MINUTES OF THE MEETING HELD ON 27-02-2013 UNDER CHAIRMANSHIP OF DGHSFOR 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. Ashok Kumar Das, Director – Professor of Medicine & Medical Superintendent, JIPMER, Puduchery-605006.	Member
3.	Dr. Jaspal Sharma, Prof. & Head, Dept. of Cardiology, PGIMER, Chandigarh.	Member
4.	Dr. Nikhil Tandon, Professor, Dept. of Endocrinology & Metabolism, AIIMS, New Delhi.	Member
5.	Dr. KamlakarTripathi, Prof., Dept. of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi – 221005.	Member
6.	Dr.DebasisBasu, Prof. & Head, Dept. of Neurology,KolkataMedicalCollege, Kolkata.	Member
7.	Dr. P.K. Dalal, HOD, Dept. of Psychiatry, CSMU Medical College, Lucknow.	Member
8.	Dr.RajutitusChacko, Prof. & Head, Dept. of Medical oncology, CMC, Vellore.	Member
9.	Dr. B.L. Sherwal, Director-Professor, Dept. of Microbiology, LHMC & Associated Hospitals, New Delhi	Member

10. Dr. Nandini Kumar, Member
Former Deputy Director General Sr. Grade,
Co-Investigator, NIH Bioethics Project, National Institute of Epidemiology, ICMR, Chennai

From CDSCO:

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

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

3. Dr. Ravi Kant Sharma,
Assistant Drugs Controller (India)

The Hon'ble Supreme Court of India, vide its order dated 03.01.2013 in the matter of W.P. (C) No. 33/2012 of SwasthyaAdhikarManch, Indore &Anr Vs. Ministry of Health and Family Welfare &Ors. with WP(C) No. 779/2012 regarding clinical trials, had directed that until further orders by this Court, clinical trials of new chemical entity shall be conducted strictly in accord with the procedures prescribed in Schedule Y of the Drugs and Cosmetics Act, 1940 under the direct supervision of the Secretary, Ministry of Health and Family Welfare, Government of India.

In compliance to the said order of the Hon'ble Court, Ministry of Health & Family Welfare has put into place a system of supervision of clinical trial of new chemical entities. In order to supervise the clinical trial, the Ministryhas constituted an Apex Committee and a Technical Committee vide order no. 12-01/12-DC (Pt-133)/DFQC dated 06-02-2013. The Apex Committee consisting of Secretary-cum-DG, Indian Council of Medical Research, Director General, Health Services, and Secretary, Health and Family Welfare (as Chairman) has started meeting monthly basis to take stock of new approvals of clinical trials. The Secretary (HFW) will take the assistance of the Technical Committee to supervise and monitor the conduct of the clinical trials in the country. The Technical Committee will meet every month to oversee the conduct of clinical trials and give its recommendation to the Apex Committee for taking further appropriate action.

Accordingly, the first meeting of the Technical Committee was held on 27-02-2013 to give input related to such clinical trials to the Apex Committee for supervising and monitoring the conduct of clinical trials in the country.

The Committee was appraised that as per the Schedule-Y, for new drug substances discovered in countries other than India, Phase-I (First-in-Human) studies are not

permitted. In such case, Phase I data from other countries and along with data as per Appendix I of Schedule-Y should be submitted. After submission of Phase I data generated outside India, permission may be granted to repeat Phase I trials and/or to conduct Phase II trials and subsequently Phase III trials concurrently with other global trials for that drug. However, for any new drug substances discovered in India, clinical trials are required to be carried out in India right from Phase I and the data should be submitted as required under Schedule Y.

Committee was also appraised that, in order to strengthen the review process of applications of global clinical trial including clinical trials of New Chemical Entities (NCEs) other than IND and approval of new drug molecules and new Fixed Dose Combinations, Ministry of Health and Family Welfare has constituted following twelve New Drug Advisory Committees (NDACs) of different therapeutic categories vide orders dated 31.03.2011, to advise DCG(I) in matters related to regulatory approval of such applications. The committees are as under

a) NDAC- Oncology &Hematology
b) NDAC- Cardiovascular and Renal
c) NDAC-Metabolism & Endocrinology
d) NDAC- Antimicrobial, Antiparasitic& Antifungal, Antiviral
e) NDAC- Reproductive & Urology
f) NDAC-Gastroenterology &Hepatology
g) NDAC-Dermatology & Allergy, immunology
h) NDAC- Pulmonary
i) NDAC- Neurology &Psychiatry
j) NDAC- Analgesic, Anesthetics& Rheumatology
k) NDAC- Ophthalmology
l) NDAC- Vaccines

Each of the above committees comprise of ten members including two Pharmacologists and eight medical specialists from Government Institutes, Medical Colleges across the country.

All applications of clinical trial proposals of new drug including NCEs excluding Investigation New Drugs (INDs) are being evaluated by the NDACs. In case of Investigational New Drug (IND), the proposals are referred to IND Committee headed by Secretary, Department of Health Research and Director General, Indian Council of Medical Research and decision to approve or otherwise is taken as per recommendation of that Committee.

The functioning of these twelve NDACs in respect of approval of Global Clinical Trial (GCT) including clinical trials of new chemical entities are as under:

i. Till 31.12.12, these twelve NDACs have met 47 times wherein a total of 638 applications for approval of clinical trials, new drugs and fixed dose combinations, were evaluated.

ii. Out of these 638 applications, 234 were related to approval of GCT including clinical trials of new chemical entities. Of these 234 GCT applications, NDACs after deliberation have recommended for approval of 201 applications and have not recommended approval in case of the remaining 33 applications.

iii. These 201 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. The Committees have recommended these cases after detailed evaluation of safety, efficacy data including pharmacological, toxicological data, clinical data and protocol for the clinical trials including the objective of the study, eligibility criteria of the subjects, treatment, safety & efficacy assessments etc. Out of these 201 applications, based on recommendations of the Committees, so far, DCG (I) has given approval to conduct clinical trials in 158 cases. Other cases are under process.

iv. 33 applications of GCT which have not been recommended by NDACs for approval are related to psychiatry, neurology, cardiology, metabolism and endocrinology etc. These have not been recommended by NDACs due to various reasons like administration of placebo, inadequate safety & efficacy data, proposal to conduct study in India only etc.

The functioning of IND Committee in respect of approval of INDs is as under:-

i. Within last two years, IND Committee has met 10 times wherein a total of 80 applications for approval of clinical trials were evaluated. These 80 applications include clinical trials for products relating to Anti-HIV, Anti-T.B., Anti allergic, Cardiology, Oncology, Metabolism & Endocrinology, Gastroenterology etc.

ii. Out of these 80 applications evaluated by the IND Committee, this office has granted NOC to conduct clinical trial in 40 cases based on the recommendations of the IND Committee. Remaining applications are still under processing wherein applicants have been asked to submit different types of additional data / information as recommended by IND Committee during its meetings.

iii. Further, in addition to the above mentioned cases committee has also evaluated and recommended for grant of market authorization of two investigational new drugs developed in the country. Based on the recommendations of IND Committee, DCG(I) has granted approval to market these two new drug molecules (FDC of ArterolaneMaleate+Piperquine Phosphate &Saroglitazar) in India.

Committee advised that these approval details of NDAC's and IND should be forwarded to the members of Technical Committee through e-mail for their review. Committee also recommended that clinical trials should only be conducted in government medical college / institutions and institutes of reputes including reputed corporate hospitals under the supervision of investigators who have experience, knowledge and are known for their integrity.

The committee also felt that it is absolutely necessary to develop an IT enabled database of clinical trials which can give information about all elements of a clinical trial (CT) related to Sponsors (or his representatives), Investigators, Ethics Committees (EC)and the trial subjects for monitoring and enforcement in clinical trials to ensure the protection of rights, safety and well beings of trial subjects and authenticity of the data generated. The database shall be updated continuously on day to day basis by Sponsors (or his representatives), Investigators, Ethics Committees (EC)for correct and updated information. The Committee was appraised that the matter is being taken up on priority with NIC. A detailed concept note in this regard was provided to NIC for their project evaluation and the NIC has forwarded a project plan of Rs. 24 Lacs for creating the data base. Further, action in this regard is under consideration of the Ministry of Health & Family Welfare.

The Committee appreciated the various efforts being taken by the Government to strengthen regulationof clinical trials, including three recent amendments in Drugs & Cosmetics Rules related to (a) examination of Serious Adverse Events & procedures for payment of compensation in case of clinical trial related injury or death, (b) Inspection and monitoring of clinical trials and (c) Registration requirements for Ethics Committees.

However, there are concerns on certain clauses, viz,providing free medical management to clinical trial as along as required in case of any injury irrespective of whether the injury is related to clinical trial or not, providing financial compensation in case of injury or death due to failure of investigational product to provide intended therapeutic effect and use of placebo in placebo controlled trial.

The committee deliberated the various clauses of the notification and opined as under:

a) The Committee felt that providing free medical management to the subject in case of any injury irrespective of whether the injury is related to clinical trial or not may

besuitably amended to ensure that medical management is provided in case of injury due to clinical trial related activities.

b) Committee opined that there is a possibility that Investigational product may fail to provide intended therapeutic effect. This is explained to trial subjects during consent process. Similarly placebo used in placebo-controlled trial, will not give any therapeutic effect. In certain cases placebo controlled trial is necessary to evaluate efficacy of Investigational drug. Lack of therapeutic effect of placebo is explained to the subject during consent process.Therefore, the said clauses of the notification requires modification as under:
    i. The clause requiring to provide financial compensation in case of injury or death due to failure of investigational product to provide intended therapeutic effect should be deleted.
    ii. The clause requiring to provide financial compensation in case of injury or death due to use of placebo in a placebo-controlled trial should be modified as below:

    " use of placebo in a placebo-controlled trial if the standard of care is denied."

c) Committee also felt that the timeline requirement of submitting the Serious Adverse Events reports after due analysis, by the Sponsor, Investigator within ten calendar days as mentioned in the notification may be modified to fourteen calendar days as practiced internationally.

d) The committee also noted that the notification related to compensation in clinical trials is applicable to both company sponsored trial as well as investigator initiated institutional clinical trial for academic purpose. However, concerns were raised by the members of the committee as to how the Institutions will be able to provide financial compensation in case of clinical trial related injury or death in Investigator initiated institutional trials. After deliberation committee recommended that Department of Health Research should maintain a corpus fund to compensate subjects who suffer injury or death during such institutional clinical trials.

e) As regards to reporting of Serious Adverse Events by the sponsor companies, the committee felt that it should be made mandatory for the sponsor to submit reports of serious adverse events occurring in other countries in a global clinical trial in which India is also a participating country.

Some of the members of the committee also raised concerns about delays in approval of institutional clinical trials by DCG(I). One of the reasons for such delays was cited to be the procedures of evaluation of such proposals through NDAC committees. The committee recommended that in case approval of institutional clinical trial is delayed due to meetings of NDAC etc. the same may be placed before this Technical Committee for evaluation and speedy processing.

DCG(I) mentioned that some proposals of new drug approvals which have been recommended by NDACs for approval in the country without conducting local clinical trials. However, there are concerns on approval of such new drugs without local clinical trial on Indian population. The committee deliberated the issue of waiver of local clinical trials on Indian population for approval of new drugs and suggested that such new drug proposals in which NDAC has already recommended for waiver of local clinical trials should be placed before this Technical Committee for evaluation and recommendation.

The meeting ended with the vote of thanks to the chair.