MINUTES OF THE FIFTH MEETING OF THE APEX COMMITTEE HELD ON 02-07-2013 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 and Family Welfare
6. Dr. G.N. Singh,
   Drugs Controller General (India)

The Apex Committee was apprised that the fifth meeting of the Technical Committee was held on 01.07.2013 under the Chairmanship of DGHS and the Committee deliberated on various issues related to various categories of Clinical Trials. The proposals were related to Investigational New Drugs (IND), Global Clinical Trials, FDCs, Medical Devices, Biologicals and New Drugs. It also considered the issue of reconstitution of NDACs, timelines for processing of clinical trial applications, formula for deciding compensation in case of clinical trial related deaths, etc.

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

In the previous meeting, the Committee desired that the 33 cases of Global Clinical Trials should be submitted as per the format approved by the Technical Committee. The Committee was briefed that out of 33 cases one was repeated twice and five applications have since been withdrawn. Thus, there were 27 proposals for Global Clinical Trials under consideration. 54 cases of clinical trials including the above 27 cases and fresh proposals of 8 IND applications, 3 fixed dose combinations (FDCs), 2 subsequent new drugs, 7 biologicals, 2 medical devices were forwarded to the members of the Technical Committee beforehand for their consideration. Besides, five proposals of institutional clinical trials recommended for approval by NDAC were also placed before the Technical Committee in the same meeting for deliberation. Details of these 54 cases are **annexed.**

The Technical Committee recommended for approval of these cases subject to the concurrence of the Apex Committee except in two cases (one each in global clinical trial and medical device Sr no. 34 and 48 of the annexure) where only two NDAC members recommended for approval. For these two cases, the Committee desired that these should be further deliberated by the NDAC / MDAC concerned in their meetings with a proper representation of members during the meeting.

The Technical Committee also recommended that as and when approval is granted, details of these proposals as per the format including the details of the trial sites, Ethics Committees, Investigators, etc should be uploaded on the CDSCO website except the information which the concerned applicant / companies would not like to be disclosed.

The details of the 54 cases alongwith the recommendations of the Technical Committee as above were considered by the Apex Committee. The Committee was also apprised that the number of subjects and study sites in all these cases are adequate.

After due deliberation, the Committee agreed to the recommendations of Technical Committee for approval of the 52 cases. The Committee, however, desired that Sh. Sidharth Luthra, Additional Solicitor General in the case on clinical trial in the Supreme Court should be informed about the above decision of the Apex Committee before issue of formal approvals by DCG (I). The Committee also agreed to the

recommendation of the Technical Committee that the remaining two cases should be deliberated again by NDAC / MDAC.

DCG (I) informed the Committee that the NDACs have recommended for approval of 8 new drugs without local clinical trials in the country. The Committee opined that it would be appropriate to wait till the report of Ranjit Roy Chaudhury Committee on guidelines for approval of new drugs and clinical trials is made available.

As regards the compensation formula for clinical trial related death cases, the Apex Committee opined that the issue may be further deliberated after receiving the final report from the independent Expert Committee.

The Committee considered the recommendation of Technical Committee on broadening the New Drug Advisory Committees (NDACs) for various therapeutic areas. It opined that broad panels of medical specialists for each of the therapeutic areas including pharmacologists may be created for evaluation of proposals of clinical trials and new drugs. These experts may be indentified from Government Medical Colleges / Institutions of repute. The experts may be at the level of Assistant Professor or above. In a specific therapeutic area, there may be multiple Committees consisting of randomly selected members from the panel. The proposals of new drugs and clinical trials of a particular therapeutic area received in a month may be forwarded to one Committee constituted from that panel. The proposal in the same area received in the next month may be referred to another Committee of the same panel. The process may be repeated every month. The selection of members of these Committees should be done randomly.

The Committee was apprised about the concerns raised regarding the delay in the approval of clinical trials. After deliberation, the Committee recommended that a timeline of 8-12 weeks should be followed by DCG (I) for taking final decision for approval or otherwise of clinical trial proposals.

The Committee was also apprised about the updated status of evaluation of various applications of new drugs and clinical trials by the twelve New Drugs Advisory Committees (NDACs), payment of compensation in cases of trial related deaths, status of registration of Ethics Committees, clinical trials site inspections as under:-

- As regards the payment of compensation in cases of clinical trials related death the Committee was informed that out of 89 cases of SAEs of related deaths tha occurred during clinical trials between January, 2005 to December 2012 payment of compensation has already been made by the companies in 75 cases In 9 cases, the amount has been decided and payments by the companies are under process. The matter is being pursued further with the companies in remaining cases for payment of compensation. The Committee was informed that in one case where the whereabouts of the subject could not be traced and the payment could not be made by the company, as recommended in the last meeting, the company has been directed by DCG (I) to deposit the amount of compensation to the institution.
- Out of total 1070 applications received for approval of clinical trials and various categories of new drugs including biological and fixed dose combinations, the NDACs have, so far, evaluated 814 applications in 68 meetings. Out of these 814 applications, 288 were related to approval of Global Clinical Trials (GCTs) including clinical trials of new chemical entities. Of these 288 applications, NDACs after deliberation have recommended for approval of 248 applications and have not recommended for approval in case of the remaining 40 applications.

Since 03.01.2013, CDSCO has received a total of 124 applications for approval of clinical trials and new drugs including biological and fixed dose combinations. Since then the New Drug Advisory Committees have met 21 times and have evaluated 311 proposals of clinical trials and New Drugs, out of which 57 applications pertain to global clinical trials. Out of these 57 applications of global clinical trials, NDACs have recommended 50 cases for approval.

- As regards the status of applications for EC registration, 841 applications for registration of Ethics Committees have so far been received which includes 650 applications from Institutional and 191 applications from Independent Ethics Committees. Out of this, CDSCO has granted registration to 413 Institutional Ethics Committees and 76 Independent Ethics Committees. Further, rejection has been issued in 11 cases. 243 Ethics Committees (150 institutional and 93 independent) have been asked to submit further information.

- Clearance of a total of 223 proposals for protocol amendments, grant of test license, NOC for export of biological samples and addition of study sites related to global clinical trials approved before 03.01.2013, have been considered and NOCs/Test Licenses were granted by CDSCO.

The Committee was further informed that since 03.01.2013, CDSCO has granted approval of 8 institutional clinical trials. These clinical trials are of approved drugs and not of new chemical entities.

- The Committee was also informed that zonal offices of CDSCO have conducted inspections at various clinical trial sites in the country and submitted the inspection reports to CDSCO. A total of 574 inspection reports have been received by CDSCO which are under examination. So far, show cause notices have been issued in 156 cases.

The meeting ended with a vote of thanks to the Chair.

Annexure

LIST OF 54 CASES OF CLINICAL TRIALS PROPOSALS

S.No.	Drug	Applicant	Category
1.	GRC 17536	Glenmark Pharma	IND
2.	Human Monoclonal Antibody on rabies (SIIR Mab)	Serum Institute	IND
3.	Rabies G Protein Vaccine	Cadila Pharma	IND
4.	S0597	Sun Pharma	IND
5.	DRL-17822	Dr. Reddy's Labs	IND
6.	PMZ-2010	Pharmazz India	IND
7.	Endoxifen	Intas Pharma	IND
8.	RBx11160 + PQP	Ranbaxy Labs	IND
9.	Transtuzumab	Roche Scientific	GCT
10.	MV25599 (PegBase)	Roche Scientific	GCT
11.	Exenatide	Parexel	GCT
12.	Belimumab	Parexel	GCT
13.	LY2127399	Parexel	GCT
14.	Mometasone Furoate/Formoterol Fumarate MDI	Covance	GCT
15.	Ceftazidime Avibactum	PPD Pharmaceutical	GCT
16.	Fluticasone + Salmetrol MDI	Parexel	GCT
17.	Tenofovir Disoproxil	KlinEra	GCT
18.	RAD001 (Everolimus)	PPD Pharmaceutical	GCT
19.	Lixisenatide	Sanofi Synthelabo	GCT
20.	Solifenacin Succinate	PPD Pharmaceutical	GCT
21.	Tofacitinib	Pfizer Ltd.	GCT
22.	Fesoterodine	Pfizer Ltd.	GCT
23.	Liraglutide	Novo Nordisk	GCT
24.	AMG 145	Amgen Technology	GCT
25.	Lanthanum Carbonate	ICON	GCT
26.	Vildagliptin	Novartis	GCT
27.	MK-8457	MSD Pharma	GCT
28.	Delamanid	Jubliant	GCT
29.	ART-123	Asiatic Clinical Research	GCT
30.	Human Cell Line Recombinant Factor	Max Neeman	GCT
31.	Octafibrin	Max Neeman	GCT
32.	Evacetrapib	Covance	GCT
33.	Sebelipase Alfa	Clintec (India)	GCT

		International	
34.	Semaglutide	Novo Nordisk	GCT
35.	MK 3415	MSD Pharma	GCT
36.	Pegylated Recobinant Human Erythropoeitin	Intas Pharma	Biological (Recombinant)
37.	Etanercept	Intas Pharma	Biological (Recombinant)
38.	Adalimumab	Cadila Healthcare	Biological (Recombinant)
39.	Tetanus Toxoid Vaccine	Cadila Healthcare	Biological (Vaccine)
40.	Diptheria & Tetanus Vaccine	Cadila Healthcare	Biological (Vaccine)
41.	Diptheria, Tetanus and Pertussis Vaccine	Cadila Healthcare	Biological (Vaccine)
42.	Diptheria, Tetanus Pertussis and Haemophilus Type B conjugate Vaccine	Cadila Healthcare	Biological (Vaccine)
43.	Diltiazem + Lignocaine	Themis Medicare	FDC
44.	Artesunate + Piperaquine Phosphate	Ipca Labs	FDC
45.	Naftopidil + Dutasteride	Intas Pharma	FDC
46.	Tapentadol Hydrochloride Nasal Spray	Torrent Pharma	SND
47.	Lubiprostone	Sun Pharma	SND
48.	On X mechanical heart versus SJM mechanical heart	iProcess Clinical	Medical Device
49.	Simplicity Renal Denervation System	India Medtronic	Medical Device
50.	Levamisole	Dr. H.K. Kar, RML Hospital	Institutional Clinical Trial
51.	Rebamipide	Dr. Radhika Tandon, AIIMS	Institutional Clinical Trial
52.	Primaquine	NIMR	Institutional Clinical Trial
53.	Platelet rich plasma	Dr. Vijay Kumar Jain, RML Hospital	Institutional Clinical Trial
54.	Platelet rich plasma	Dr. P.P. Kotwal, AIIMS	Institutional Clinical Trial

5TH Meeting of the Apex Committee on 02.07.2013

Actions Taken on recommendations made by the Committee

S.No.	Recommendations	Action Taken
1.	Proposals of 33 Global Clinical Trials (GCT) which deliberated in the last meeting of the committee held on 29.04.13, was deliberated by the technical committee. The Technical Committee also deliberated the recommendations of IND Committee in respect of 8 clinical trials of INDs. However, the Technical Committee recommended that office of DCG(I) should prepare a format in consultation with the members of the committee for the purpose of the submission of the details of all clinical trial proposals including global clinical trials, clinical trials of new drugs, biologicals, medical devices, INDs along with recommendations of NDACs / IND Committee.	Out of 33 proposals of GCT, one was repeated twice in the list and 5 have been withdrawn by the applicants. Details of remaining 27 cases alongwith 8 proposals of IND, 3 proposals of fixed dose combinations, 2 proposals of subsequent new drugs, 7 proposals of biological, 2 proposals of medical devices as per the approved format forwarded to the members of the technical committee, were deliberated by the Committee in its meeting held on 01.07.13. Further, 5 proposals of institutional clinical trials recommended by the NDAC were also placed before the technical committee in the same meeting for deliberation. The technical committee members opined that there are no issues for approval of these proposals. However in two cases only two NDAC members participated in the meeting and recommended for approval. The committee recommended for grant of approval for 52 proposals subject to concurrence of the Apex Committee except those two cases. The committee recommended that these two cases recommended by only two members shall be further deliberated by concerned NDACs in their meetings with a proper representation of members during the meeting. Technical Committee also recommended that as and when approval is granted, details of these proposals as per