td>
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<td>7.</td>
<td>Dr. V. Deshmane</td>
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<td>8.</td>
<td>Dr. Soonu Udani</td>
<td>Member</td>
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<td>9.</td>
<td>Dr. Rachna Adsule</td>
<td>Member</td>
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It is hereby confirmed that neither you nor any of the study team members have participated in the voting/decision making procedures of the committee.

The Project is approved in its presented form. For renewal / extension of the study you are requested to submit a written application along with the submission of annual status report. The total budget Rs.117024/- is approved. Following points must be noted:
Following points must be noted:

1. Ethics committee (EC) should be informed of the yearly progress in the form of annual report of the study (annual report format as given in IRBI CREC SOP or it can be obtained from Research department).

2. EC has approved recruitment of 6 number of patients on this study.

3. It is essential that all patients included in research studies should have an H. H. No. They could, if necessary be registered as Free OPD patients.

4. Outside patients must be registered at Hinduja Hospital (free OPD) Money from incidental expenses, can be used for this purpose.

5. Hinduja Hospital research patient files (MRD files) must have RED label to identify them as research patients.

6. If the company has sponsored the project, all the cheques should be drawn in the name of "National Health and Education Society".

7. In case of sponsored projects it is essential that the sponsors pay advance in time.

8. The usual procedures for utilization of funds sanctioned for the project should be followed and patients covered by the study, if any, should not be charged for relevant items/investigations (related to the study).

9. All requests for investigations advised to the patients covered by the study should be accompanied by a voucher request form (format available with research department). You should get the voucher request form signed and approved in advance by Director Research. Please note this is essential and No voucher will be generated without the producing duly approved voucher request form at the reception counter. Only those investigations, which are pertinent to the project and mentioned in your research proforma should be asked for.

10. Kindly ensure that every consultation/ investigation voucher generated for research patients must contain project code number. This project number is inserted by the receptionist (in remark column) before generating voucher. This is essential for accounts.

11. If a research fellow / technician is to be appointed on the research project, please first process the approved application of the candidate through the research department which will then be forwarded to the HR department. The concerned person will / can start working on the project only after ‘Appointment Order’ is issued.
12. If you have a Research Fellow assigned to your project, he/she should punch the ID card daily. If he/she wishes to proceed on leave an application for this must be submitted by him/her to this office duly signed by the PI.

13. At the end of the study all documents are to be handed over to research society. These will be retained for as per the regulations.

14. As required by ICH-GCP & ICMR guidelines for good clinical practice. Clinical Trial Monitor designated by research department will periodically visit the trial/study sites with prior intimation to you to review the projects.

15. In case of PI's retirement/leaving the institute, study responsibility should be transferred to the Co-investigator after obtaining clearance from EC.

16. The CREC functions in accordance with the ICH-GCP/ICMR/Schedule Y guidelines.

17. In case of any new information or an SAE, which could affect the study, it must be informed to EC. The PI should report SAEs to EC within 7 days of the occurrence of the SAE. If the SAE is 'Death', the EC (IRB/ CREC) Secretariat should receive the SAE reporting form within 24 hours of the occurrence.

(Please keep the SAE reporting form with you. This is available with research department)

18. In the event(s) of any protocol amendments, EC must be informed and only after approval the amendment(s) then can be implemented. Amendments should be highlighted in clear terms as follows:

   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)

   b. Alteration in the budgetary status should be clearly indicated and the revised budget form should be submitted.

   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval.

   d. If there are any amendments in the study design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval to the EC.

   e. Approval of amendment changes must be obtained prior to implementation of changes. Without including all the above points, the amendment is unlikely to be approved by the Ethics committee.

   f. Any deviation/violation/waiver in the protocol must be informed to the EC in the reporting form (available with the research department).
All the above instructions/ procedure should be followed strictly without exception. Please feel free to contact the undersigned if you have any queries concerning the project.

Thanking You,

Yours Sincerely,

Dr. V. R. Joshi
Member Secretary
Clinical Research Ethics Committee

Dr. V.R. Joshi
Member Secretary
National Health & Education Society
Clinical Research & Ethics Committee
P. D. Hinduja National Hospital & Medical Research Centre,
Veer Savarkar Marg, Mahim, Mumbai - 400 016.