MINUTES OF 18th MEETING OF THE TECHNICAL COMMITTEE HELD ON 13.10.2014 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	Chairman
2.	Dr. Nandini Kumar, Former Dy. Director (Sr. Grade) National Institute of Epidemiology, ICMR, New Delhi	Member
3.	Dr. Kamlakar Tripathi, Prof., Dept. of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi – 221005.	Member
4.	Dr. Yash Paul, Prof. & Head, Dept. of Cardiology, PGIMER, Chandigarh.	Member
5.	Dr. Rajutitus Chacko Prof & Head, Dept. of Medical Oncology CMC Vellore	Member
6.	Dr. Nikhil Tandon Prof & Head, Dept of Endocrinology and Metabolism, AIIMS, New Delhi	Member

Special Invitee:

1. Dr. Radhika Tandon,
   Prof of Ophthalmology, Cornea and Refractive Surgery Unit and Officer–in-charge National Eye bank, AIIMS, New Delhi.
   (For evaluation of proposals of ophthalmology drugs)

2. Dr. Ramanjit Sihota,
   Professor of Ophthalmology, AIIMS, New Delhi
   (For evaluation of proposals of ophthalmology drugs)

3. Dr. R. S. Gupta,
   DDG(TB), DGHS, New Delhi
   (For evaluation of one proposal of anti-TB drugs)

4. Dr. S.K. Sharma,
   Prof & Head, Dept. of Medicine, AIIMS
   (For evaluation of one proposal of anti-TB drugs)

5. Dr. Rohit Sarin, Director, National Institute of Tuberculosis and Respiratory Diseases, New Delhi
   (For evaluation of one proposal of anti-TB drugs)

From CDSCO:

1. Dr. G.N. Singh,
   Drugs Controller General (India)
2. Dr.V.G.Somani,
   Joint Drugs Controller (India)
3. Sh. A.K. Pradhan,
   Deputy Drugs Controller (India)
4. Sh. R.Chandrashekar
   Deputy Drugs Controller (India)
5. Mrs. A Visala
   Deputy Drugs Controller (India)

DCGI welcomed the members and with permission of the Chairman, he stated that certain issues/ modalities related to evaluation of clinical trial proposals by Technical Committee needs to be discussed. Accordingly he placed following two issues before the Committee for deliberation and recommendations.

i) Categories of clinical trial proposals to be evaluated by Technical Committee:

DCGI stated that as per the order of Hon'ble Supreme Court dated 03.01.2013 in the matter of W.P. (C) No. 33/2012 of Swasthya Adhikar Manch in the case of clinical trials of new chemical entity shall be conducted strictly in accord with the procedure prescribed in Schedule 'Y' of Drugs & Cosmetics Act, 1940 under the direct supervision of the Secretary, Ministry of Health & Family Welfare, Government of India.

In view of the same, Ministry of Health & Family Welfare constituted Technical Committee under the Chairmanship of DGHS and Apex Committee under the Chairmanship of Secretary, Ministry of Health & Family Welfare, to evaluate the clinical trial proposals vide its order no 12-01/12-DC(Pt-133/DFQC) dated 06.02.2013.

Presently all clinical trial proposals including proposals of New Chemical Entity (NCE), Global Clinical Trial (GCT), clinical trial of New Drugs already approved in other countries, Fixed dose combination, Subsequent New Drugs and vaccines are being evaluated through a three tier system viz. (1) NDAC (presently renamed as SECs), (2) Technical Committee and (3) Apex Committee.

Hon'ble Supreme Court in its order dater 21.04.2014 have directed that henceforth the Format seeking information from the applicants, three specific columns viz. (i)risk versus benefits to the subjects, (ii) innovation *vis* a *vis* existing therapy and (iii) unmet need to the country shall be inserted for the purpose of New Clinical Entities/Global Clinical Trials.

In view of the above fact and circumstances, DCGI placed before the Committee that it may be appropriate for the Technical Committee to consider the evaluation of the proposals of clinical trial which are related to GCTs/NCEs only and clinical trial proposals of drugs related to other than GCT/NCEs may be disposed of at CDSCO level.

After detailed deliberations, the Committee agreed to the suggestion and recommended that henceforth only clinical trial proposals of GCTs & NCEs should be placed before the Committee for evaluation. Other proposals of clinical trial of New Drugs already approved in other countries, Fixed dose combination, Subsequent New Drugs and vaccines etc., may be disposed of at CDSCO level.

ii) **To fix specific day of every month for conduct of meeting of Technical Committee.**

DCGI has requested the Committee to consider fixing a specific day of every month for holding of the meetings of the Committee so that the members can plan their schedule well in advance accordingly.

After detailed deliberation, Committee decided that the meeting may be held on first week of every month preferably Friday. The Committee also decided that in case the Chairman, DGHS is not available on the day of the meeting, DGHS may nominate a Chairman for conduct of the meeting on the same day.

The Committee also deliberated regarding the inspection of clinical trial by CDSCO. It was appraised that CDSCO Zonal offices are involved in conduct of inspection of clinical trial sites in their respective jurisdiction as per CDSCO (HQ) direction.

The Committee after deliberation recommended that CDSCO Zonal, Sub zonal offices may start initially to conduct inspection of clinical trial for 3 sites per month per inspector.

The Committee then discussed the clinical trial proposals one by one as under.

1. <u>Proposals of Clinical Trials recommended by SEC / IND.</u>

The Committee deliberated the 35 cases related to approval of clinical trials /protocol amendments.

Out of these 35 cases, 19 cases are related to global clinical trials (GCT), remaining 16 cases are related to clinical trials for approval of New Drugs including fixed dose combination, subsequent new drugs and biologicals. Out of 19 GCT cases, 11 are for approval of clinical trial and remaining 8 cases are for approval of protocol amendments.

The Committee evaluated the 19 cases related to global clinical trials one by one and made recommendations considering all aspect 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 deliberation, the Committee recommended approval for 10 out of 11 cases of global clinical trials (Sr. No 1, 2,3,4,5,6,7,17, 18 & 19 of Annexure-I) and all 8 cases of protocol amendments as per recommendations of the SECs. In one case of global clinical trial of anti-TB drugs (Sr.No14 in Annexure-I), the Committee recommended that the applicant should be asked to make a presentation before the Committee in presence of HIV and TB experts. The recommendations of the Committee in respect of these 19 cases is enclosed as **Annexure-I.**

The Committee also evaluated the remaining 16 cases which were other than GCT/clinical trial of NCEs. After detailed deliberation, out of these 16 cases, the

Committee recommended for approval of 15 cases as per recommendations of the SECs. In the remaining one case (Sr No 5 of Annexure-II), the Committee recommended that the firm should conduct the same study in rabbit as proposed for human and the data should be submitted for consideration of the proposed study in human.

The recommendations of the Committee in respect of other 16 cases is enclosed as **Annexure-II.**

Out of total 35 cases of clinical trial proposals, the Committee recommended for approval of 33 cases as per recommendations of the SECs. In remaining two cases the Committee sought certain additional data/ information as above.

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

As per the D&C 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 be thus 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 03 proposals (02 proposals from biologicals and 01 proposal from Subsequent New Drug) 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 alongwith recommendations of SEC are placed before the Committee for perusal and comments:

Sr. no.	Drug Name	Indication	SEC Recommendations
1.	Aflibercept	For patients with metastatic colorectal cancer (MCRC) previously treated with an oxaliplatin containing regimen.	Firm presented that there is an unmet need for this drug. The committee reviewed the presentation made in light of the Action taken report on Prof Ranjit Roy Committee Report and reiterate its previous observations which are as follows: ✓ There is an unmet need as a second-line therapy for metastatic colorectal cancer. ✓ The firm has conducted clinical trial in other indications as part of Global clinical trial which showed no difference in the pharmacokinetic parameters in 14 Indian patients and there was no safety issue. ✓ Pharmacokinetic data in Indian patients shows that there is no pharmacokinetic difference when compared to Caucasians. ✓ The Drug has been found to be effective for the proposed indication as per the data generated in other countries. Committee recommended for import and market subject to condition that firm should conduct a structured India specific Phase IV trial after getting approval by this office.
2.	Trastuzumab emtansine	For the treatment of patients with HER2-Positive, unresectable locally advanced or metastatic breast cancer who have received prior treatment with Trastuzumab and a taxane	"The proposal for the import and market the Trastuzumab Emtansine has been submitted for the NDAC approval with clinical trial waiver. TDM 1 is a novel drug indicated "for the treatment of patients with HER2-Positive, unresectable locally advanced or metastatic breast cancer who have received prior treatment with trastuzumab and a taxane" which is an unmet need. This drug is approved in 52 countries including countries such as US, Switzerland, Australia, Canada, Japan, Ecuador, Uruguay. Currently there is no standard of care for this condition and there is genuine unmet need. Overall 3000 patients have been exposed to the drug in various clinical trials globally. It shows significant improvement in overall survival. In addition to improving the Progression free survival, it also improves the overall survival based on the presentation made by firm. In view of the fact there is no therapy available for this condition and in the interest of public. Committee recommended for the permission to

			import and market for the subject drug may be granted subject to condition of adequately powdered phase IV clinical trial with a review of data in 2 years. The phase IV protocol should be duly approved by the CDSCO."
3.	Medroxyprogesterone Acetate (MPA) 104mg in 0.65mL suspension for injection	For long term female contraception and management of endometriosis associated pain.	Medroxyprogesterone Acetate 150mg/ml sterile aqueous suspension USP injection (intra-muscular) is approved by this Directorate in the year 1998. Firm has proposed a new drug delivery system of Medroxyprogesterone Acetate (MPA) 104 mg in 0.65 ml suspension by subcutaneous route. The committee opined that this particular formulation has been approved and marketed for several years in other countries and is also recommended by WHO. The proposed formulation is a reduced dose than intramuscular dose and the delivery system is novel and it is convenient for use when compared to the intra muscular route. Firm has also submitted the published reports on over 16,000 patients. Therefore committee recommended for import and marketing of Medroxyprogesterone acetate (MPA) 104mg in 0.65 ml suspension for injection in new delivery system and route of administration (subcutaneous). The committee has recommended for the approval subject to submission of PSUR every six month to the office of DCG (I).

The Committee after detailed deliberation agreed to the recommendations of the SEC for marketing authorization of these drugs without conducting local clinical trial.

The Meeting ended with vote of thanks to Chair.

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Annexure-I

List of 19 cases of global clinical trials/ clinical trials of NCEs along with their evaluations and recommendations of the Technical Committee in its 18th Meeting.

Sr. No.	Drug	Applicant Name	Protocol No	Parameters 1. risk versus benefit to the patients 2. innovation vis-a-vis existing therapeutic option 3. unmet medical need in the country	Recommendations
1.	CT-P10 (Biosimilar Rituximab	PPD	CT-P10 3.3 (Version 1.1)	**Risk Versus Benefit To The Patients** The risk vs benefit profile of the test drug from Pre clinical repeated dose toxicity studies, phase I, clinical study etc justify the conduct of the study. **Innovation Vis-A-Vis Existing Therapeutic Option** The purpose of the study is to demonstrate pharmacokinetic equivalence and noninferiority of efficacy of CT-P10 in comparison with a comparator administered in combination with cyclophosphamide, vincristine,and prednisone (cvp) in patients with advanced follicular lymphoma. **Unmet Medical Need In The Country** Availability of rituximab from multisource may potentially benefit Indian patients.	**NDAC/SEC Recommendation:** NDAC/SEC recommends the conduct of the study with subjects of upper age limit up to 75 years subject to submission of the MA / clinical trial approval from the country of origin. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC

2.	CT-P6 (Trastuzumab biosimilar)	PPD	CT-P6 3.2 (Version 2.0)	**Risk Versus Benefit To The Patients** The risk vs benefit profile of the test drug from repeated dose toxicity studies; in-vitro and in-vivo characterization studies justify the conduct of study. **Innovation Vis-A-Vis Existing Therapeutic Option** The purpose of the study is to compare the efficacy and safety of ct-p6 and the innovator/comparator as neo adjuvant and adjuvant treatment in patients with Her2-positive early breast cancer **Unmet Medical Need In The Country** Availability of Trastuzumab from multisource may potentially benefit Indian patients**.**	**NDAC/SEC Recommendation:** After deliberation, the committee recommended permission for conduct of the trial. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC

3.	Bosutinib	Wyeth	B1871040 (Dated 25 Feb 2013)	**Risk Versus Benefit To The Patients** The risk vs benefit profile of the test drug from various preclinical toxicity studies including repeated dose, carcinogenicity, reproductive toxicity studies, phase I, II, III clinical studies etc justify the conduct of the study. **Innovation Vis-A-Vis Existing Therapeutic Option** Bosutinib is a dual SRC – ABL TKI which inhibits the majority of mutated BCR-ABL proteins conferring imatinib resistance and is being developed for the treatment of PH+ CML. The purpose of the study is to assess the long term safety, tolerability and duration of clinical benefit of bosutinib. **Unmet Medical Need In The Country** The test drug may potentially provide treatment to subjects with chronic, accelerated, or blast phase Ph+ CML with resistance or intolerance to prior therapy	**NDAC/SEC Recommendation:** NDAC/SEC recommends the conduct of the study **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC

4.	Glycopyrronium Bromide/NVA237	Novartis	CNVA237B2301	**Risk Versus Benefit To The Patients** The risk vs benefit to the patients of the test drug from safety pharmacology and pre clinical toxicity including single dose, repeated dose, genotoxicity, carcinogenecity and phase I, II, III clinical studies justifies the conduct od study. **Innovation Vis-A-Vis Existing Therapeutic Option** The purpose of the study is to evaluate the efficacy, safety, and tolerability of test drug in patients with poorly controlled asthma. **Unmet Medical Need In The Country** The test drug will provide the better treatment option in patients with poorly controlled asthma.	**NDAC/SEC Recommendation**: The committee recommended the proposed study subject to condition that there should be periodic monitoring of female patients of child bearing age for pregnancy. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC. Further the committee recommended that there should be two more sites from government hospital.

5.	LDK378 (NCE)	Novartis	CLDK378A2402	**Risk Versus Benefit To The Patients** The risk vs benefit profle of the test drug from preclnical studies including single dose, repeat dose toxicity and phase I clinical trial etc, justify the conduct of this study. **Innovation Vis-A-Vis Existing Therapeutic Option** The purpose of the study is to evaluate safety of the test drug (LDK378) when used in patients with ALK positive locally advanced or metastatic non small cell lung carcinoma. **Unmet Medical Need In The Country** ALK targeted therapy with LDK378 may provide impproved anticancer activity over standard first line chemotherapy in treatment naïve patients with ALK-rearranged non squamous non small cell lung carcinoma.	**NDAC/SEC Recommendations:** The committee reviewed the proposed phase III study protocol and recommended the conduct of the study. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC

6.	MK-0431A XR (Sitagliptin and Metformin HCl Extended Release, FDC tablet)	MSD	MK-0431A-XR-289	**Risk Versus Benefit To The Patients** The risk vs benefit profle of the test drug from preclnical studies including single dose, repeat dose toxicity and phase I clinical trial etc, justify the conduct of this study. **Innovation Vis-A-Vis Existing Therapeutic Option** The purpose of the study is l to evaluate the safety and efficacy of mk-0431a xr (a fixed-dose combination tablet of sitagliptin and extended-release metformin) in pediatric subjects with type 2 diabetes mellitus with inadequate glycemic control on metformin monotherapy. **Unmet Medical Need In The Country** The data from study will provide information about efficacy and safety of MK-0431A XR (Sitagliptin and Metformin HCl Extended Release, FDC tablet) in Pediatric subjects.	**NDAC/SEC Recommendation:** The committee recommends the conduct of the trial subjects to following condition 1. Inclusion of 50% govt sites. 2. The children's obesity criteria should be included with range of BMI 3. Glutamic acid de-carboxylase antibody should be negative 4. C-peptide should be more than 0.6 ng/ml and type 1 diabetes mellitus should be excluded. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC

7.	Hercules (Trastuzumab)	INC Research	MYL-Her3001	**Risk Versus Benefit To The Patients** The risk vs benefits profile of the test drug from preclinical repeated dose toxicity studies and phase I pharmacokinetics, Phase III bioequivalence study justify the conduct of the study. **Innovation Vis-A-Vis Existing Therapeutic Option** The study drug is biosimilars of Trastuzumab which is the existing therapeutic option for metastatic HER2 positive breast cancer patients. **Unmet Medical Need In The Country** Multisource availability of Trastuzumab may be beneficial to Indian subjects.	**NDAC/SEC Recommendation:** . The committee reviewed the proposed phase III study protocol and recommended the conduct of the study. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC

8.	Dasatinib	BMS	CA180226	**Risk Versus Benefit To The Patients** The risk vs benefit profile of the test drug from preclinical pharmacology, single dose and repeat dose toxicity studies and phase I clinical trials etc justify the conduct of this study. **Innovation Vis-A-Vis Existing Therapeutic Option** The purpose of the study is to estimate the complete cytogenic response (CCyR) rate to Dasatinib therapy in children and adolescent with newly diagnosed CP-CML in first chronic Phase with no prior therapy (except hydroxyurea) and to estimate the major cytogenic response rate (MCyR) to Dasatinib therapy in subjects to prove resistant to or intolerant to Imatinib **Unmet Medical Need In The Country** The test drug may potentially provide an alternate choice for children and adolescents with newly diagnosed CP-CML or progressive Ph+ leukemia which has become resistant to imatinib.	**NDAC/SEC Recommendation:** The committee recommended all the three protocol amendments. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC

9.	BIBW2992(Afatinib)	Boehringer	1200.98	**Risk Versus Benefit To The Patients** The risk vs. benefit profile of the test drug from preclinical pharmacology, single dose and repeat dose toxicity studies and phase I, II and III clinical trials with afatinib alone or in combination with other drugs justify the conduct of this study. **Innovation Vis-A-Vis Existing Therapeutic Option** The purpose of the study is to investigate the efficacy and safety of Afatinib alone and in combination with weekly paclitaxel or vinorelbine upon progression with afatinib monotherapy. **Unmet Medical Need In The Country** The test drug may potentially provide an alternate choice for patients who relapse after receiving taxanes and both registered targeted agents (Trastuzumab and lapatinib).	**NDAC/SEC Recommendation:** The committee recommended the protocol amendment. The committee opined that the subjects who are on going in the study and clinically benefiting should be continued in the trial. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC

10.	Trastuzumab emtansine	Roche	TDM4997G/BO25734	**Risk Versus Benefit To The Patients** The Risk vs Benefit profile of the test drug from preclinical pharmacology, single dose and repeat dose toxicity studies and phase I, II and III clinical trials justify the conduct of this study. **Innovation Vis-A-Vis Existing Therapeutic Option** The test drug is a novel antibody drug conjugate /targeted drug delivery system for the treatment of Her2+ve metastatic breast cancer. The purpose of the study is to to evaluate the efficacy of Trastuzumab emtansine compared with treatment of physician's choice in patients with her2-positive metastatic breast cancer who have received at least two prior regimens of her2-directed therapy.\ **Unmet Medical Need In The Country** The test drug may potentially provide an alternate choice for HER2 positive patients' who progress on two regimens of HER2-directed therapy, including Trastuzumab and Lapatinib.	**NDAC/SEC Recommendation:** The committee recommended the protocol amendments (B to F) ie the inclusion, exclusion criteria, criteria for women of child bearing age and recommends for the same. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC

11.	Axitinib	Pfizer	A4061051	**Risk Versus Benefit To The Patients** The risk vs benefit profile of the test drug from preclinical pharmacology, single dose and repeat dose toxicity studies and phase I and II clinical trials justify the conduct of this study. **Innovation Vis-A-Vis Existing Therapeutic Option** The purpose of the study is to compare the progression free survival (PFS) of treatment naïve patient with mRCC receiving Axitinib vs Sorafenib **Unmet Medical Need In The Country** The test drug may potentially provide an alternate choice for patients with metastatic renal cell carcinoma.	**NDAC/SEC Recommendation:** The committee recommended the protocol amendments. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC

12.	TenofovirDisaproxilFumarate	Klinera	GS-US174-0149T	**<u>Assessment of Risk vs. Benefit to the Assessment of Risk vs. Benefit to the patients:</u>** The risk vs benefit profile of the test drug from mutagenicity, and reproductive toxicity and carcinogenicity studies and phase I, II and III clinical trials justify the conduct of this study. **<u>Innovation vis-à-vis Existing Therapeutic Option:</u>** The purpose of the study is to evaluate the efficacy and safety of Tenofovir Disoproxil Fumarate (TDF) in combination with peginterferon α-2a (Pegasys) versus Standard of care Tenofovir Disoproxil Fumarate (TDF) monotherapy or peginterferon α-2a monotherapy for 48 Weeks in Non-Cirrhotic Subjects with HBeAg-Positive or HBeAg-Negative Chronic Hepatitis B (CHB). **<u>Unmet Medical Need in the country:</u>** The test drug combination may potentially provide alternative treatment option for Chronic Hepatitis B.	**NDAC/SEC Recommendation:** The committee recommended the permission for the protocol amendment. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC

13.	ART-123 (Thrombomodulin Alfa)	Asiatic	3-001	**<u>Assessment of Risk vs. Benefit to the patients:</u>** The risk vs benefit profile of the test drug from preclinical pharmacology, single dose and repeat dose toxicity studies and Phase I and II clinical trials justify the conduct of this study. **<u>Innovation vis-à-vis Existing Therapeutic Option:</u>** The purpose of the study is to assess the safety and efficacy of ART-123 in subjects with Severe Sepsis and Coagulopathy. **<u>Unmet Medical Need in the country:</u>** No approved drug for the treatment of severe sepsis and coagulopathy. The test drug may potentially provide treatment for severe sepsis and coagulopathy.	**NDAC/SEC Recommendation:** The committee recommended the approval for the proposed amendment version 2. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC.

14.	Rifapentine, Isoniazid **(*)**	BJ Med, YRG, NARI	A5279	**Risk Versus Benefit To The Patients** In light of the fact that the test drugs are already approved for treatment of tuberculosis, the risk vs benefit profiles of the drugs justify the conduct of the study. **Innovation Vis-A-Vis Existing Therapeutic Option** The purpose of the study is to assess ultra-short-course rifapentine/isoniazid for the prevention of active tuberculosis in HIV-infected individuals with latent tuberculosis infection. **Unmet Medical Need In The Country** The study will potentially provide new regimen for treatment of latent tuberculosis infection in HIV-infected individuals.	**NDAC/SEC Recommendation dated 11.02.2012:-** Proposed study is to compare 4 weeks daily rifapentine/isoniazid regimen to a standard 9 months daily isoniazid for prevention of TB in HIV infected patients without active TB. Committee desires sound justification for the proposed regimen of Rifapentine/isoniazid in view of recently published articles in NEJM showing efficacy of weekly rifapentine/NH 900mg doses equivalent to 9 months efficacy of daily dose of INH. Compliance issue and post-trial cost implementation should also be submitted. **NDAC/SEC Recommendation dated 28.092012:-** Data submitted is not adequate to address the following issues:- i) The possibility of increased serious adverse effects of daily dose of Rifapentine vs. once weekly use. ii) PK study has shown that peak conc. of rifapentine is associated with better efficacy than increased AUC in daily dose schedule. This also raises doubt about the efficacy of daily dose. Hence committee did not recommend for giving permission to conduct the proposed study. **Technical Committee Recommendation :** The committee opined that the applicant should make a presentation on the proposal in the presence of HIV and TB experts in the next meeting.

15.	AMG 145	Amgen Technology	20110118	**<u>Assessment of Risk vs. Benefit to the patients:</u>** The risk vs benefit profile of the IMP from preclinical pharmacology, single dose and repeat dose toxicity studies and phase I and II clinical trials justify the conduct of this study. **<u>Innovation vis-à-vis Existing Therapeutic Option:</u>** The purpose of the study is to assess the impact of additional LDL-Cholesterol reduction on major CV events when study drug is used in combination with statin therapy in patients with clinically evident CV disease. **<u>Unmet Medical Need in the country:</u>** The test drug may potentially provide alternative treatment option for cardiovascular disease.	**NDAC/SEC Recommendation:** The firm presented the protocol amendment version 04. After detail deliberation the committee opined that the protocol amendment is acceptable. However the committee did not recommend the increase in age limit from 80 yrs to 85 yrs. Accordingly the revised protocol shall be submitted by the firm to CDSCO for approval. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC.

16.	GZGD03109	Siro Clinpharm	Genz-112638, Eliglustat Tartrate	**Risk versus benefit to the patients-** The risk vs benefit profile of the test drug from preclinical single dose and repeat dose toxicity, genotoxicity, reproductive toxicity and carcinogenicity studies and phase I, II and III clinical trials justify the conduct of this study. **Innovation vis-a-vis existing therapeutic option-** The Purpose of the study is to evaluate the efficacy, safety and pharmacokinetics of Once daily versus twice daily treatment with Genz-112638 (eliglustat) in Gaucher disease patient Type 1 who have Demonstrated Clinical Stability on twice daily dose of Genz-112638. **Unmet medical need in the country-** The test drug may potentially provide treatment option for Gaucher disease	**NDAC/SEC Recommendation:** The committee reviewed the data in respective of the interim efficacy and safety data along with DSMB report. The committee recommended for approval of protocol amendment 4 which is for extension of trial from 42 wks to 60 wks and also the committee recommended for amendment no 5. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC.

17.	LY2963016	Eli Lilly	I4L-MC-ABEL	**Risk Vs Benefits to the patients:** The Risk Vs Benefits profile of the test drug from pre clinical repeated dose toxicity studies and phase I, III clinical study justify the conduct of study **Innovation vis a vis existing therapeutic option:** The purpose of the study is comparison of long acting basal insulin analogue LY2963016 to Lantus in combination with mealtime insulin Lispro in adult patients with type I diabetes mellitus. **Unmet Medical Need in the Country:** Availability of Long acting basal insulin analogue from multisource may potentially benefits Indian patients.	**NDAC/SEC Recommendation:** After detailed deliberation NDAC/SEC recommended approval of the study as per submitted protocol. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC.
18.	LY2963016	Eli Lilly	I4L-MC-ABEG	**Risk Vs Benefits to the patients:** The Risk Vs Benefits profile of the test drug from pre clinical repeated dose toxicity studies and phase I, III clinical study justify the conduct of study **Innovation vis a vis existing therapeutic option:** The purpose of the study is comparison of long acting basal insulin analogue LY2963016 to Lantus in adult patients with type 2 diabetes mellitus when used in combination with oral anti-hyperglycaemic medications. **Unmet Medical Need in the Country:** Availability of Long acting basal insulin analogue from multisource may potentially benefits Indian patients.	**NDAC/SEC Recommendation:** After detailed deliberation NDAC/SEC recommended approval of the study as per submitted protocol. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC.

19.	QPI-1007	Manipal	QRK-207	**Risk Vs Benefits to the patients:** The Risk Vs Benefits profile of the test drug from pre clinical single, repeated dose toxicity studies, genotoxicity and phase I clinical study justify the conduct of study **Innovation vis a vis existing therapeutic option:** The purpose of the study is to assess the safety, efficacy and tolerability of QPI-1007 administration as three bimonthly intravitreal injection on visual acuity in subjects with recent onset NAION . **Unmet Medical Need in the Country:** NAION is an unmet medical need. There are no therapeutic options currently approved for the disease.	**NDAC/SEC Recommendation:** The committee during its deliberation on 17-06-2014 recommend that only severe cases of NAION should be included in the study ie the subject with visual acuity of finger counting close to face to 6/36, field defects on perimetry, retinal fiber thinning on OCT machine and FFA changes. Before phase III is initiated the phase II trial data from all the centers should be submitted to CDSCO for further review by the experts. The committee opined that all the investigator must have MS degree or alternate such as DNB. **Technical Committee Recommendation :** Recommended for approval as per recommendations of NDAC/SEC dated 17-06-2014.

Annexure-II

A. List of 16 cases of clinical trial proposals other than GCT/NCE along with evaluations and recommendations of the Technical Committee in 18th Meeting.

Sl No	Drug	Applicant Name	Protocol No	Recommendation
1.	Bevacizumab	M/s Reliance Life Sciences Pvt Ltd		The Committee has recommended to conduct the clinical trial study as per SEC recommendation.
2.	Brinzolamide + Timolol	M/s Ajanta Pharma limited		The Committee has recommended to conduct the clinical trial study as per SEC recommendation
3.	Brinzolamide + Brimonidine +Tartrate	M/s Ajanta Pharma limited		The Committee has recommended to conduct the clinical trial study as per SEC recommendation subject to condition that with all requirements of stability studies as per appendix-IX of Schedule Y of Drugs and Cosmetics Rule, 1945.
4.	Rebamipide pthalmic suspension 2%w/v	Ajanta Pharma Ltd.	APL/CT/13/02	The Committee has recommended to conduct the clinical trial study as per SEC recommendation
5.	Poly Lactide-co-Glycolic Acid (PLGA)biodegradable, synthetic carrier membrane / LECPLGA50:50 P1	M/s LV Prasad Eye Institute	LVPEI-2012-11	The Committee has recommended that one more level of animal study in rabbit has to be done replicative of human study with the same membrane and submit the report to the committee.

6.	Influenza vaccine (Human, live attenuated) Freeze dried (Type A & B) (Seasonal, Trivalent) (SII LAIV)	M/s Serum Institute of India Ltd., Pune-411028.	SIV 04	The Committee has recommended to conduct the clinical trial study as per SEC recommendation
7.	Mometasone furoate 200mcg/400mcg	Cadila Healthcare Limited,		The Committee has recommended to conduct the clinical trial study as per SEC recommendation.
8.	Brinzolamide 1% ophthalmic suspension	Cipla Ltd.	MA-CT13-001	The Committee has recommended to conduct the clinical trial study as per SEC recommendation.
9.	Hydroxychloroquine sulphate 100mg	Ipca Laboratories		The Committee has recommended to conduct the clinical trial study as per SEC recommendation.
10.	Lacosamide Injection 10mg/ml	Torrent Pharmaceuticals Ltd.		The Committee has recommended to conduct the clinical trial study as per SEC recommendation
11.	Diclofenac Diethylamine Non Aqueous Topical Solution (4.64%)	Troikka Pharmaceuticals		The Committee has recommended to conduct the clinical trial study as per SEC recommendation.

12.	Tafluprost 0.0015% + Timolol 0.5% eye drops	M/s Ajanta Pharma Ltd		The Committee has recommended to conduct the clinical trial study as per SEC recommendation
13.	Seroflo® MDI (Salmeterol/ Fluticasone(25µg/250µg)	M/s Cipla Ltd.,		The Committee has recommended to conduct the clinical trial study as per SEC recommendation subject to condition that 50% of the sites should be Govt. Hospital and sites should be geographically distributed across the country.
14.	Leuprolide acetate for depot suspension 7.5 mg	M/s Sun Pharmaceutical Industries Ltd	CLR_13_14 ,	The Committee has recommended to conduct the clinical trial study as per SEC recommendation.
15.	Paclitaxel injection concentrate for nanodispersion 10 % w/w (PICN)	M/s Sun Pharma Advanced Research Company Limited,	CLR_12-_04	The Committee has recommended to conduct the clinical trial study as per SEC recommendation
16.	Garenxoacin Mesylate 200mg tablets	M/s. Glenmark Generics Ltd.	GPL/Garenoxacin/1213; version No. 3.0	The Committee has recommended to conduct the clinical trial study as per SEC recommendation