MINUTES OF THE 9th MEETING OF THE APEX COMMITTEE HELD ON 31-10-2013 UNDER THE CHAIRMANSHIP OF SECRETARY, HEALTH AND FAMILY WELFARE FOR SUPERVISING CLINICAL TRIALS ON NEW CHEMICAL ENTITIES IN THE LIGHT OF DIRECTIONS OF THE HON'BLE SUPREME COURT OF INDIA DATED 03.01.2013

Present:

1. Shri Keshav Desiraju,
   Secretary,
   Department of Health and Family Welfare.

2. Dr. V. M. Katoch
   Secretary, DHR & DG ICMR
   New Delhi

3. Dr. Jagdish Prasad,
   Director General of Health Services,
   New Delhi

4. Shri R.K. Jain,
   Addl. Secretary & DG (CGHS)
   Ministry of Health and Family Welfare

5. Dr. Arun K.Panda
   Joint Secretary,
   Ministry of Health & Family Welfare

The Apex Committee was apprised that the 9th meeting of the Technical Committee was held on 29.10.2013 under the Chairmanship of DGHS and the Committee deliberated on the modalities to be followed for evaluation of 157 global clinical trials granted by DCGI before 03.01.13, in light of order of Hon'ble Supreme Court dated 21.10.213 in the matter of W.P. (C) No. 33/2012 of Swasthya Adhikar Manch, Indore & Anr Vs. Ministry of Health and Family Welfare &Ors. WP(C) No. 779/2012 as well as proposals of clinical trials.

The minutes of the 9th meeting of Technical Committee were circulated to the members.

The Committee discussed about the various actions need to be taken in light of the order of Hon'ble Supreme Court of India, dated 21.10.2013. The directions of the Hon'ble Court related to 162 global clinical trials is reproduced below.

> "Out of 285 applications which have been recommended for approval by NDACs include clinical trials for investigational products relating to Anti-AIDS, Oncology, Cardiology, Neurology, Psychiatry, Metabolism, Endocrinology, etc. NDACs have evaluated carefully pharmacological, toxicological data, clinical data and protocol for the clinical trials including the objective of the study, eligibility criteria of the subjects, treatment, safety and efficacy assessments, etc. Of these 285 applications, DCG(I) has given approval to conduct clinical trials in 162 cases till 31.08.2013.
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> Out of 162 approvals, 157 approvals were given by the DCG(I) before 31.12.2012 which were prior to directions of this Court on 03.01.2013. The DCG(I) has given the approval to conduct clinical trials in the remaining 5 cases from 01.01.2013 till 31.08.2013 after the approval of the Apex Committee assisted by the Technical Committee.
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> The above facts show that in so far as 5 cases out of 162 cases which were given approval by DCG(I) are concerned, these 5 cases had undergone the three-tier screening. First by NDACs, then by the Technical Committee and the Apex Committee and thereafter the approval has been given by the DCG(I).
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> However, as regards 157 approvals which were given by the DCG(I) before 03.01.2013, learned Additional Solicitor General fairly submits that these cases have not been evaluated by the Technical Committee and the Apex Committee. He submits that the Central Government is agreeable that these 157 cases may be evaluated by the Technical Committee and the Apex committee as well, as has been done for the 5 cases for which approval was given after 03.01.2013.
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> We accept the statement of the learned Additional Solicitor General. We, however, observe that the Technical Committee and the Apex Committee while evaluating the above 157 cases shall keep in view all relevant aspects of safety and efficacy particularly in terms of assessment of risk versus benefit to the patients, innovation vis-a-vis existing therapeutic option and unmet medical need in the country.
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> In the light of the above, it is not possible to pass any order today with regard to 157 cases and the same will be considered after the reports of the Technical Committee and the Apex Committee in respect of 157 cases are submitted before this Court. As regards 5 cases for which approval has been given by the

DCG(I) after 03.01.2013, we record and accept the statement of Mr. Siddharth Luthra, learned Additional Solicitor General that before the clinical trials are conducted, appropriate provision shall be made or administrative direction shall be issued which ensures that audio- visual recording of the informed concerned process of the participants is done and the documentation preserved, adhering to the principles of confidentiality. In other words, the clinical trials in respect of five cases shall commence after proper framework is in place concerning audio-visual recording of the informed concerned process and the preservation of documents while adhering to the principals of confidentiality."

With regard to the evaluation of 157 cases of Global Clinical Trials approved by the DCG(I) before 03.01.2013, the Committee recommended that DCGI should write to each of the applicants of these clinical trials mentioning the observations / directions of the Hon'ble Court for necessary action and for submission of status report of these trials viz. initiated / not initiated / on-going / completed / suspended, along with subject enrolment status within two weeks. The Committee also agreed to the recommendations of the Technical Committee for obtaining other details of the trials like details of sites, Investigators etc. in these cases. The details of the trials along with their status report should be submitted to the Technical Committee so that the Committee can initiate evaluation of these cases at the earliest.

With regard to the observation / direction of the Court on 5 cases of Global Clinical Trials for which approval has been given by DCGI between 03.01.13 to 31.08.13, the Committee recommended that initially appropriate administrative direction should be issued by DCGI to ensure that audio-visual recording of the informed consent process of the trial participants and documentation preserved, adhering to the principles of confidentiality. The Committee also recommended that this direction of audio- visual recording would be applicable for participants to be enrolled in all categories of clinical trials including Global Clinical Trials.

The Committee also desired that the suggestions / comments received on draft notification of the amendments on audio-visual recording of the informed consent, notified on 07.06.13 should be processed for finalization of the amendment at the earlieast.

With regard to the evaluation of fresh proposals of clinical trials, the Apex Committee noted that the Technical Committee in its 9th meeting has deliberated the proposals of CSIR for conducting clinical trial with PA-284 (an IND) along with other 34 fresh proposals of clinical trials of new drugs including fixed dose combinations, subsequent new drugs, biological and global clinical trials. Out of the 34 proposals there were 14 cases of Global Clinical trials and remaining were clinical trial proposals related to new drugs including fixed dose combinations, subsequent new drugs and biologicals. Details of these 34 cases are placed at **Annexure I.**

With regard to the proposal of CSIR for conducting clinical trial with PA-284 the Committee noted that the Technical Committee has recommended that the study can't be approved in its present form. The protocol of the study should be modified by deleting the first arm of the study in which the trial participants will not receive the standard treatment. This is because, in a scenario, if experimental drug is not effective it will not only harm the participants of the arm but also it could lead to development of XDR. Accordingly, the protocol should be modified and submitted to the Committee for review.

The Committee agreed to the above recommendation of the Technical Committee.

The Committee noted recommendations of the Technical Committee in respect of 34 proposals as under.

- For the proposals at Sr. No. 1, 2, 4, 5, 6, 12, 13, 14, 29, which are related to the clinical trial applications submitted by CROs, the Technical Committee recommended that following information should be obtained for review in the next meeting.

    1. Name of sponsors/manufacturer of the experimental drug.
    2. Financial status of these CROs in light of requirements as per the rules, for medical management and payment of compensation in case of injury/death in clinical trial.

- For the proposal at Sr. No. 18, which is related to clinical trial of platelet rich plasma (PRP), the Technical Committee recommended that details of the proposal as per the format should be forwarded to the members for further review, as the information forwarded was not adequate.

- For proposal at Sr. No. 23, which is related to clinical trial of albumin in hypoalbuminemic patients, the Technical Committee raised a concern regarding the patients in control group who will receive placebo (0.9% sodium chloride solution) in place of albumin. All such hypoalbuminemic patients are required to be administered with albumin. Clarification/justification should be submitted to the Technical Committee for further review.

- The proposal at Sr. No. 27, the Technical Committee noted that NDAC has recommended that firm should increase the sample size and number of centers in the study. The action taken in this regard should be submitted to the Technical Committee for further review.

- For proposals at Sr. No. 30, 31, 32, 33, 34, which are related to clinical trials of cell therapy, the Technical Committee noted that the Cellular Biology Based Therapeutic Drug Evaluation Committee (CBBTDEC) has given conditional recommendation/ sought clarification. Therefore, the Technical Committee recommended that the actions taken on the recommendations of CBBTDEC should be submitted for further consideration.

- For remaining 17 proposals, the Technical Committee recommended for giving permission to conduct the trials.

The Apex Committee agreed to the above recommendations of the Technical Committee for taking further action by CDSCO.

Meeting ended with the vote of thanks to and from the Chair.

LIST OF 34 CASES OF CLINICAL TRIALS PROPOSALS **Annexure I**

Sr. No.	Drug	Names of the Applicant	Division
1	UT-15C	M/s PRA Pvt. Ltd.	GCT
2	UT-15C	M/s PRA Pvt. Ltd.	GCT
3	Daclizumab High Yield Process (DAC HYP), Inj.	M/s Biogen Idec Pvt. Ltd. Gurgaon.	GCT
4	SB4	M/s Quintiles Res. (P) Ltd.	GCT
5	SB2	M/s Quintiles Res. (P) Ltd.	GCT
6	Belimumab (Benlysta™) Inj.	M/s Quintiles Res. (P) Ltd.	GCT
7	Alglucosidase alfa Inj.	M/s Genzyme India (P)	GCT
8	Faster-acting insulin aspart (FIAsp)	M/s Novo Nordisk (P) Ltd.	GCT
9	Faster-acting insulin aspart (FIAsp)	M/s Novo Nordisk (P) Ltd.	GCT
10	Insulin Lispro Mix 25 AND Insulin Lispro Mix 50 Inj.	M/s Eli Lilly Co. (P) Ltd.	GCT
11	Semaglutide	M/s Novo Nordisk (P)	GCT
12	Rituximab Inj.	BIOCAD India (P) Ltd.	GCT
13	Linagliptin	M/s Manipal Accunova (P) Ltd. Manipal, Karnataka.	GCT
14	Xprenor (buprenorphine oral lyophilisate)	M/s Clingene International Ltd. Bangalore	GCT
15	VSL#3	Dr. Varsha Gupta, GMCH, Chandigarh	Institutional CT
16	Simvastatin	Dr. Deppak Thappa, GMCH, Chandigarh	Institutional CT
17	Palonosetron	Dr. Yogesh Roy, ESIC-PGIMSR, Delhi	Institutional CT
18	Platelet Rich Plasma	Dr. Aarti Sharma, KGMU, Lucknow	Institutional CT
19	Pulse Steroids	Dr. Nilesh Kolkha, KGMU, Lucknow	Institutional CT

20	Dexlansoprazole	M/s. MSN Labs	NDA
21	Lurasidone	M/s. MSN Labs	NDA
22	FDC of MultiBic potassium-free, MultiBic 2 mmol/l potassium, MultiBic 4 mmol/l potassium solution	M/s Fresenius Medical Care India	FDC Division
23	Albumin	Dr. Kapil Dev, AIIMS	Bioloogical (Blood Products)
24	Tenectaplase	Gennove Biopharma	Biological (Recombinant)
25	Abciximab	Reliance Life Sciences	Bioloogical (Recombinant)
26	Adalimumab	Reliance Life Sciences	Bioloogical (Recombinant)
27	Recombinant Human Chorionic Gonadotrophin (r-hCG)	Bharat Serums & Vaccines	Bioloogical (Recombinant)
28	Hydrochlorothiazide	IPCA Labs	SND
29	Guaifensin	Manipal Accunova	SND
30	Autologus Cultured Chondrocytes	Reliance Life Sciences	Biological (Stem Cells)
31	Autologous Myoblasts	Reliance Life Sciences	Biological (Stem Cells)
32	Allogenic Placental Derived Cells	ClinRx Labs.	Biological (Stem Cells)
33	Autologous Adipose Derives Adult Stem Cells (Idiopathic pulmonary fibrosis)	Kasiak Research	Biological (Stem Cells)
34	Autologous Adipose Derives Adult Stem Cells	Kasiak Research	Biological (Stem Cells)