MINUTES OF THE 7th MEETING OF TECHNICAL COMMITTEE HELD ON 23-08-2013 UNDER CHAIRMANSHIP OF DGHS FOR SUPERVISING CLINICAL TRIALS ON NEW CHEMICAL ENTITIES IN THE LIGHT OF DIRECTIONS OF THE HON'BLE SUPREME COURT OF INDIA ON 03.01.2013

Present:

1.	Dr. Jagdish Prasad, Director General of Health Services.	Chairman
2.	Dr. Yashpaul Sharma, Prof. & Head, Dept. of Cardiology, PGIMER, Chandigarh	Member
3.	Dr.Rajutitus Chacko, Prof. & Head, Dept. of Medical Oncology, CMC, Vellore.	Member
4.	Dr. Nandini Kumar, Former Deputy Director General Sr. Grade, ICMR.	Member
5.	Dr. Kamlakar Tripathi, Prof., Dept. of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi	Member
6.	Dr. P.K Dalal, HOD, Dept of Psychiatry, KGMU Medical College, Lucknow.	Member
7.	Dr. Nikhil Tandon, Professor, Dept of endocrinology & Metabolism, AIIMS, New Delhi.	Member

From CDSCO:

1. Dr. V. G. Somani,
   Joint Drugs Controller (India)

2. Sh. A.K. Pradhan
   Deputy Drugs Controller (India)

Dr. Jagdish Prasad, DGHS welcomed the members and briefed them about the outcome of the sixth meeting of the Technical Committee which was held on 25.07.13. The minutes of the fifth meeting approved by the Chairman were already circulated to the members.

Sh. A.K. Pradhan, DDC(I) informed the Chairman that as decided in the last meeting of Technical Committee held on 25.07.13, a list of approx. 2000 experts identified from Govt. medical colleges / institutes as well as from Private Institutions across the country in respect of Oncology & hematology, Cardiovascular, renal, Metabolism & Endocrinology, Antimicrobial, Antiparasitic & Antifungal, Antiviral, Reproductive & Urology, Gastroenterology & Hepatology, Dermatology & Allergy, immunology, Pulmonary, Neurology & Psychiatry, Anesthetics & Rheumatology, Ophthalmology and Vaccines have been prepared and forwarded through e-mail to Dr. Ashok Kumar Das for finalization in consultation with other members of the committee.

Thereafter, the details of 29 proposals of clinical trials were deliberated. Out of these 29 proposals there were 4 cases of clinical trials of New drugs, 13 cases of Global Clinical trials and remaining were clinical trial proposals related to fixed dose combinations, subsequent new drugs, biological, medical devices and institutional trial. Detailed information on these proposals as per the prescribed format was forwarded to the members through e-mail. List of these proposals is as under:

S.No.	Drug	Applicant	Category
1.	Empagliflozin	Boehringer	GCT
2.	Empagliflozin + Linagliptin	Boehringer	GCT
3.	Dapagliflozin	Brostol Myers	GCT
4.	MK-0859 (Anacetrapib)	MSD Pharma	GCT
5.	Empagliflozin + Linagliptin	Boehringer	GCT
6.	MK-3102	Parexel	GCT
7.	MK-3102	MSD Pharma	GCT
8.	MK-3102	Parexel	GCT
9.	SAR153191 (Sarilumab)	Sanofi Synthelabo	GCT
10.	SAR153191 (Sarilumab)	Sanofi Synthelabo	GCT
11.	Ixekizumab (LY2439821)	Eli Lilly	GCT
12.	Volasertib	Boehringer	GCT
13.	Nepadutant	Karmic Labs	GCT
14.	Inactivated Japanese Encephalitis Vaccine	Bharat Biotech	Biological (Vaccine)
15.	Measles Vaccine, (Live, Freeze Dried, Single and Multi Dose)	Cadila Healthcare	Biological (Vaccine)
16.	Measles Mumps and Rubella (MMR) vaccine, (Live, Freeze Dried, Single and Multi dose)	Cadila Healthcare	Biological (Vaccine)
17.	Suspension of heat killed (autoclaved) Mycobacterium W	Cadila Pharma	Biological (Vaccine)
18.	Typhoid Vi Polysaccharide –Diphtheria Toxoid conjugate vaccine	Shantha Biotech	Biological (Vaccine)
19.	Pneumococcal polysaccharide conjugate vaccine (adsorbed) 13-valent-Prevenar 13.	Wyeth Ltd.	Biological (Vaccine)
20.	FDC of Silver Sulfadiazine (Nanonized) 0.5%w/w/0.75% w/w + ChlorhexidineGluconate 0.2% w/w Topical Cream	Ranbaxy Labs	FDC
21.	Azilsartan Medoxomil	Synokem Pharma	NDA

22.	Azilsartan Kamedoxomil	Hetero Labs	NDA
23.	Vilazodone Hyderochloride	Hetero Labs	NDA
24.	Meclofenamate Sodium Capsule	Lupin Ltd.	NDA
25.	Combination of Moxifloxacin 400 mg + Rifampicin 600mg + Minocycline 200 mg (MRM)	Dr. H.K. Kar, RML Hospital, Delhi	Institutional
26.	Aceclofenac Gel 5%w/w	Inventia Healthcare	SND
27.	Salbutamol Pressurised Inhalation (100 mcg per actuation) CFC free pMDI.	Glenmark Pharma	SND
28.	Teriparatide	Lupin Ltd.	Biological (Recombinant)
29.	PEG-Filgrastim	GVK Biosciences	Biological (Recombinant)

One of the members of the committee pointed out that in case of proposal of clinical trial with Azilasartan (case no. 21 & 22) there is a washout period of 15 days, where subjects will not be given any antihypertensive drug which needs to be discussed from ethical angle. The Committee after detailed discussion recommended that the study in first 20 patients should be conducted in ICU setting. Based on result of 20 patients, the study can be extended on the subjects under OPD setting.

The Committee, thereafter discussed about the proposed sites for the above clinical trial proposals and opined that there are many sites proposed for clinical trial proposal mentioned at item no. 1, 2, 3, 4, 7, 8, 12, 13 and 20 which are having Independent Ethics Committees. Clinical trial should not be allowed to be conducted at these sites. The clinical trial sites should be multispecialty hospital, Institute having emergency facilities and Institutional Ethics Committee registered with CDSCO.

The Committee recommended for approval of these 29 clinical trials subject to the condition that these studies should be conducted only in multispecialty hospital/institute with emergency facilities and Institutional Ethics Committee registered with CDSCO.

The committee also recommended that DCGI should inform all the NDAC members in-writing that while evaluating the clinical trial proposals they should ensure that clinical trial sites, which are multispecialty hospitals/institutes having emergency facility and having Institutional Ethics Committee registered with CDSCO are only recommended for the conduct of clinical trial.

One of the members of the committee raised an issue that many a times in Ethics Committee meeting Chairman does not attend the meeting. Therefore it was deliberated that there should be a mechanism, so that a Vice-Chairman of Ethics Committee can conduct the meeting and discharge the responsibility of Chairman. Committee agreed to the suggestion and stated that such mechanism should be defined by the individual Ethics Committee in their SOP.

While discussing the procedures followed for processing of clinical trial applications, the Committee recommended that as and when clinical trial application is filed to CDSCO, the status of each application should be uploaded in CDSCO website so that the members of this Committee may came to know well in advance about the processing of application by CDSCO/NDAC, which will help them to review the application in a better way when it is referred to them.

The Committee was apprised that the three Independent Expert committees under Dr. Arun Agarwal have deliberated and given their report regarding the formula to be followed in deciding the quantum of compensation in cases of clinical trial related deaths which is as under:

$$\text{Compensation} = \frac{B \times F \times R}{99.37}$$

Where,

B = Base amount (i.e. 8 lacs)

F = Factor depending on the age of the subject as per Annexure 4 (based on Workmen Compensation Act, **Annexure**-I)

R = Risk Factor depending on the seriousness and severity of the disease, presence of co-morbidity and duration of disease of the subject at the time of enrolment in the clinical trial between a scale of 0.5 to 4 as under:

1 .0.50 Terminally ill patient (expected survival not more than (NMT) 6 months)
2. 1.0 Patient with high risk (expected survival between 6 to 24 months)
3. 2.0 Patient with moderate risk
4. 3.0 Patient with mild risk
5 4.0 Healthy Volunteers or subject of no risk

However, in case of patients whose expected mortality is 90 % or more within 30 days, a fixed amount of Rs. 2 lacs should be given

As per the above formula, the compensation amount will vary from a minimum of 4 lacs to a maximum of 73.60 lacs depending on the age of the deceased and the risk factor. However, in case of patients whose expected mortality is 90 % or more within 30 days, a fixed amount of Rs. 2 lac should be given.

The Committee agreed to the above formula for determining the quantum of compensation in case of clinical trial related death. However the Committee recommended that amendment in certain clauses of Drug & Cosmetic Rule related to the payment of compensation in case of injury/death occurring during clinical trial as recommended by DTAB, should be made expeditiously, So that causality analysis

of Serious Adverse Events is done following appropriate criteria and compensation is decided as per the above formula.

The Committee members also deliberated on the requirements of Serious Adverse Event reporting by the Investigator within 24 hrs. of their occurrence. It was deliberated that there is always possibilities that in a clinical trial on OPD patients, the Investigator may not came to know about an SAE within 24 hrs of occurrence, if subject or his relative do not inform it to the Investigator within 24 hrs of its occurrence. The Committee after detailed deliberation recommended that a clause should be included in the D&C Rules mentioning that in case an Investigator fails to report any SAE within 24 hrs of its occurrence, reason for the delay to the satisfaction of the Licensing Authority (DCGI) should be submitted along with the SAE.

The committee was apprised about by status of various regulatory activities related to clinical as under:

1. Out of 89 cases of SAEs of related deaths occurred during clinical trials between January, 2005 to December 2012, payment of compensation has already been made by the companies in 83 cases. In 2 cases, the amount has been decided and payments by the companies are under process.

2. Clearance of a total of 239 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.

3. 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 577 inspection reports have been received by CDSCO which are under examination. So far notices have been issued in 213 cases seeking clarification.

4. A total of 907 applications for registration of Ethics Committees have been received which includes 667 applications from Institutional and 200 applications from Independent ethics committee. Out of this, CDSCO has granted registration to 463 Institutional Ethics Committees and 95 Independent Ethics Committees. Further, rejection has been issued in 11 cases and 238 ethics committees (153 institutional and 85 independent) have been asked to submit further information.

The meeting ended with the vote thanks to the chair.

ANNEXURE - I

	Completed years of age on the last birthday of the workman immediately preceding the date on which the compensation fell due	Factor (F)
	1	2
Not more than	16	228.54
	17	227.49
	18	226.38
	19	225.22
	20	224.00
	21	222.71
	22	221.37
	23	219.95
	24	218.47
	25	216.91
	26	215.28
	27	213.57
	28	211.79
	29	209.92
	30	207.98
	31	205.95
	32	203.85
	33	201.66
	34	199.40
	35	197.06
	36	194.64
	37	192.14
	38	189.56
	39	186.90
	40	184.17
	41	181.37

42	178.49
43	175.54
44	172.52
45	169.44
46	166.29
47	163.07
48	159.80
49	156.47
50	153.09
51	149.67
52	146.20
53	142.68
54	139.13
55	135.56
56	131.95
57	128.33
58	124.70
59	121.05
60	117.41
61	113.77
62	110.14
63	106.52
64	102.93
65 or more	99.37