MINUTES OF THE 10th MEETING OF THE APEX COMMITTEE HELD ON 06-12-2013 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. Arun K.Panda
   Joint Secretary,
   Ministry of Health & Family Welfare

Special Invitee:

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

The Apex Committee was apprised that as decided in the 9th meeting of the Committee with regard to the observation / direction of the Hon'ble Supreme Court on 5 cases of Global Clinical Trials for which approvals were given by DCGI between 03.01.13 to 31.08.13, DCGI vide its order dated 19.11.13, with the approval of the Ministry of Health and Family Welfare, has issued directions making audio-visual recording of Informed Consent process mandatory in all clinical trials. As per the direction, in addition to the requirements of obtaining written informed consent, audio-visual recording of the informed consent process of each trial subject, including the procedure of providing the information to the subject & his/her understanding on such consent is required to be done while adhering to the principles of confidentiality. Such audio-visual recording and related documentation would be preserved. This is applicable to the new subjects to be enrolled in all clinical trials including Global Clinical

Trials. The Committee noted the same and recommended that DCG(I) should prepare detailed guidelines specifying procedures for such audio-visual recording of Informed Consent Process and adherence to the principles of confidentiality, preservation of the audio-visual recordings and other related documents.

The Committee further noticed that DCG(I) vide office order dated 30.08.2013 has made it mandatory for all the applicants while submitting the application for conducting clinical trials to furnish information in respect of financial support, fees, honorarium, payments in kind etc. to be paid to the Investigator as per the contract entered into by the sponsor with investigator/institution in clinical trials. The Committee recommended that DCG(I) should devise a procedure to the make this information public.

The Committee was further apprised that the 10th meeting of the Technical Committee was held on 28.11.2013 under the Chairmanship of DGHS and the Committee deliberated the details 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 other proposals of clinical trials.

As decided in 9th meetings of the Technical Committee and the Apex Committee, DCGI had written to each of the applicants of these clinical trials mentioning the observations / directions of the Hon'ble Supreme Court and asked for submission of status report of these trials viz. initiated / not initiated / on-going / completed / suspended, along with other details of such trials. Accordingly, the information in respect of 148 cases has been collected so far, which is as under:

Ongoing	64
Completed	35
Not initiated	19
Terminated / Suspended	11
Discontinued	19

Out of 64 cases of ongoing global clinical trials, detailed information of 50 cases were already circulated to the members of the Technical Committee through e-mail. List of these cases is enclosed at **Annexure-I**.

The Committee noted that the Technical Committee has evaluated these 50 cases in detail keeping 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 in its meeting held on 28.11.13. After detailed deliberation, the Technical Committee has recommended that all these 50 cases of GCTs meet the requirements of safety and efficacy aspects especially in terms of risk versus benefits to the patients, innovation vis-a-vis existing therapeutic options and unmet medical need in the country and these studies should be continued.

However, in case of proposal at Sr. No. 29, the Technical Committee noted that at one of the clinical trial sites, a case of pregnancy has been reported. The Committee recommended that this case of pregnancy should be followed-up and there should not be further patient enrollment at this site.

The Technical Committee further recommended that in case of those proposals, out of 50 cases, where there is no Govt. Hospitals/ Medical Colleges/Institutions as sites, the DCG(I) should advise the applicants to include at least two Govt. Hospitals/ Medical Colleges/Institutions as sites.

Apex Committee agreed to the above recommendations of the Technical Committee with regard to the 50 cases of ongoing trials as mentioned above. However, the Committee desired that following information / clarification should be placed before the Committee in its next meeting.

1. How the terms Terminated, Suspended, Discontinued differ from each other?
2. How many of the 11 clinical trials mentioned as terminated/suspended, have been terminated and how many have been suspended?

3. Who has suspended or terminated the clinical trials and what are the reasons for termination/suspension?

4. Out of ongoing 50 clinical trials, how many cases are there where there is no site in any Govt. hospital/medical college?

The Apex Committee, then noted that the Technical Committee in its 9th meeting had evaluated the proposal of CSIR for the conduct of Phase II clinical study with PA-824 and that study could not be approved in its present form and recommended that the protocol of the study should be modified by deleting 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 develop XDR. Accordingly, the protocol should be modified and submitted to the committee for review. The Apex committee also agreed on the recommendation of the Technical committee.

However, the DG, CSIR requested the Secretary, Ministry of Health & Family Welfare, to hear the experts on TB from CSIR, before arriving at a decision. Accordingly, experts on TB from CSIR presented their case before the Technical Committee in its 10th meeting. The Committee has observed the following:

- The treatment duration in the proposed study of PA- 824 is only two months. The patients in first arm will not receive the standard care only for two months. After the end of two months, these patients will receive standard care as part of their routine treatment. Therefore, the chance of development of XDR is very less.
- The study will be conducted at Govt. Hospital i.e Lala Ram Swarup Institute of Tuberculosis & Respiratory Diseases (upgraded as National Institute of Tuberculosis and Respiratory Diseases), Mehrauli, New Delhi, which has adequate facilities for conducting such studies.
- All the subjects enrolled in the study will be admitted in the hospital for two months during the treatment period. Therefore, they will be under close supervision of the Investigator and Co-Investigator, and there will be rescue management in case of any emergency.

In view of above, after detailed deliberation, the Technical Committee has recommended for the grant of permission for the proposed clinical trial as per the protocol submitted. The Apex Committee agreed to this recommendation of the Technical Committee for giving permission to conduct the trial as per the protocol submitted.

The Committee also noted that the Technical Committee has evaluated following 8 fresh proposals of clinical trials of new drugs (including institutional, fixed dose combinations, subsequent new drugs, biological) details of which were forwarded through e-mail to the members as per the format.

Sr. No.	Drug	Names of the Applicant	Division
1	Platelet rich plasma	Dr.Aarti Sharma, KGMU, Lucknow	Institutional CT
2	Ambrisentan + Tadalafil	Dr. Saibal Mukhopadhyay, Associate Professor, Department of Cardiology, G B Pant Hospital, Delhi	Institutional CT
3	Cabazitaxel	M/s Sanofi-Synthelabo (India) Limited	NDA
4	Atorvastatin and vitamin D3 tablets (10 mg + 1000 IU) and (20 mg + 1000 IU)	M/s Sun Pharmaceutical Industries Ltd.	FDC Division
5	Losartan potassium, amlodipine and hydrochlorothiazide tablets (50 mg + 5 mg + 12.5 mg)	M/s Sun Pharmaceutical Industries Ltd.	FDC Division
6	Salbutamol Pressurised Inhalation	M/s Glenmark Pharmaceuticals Ltd	SND
7	Etanercept	M/s Lupin Limited	Biological (Recombinant)
8	Panitumumab (Vectibix)	M/s Glaxosmith Kline Pharma. Ltd	Biological (Recombinant)

Out of these 8 cases, one case (S.No.1 above) was of Dr. Aarti Sharma, KGMU, Lucknow for conducting an institutional clinical trial study with Platelet rich plasma which was earlier deliberated by the committee in its 9th meeting wherein the

Committee recommended that detailed information in respect of the proposal as per the format should be forwarded to the members for further review. Accordingly, the details were forwarded to the members of the Committee through e-mail. The Committee deliberated on the proposal and recommended for the grant of permission to conduct the proposed study.

The remaining 7 cases were fresh proposals of clinical trials which have been recommended by NDAC for approval. The Technical Committee deliberated these 7 cases in detail and recommended for the grant of permission to conduct the clinical trials.

The Apex Committee agreed to the above recommendations of the Technical Committee for giving permission to conduct the above 8 fresh cases of clinical trials as mentioned above.

The Apex Committee further noted that the Technical Committee deliberated on the representation received from M/s Glenmark Pharmaceuticals Ltd., in respect of the condition being laid while granting CT permissions for inclusion of at least 50% sites from Govt. Medical College/Hospitals. The firm has stated that majority of the sites (85%) in India are private medical college/multi-specialty Hospitals. Government Medical Colleges/Hospitals in fact contribute only 15% of total clinical trial sites. It is therefore impractical to suddenly insist on 50% sites to be from Government hospital/medical college pool. This number should be 15% or at best 20% of the overall sites pool.

The Technical Committee also deliberated on the concerns raised by the stakeholders that in all cases multispecialty hospital should not be made mandatory. There are certain clinical trials such as in ophthalmological trials where these studies are proposed to be conducted in reputed ophthalmological centers e.g. Shankar Netralaya etc. In such cases, multispecialty hospitals should not be insisted upon.

The Technical Committee deliberated the above issues in detail and noticed that in every case it might not be feasible to comply with these conditions for conducting clinical trials in multispecialty hospitals with at least 50% Govt. Medical

College/Hospitals. The Technical Committee, therefore, recommended that the decision in this regard would be taken on case by case basis depending on the nature of clinical trial.

The Apex Committee agreed to the recommendations made by the Technical Committee that while evaluating clinical trial applications, decision on the requirement of Govt. Medical College/Hospitals/ Multispecialty hospitals shall be taken on case by case basis.

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

Annexure I

LIST OF 50 CASES OF CLINICAL TRIALS PROPOSALS

Sr. No.	Drug	Names of the Applicant
1	Daclizumab high yield process (DAC HYP)	Biogen Idec
2	Xprenor(buprenorphine oral lyophilisate)	Clinigene
3	Asenapine	PAREXEL
4	PF-03049423	Pfizer
5	RO4917838	Quintiles
6	RO4917828	Quintiles
7	Cariprazine	Quintiles
8	Recombinant Human Coagulation Factor IX Fusion Protein (rFIXFc)	Biogen Idec
9	Recombinant Human Coagulation Factor VIII Fusion Protein (rFVIIIFc)	Biogen Idec
10	VGX-3100	Max Neeman
11	Factor VIII	Max Neeman
12	Nilotinib	Novartis
13	Pertuzumab	Roche
14	SUNITINIB MALEATE (Tyrosine Kinase inhibitor)	Pfizer
15	PF-00299804	Pfizer
16	Crizotinib Capsules 200 mg and 250 mg	Pfizer
17	AFATINIB	Boehringer
18	Panitumumab	Amgen
19	Denosumab	Amgen
20	Axitinib	Quintiles
21	Symbicort - Budesonide + Formoterol	AstraZeneca
22	QVA149	Novartis
23	Fluticasone Furoate /Vilanterol Inhalational powder 100/25 mcg	Parexel
24	Nintedanib (BIBF 1120)	Boehringer
25	Tiotropium + olodaterol fixed dose combination	Boehringer
26	Fixed dose combination of Tiotropium + Olodaterol solution for inhalation	Boehringer
27	BIBF 1120	Boehringer
28	BIBF 1120	Boehringer
29	Sifalimumab	AstraZeneca
30	PF-04171327 (5mg / 10 mg / 25 mg) Tablets.	Pfizer
31	DEB025 (alisporivir)	Novartis

32	NVC-422	Quintiles
33	Vildagliptin	Novartis
34	Mipomersen	Sanofi
35	Velaglucerase Alfa	Quintiles
36	Saxagliptin	BMS
37	Denosumab	Amgen
38	NT 201	Kendle
39	Doxorubicin-EMCH	GVK/INC Research
40	Estradiol valerate (EV) / Dienogest (DNG) (Qlaira)	Bayer
41	CXA-201 (CXA-101/ tazobactam) for Injection	PRA
42	AMR101	Pharmant
43	Tasquinimod	PPD
44	GP2013	PPD
45	Ceftazidimeavibactam	PPD
46	Topiramate (USL 255)	PPD
47	STAVUDINE (app. In INDIA)	PPD
48	Adjunctive Perampanel	PPD
49	BOCEPREVIR	MSD
50	Lapatinib	GSK