MINUTES OF 24th MEETING OF THE TECHNICAL COMMITTEE HELD ON 06.05.2015 UNDER THE 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, Nirman Bhawan, New Delhi	Chairman
2.	Dr. Ranjit Roy Chaudhury, National Professor of Pharmacology, Former Member, BOG – MCI, Y-85, Hauz Khas, New Delhi-110 016.	Member
3.	Dr. Nandini Kumar, Former Dy. Dire. Gen. Sr. Grade, Adjunct Professor, KMC, Manipal, 5/1 (New) Padmalaye Apt. Chennai.	Member
4.	Dr.Rajutitus Chacko, Prof. & Head, Dept. of Medical Oncology, CMC, Vellore	Member
5.	Dr. Ashok Kumar Das, Professor of Medicine & Professor and Head of Endocrinology, Pondicherry Institute of Medical Sciences, Pondicherry – 605014	Member
6.	Dr. Yash Paul, Prof. & Head, Dept. of Cardiology, PGIMER, Chandigarh.	Member
7.	Dr. B.L Shrerwal, Additional Medical Supdt. Director-Professor, LHMC, Delhi	Member

From CDSCO:

1. Dr. G.N Singh,
   Drugs Controller General (I)
2. Dr.V.G.Somani,
   Joint Drugs Controller (I)
3. Mrs. Rubina Bose
   Deputy Drugs Controller (I)

Dr. G.N.Singh, DCG (I) welcomed the members of the meeting and Dr.V.G.Somani, JDC (I) initiated the proceedings of the Committee.

Before taking up evaluation of the clinical trial proposals as per the agenda, the Committee deliberated various issues including streamlining the procedure of evaluation of clinical trial proposals and recommended that policy issues related to new drug and clinical trial approval etc., where further guidance or clarity is required, may be deliberated in the Technical Committee for streamlining the procedures. The outcome of these deliberations shall be placed before the DTAB for further consideration. Advance intimation of DTAB meeting shall be posted on the CDSCO website before the proposed date and all stakeholders shall be invited to give suggestion for any policy related matter for discussion in the DTAB. A workshop shall be organized in the mid of June to frame uniform format for deliberation of clinical trial proposal in the SEC and Technical Committee, based on which SOPs for the SEC shall be prepared. Once the format is finalised, the scope shall be provided for inclusion of any other additional information related to specific proposal at the footnote of the format. In this regard, a proposal of visit of DCG (I) and Technical team of CDSCO to the other regulatory agencies like USFDA, EMA, PMDA shall be made.

Thereafter the Committee discussed the clinical trial proposals one by one as under:

1. **Proposals of Clinical Trials recommended by SEC / IND.**

The Committee deliberated 17 cases related to approval of clinical trials. Out of these 17 cases, 02 cases were related to clinical trials of NCEs (01 case of GCT and 01 case of Biological) and 02 cases were related to global clinical trials (GCT). Remaining 13 cases were related to clinical trials for approval of New Drugs, medical devices and biologicals.

The Committee evaluated the 02 cases related to clinical trial of NCEs one by one and made recommendations considering all aspects of safety, efficacy especially in terms of the three parameters viz. risk versus benefit to the patients, innovation *vis-a-vis* existing therapeutic option and unmet medical need in the country. After detailed deliberations, the Committee recommended for approval of both the cases. The recommendations of the Committee in respect of these 02 cases related to clinical trial of NCEs are enclosed as **Annexure-I.**

Thereafter, the Committee evaluated 02 cases related to global clinical trial. After detailed deliberations, the Committee recommended for approval of 02 cases.The recommendations of the Committee in respect of these 02 cases related to GCTs are enclosed as **Annexure-II**

The Committee also evaluated the remaining 13 cases of other than GCT/clinical trial of NCEs. After detailed deliberation, the Committee recommended for approval of 09 cases out of 13 cases. Out of 09 recommended cases, the Committee recommended 01 case (S. No 07 in annexure-III) subject to certain conditions. The Committee did not recommend the 02 (S. No 05 and 11 in annexure-III) cases and deferred the 02 (S. No 9 and 12 in annexure-III) proposals for seeking clarification. The recommendations of the Committee in respect of these 13 cases are enclosed as **Annexure-III.**

Thus, the Committee recommended for approval of 13 cases, out of total 17 cases of clinical trial proposals.

2. Waiver of Clinical Trial in Indian population for approval of new drugs, which have already been approved outside India

As per the Drugs & Cosmetics Rules, for new drugs substance approved in other countries, phase III clinical trial is required before granting permission to manufacture / import of finished formulation of the new drug.

However, requirements of local clinical trial may be waived off / relaxed under certain conditions as per Drugs & Cosmetics Rules (122 A (2) ,122 B (3) & clause 1 (3) of Schedule Y as mentioned above depending on nature of drugs and diseases for which it is indicated.

Under Rule-122A(2) & Rule-122B(3) of Drugs & Cosmetics Rules the requirement of submitting the results of local clinical trials may not be necessary if the drug is of such a nature that the licensing authority may, in public interest decide to grant such permission on the basis of data available from other countries. Further the submission of requirements relating to animal toxicology data may also be modified or relaxed under the same rules in case of new drugs approved and marketed for several years in other countries and adequate published evidence regarding the safety of the drug is available.

As per clause 1(3) of Schedule Y to Drugs & Cosmetics Rules, for drugs indicated in life threatening / serious diseases or diseases of special relevance to the Indian health scenario, the toxicological and clinical data requirements may be abbreviated, deferred or omitted, as deemed appropriate by the Licensing Authority.
It would thus be observed that there are certain conditions specified in the Drugs & Cosmetics Rules under which the licensing authority may grant permission to manufacture / import of new drugs without local clinical trials.

However, Parliamentary Standing Committee in its 59th report has raised concerns on approval of certain new drugs in the country without local clinical trials. In light of the same the Ministry constituted a Committee under chairmanship of Prof. Ranjit Roy Chaudhury, the Committee submitted its report. The action to be taken on the recommendations of the Expert Committee has been finalized by the Ministry of Health & Family Welfare.

As per the action, "The waiver of Clinical Trial in Indian population for approval of new drugs, which have already been approved outside India, can be considered only in cases of **national emergency, extreme urgency, epidemic and for orphan drugs for rare diseases and drugs indicated for conditions/diseases for which there is no therapy**.

The Apex Committee in its meeting held on **24.01.2014** has recommended that waiver of local clinical trial of such cases should be granted only under the criteria as already decided by the Ministry viz national emergency, extreme urgency, epidemic and for orphan drugs for rare diseases and drugs indicated for conditions/diseases for which there is no therapy. In case local clinical trial waiver is required for any other category, the matter should be brought before the Committee for consideration along with the recommendations of the Technical Committee.

Following 04 proposals (02 from New Drug and 02 from Subsequent New Drugs) have been recommended by the SECs for their approval for manufacture/ import for marketing in the country without local clinical trial. The details of the same along with recommendations of SEC were placed before the Committee. The recommendation of the Technical Committee is as under.

Sr. no.	Drug Name	Name of the Firm	Indication	Recommendation
1.	Panobinostat Hard Gelatin Capsules, 10/15/20mg	M/s. Novartis Healthcare	For the treatment of patients with relapsed or relapsed-and-refractory multiple myeloma, who received at least 1 prior therapy	**Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended the waiver of local clinical trial for this orphan drug as per the recommendation of the SEC. **SEC Recommendation:** The Committee recommended the waiver of Phase-III study for the drug and import and marketing approval of the drug as it has been approved as orphan drugs by USFDA "in combination with Bortezomib and Dexamethasone for the treatment of patients with multiple myeloma who have received at least 2 prior regimens, including Bortezomib and an immunomodulatory agent".. However the firm should conduct a Phase-IV trial in Indian subjects. The continued marketing of the drug will depend on the safety & efficacy data on the Phase-IV trial subjects which are to be generated and submitted to the SEC for evaluation within eighteen months. Accordingly, the firm should submit Phase-IV protocol etc. within two months to the office of DCGI.

2.	Pasireotide solution for injection	M/s Novartis Healthcare Pvt. Ltd	For the treatment of patients with Acromegaly for whom medical therapy is appropriate	**Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended the waiver of local clinical trial for this rare disease as per the recommendation of the SEC. **SEC Recommendation:** The Committee deliberated the proposal in detail and agreed that Acromegaly is a rare disease. Therefore, the Committee recommended for grant of permission for import and marketing of the drug with local clinical trial waiver subject to condition that a Phase IV Post Marketing Study to be conducted in adequate no. of patients and duration.
3.	Everolimus 0.25/0.5/0.75/1 mg tablets & 0.1/0.25 mg dispersible tablets	M/s Novartis India Ltd	For the treatment for the prophylaxis of organ rejection in patients receiving a hepatic transplant.	**Recommendation of the Technical Committee:** The Committee noted that Everolimus is an Immuno-suppressant and is already approved for use in Renal Transplant in the country. Drug is already approved in US, EU and other countries for the proposed additional indication i.e. for use in patients receiving hepatic transplant. The Committee recommended for granting permission for the proposed additional indication as it is unmet need in the country and it will help to reduce CNI (Calcineurine inhibitor) related nephrotoxicity, high morbidity rate etc., as observed from the literature and the drug is approved by other robust regulatory authorities. The Committee further noted that there is a constant request from specialists involved in hepatic transplant and post operative care for this drug based on their information. The Committee opined that the further data may be collected by conducting Phase IV trial. **SEC Recommendation:** The Committee noted that Everolimus is already approved in proposed indication in USA, EU, Uk etc. The Committee noted that the liver translation is done for life threatening conditions. Currently Hepatic transplantation is managed by Tacrolimus/cyclosporine, Corticosteroids and MMF/Azathioprine. As per the trial data generated in other countries and presented before the Committee, it shows that use of Everolimus in combination with Tacrolimus and corticosteroids provide promising results in reducing kidney injuries post liver transplantation. Based on the presentation made by the firm, the Committee noted that

				there is an unmet need for the use of Everolimus in management of hepatic transplant patients. However there is no data on Indian patients for the proposed Indication. The Committee opined that the proposal is not meeting the criteria laid down for this purpose for waiver of local clinical trial. The firm represented to DGHS for clinical trial waiver in which the firm has submitted the justification for same. **Justification submitted by the firm for clinical trial waiver:** The Firm has stated that the proposed indication is a life threatening serious condition and there is still an unmet need of immunosuppressive regimens to reduce long term complications, particularly CNI-related nephrotoxicity in liver transplant, high morbidity rate and favourable global data derived from number of clinical studies on Everolimus in liver transplant patients. Product for the said indication was approved in 76 countries worldwide including US and EU. As desired by DGHS, the matter is placed before the Committee.
4.	Medroxyproges terone Acetate (MPA) 104mg in 0.65mL suspension for injection	M/s Pfizer Products India Pvt Ltd.	For long term female contraception	**Recommendation of the Technical Committee:** The matter was deliberated and the Committee noted that there are various alternatives available in respect of the proposed additional indication and being a Sub-cutaneous route which is new for its use and operationalization for the purpose of contraception, the Committee recommended that a Phase III trial shall be conducted. **SEC Recommendations:** The Committee recommended for approving for the proposed indication i.e for long term female contraception without conducting clinical trial as it is satisfactory subcutaneous therapy for the proposed indication which is not yet available in the country and further dose is also reduced with SC route when compared to IM route.

The meeting ended with vote of thanks to the Chair.

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Annexure-I

List of 02 cases of clinical trials of NCEs along with their evaluations and recommendations of the Technical Committee in its 24th Meeting.

Sr No.	Name of the Drug	FIRM	PROTOCOL	Parameters 1. risk versus benefit to the patients 2. innovation vis-a-vis existing therapeutic option 3. unmet medical need in the country	Recommendation
1	Masitinib	Maya Clinicals	AB11003	**Assessment of Risk vs. Benefit to the patients:** The safety profile of the study drug from preclinical pharmacology, single dose, repeat dose toxicity, reproductive toxicity and phase I, II clinical studies justify the conduct of the trial. **Innovation vis-à-vis Existing Therapeutic Option**: The purpose of the study is to evaluate the efficacy and safety of masitinib with dexamethasone, gemcitabine with dexamethasone and the combination of masitinib, gemcitabine and dexamethasone in patients with relapsed or refractory peripheral T-cell lymphoma. **Unmet Medical Need in the country**: The test drug may potentially provide alternative treatment option in patients with relapsed or refractory peripheral T-cell lymphoma.	**Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation. **SEC Recommendation** After detailed deliberation the committee recommended to conduct of the trial as per protocol presented by the firm with the condition that the study sites/ Investigators need to be appropriately selected to the trial considering the indication, PI preferably should be from high volume oncology centers for patients with relapse or refractory peripheral T-Cell Lymphomas and should medical oncologist / hematologist

	Recombinant Lysostaphin gel (150µg/g) - BIOSTAPHIN™	M/s Bharat Biotech International Limited,	BBIL/LYS/IIB/III/2013		**Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended to conduct the study as per the IND committee recommendation. **IND Committee recommendations**: The firm presented the amendments made to the protocol in line with the recommendations made in the earlier IND meeting dated 14.10.14.The amendments have been deliberated and the firm proposal for phase IIb/III clinical study as per the revised protocol (BBIL/LYS/IIb/III/2013,version 1.1,dated 17.01.2015)has been recommended by the committee.

Annexure-II

List of 02 cases of Global Clinical Trials along with their evaluations and recommendations of the Technical Committee in its 24th Meeting.

Sr No.	Name of the Drug	Name of Firm	PROTOCOL	Parameters 1. risk versus benefit to the patients 2. innovation vis-a-vis existing therapeutic option 3. unmet medical need in the country	Recommendation
1	CT/06/15	Max Neeman	FORMA-04	**Risk Versus Benefit to the Patients:** The risk vs benefit profile of the test drug from preclinical single dose toxicity studies and reproductive toxicity study justify the conduct of this study. **Innovation vis-a-vis Existing Therapeutic Option:** The purpose of the study is to demonstrate the efficacy of Octafibrin for on demand treatment of acute bleeding episodes (spontaneous or after trauma). **Unmet Medical Need in the Country:** Fibrinogen concentrates availability may help in decreasing the volumes to be infused in emergency and serious bleeds.	**Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation. **SEC Recommendation:** After detailed deliberation, the Committee recommended for the conduct of phase III trial in Indian Patients as per the submitted protocol.

2.	CT/08/15	Excel Life Science	32-009	**Risk Versus Benefit to the Patients:** The risk vs benefit profile of the test drug from preclinical single dose toxicity, repeated dose toxicity, genotoxicity studies and phase I, II clinical studies justify the conduct of this study. **Innovation vis-a-vis Existing Therapeutic Option:** The purpose of the study is to evaluate the long-term safety of treatment with DE-109(440µg) in subjects with NonInfectious Uveitis of the posterior segment of the eye who have participated in the SAKURA development program. **Unmet Medical Need in the Country:** The study may provide continued access to the drug who have participated in the previous study as this is the extension study of protocol number 32-007.	**Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation. **SEC Recommendation** After detailed deliberation the committee has approved the conduct of the study as per the presented protocol.

Annexure-III

List of 13 cases of clinical trial proposals other than GCT/NCE along with evaluations and recommendations of the Technical Committee in 24th Meeting.

Sl No	Name of the Drug	Firm Name	Recommendation of the Technical Committee
1.	SYSTANE® BALANCE Lubricant Eye Drops Chemical name - Propylene Glycol 0.6%	M/s Alcon Laboratories India Pvt Ltd	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
2.	Cabazitaxel Lipid Suspension for injection 50 mg/vial	M/s Intas Pharmaceuticals Limited	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
3.	Nanosomal Paclitaxel Lipid Suspension for Injection	M/s Intas Pharmaceuticals Limited	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
4.	Intrauterine Contraceptive Device Cu-380 Ag (3-sizes; Mini, normal & maxi)	M/s SMB Corporation of India, Mumbai-60.	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
5.	Inter-Atrial Shunt Device (.IA SD™) System - II	M/s 8C Healthcare Private Limited, Hyderabad	After detailed deliberation, the Committee felt that there is inadequacy of evidence for safety & performance of this "medical device" and cannot be considered to conduct the study at this stage.
6.	Pentavalent vaccine (DTwP-HepB-Hib) Shan5 (with Shantha pertussis)	M/s Shantha Biotechnics Ltd., Hyderabad	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation. However, the Committee desired to obtain the details of environment described in the statement in the Assessment of Risk versus benefit to the patients that "The subjects will be in an environment where appropriate medical care can be provided for any adverse events that may be observed"

7.	Seasonal Live Attenuated and Inactivated Influenza Vaccine	Dr. Anand Krishnan, AIIMS, New Delhi	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation. However, the applicant has to clarify following points: 1. The committee observed that there are no. of Co-Investigators and recommended that the roles and responsibilities of each Investigator and Co-Investigators be clarified and reviewed by the office of DCG (I). 2. Clarification be sought regarding the statement in the Inclusion Criteria that "Children aged above 7 years will provide written assent and those below 7 years will provide verbal assent". The detail meaning and procedure of verbal assent and whether it is addition to written inform assent shall be enquired from the applicant.
8.	Cadisurf (Goat lung surfactant extract 25 mg & 80 mg)	Dr. Ramesh Agarwal, AIIMS, New Delhi	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
9.	Ulinastatin for Injection 50000 IU/100000 IU	M/s Lupin Limited	After detailed deliberation, the Committee noted that it is not clear in the protocol as what is meant by standard supportive care. Therefore, the Committee recommended that the firm shall clarify it and provide a proper protocol within 15 days from receipt of letter, failing which the marketing authorization which was granted subject to the conduct of phase-IV trial in 200 patients shall be made invalid. Further, whether standard care of treatment will be provided in Placebo arm needs to be clarified. Hence the Committee did not recommend the trial as per protocol submitted.
10.	Fentanyl Citrate Injection	Dr. Smita Prakash, VMMC College and Hospital, New Delhi	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
11.	Ampucare (Wound Care Solution)	M/s Venus Remedies Limited	The Committee did not recommend the proposal as sufficient clinical development data prior to phase-III studies for the said drug in the diabetic foot ulcer is not available to justify the permission to conduct phase-III clinical trial for the purpose of marketing approval.

12.	Ulinastatin for Injection 50000 IU/100000 IU	M/s Bharat Serum and Vaccine Ltd	After detailed deliberation, the Committee noted that it is not clear in the protocol as what is meant by standard supportive care. Therefore, the Committee recommended that the firm shall clarify it and provide a proper protocol within 15 days from receipt of letter, failing which the marketing authorization which was granted subject to the conduct of phase-IV trial in 200 patients shall be made invalid. Further, whether standard care of treatment will be provided in Placebo arm needs to be clarified. Hence the Committee did not recommend the trial as per protocol submitted.
13.	Recombinant human follicle stimulating hormone (rhFSH)	M/s Serum Institute of India Limited	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.

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