MINUTES OF 16th MEETING OF THE TECHNICAL COMMITTEE HELD ON 10.07.2014 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. Rajit Roy Chaudhury, National Professor of Pharmacology, Y-85, Hauzkhas, New Delhi-16	Member
3.	Dr.Nandini Kumar, Former Dy. Director (Sr. Grade) National Institute of Epidemiology, ICMR, Delhi	Member
4.	Dr. Ashok Kumar Das, Director-Professor of Medicine & Medical Superintendent, JIPMER, Puducherry.	Member
5.	Dr. S.N. Gaur, Prof. & Head, Dept. of Respiratory Medicine, V.P. Chest Institute, New Delhi	Member
6.	Dr. P.K. Dalal, HOD, Dept. of Psychiatry, KGMU Medical College, Lucknow.	Member
7.	Dr. Kamalakar Tripathi Prof. Dept of Medicine, Sciences, BHU, Varanasi	Member
8.	Dr. Rajutitus Chacko Prof & Head, Dept. of Medical Oncology CMC Vellore	Member
9.	Dr. Yash Paul Prof & Head Dept of Cardiology PGIMER, Chandigarh	Member

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)

The Chairman welcome the members and stated that this Committee is an important Committee not only for evaluation of clinical trial proposals but the Committee can also recommend measures for strengthening the functioning of CDSCO in respect of its various activities including approval of new drugs, clinical trials, imports etc.

Before taking up evaluation of the clinical trial proposals as per the agenda, the Committee deliberated various issues for strengthing of CDSCO and recommended as under:

1. The Technical Committee should be expanded to have at least 1 member from each of the various therapeutic areas.
2. The Committee should invite the industry representative/stakeholders within 3 months to consider their suggestions/issues to improve the regulatory process in respect of approval of clinical trials, new drugs etc. as well as improvement in overall drug regulatory activities in the country.
3. In certain situations where the matters related to CDSCO activities needs to be addressed urgently, the Chairman can take decision in his wisdom and the decision may be placed before the Committee in its next meeting for consideration.
4. The Zonal offices of CDSCO should submit report regularly to CDSCO (HQ) giving details of the activities performed by these offices. CDSCO(HQ) should assess the report and resolve the unaddressed issues.
5. Involvement of CDSCO in granting various certificate/ NOCs for export of drugs to five countries viz. USA,UK, Canada, Japan & Australia which have well developed drug regulatory system may not be required as these countries assess the suitability of import of drugs from India before they allow import of such drugs into their country.
6. In order to address pending issues raised by the applicants for grant of various approval/ licenses granted by CDSCO, the office should create a Grievance Cell which will address such issues regularly on daily basis.
7. As regards to issues of quality of generic drugs, the Committee recommended that consideration should be given to make Bioequivalent study as a requirement for grant of manufacturing license to manufacture such drugs in the country.
8. The generic drug manufacturer should have R &D facility either of their own or use such facilities of other companies for product development, process validation, analytical testing etc. before such drugs are released for marketing.

The Chairman stressed the need of regular follow up to take necessary actions in respect of above recommendations for strengthening the drug regulatory system in the country.

The Committee then deliberated the proposal of clinical trials as under:

1. **Evaluation details with respect to risk *vs* benefit, innovation vs existing therapies & unmet medical need in the country for 157 Global clinical trial proposals which were earlier considered by the Technical Committee as per the order of Hon'ble Supreme Court.**

Committee was appraised that the Hon'ble Supreme Court of India, vide its order dated 21.04.2014 in the matter of W.P. (C) No. 33/2012 of Swasthya Adhikar Manch, Indore &Anr Vs. Ministry of Health and Family Welfare &Ors. with WP(C) No. 779/2012 regarding clinical trials, has issued following observations/ directions :

- Sanjay Parikh, learned counsel for the petitioners in Writ Petition (Civil) No. 33 of 2012, with regard to non-compliance of our previous orders dated 21.10.2013 and 10.03.2014, Mr. Siddharth Luthra, learned Additional Solicitor General, prays for time to seeks instructions and file comprehensive affidavit on behalf of the Union of India through competent authority. Comprehensive affidavit shall be filed by the Union of India within eight weeks.
- From the additional affidavit dated 10.03.2014 (filed on 17.04.2014) filed by Mr. Lov Verma, Secretary, Ministry of Health and Family Welfare, Government of India, it is not clear whether the Technical Committee and the Apex Technical Committee have evaluated Global Clinical Trials (GCTs)/New Clinical Trials (NCEs) having regard to three parameters, namely, (i) assessment of risk versus benefit to the patients, (ii) innovation vis-à-vis existing therapeutic option and (iii) unmet medical need in the country as indicated in the order dated 21.10.2013.
- To obviate any controversy in future in this regard, we direct that henceforth in the Format seeking information from the applicants, three specific columns regarding the above parameters shall be inserted for the purpose of New Clinical Entities/Global Clinical Trials.

As per the order of Hon'ble Supreme Court the three parameters namely , (i) assessment of risk versus benefit to the patients, (ii) innovation vis-a-vis existing therapeutic option and (iii) unmet medical need in the country have already been inserted in the format seeking information from the applicant.

With regard to evaluation of 157 cases of Global Clinical Trials, the Committee noted that these cases of the clinical trials were considered by the Committee in the meetings on 28.11.2013, and 15.01.2014, 16.01.2014 in terms of i) assessment of risk versus benefit to the patients, (ii) innovation vis-à-vis existing therapeutic option and (iii) unmet medical need in the country.

The details of the status of the total 157 Global clinical trial proposals at the time of their evaluation were as under:

S. No	Status	No. of Trials
01	Ongoing	65
02	Completed	39
03	Not initiated	13
04	Withdrawn by the respective applicant without any patient enrolment	25
05	Suspended by the respective applicant prematurely	15
06	**Total**	**157**

The Committee considered the details of the data relating to the safety and efficacy of the study drugs, details of protocols containing the objective of the of studies, inclusion and exclusion criteria for enrollment of patient, treatment, assessment of safety and efficacy parameters etc. keeping in view the following aspects:

(a) risk versus benefits to the subjects,

(b) innovation vis-à-vis existing therapy and

(c) unmet need to the Indian population

After considering these details, the Technical Committee recommended the continuance of the 64 out of 65 ongoing trials as they meet all the relevant aspects of safety and efficacy.

In respect of one case relating to clinical trial in patients with advanced HIV disease entitled “Reducing early mortality and early morbidity by empiric tuberculosis treatment regimen”, the Committee had opined that prophylactic anti TB treatment is acceptable. However, empiric treatment with anti-TB drugs in HIV patients may not be justified given the risk vs. benefit to the patients. Therefore, the Committee recommended that the report of the Data Safety Monitoring Board (DSMB) as constituted by the Sponsor for this trial shall be submitted to the Committee for evaluation. Till such time the DSMB report is evaluated by the Committee, there should be no further enrolment of any new subject in this trial. However, the trial should continue with the subjects already recruited in the study.

In respect of the 13 cases which have not yet been initiated by the respective applicants, one case refers to the same study relating to clinical trial in patients with advanced HIV disease entitled “Reducing early mortality and early morbidity by empiric tuberculosis treatment regimen”. The Committee recommended that the other 12 cases meet all the requirements of safety and efficacy particularly in terms of assessment of risk versus benefit to the patients, innovation vis-à-vis existing therapeutic option and unmet medical need in the country.

The remaining cases, 39 were completed, 25 cases were withdrawn by the respective applicants without any patient enrolment and 15 cases were suspended by the applicants. The Technical Committee did not recommend any specific actions in these cases.

The Apex Committee in its meeting considered and approved the recommendations of the Committee, in its meeting held on 06.12.2013 and 24.01.2014.

However, in respect of the 25 withdrawn cases and 15 suspended cases, the Apex Committee after detailed deliberation recommended that the respective applicants of these cases should be informed by DCGI that the permissions granted to conduct these clinical trials should be treated as withdrawn and these studies should not be initiated/re-started without prior permission from CDSCO.

However, in light of the order of Hon’ble Supreme Court dated 21.04.2014 as mentioned above, the Committee considered mentioning the evaluation details with respect to i) assessment of risk versus benefit to the patients, (ii) innovation vis-à-vis existing therapeutic option and (iii) unmet medical need in the country for the GCTs which were either ongoing or not initiated at the time of their evaluation by the Committee.

Accordingly, the Committee mentioned the evaluation details with respect to the above three parameters for the GCTs which were either ongoing or not initiated at the time of their evaluation by the Committee. Details of the same is enclosed as **Annexure-I.**

2. <u>Fresh proposals of Clinical Trials recommended by NDAC / IND and earlier proposals where opinion of pharmacologist / expert was needed.</u>

The Committee deliberated the 43 cases of fresh proposals of clinical trials. These cases have already been recommended by the NDACs.

Out of these 43 cases, 18 cases were proposals of global clinical trials/ clinical trials of NCEs (11 cases of fresh proposal and 07 cases of re-deliberation in which there was no pharmacologist in the NDAC meetings), remaining 25 cases were related to clinical trials for approval of New Drugs including fixed dose combination, subsequent new drugs and biologicals (24 cases of fresh proposal and 01 cases of re-deliberation of New Drugs in which there was no pharmacologist in the NDAC meetings).

The Committee evaluated these cases one by one and made recommendations. The Committee evaluated the 18 cases of global clinical trials/ clinical trials of NCEs considering all aspect of safety efficacy especially in terms of the three parameter viz. risk versus benefit to the patients, innovation *vis-a-vis* existing therapeutic option and unmet medical need in the country.

The recommendation of the Committee in respect of these 18 cases is enclosed as **Annexure-II.**

The recommendation of the Committee in respect of other 25 cases is enclosed as **Annexure-III.**

Out of total 43 fresh cases, the Technical Committee recommended for approval of 38 cases as per recommendation of the NDAC. In one case at Sr. No 7 in Annexure-II, the Committee recommended for approval subject to condition that if the subjects in the placebo arm are found refractory to standard of care after 3 months they should be withdrawn from the study. In 4 of the remaining 5 cases at Sr. No 5 & 6 in Annexure-II and at Sr. No 5 & 13 in Annexure-III the committee recommended to obtain opinion of the pharmacologist/ specialist. Based on positive opinion the proposal can be approved as per the recommendation of the NDAC without referring to Technical Committee. In one case at Sr. No 23 in Annexure-III, the Committee recommended that the clinical trial protocol etc. should be reviewed and recommended by the SEC (NDAC).

The Meeting ended with vote of thanks to Chair.

Annexure-I

Ongoing clinical trials

Sr No	Drug	Names of the Applicant	Protocol No	Evaluations in respect of 1. risk versus benefit to the patients 2. innovation vis-a-vis existing therapeutic option 3. unmet medical need in the country
1	**Daclizumab high yield process (DAC HYP)**	**M/s Biogen Idec**	**205MS203**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinical pharmacology, safety pharmacology and toxicology studies and clinical studies including Phase I , II clinical trials justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** Daclizumab is a monoclonal antibody (IgG1 isotype) which binds to CD25, a receptor on the surface of lymphocytes for interleukin 2, a chemical messenger in the immune system. This prevents activation and growth of lymphocytes which are involved in the immune attack in multiple sclerosis (MS). The purpose of this clinical study is to assess the safety of extended treatment with daclizumab high yield process monotherapy in subjects with relapsing remitting multiple sclerosis (RRMS) and to assess the long term effects of daclizumab high yield process treatment on patients. **Unmet medical need in the country-** The study may provide a better formulation option for the treatment of multiple sclerosis.
2	**Xprenor** **(Buprenorphine oral lyophilisate)**	**Clingene**	**MD2012/01XP**	**Assessment of Risk versus Benefit to the Patients:** The risk vs benefit of the test drug in various animal toxicity studies which include single and repeated dose studies and clinical phase I studies, justify the conduct of the study.

				Innovation vis-à-vis Existing Therapeutic Option The test drug is a novel dosage form (oral lyophilisate) of buprenorphine The purpose of the study is to establish the safety and efficacy of the test drug with that of a comparator product, in opioid dependent patients. **Unmet Medical Need in the Country (if any)-** The study may provide a novel oral dosage form of buprenorphine for opioid dependent patients.
3	**Asenapine**	**Parexel**	**P06384**	**Assessment of Risk- vs.- Benefit to the Patients:** The risk vs benefit of the test drug from various animal pharmacology and toxicity studies including single dose, repeat dose, carcinogenicity, reproductive and developmental toxicity and clinical phase I,II and III studies justify the conduct of this study. **Innovation vis-à-vis Existing Therapeutic Option-** The purpose of the study is to determine the efficacy and safety of the test drug compared with placebo in preventing the recurrence of any mood episodes. **Unmet Medical Need in the Country (if any)-** The data generated from this study may provide long term use of the test drug for the prevention of the recurrent mood episode associated with bipolar I disorder.
4	**PF-03049423**	**M/s Pfizer**	**A9541004**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinical pharmacology and safety pharmacology studies and toxicology in animals and clinical studies including Phase I, II clinical studies justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The objective of the study is to assess the efficacy of PF-03049423and evaluate the safety and tolerability of PF-

				03049423 relative to placebo in subjects with ischemic stroke. Unmet medical need in the country- PF-03049423 is a high affinity, selective, competitive and reversible phosphodiestrase 5 inhibitor. This study may provide a better treatment option for stroke to the Indian patients.
5	**RO4917838**	**Quintiles**	**NN25307**	**Assessment of Risk versus Benefit to the Patients-** The risk vs benefit of the test drug in various safety pharmacology and toxicology studies which include single and repeat dose, reproductive developmental studies, genotoxicity studies and Clinical Phase I and II studies justify the conduct of the study. **Innovation vis-à-vis Existing Therapeutic Option-** The purpose of the study to evaluate the efficacy and safety of the test drug in patients with sub-optimally controlled symptoms of schizophrenia treated with antipsychotics followed by a 40-week double-blind, parallel-group, placebo-controlled treatment period. **Unmet Medical Need in the Country (if any) –** The test drug along with current antipsychotic regimens may potentially provide an alternate therapy to achieve better control of schizophrenia**.**
6	**R04917838**	**Quintiles**	**NN25310**	**Assessment of Risk versus Benefit to the Patients-** The risk vs benefit of the test drug in various safety pharmacology and toxicology studies which include single and repeat dose studies in rats, mouse and monkeys and Clinical Phase I and II studies justify the conduct of the study. **Innovation vis-à-vis Existing Therapeutic Option-** The purpose of the study is to evaluate the safety and efficacy of the test drug in stable patients with persistent,

				predominant negative symptoms of schizophrenia. **Unmet Medical Need in the Country (if any) –** Present antipsychotic medications have minimal effects on negative symptoms and cognitive function in patients with Schizophrenia. The test drug may potentially provide an alternative /adjunctive therapy for schizophrenia.
7	**Cariprazine**	**Quintiles**	**RGH-MD-06**	**Assessment of Risk versus Benefit to the Patients** The risk vs benefit of the test drug in various safety pharmacology and toxicology studies which include single dose and repeated dose toxicity studies in rats, mice, dogs, rabbits and phase I,II clinical trials justify the conduct of the study. **Innovation vis-à-vis Existing Therapeutic Option** The purpose of the study is to evaluate the safety and efficacy of the test drug in the prevention of symptoms in patients with schizophrenia. **Unmet Medical Need in the Country (if any)-** A test drug may potentially provide an improved /alternative antipsychotic therapy.
8	**Recombinant Human Coagulation Factor IX fusion protein (rFIXFc)**	**Biogen Idec**	**9HB01EXT**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinical pharmacology, toxicity and clinical studies including Phase I, II, III studies justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The objective of the study is to evaluate the long term safety and efficacy of rFIXFc in Haemophilia-B male patients who have completed the preceding studies of recombinant human coagulation factor IX fusion protein.

				Unmet medical need in the country- Recombinant human coagulation factor IX fusion protein is a fully recombinant coagulation Factor IX protein consisting of the human coagulation Factor IX sequence linked to human IgG_1. It is indicated for control and prevention of bleeding episodes, perioperative management, and routine prophylaxis to prevent or reduce the frequency of bleeding episodes. The test drug may provide an alternate treatment option for Hemophilia B patients.
9	**Recombinant Human Coagulation Factor VIII fusion protein (rFVIIIFc)**	**Biogen Idec**	**8HA01EXT**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinical pharmacology, pharmacokinetic and toxicity studies and clinical studies including Phase I/IIa and IIa/III studies justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The objective of the study is to evaluate the long term safety and efficacy of recombinant human coagulation factor viii fusion protein in the prevention and treatment of bleeding episodes in Haemophilia-A patients. **Unmet medical need in the country-** Haemophilia-A, treatment focuses on replacement of factor VIII, the test drug i.e. recombinant human coagulation factor viii fusion protein is designed to provide longer circulating $t_{1/2}$ than currently available factor VIII products and may provide an alternative treatment option for Haemophilia-A patients.
10	**VGX-3100 (DNA vaccine for cervical cancer)**	**M/s Max Neeman**	**HPV-003**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in the pre-clinical safety, toxicology, and bio-distribution data generated for this candidate vaccine (VGX-3100) which includes plasmids for both human papiloma viruses HPV-16 and HPV-18 and Phase I clinical studies justify the conduct of this study.

				Innovation *vis-a-vis* existing therapeutic option- The objective of this study is to evaluate the safety and efficacy of VGX-3100 administered by IM injection in combination with EP delivered by CELLLECTRA®-5 P in adult females with biopsy proven HPV 16 or 18. **Unmet medical need in the country-** The study may potentially provide a candidate vaccine for treatment of cervical cancer.
11	**OBI-1 Factor VIII**	**M/s Max Neeman**	**OBI-1-301**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinical pharmacology studies, product metabolism, toxicity studies and clinical studies including Phase I, II etc justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The objective of the study is to evaluate the efficacy and safety of OBI-1 for the treatment of serious bleeding episodes in subjects with acquired hemophilia A with autoimmune inhibitory antibodies to human factor VIII. **Unmet medical need in the country-** **OBI-1** is a recombinant porcine coagulation factor VIII being developed for the treatment of bleeding episodes in subjects with congenital hemophilia A and acquired hemophilia with inhibitors to human factor VIII. This study may provide a treatment option for the acquired hemophilia A patients in India**.**
12	**Nilotinib**	**Novartis**	**CAMIN107E2401**	**Risk versus benefit to the patients** The risk vs benefit of the test drug in repeat dose toxicity studies in mice, rat, dogs, and cynomolgus monkey, genotoxicity study, reproductive-developmental toxicity, pre-post natal developmental study 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 efficacy, safety and tolerability of nilotinib using molecular response in the treatment of newly diagnosed Chronic Myelocytic Leukemia Cells in Chronic Phase patients. **Unmet medical need in the country** The study will provide information regarding the efficacy and safety of frontline therapy with nilotinib in patients with newly diagnosed Chronic Myelocytic Leukemia Cells in Chronic Phase
13	**Pertuzumab**	**Roche**	**MO27775**	**Risk versus benefit to the patients** The risk vs benefit of the test drug in repeated dose intravenous toxicity and reproductive study in cynomolgus monkey and phase I, Ia, Ib, II and III clinical study justify the conduct of this study **Innovation vis-a-vis existing therapeutic option** Pertuzumab is a humanized monoclonal antibody to human epidermal growth factor receptor 2 receptor, with novel mechanism of action targeting inhibition of human epidermal growth factor receptor 2 dimerization. Trastuzumab and pertuzumab monoclonal antibodies bind to distinct epitopes on the human epidermal growth factor receptor 2 receptor without competing with each other and this mechanism may be complementary and result in augmented therapeutic efficacy when given in combination. The purpose of the study is to assess the efficacy and safety of pertuzumab given in combination with trastuzumab plus an aromatase inhibitor in first line patients with human epidermal growth factor receptor 2 - positive and hormone receptor-positive advanced

				(metastatic or locally advanced) breast cancer. **Unmet medical need in the country** The combination of pertuzumab, transtuzumab and chemotherapy may significantly improve overall survival in patients with human epidermal growth factor receptor 2 positive metatstatic breast cancer, compared with Trastuzumab and chemotherapy alone.
14	**Sunitinib (tyrosine kinase inhibitor)**	**M/s Pfizer**	**A6181202**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinical pharmacology studies and product metabolism study in animals and toxicity studies in rats and monkeys, carcinogenicity, genotoxicity, and reproductive toxicity and clinical studies including Phase I, II, III and clinical pharmacokinetic and drug metabolism studies justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The purpose of the study is to confirm the safety and efficacy of the drug in subjects with unrespectable pancreatic neuroendocrine tumours. **Unmet medical need in the country-** Sunitinib is an oral, small-molecule, multi-targeted receptor tyrosine kinase (RTK) inhibitor proposed for the treatment of unresectable pancreatic neuroendocrine tumours which may provide a treatment option for the Indian patients.
15	**PF-00299804 (Dacomitinib)**	**M/s Pfizer**	**A7471009**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinical pharmacology and safety pharmacology studies, toxicity studies and clinical studies including Phase I, II studies justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The objective of the study is to demonstrate that PF-00299804 treatment is superior to erlotinib treatment with

				respect to progression free survival and further to evaluate the safety and tolerability of PF-00299804 in advanced Non-small-cell lung carcinoma patients. **Unmet medical need in the country-** This study data may provide a more advanced anticancer drug for advanced and metastatic non-small cell lung cancer patients
16	**Crizotinib**	**M/s Pfizer**	**A8081014**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinical pharmacology and safety pharmacology studies, and product metabolism in animals and toxicokinetics studies in rats, dogs, mouse, rabbit and monkeys, carcinogenicity, genotoxicity, developmental and reproductive toxicity and clinical studies including Phase I, II and clinical pharmacokinetic and drug metabolism studies etc. justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The purpose of the study is to demonstate that Crizotinib is superior to the first line chemotherapy in prolonging progression free survival in patients with advanced non-squamous Non-small-cell lung carcinoma whose tumours harbour a translocation or inversion event involving the Anaplastic lymphoma kinase gene locus. **Unmet medical need in the country-** Crizotinib is a kinase inhibitor approved by USFDA on Aug 2011 and indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK)-positive. The study may potentially provide an alternative treatment option/better option for the Indian patients.
17	**Afatinib**	**Boehringer**	**1200.125**	**Risk versus benefit to the patients** The risk vs benefit of the test drug in single and repeated dose intravenous and subcutaneous toxicity study in cynomolgus monkey and phase I, II, III clinical study

				justify the conduct of this study **Innovation vis-a-vis existing therapeutic option** Afatinib is a member of the second generation tyrosin kinase inhibitiors which binds irreversibly to the epidermal growth factor receptor family of receptors. The prolonged and irreversible inhibition of the receptor has the potential for further improvement in response to treatment over the first generation tyrosin kinase inhibitiors The purpose of the study is to assess efficacy of afatinib with erlotinib as second line treatment for patients with squamous cell carcinoma of the lung. **Unmet medical need in the country-** The study may potentially provide 2nd line options for treatment of squamous cell non-small-cell lung carcinoma.
18	**Panitumumab**	**M/s Amgen**	**20100007**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinical pharmacology and various toxicity studies, antigenicity and clinical studies including Phase I, II studies justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** Panitumumab is a fully human IgG2 antibody selectively inhibits the growth and survival of selected tumor cells expressing epidermal growth factor receptor (EGFR). The objective of this study is to evaluate the effect of Panitumumab and best supportive care (BSC) versus and best supportive care alone on overall survival in subjects with Chemo refractory Wild-type Kirsten rat sarcoma viral oncogene Metastatic Colorectal Cancer' **Unmet medical need in the country-** This study may potentially provide an additional/alternative therapy for the treatment of

				Metastatic Colorectal Cancer along with the Cetuximab and Bevacizumab.
19	**AMG-162 [Denosumab (IgG2 Monoclonal Antibody)]**	**AMGEN**	**20110113**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinical pharmacology, single dose pharmacokinetics and multiple dose toxicokinetics (TK) studies following IV or SC administration and clinical studies including Phase I, II and III. studies etc justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The purpose of the study is to facilitate the access of Denosumab for subjects with advanced cancer who have participated in a Denosumab Phase III study until Denosumab is approved and available for use and to further assess the safety of Denosumab for subjects who have participated in open label extensions of a Denosumab advanced cancer phase III study. **Unmet medical need in the country-** The study may provide long term safety data of Denosumab for the prevention of skeletal related events in patients with advanced malignancies involving bone which will be made available via this clinical trial
20	**Axitinib**	**Quintiles**	**AP311736**	**Assessment of Risk versus Benefit to the Patients-** The risk vs benefit of the test drug in various safety pharmacology and toxicology studies which include Single and repeat dose studies in mice and dogs and several Phase I,II, III clinical trials justify the conduct of the study . **Innovation vis-à-vis Existing Therapeutic Option-** Already existing therapeutic options (Nephrectomy, hormonal chemotherapeutics and radiation therapies) have failed to significantly improve clinical outcomes. The purpose of this study is to demonstrate an improvement with the test drug in disease free survival in

				patients at high risk of recurrent renal cell carcinoma. **Unmet Medical Need in the Country-** This Study may provide an alternative /effective treatment in patients at high risk of recurrent renal cell carcinoma, in addition to the existing options.
21	**Symbicort®, a fixed combination of inhaled budesonide and formoterol**	**Astrazeneca**	**D589C00027**	**Risk versus benefit to the patients** The risk vs benefit of the study drug assessed in the pre-clinical single dose, repeated dose inhalation toxicity study, embryo fetal developmental study and phase I, II, III clinical studies justify the conduct of this study. **Innovation vis-a-vis existing therapeutic option** The purpose of this trial is to evaluate whether the addition of formoterol to budesonide maintenance therapy increases the incidence of serious asthma related events compared to budesonide in patients with persistent asthma. **Unmet medical need in the country** This trial will provide data on the safety of long acting beta agonist when taken in combination with inhaled corticosteroid.
22	**QVA149** **(is fixed dose combination indacaterol and glycopyrronium bromide)**	**Novartis**	**CQVA149A2339**	**Risk versus benefit to the patients** The risk vs benefit of the test drug in repeated dose inhalation toxicity study, embryo fetal development study and phase I, II, III clinical study justify the conduct of this study. **Innovation vis-a-vis existing therapeutic option** QVA149 is fixed dose combination of long acting beta 2 agonist indacaterol approved in country and long acting muscarinic antagonist glycopyrronium bromide developed for once daily treatment of chronic obstructive pulmonary disease. The long acting beta agonist and long acting muscarinic antagonist have complimentary mechanism of

				action in improving broncho dilation in chronic obstructive pulmonary disease compared to the respective monotherapies. The purpose of study is to assess the long-term safety of once daily QVA149 for 52 weeks in Chronic Obstructive Pulmonary Disease (COPD) patients with moderate to severe airflow limitation. **Unmet medical need in the country** This fix dose combination may potentially improve broncho dilation in chronic obstructive pulmonary disease and may provide more convenient dosing as compared to taking two compounds as separate agents**.**
23	**Fluticasone Furorate/Vilanterol Inhalational powder 100/25 mcg**	**Parexel**	**HZC113782**	**Assessment of Risk versus Benefit to the Patients:** The risk-vs-benefit of the test drug from various animal toxicity studies which include single and repeated dose studies in rats, mice and dogs and clinical phase I, II studies justify the conduct of the study **Innovation vis-à-vis Existing Therapeutic Option** The purpose of the study is to prospectively evaluate the effect of the once daily ICS (Inhaled Corticosteroid) /LABA (Long Acting Beta Agonist) combination. **Unmet Medical Need in the Country (if any)-** ICS (Inhaled Corticosteroid) /LABA (Long Acting Beta Agonist) combinations are currently available require twice daily administration. A once daily administration Inhaled Corticosteroid / Long Acting Beta Agonist combination has the potential to improve patient compliance and as a result overall disease management.
24	**BIBF 1120** **(Nintedanib)**	**Boehringer**	**1199.33 (Extension Open Label Trial)**	**Risk versus benefit to the patients** The risk vs benefit of the test drug in single dose toxicity study in rat and mice, repeated dose toxicity study in rat, minipigs, cynomolgus monkey, dogs, genotoxicity study, reproductive toxicity study and phase I, II, III clinical study justify the conduct of this study.

				Innovation vis-a-vis existing therapeutic option BIBF 1120 is small molecule which inhibits Fibroblast growth factor receptor -1/3, Platelet derived growth factor receptor α and β, Vascular Endothelial Growth Factor Receptors 1-3 tyrosine kinase receptor. The anti fibrotic kinase inhibition interfere in fibrotic signally cascade which is beneficial in treatment of idiopathic pulmonary fibrosis. The purpose of this study to assess the long term safety of oral BIBF 1120 in patients with Idiopathic Pulmonary Fibrosis **Unmet medical need in the country** The study drug may provide an alternative therapeutic option in the treatment of idiopathic pulmonary fibrosis as the therapeutic options currently available are limited
25	**Tiotropium and olodaterol fix dose combination**	**Boehringer**	**1237.5**	**Risk versus benefit to the patients** The risk vs benefit of study drug in the acute and repeated dose inhalation toxicity study and phase I and II clinical studies(with the fixed dose combination of Tiotropium and olodaterol) justify the conduct of this study. **Innovation vis-a-vis existing therapeutic option** The purpose of the study is to assess the efficacy and safety of once daily treatment of orally inhaled tiotropium + olodaterol fixed dose combination compared with the individual components in patients with Chronic Obstructive Pulmonary Disease. **Unmet medical need in the country** This fixed dose combination may potentially improve airflow, convenience and patient compliance compared with tiotropium and olodaterol given alone //separately.
26	**Tiotropium and olodaterol fix**	**Boehringer**	**1237.6**	**Risk versus benefit to the patients**

	dose combination			The risk vs benefit of study drug in acute and repeated dose inhalation toxicity study and phase I and II clinical study with the fixed dose combination of Tiotropium and olodaterol justify the conduct of this study. **Innovation vis-a-vis existing therapeutic option** The purpose of the study is to assess the efficacy and safety of once daily treatment of orally inhaled tiotropium + olodaterol fixed dose combination compared with the individual components in patients with Chronic Obstructive Pulmonary Disease. **Unmet medical need in the country** The tiotropium and olodaterol fixed dose combination may improve airflow, convenience and compliance compared with the free combination of tiotropium and olodaterol
27	**BIBF 1120 (Nintendanib)**	**Boehringer**	**1199.32**	**Risk versus benefit to the patients** The risk vs benefit of study drug in single dose toxicity study in rat and mice, repeated dose toxicity study in rat, minipigs, cynomolgus monkey, dogs, genotoxicity study, reproductive toxicity study and phase I, II, III clinical study justify the conduct of this study. **Innovation vis-a-vis existing therapeutic option** BIBF 1120 is small molecule which inhibits Fibroblast growth factor receptor -1/3, Platelet derived growth factor receptor α and β, Vascular Endothelial Growth Factor Receptors 1-3 tyrosine kinase receptor. The anti fibrotic kinase inhibition interferes in fibrotic signaling cascade which is beneficial in treatment of idiopathic pulmonary fibrosis. The purpose of this study is to assess efficacy of oral BIBF 1120 in annual forced vital capacity decline in patients with Idiopathic Pulmonary Fibrosis. **Unmet medical need in the country**

				The study drug may provide an alternative therapeutic option in the treatment of idiopathic pulmonary fibrosis as the therapeutic options currently available are limited
28	**BIBF 1120 Nintendanib**	**Boehringer**	**1199.34**	**Risk versus benefit to the patients** The risk vs benefit of study drug in single dose toxicity study in rat and mice, repeated dose toxicity study in rat, minipigs, cynomolgus monkey, dogs, genotoxicity study, reproductive toxicity study and phase I, II, III clinical study justify the conduct of this study. **Innovation vis-a-vis existing therapeutic option** BIBF 1120 is a small molecule which inhibits Platelet derived growth factor receptor -1/3, Platelet derived growth factor receptor α and β, Vascular Endothelial Growth Factor Receptors 1-3 tyrosine kinase receptor. The anti fibrotic kinase inhibition interferes in fibrotic signaling cascade which is beneficial in treatment of idiopathic pulmonary fibrosis. The purpose of this study is to assess efficacy of oral BIBF 1120 in annual forced vital capacity decline in patients with Idiopathic Pulmonary Fibrosis. **Unmet medical need in the country:** The study drug may provide an alternative therapeutic option in the treatment of idiopathic pulmonary fibrosis as the therapeutic options currently available are limited
29	**Sifalimumab**	**Astra Zeneca**	**CD-IA-MEDI-545/1067/D2800L00004**	**Risk versus benefit to the patients** The risk vs benefit of the test drug in single and repeated dose intravenous and subcutaneous toxicity study in cynomolgus monkey and phase I, II, clinical study justify the conduct of this study. **Innovation vis-a-vis existing therapeutic option** Systemic lupus erythomatosus is a life threatening condition and interferon α having pivotal role in the genesis and maintenance of active Systemic lupus erythomatosus. Sifalimumab is a human immunoglobulin G1 kappa

				monoclonal antibody that neutralizes human interferon -α. The purpose of the study is to evaluate the efficacy and safety of sifalimumab in adults with systemic lupus erythematosus. **Unmet medical need in the country** The study drug may provide an alternative therapy for the treatment of Systemic lupus erythomatosus where limited options exist.
30	**PF-04171327**	**M/s Pfizer**	**A9391010**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinical pharmacology, safety pharmacology studies, pharmacokinetic and product metabolism in animals, toxicokinetic studies in animals, carcinogenicity, genotoxicity, and developmental and reproductive toxicity studies and clinical studies including Phase I and clinical pharmacokinetic and drug metabolism studies justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** PF-04171327 represents a therapeutic improvement relative to current glucocorticoids (GC). The purpose of the study is to compare efficacy and safety of PF-041713227 against different doses of prednisolone and placebo in subjects with active rheumatoid arthritis (RA) on a stable background of methotrexate. **Unmet medical need in the country-** The study drug may provide an alternate treatment option for rheumatoid arthritic patients.
31	**Alisporvir**	**Novartis**	**CDEB025A2312**	**Risk versus benefit to the patients** The risk vs benefit of the test drug in single, repeat dose toxicity studies in mice, rat and cynomolgus monkey, genotoxicity study, reproductive-developmental toxicity studies and phase I and II clinical trials justify the conduct of this study

				Innovation vis-a-vis existing therapeutic option Alisporvir is a cyclophilin inhibitor with a new mechanism of action involving interaction at the host viral interface. The proposed study is a follow up study on the patients from the CDEBO25A2211 protocol who achieved sustained virological response 24 to assess the durability of sustained viriologic response. For new therapies the pattern of relapse following undetectable viremia at the end of treatment is unknown and needs long term follow up in these patients. **Unmet medical need in the country** This study will provide confirmation whether sustained virological response 24 is a reliable predictor of long term hepatitis C cure.
32	**NVC 422**	**Quintiles**	**CL1104**	**Assessment of Risk versus Benefit to the Patients** The risk vs benefit of the test drug in various animal pharmacology and toxicity studies which include single and repeated dose studies in rats, dogs, rabbits, cynomolgus monkeys and minipigs and Clinical phase I and II studies justify the conduct of the study **Innovation vis-à-vis Existing Therapeutic Option** The purpose of the study is to evaluate the safety and efficacy of test drug in treatment of adenoviral keratoconjuctivitis. **Unmet Medical Need in the Country (if any)-** The test drug may potentially benefit patients with adenoviral kerato-conjunctivitis.
33	**Vildagliptin**	**Novartis**	**CLAF237A23 156**	**Risk versus benefit to the patients** The risk vs benefit of study drug in the single, repeated dose toxicity, genotoxicity, reproductive toxicity, carcinogencity studies and phase I, II, III clinical studies justify the conduct of this study.

				Innovation vis-a-vis existing therapeutic option Vildagliptin is a Dipeptidyl peptidase -4 inhibitor and highly selective substrate for Dipeptidyl peptidase -4 catalytic site with a slow reaction rate and blocks rapid degradation of Glucagon-like peptide -1 and glucose-dependent insulinotropic polypeptide. The purpose of the study is to demonstrate the superiority of combination of vildagliptin plus metformin for the risk of initial treatment failure over metformin monotherapy in treatment-naïve patients with type 2 diabetes mellitus. **Unmet medical need in the country** The study will determine whether the vildagliptin plus metformin combination regimen would result in more durable glycemic control than metformin monotherapy in treatment-naïve patients with type 2 diabetes mellitus.
34	**Mipomersen**	**Sanofi Synthelabo**	**MIPO 3801011**	**Assessment of Risk versus Benefit to the Patients-** The risk vs benefit of the test drug in various safety pharmacology and toxicology studies which include single and repeat dose study mice, monkeys and rats and Clinical phase I,II and III studies justify the conduct of the study **Innovation vis-à-vis Existing Therapeutic Option-** The purpose of the study is to determine whether mipomersen significantly reduces atherogenic lipid levels in patients with severe heterozygous familial hypercholesterolemia. **Unmet Medical Need in the Country (if any) –** Prevalence of Familial Hypercholesterolemia (FH) in India is comparable to other countries but there are certain genetic mutations associated with Familial Hypercholesterolemia found in some specific part of the country (Maharashtra, Surat, Gujarat). The study will explore the differences in efficacy parameters between

				the reference and test regimens and will help in collecting extended safety and efficacy data.
35	**Velaglucerase alfa (VPRIV®)**	**Quintiles**	**HGT-GCB-068**	**Assessment of Risk versus Benefit to the Patients-** The risk vs benefit of the test drug in various safety pharmacology and toxicology studies which include single and repeat dose, reproductive toxicity and phase I/II/III clinical studies justify the conduct of the study. **Innovation vis-à-vis Existing Therapeutic Option-** **Innovation vis-à-vis Existing Therapeutic Option-** The purpose of the study is to evaluate the efficacy and Safety of Velaglucerase alfa enzyme replacement therapy in children and adolescents with type 3 Gaucher Disease. **Unmet Medical Need in the Country (if any) –** Gaucher Disease is a rare disease and no specific treatment is available. The test drug may be alternate choice for enzyme replacement therapy in children and adolescents with Type 3 Gaucher Disease.
36	**Saxagliptin**	**BMS**	**CV181147**	**Risk versus benefit to the patients** The risk vs benefit of study drug in the pre clinical animal pharmacology,repeated dose toxicity, reproductive toxicity study, carcinogenecity and phase I,II, and III clinical studies justify the conduct of this study **Innovation vis-a-vis existing therapeutic option** The purpose of the study is to investigate the safety, tolerability, and efficacy of saxagliptin in combination with metformin Instant Release or metformin Xtended Release in pediatric patients with type 2 diabetes who have inadequate glycemic control on metformin alone. **Unmet medical need in the country** The data emerging from the study may benefit pediatric patients having type 2 diabetes. Saxagliptin in combination with metformin may provide a better

				alternative for such patients.
37	**Denosumab (AMG-162)**	**Ms/ Amgen**	**20080560**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinical pharmacology, drug metabolism and toxicology studies in animals and clinical studies including Phase I, II studies justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The objective of this study is to Evaluate New or Worsening Lens Opacifications in Subjects with Non-metastatic Prostate Cancer Receiving Denosumab for Bone Loss due to Androgen-deprivation **Unmet medical need in the country-** The study will provide additional safety data of the test drug in patients with non-metastatic prostate cancer receiving denosumab for bone loss.
38	**NT 201(Botulinum Neurotoxin Type I)**	**Kendle India**	**MRZ60201/SP/3001**	**Assessment of Risk versus Benefit to the Patients:** The risk vs benefit of the test drug from various preclinical toxicity studies including single dose, repeat dose toxicity, reproductive/ fertility toxicity studies and phase I, II.III clinical studies etc. justify the conduct of this study. **Innovation vis-à-vis Existing Therapeutic Option-** The purpose of the study is to assess the efficacy and safety of test drug in the treatment of post stroke spasticity of the upper limb. **Unmet Medical Need in the Country (if any)-** The data generated from this study may contribute to the use of test drug in the treatment of post stoke spasticity of the upper limb as new indication.

39	**INNO-206 (Doxorubicin-EMCH)**	**INC GVK Bio**	**INNO-206-P2-STS-01**	**Assessment of Risk versus Benefit to the Patients-** The risk vs benefit of the test drug in various safety pharmacology and toxicology studies which include single and repeat dose study in mice, rats and dogs and Clinical phase I study, justify the conduct of the study . **Innovation vis-à-vis Existing Therapeutic Option-** The purpose of this study is to determine the preliminary efficacy and tolerability of administration of INNO-206 compared to Doxorubicin in subjects with metastatic, locally advanced, or unresectable soft tissue sarcoma. **Unmet Medical Need in the Country (if any)-** INNO-206 is an albumin binding pro-drug of doxorubicin. It is being developed to circumvent the limitations (toxic dose related side effects) possessed by Doxorubicin (used for the treatment of haematological and solid cancers) and to improve the therapeutic potential of anthracyclines.
40	**SH T00658ID** **-Estradiol valerate (EV)/ Dienogest (DNG) (Qlaira)**	**M/s Bayer**	**BAY 86-5027/91773**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinical pharmacology, safety pharmacology and toxicity studies carcinogenicity, genotoxicity, reproductive toxicity & teratogenicity, immunotoxicity and antigenicity studies and clinical studies including Phase I, II, III studies justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The objective of the study is to investigate the contraceptive efficacy and safety of 4 phasic oral contraceptive SH TOO658ID containing Estradiol valerate (EV)/ Dienogest in 28 days regimen for 13 day cycle in healthy female subjects. **Unmet medical need in the country-**

				SH T00658ID is a combined oral contraceptive (COC) intended for use by women between the ages of 18 and 50 years requiring contraception. This study may provide an alternative oral contraceptive for women of child bearing potential.
41	**CXA-201**	**PRA**	**CXA-cUTI-10-05**	**Assessment of Risk versus Benefit to the Patients** The risk vs benefit of the test drug in various safety pharmacology and single dose and repeat dose toxicity studies and phase I, II clinical trials justify the conduct of the study **Innovation vis-à-vis Existing Therapeutic Option** The purpose of the study is to demonstrate non-inferiority of test drug versus comparator in adult subjects with complicated urinary tract infection. **Unmet Medical Need in the Country (if any)-** The study may potentially provide an alternative treatment option for the treatment of complicated urinary tract infection.
42	**AMR 101**	**PharmaNet**	**AMR-01-01-0019**	**Assessment of Risk versus Benefit to the Patients:** The risk vs benefit of the test drug from various animal toxicity studies includingsingle dose, repeat dose, genotoxicity, carcinogenicity, developmental toxicity and clinical phase I, III studies justify the conduct of this study. **Innovation vis-à-vis Existing Therapeutic Option-** The purpose of this study is to evaluate whether the triglyceride lowering test drug, combined with a statin therapy, will be superior to the satin therapy alone, when used as prevention in reducing long term clinical events in patients with mixed dyslipidemia at a high risk for cardiovascular events. **Unmet Medical Need in the Country (if any)-**

				The test drug in combination with existing statins therapy may be beneficial in the treatment of hypertriaglyceridemic patients with cardiovascular disease.
43	**Tasquinimod**	**PPD**	**10TASQ10**	**Assessment of Risk versus Benefit to the Patients-** The risk vs benefit of the test drug in various animal toxicity studies which include single and repeated dose studies in rats, mice and dogs, Clinical phase I and II studies, justify the conduct of the study **Innovation vis-à-vis Existing Therapeutic Option** The purpose of the study is to assess the safety and to confirm the effect of tasquinimod on delaying disease progression or death in metastatic castrate resistant prostate cancer. **Unmet Medical Need in the Country (if any)-** The study may provide an alternative treatment therapy for metastatic castrate resistant prostate cancer.
44	**GP2013 (Rituximab Biosimilar)**	**PPD**	**GP13-301**	**Assessment of Risk versus Benefit to the Patients:** The risk vs benefit of the test drug in various animal toxicity studies which include repeated dose studies in monkeys, and clinical study justify the conduct of the study. **Innovation vis-à-vis Existing Therapeutic Option** The purpose of the study is to demonstrate the clinical comparability of GP2013 to the innovator/comparator product **Unmet Medical Need in the Country (if any)-** Availability of biosimilar GP2013 is expected to enhance patient access and availability of sufficient supplies.
45	**ceftazidimeavibactam**	**PPDPharma** **ceftazidimeavib**	**D4280C00001 and**	**Assessment of Risk versus Benefit to the Patients:** The risk vs benefit of the test drug from various

		actam	**D4280C00005**	preclinical toxicity studies including repeat dose toxicity, reproductive, fertility toxicity, local toxicity studies and phase I, II clinical studies justify the conduct of this study. **Innovation vis-à-vis Existing Therapeutic Option-** The purpose of the study is to assess the efficacy, safety and tolerability of the test drug with metronidazole versus meropenem in the treatment of complicated intra-abdominal infections in hospitalized adults. **Unmet Medical Need in the Country (if any)-** Currently available treatment of Gram-negative infections, especially multidrug resistant strains including extended spectrum β-lactamases producers are extremely limited. The test drug may be potentially effective in the treatment of Gram negative infections or complicated intra-abdominal infections.
46	**USL255** **(Topiramate)** .	**PPD Pharma**	**P09-005**	**Assessment of Risk versus Benefit to the Patients-** In light of the fact that the test drug are approved in India, the safety and efficacy profile justify conduct of the study. **Innovation vis-à-vis Existing Therapeutic Option-** The purpose of the study is to assess the efficacy and safety of adjunctive therapy of the test drug, compared to placebo, in patients with refractory partial onset seizures with or without secondary generalized seizures. **Unmet Medical Need in the Country (if any)-** The extended release formula of the test drug may allow once daily dose, minimizes problem associated with patient compliance related to breakthrough seizures.
47	**Stavudine**	**PPD**	**WRHI001**	**Assessment of Risk versus Benefit to the Patients:** In light of the fact that the test drug is approved for the treatment of HIV, risk vs benefit of the test drug justify conduct of the study.

				Innovation vis-à-vis Existing Therapeutic Option The purpose of the study is to demonstrate the non-inferiority of stavudine plus lamivudine and efavirenz when compared with tenofovir disoproxil fumarate plus lamivudine and efavirenz in the treatment of antiretroviral-naïve patients infected with HIV-1. **Unmet Medical Need in the Country (if any)-** The study will provide information on the dosing of stavudine i.e. whether low dose drug is non-inferior to tenofovir after 2 years in terms of both viral suppression and toxicity. The study may also help reduce the cost of anti retroviral treatment.
48	**Perampanel (Oral Tablet)**	**PPD Pharmaceutical Development India** **Private Limited**	**E2007-G000-332**	**Assessment of Risk versus Benefit to the Patients:** The risk versus Benefit of the test drug in various animal pharmacology and toxicology studies including single dose and repeat dose studies in rats, dogs, mice and monkeys and Clinical phase I, II and III studies justify the conduct of the study. **Innovation vis-à-vis Existing Therapeutic Option** The purpose of the study is to demonstrate the efficacy of adjunctive perampanel therapy in primary generalized tonic-clonic seizures (PGTC) **Unmet Medical Need in the Country (if any)-** The study with the test drug may provide an alternative/ effective treatment option for primary generalized tonic-clonic seizures (PGTC)
49	**Boceprevir**	**M/s MSD**	**Boceprevir**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinicalpharmacology and toxicology in animals and clinical studies including Phase I, II, III studies justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-**

				The objective of the study is to assess the safety and efficacy of Boceprevir/ peginterferon alfa /ribavirin in chronic Hepatitis C Virus genotype I patients. **Unmet medical need in the country-** Boceprevir is a novel orally administered potent serine protease inhibitor specifically designed to inhibit the HCV NS3 protease and may potentially benefit patient with compensated liver disease, including cirrhosis, who are previously untreated or who have failed previous interferon and ribavirin therapy, including prior null responders, partial responders,and relapsers.
50	**Lapatinib**	**GSK**	**UM2010/00099/00**	**Risk versus benefit to the patients** The risk vs benefit of the test drug in reproductive developmental toxicity study, carcinogenicity, genotoxicity and phase I, II, III clinical study justify the conduct of this study. **Innovation vis-a-vis existing therapeutic option** The purpose of the study is to demonstrate efficacy, safety and superiority of lapatinib/Trastuzumab/aromatase inhibitor combination vs Trastuzumab /aromatase inhibitor in post-menopausal subjects with hormone receptor positive, human epidermal growth factor receptor 2-positive metastatic breast cancer. This study will provide understanding of role of dual human epidermal growth factor receptor 2 suppression in this population. **Unmet medical need in the country** The study will examine the efficacy of lapatinib in subjects who have received prior neoadjuvant and /or adjuvant Trastuzumab and evaluate a potential benefits in survival when dual vs single HER2 targeted therapy is administered in combination with an aromatase inhibitor.
51	**FST-100 (0.1% Dexamethasone**	**Excel life**	**FTS100-AVC-**	**Assessment of Risk versus Benefit to the Patients:**

	and 0.6 % PVP-Iodine)	**Science**	**004**	The test drug is a new formulation of dexamethasone combined with PVP-Iodine. The risk versus benefit profile of the test drug from preclinical anti- bacterial, antiviral activity and clinical studies etc. justify the conduct of the proposed study. **Innovation vis-à-vis Existing Therapeutic Option:** The purpose of the study is to evaluate the efficacy and safety of test drug in the treatment of acute adenoviral conjunctivitis. **Unmet Medical Need in the Country (if any)-** The test drug may be a better /alternate therapy for the treatment of acute adenoviral conjunctivitis.
52	**DE-109(Sirolimus Intraverial formulation**	**Excel life Science**	**32-001**	**Assessment of Risk versus Benefit to the Patients:** The risk versus benefit profile of the test drug from preclinical toxicity studies including single dose, pharmacokinetics, ocular toxicity and phase I, II clinical studies, etc., justify the conduct of the study. **Innovation vis-à-vis Existing Therapeutic Option:** The purpose of the study is to evaluate the efficacy and safety of test drug for the treatment of active, non-infectious uveitis of the posterior segment of the eye. **Unmet Medical Need in the Country (if any)-** The test drug may be a better /alternative therapeutic option for the treatment of non-infectious uveitis of the posterior segment of the eye.
53	**Valacyclovir**	**RML Hospital, New Delhi** **(Dr. Smita. N. Deshpande)**	**-**	**Assessment of Risk versus Benefit to the Patients-** In light of the fact that **t**he test drug is already approved for chronic suppressive therapy of herpes virus infections, including HSV-1, the risk vs. benefit profile of the study drug justifies the conduct of this study. **Innovation vis-à-vis Existing Therapeutic Option-**

				Valacyclovir augmentation may improve cognitive and overall function among Herpes simplex viruses -1 exposed Early Course Schizophrenia patients. **Unmet Medical Need in the Country (if any)-** Augmentation of antipsychotic treatment by valacyclovir may provide an additional/alternative treatment option for this disabling, chronic and severe disorder.
54	**Vandetanib**	**Quintiles**	**D4200C00097**	**Assessment of Risk versus Benefit to the Patients-** The risk vs benefit profile of the test drug in various safety pharmacology and toxicology studies which include single and repeat dose studies in mice, rats and dogs and Clinical Phase I, II and III studies justify the conduct of the study. **Innovation vis-à-vis Existing Therapeutic Option-** The purpose of the study is to evaluate the safety and efficacy of test drug in patients with unresectable locally advanced or metastatic thyroid carcinoma. Study with the test drug may provide additional information to prescribers of the likely range of response rates with a starting dose of 150mg/day or a starting dose of 300 mg/day. **Unmet Medical Need in the Country (if any) –** Medullay Thyroid Carcinoma (MTC) is a rare disease for which the test drug has been granted Orphan Drug Status by USFDA. In the absence of any effective treatment for patients with Medullay Thyroid Carcinoma, the study with the test drug may provide beneficial effect to such patients.
55	**Recombinant Factor IX**	**Baxter**	**251001**	**Assessment of Risk versus Benefit to the Patients-** The risk vs benefit profile of the test drug in various safety pharmacology and toxicology studies which include single and repeat dose study in mice, rats and monkeys and phase 1/3 clinical trials justify the conduct

				of the study **Innovation vis-à-vis Existing Therapeutic Option-** The purpose of this study is to further evaluate the safety, immunogenicity and hemostatic efficacy in previously treated patients with haemophilia B. **Unmet Medical Need in the Country (if any)-** The test drug may provide an alternative to the existing therapies/approaches for treating Haemophilia B.
56	**Polycap(Simvastatin (40mg)+Ramipiril(10mg)+Atenolol(100mg)+Hydrochlorothiazide(25mg)), Aspirin (75 mg), Vitamin D (Cholecalciferol) Sachet**	**Cadila Pharmaceuticals Limited**	**TIPS 3**	**Assessment of Risk versus Benefit to the Patients:-** All the drugs are approved in India. The risk vs.benefit profile of the test drug justifies the conduct of the study. **Innovation vis-à-vis Existing Therapeutic Option: -** The purpose of the study is to determine whether Polycap reduces the risk of the composite outcome of major Cardiovascular Disease (CVD), Aspirin reduces the risk of composite outcome of Cardiovascular (CV) events and cancers and Vitamin D reduces the risk of fractures. **Unmet Medical Need in the Country (if any)-** The study will provide efficacy of the test drugs in reducing Cardiovascular diseases/ events and long term safety of Polycap , Aspirin and vitamin D.
57	**Lopinavir/Ritonavir, Raltegravir**	**YRG Care**	**A5273**	**Assessment of Risk versus Benefit to the Patients-** In light of the fact that all the test drugs are approved for the treatment of HIV, risk vs. benefit profilse of the test drugs justifies conduct of the study. **Innovation vis-à-vis Existing Therapeutic Option-** Study with the test drugs may provide a newer regimen for Anti retroviral therapy (ART) without nucleosid(t)e reverse transcriptase inhibitor (NRTI's)

				The purpose of the study is to determine whether the combination of Lopinavir plus Raltegravir is associated with virologic efficacy that is non inferior to that achieved with Lopinavir plus best available nucleoside reverse transcriptase inhibitor. **Unmet Medical Need in the Country –** There are patients where nucleosid(t)e reverse transcriptase inhibitors are problematic because of their side effects and few underlying diseases. In such cases there is a need for newer regimen without nucleosid(t)e reverse transcriptase inhibitor
58	**Atazanavir (Reyataz), Efavirenz (Stocrin), Emtricitbine/Tenofovir (Truvada), Lamivudine/Zidovudine (Combivir), Lopinavir/Ritonavir (Kaletra/Aluvia), Raltegravir (Isentress), Ritonavir (Norvir), Abacavir/Lamivudine (Epzicom), Darunavir (Prezista), Elvitegravir (Stribild)**	**YRG Care**	**START 001**	**Assessment of Risk versus Benefit to the Patients-** In light of the fact that all the test drugs are approved for the treatment of HIV, risk vs. benefit profile of the test drugs justifies conduct of the study. **Innovation vis-à-vis Existing Therapeutic Option-** The purpose of this study is to determine whether immediate initiation of antiretroviral treatment (ART) is superior to deferral of antiretroviral until the CD4+ declines below 360 cells/mm^3 in terms of morbidity and mortality in HIV-1 infected persons who are antiretroviral naïve with a CD4+ count above 500 cells/mm^3. **Unmet Medical Need in the Country (if any** The study data will provide a different therapeutic regimen option for initiating early antiretroviral treatment in HIV patients. Current data available is insufficient and do not inform whether the benefits of initiating antiretroviral at CD4+ cell counts above 500 cells/mm^3 outweigh the risks..
59	**Rifampin/isoniazid/ethambutol/**	**YRG Care**	**A5274**	**Risk versus benefit to the patients, Innovation *vis-a-vis* existing therapeutic option, Unmet medical need in**

	pyrazinamide + ARTs			**the country -** Test drugs are already approved. The purpose of this study is to reduce early mortality and early morbidity by empiric tuberculosis treatment regime in HIV infected antiretroviral naïve patients. The prophylactic anti TB treatment is acceptable. However, empiric treatment with anti TB drugs in HIV patients may not be justified, given the risk vs benefits to the patients. Therefore the report of the data safety monitoring board for this trial shall be submitted to the committee for evaluation. Till such time data safety monitoring board repot is evaluated by the committee, there should be no enrollment of any subjects in this trial.
60	**AMG-785 (Romosozumab) (Anti-Sclerostin monoclonal antibody)**	**M/s Amgen**	**20070337**	**Risk versus benefit to the patients-** The risk vs benefit of the test drug in non-clinicalpharmacology and toxicology in animals and clinical studies including Phase I, II studies.justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The objective of this study is to assess the efficacy and safety of AMG 785 treatment in Postmenopausal Women with Osteoporosis **Unmet medical need in the country-** Romosozumab (AMG-785) is humanized monoclonal antibody that targets sclerostin for the treatment of osteoporosis. This study may provide an alternative treatment option in Postmenopausal Women with Osteoporosis.
61	**CF101**	**Karmic**	**CF101-204RA**	**Assessment of Risk versus Benefit to the Patients:** The risk vs benefit profile of the test drug in various animal toxicity studies which include single and repeated dose studies and Clinical phase I, II studies justify the conduct of the study

				Innovation vis-à-vis Existing Therapeutic Option CF101 is a selective adenosine-3 (A3) receptor agonist, under development for thetreatment of RA as well as other conditions The purpose of the study is to determine the efficacy of oral CF101 when administered daily as monotherapy. **Unmet Medical Need in the Country (if any)-** The study may provide an alternative therapeutic option for rheumatoid artheritis patients.
62	**RO5185426 (Vemurafenib)**	**Roche**	**MO25512**	**Risk versus benefit to the patients** The risk vs benefit profile of the test drug in single dose and repeated dose toxicity study, reproductive development toxicity study, carcinogenicity, genotoxicity and phase I, II, III clinical study justify the conduct of this study. **Innovation vis-a-vis existing therapeutic option** The purpose of the study is to assess efficacy and safety of RO5185426 in patients with metastatic melanoma. **Unmet medical need in the country** Metastatic melanoma is one of the refractory disease for which limited treatment options are available. The study may provide better /alternate treatment options for this condition.
63	**Sativex Oromucosal Spray**	**PRA**	**GWCA11.03**	**Assessment of Risk versus Benefit to the Patients-** The risk vs benefit of the test drug in various safety pharmacology and toxicology studies which include single and repeat dose toxicity studies in mice, rats, dogs and monkeys and Clinical phaseI, II and III studies justify the conduct of the study. **Innovation vis-à-vis Existing Therapeutic Option-** Majority of patients achieve inadequate pain relief with

				existing opioid based approaches. The purpose of the study is to evaluate the efficacy of test drug in relieving uncontrolled persistent pain in patients with advanced cancer. **Unmet Medical Need in the Country (if any)-** The Study may potentially provide an adjunctive therapy in advanced cancer patients for the treatment of chronic pain
64	**Rindopepimut,**	**Novotech**	**CDX110-04**	**Assessment of Risk versus Benefit to the Patients:** The risk vs benefit profile of the test drug from various preclinical toxicity studies including repeat dose toxicity, genotoxicity, carcinogenicity, reproductive and developmental **t**oxicity studies**,** phase I, II,II/III clinical studies etc., justify the conduct of this study. **Innovation vis-à-vis Existing Therapeutic Option:** The purpose of the study is to assess if the addition of the test drug to adjuvant temozolomide improves overall survival in patient with newly diagnosed resected, epidermal growth factor receptor variant III positive glioblastoma patients. **Unmet Medical Need in the Country (if any)-** The test drug in combination with ranulocyte-macrophage colony-stimulating factor and temozolomide may improve overall survival in patient with epidermal growth factor receptor variant III positive glioblastoma patients.
65	**MEDI- 567**	**M/s Kendle India Pvt Ltd.**	**CD-IA-MEDI-546-1013**	**Risk versus benefit to the patients-** The risk vs benefit profile of the test drug from preclinical studies including single dose, repeat dosetoxicity and phase I, II clinical trials etc, justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The test drug MEDI-546 is a human IgG1k MAb directed against Type I IFNARI. Type I IFNs have been implicated

				in the pathogenesis of autoimmune and inflammatory disease such as systemic lupus erythomatous. The test drug may potentially benefit patients with autoimmune disease and similar disease such as systemic lupus erythomatous. **Unmet medical need in the country-** The test drug may potentially provide an alternative treatment option for those subjects who have had an inadequate response to steroids, anti-malarial, or slow acting immuno- suppressants.

Not Initiated Cases

Sr No	Drug	Names of the Applicant	Protocol No	Evaluations in respect of 1. risk versus benefit to the patients 2. innovation vis-a-vis existing therapeutic option 3. unmet medical need in the country
1	**Kendrion Factor VIII conc.(EMOCLOT)**	**M/s Max Neeman**	**KB053**	**Risk versus benefit to the patients-** In light of the fact that this product is already approved for replacement of the factor VIII in severe to moderate Haemophilia, the risk vs benefit profile of the drug justifies the conduct of this phase III study. **Innovation *vis-a-vis* existing therapeutic options:** The purpose of the study is to obtain data that can be used to evaluate the treatment of severe hemophilia A(FactorVIII <1 percent)in children >12 yrs of age who have been treated previously with other factor VIII product. **Unmet medical need in the country-** The data may potentially provide an alternative therapy for such Hemophilia A patients.
2	**Low anticoagulant heparin (Sevuparin/DF02)**	**M/s Max Neeman**	**TMS03**	**Risk versus benefit to the patients-** The risk vs benefit profile of the test drug from preclinical studies including single dose, 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 evaluate the safety and tolerability of test drug (Sevuparin/DF02) as adjunctive therapy on adult patients with moderate to severe plasmodium. falciparam malaria. **Unmet medical need in the country-** Due to low anticoagulant potency the test drug in combination with other anti malarial drugs, may contribute to a more efficient treatment of moderate to

				severe malaria.
3	**AR-12286**	**M/s Max Neeman**	**AR-12286-CS205**	**Risk versus benefit to the patients-** The risk vs benefit profile of the test drug from preclinical studies including single dose, repeat dose ocular toxicity and phase I, II clinical trials etc., justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** Due to Inhibitions of Rho kinase the test drug has emerged as a new class of potential glaucoma medication. The purpose of the study is to assess the safety and ocular hypertensive efficacy of test drug (AR-12286) in patients with tension glaucoma. **Unmet medical need in the country-** Currently glaucoma medication are not sufficiently potent as mono-therapy to achieve low target intra ocular pressure, and attempts to achieve lower target intra ocular pressure with combination products have met with limited success. The test drug may be a better alternate for these patients.
4	**EGT00014442**	**M/s Max Neeman**	**THR-14442-C-418 Dapagliflozin**	**Risk versus benefit to the patients-** The risk vs benefit profile of the test drug from preclinical studies including single dose, repeat dose toxicity studies and phase I, II clinical trials etc., justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The purpose of the study is to assess the efficacy and safety of the test drug (EGT0001442) in lowering HBA1c at week 24 compared with placebo. **Unmet medical need in the country-** Due to unique mechanism of action (high inhibition of renal Na+/ glucose transporter SGLT2) , the test drug may potentially benefit patient with type 2 diabetes.

5	**Esmolol hydrochloride gel (Galnobax)**	**M/s SiroClinpharma**	**Novalead-Galnobax**	**Risk versus benefit to the patients-** The risk vs benefit profile of the test drug from preclinical studies including repeated dose toxicity,12 weeks topical long term, reproductive and developmental toxicity studies justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The purpose of the study is to determine the safety and efficacy of a topical gel formulation of Esmolol Hcl for the treatment of diabetic foot ulcer. **Unmet medical need in the country-** The test drug may potentially be an alternative treatment for diabetic foot ulcer
6	**BAX 326** **(Recombinant Factor IX)**	**M/s Baxter**	**251002**	**Risk versus benefit to the patients-** The risk vs benefit profile of the test drug from preclinical studies including single dose, repeat dose toxicity and phase 1/3, 2/3 clinical trials etc., justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The purpose of the study is to evaluate the efficacy and safety of test drug (BAX 326) in previously treated patients with severe or moderate severe Hemophilia B undergoing surgical or other invasive procedures **Unmet medical need in the country-** The test drug may potentially provide a recombinant factor IX for prophylactic treatment of hemophilia B as well as for surgical prophylaxis.
7	**ATRs + Anti TB Drugs (Rifampin/** **Isoniazid/Pyrazinamide/ Ethambutol)**	**M/s NARI**	**ACTG5274**	**Risk versus benefit to the patients, Innovation *vis-a-vis* existing therapeutic option, Unmet medical need in the country -** Test drugs are already approved. The purpose of this study is to reduce early mortality and early morbidity by empiric tuberculosis treatment regime

				in HIV infected antiretroviral naïve patients. The the prophylactic anti TB treatment is acceptable. However, empiric treatment with anti TB drugs in HIV patients may not be justified, given the risk vs benefits to the patients. The report of the data safety monitoring board for this trial shall be submitted to the committee for evaluation. Till such time data safety monitoring board repot is evaluated by the committee, there should be no enrollment of any subjects in this trial.
8	**SeeMore^{TM}(EVP 1001-1) (Manganese Gluconate Injection)**	**M/s KentronBiotech**	**1001-1:221**	**Risk versus benefit to the patients-** The risk vs benefit profile of the test drug from preclinical studies including acute dose , sub-acute, genetic toxicity and clinical trial etc. justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The purpose of the study is to assess safety and efficacy of test drug (SeeMore^{TM}, a contrast media) in patients being evaluated for breast or colon cancer **Unmet medical need in the country-** The test drug SeeMore^{TM} is new manganese(Mn)based intravenous imaging agent being developed to enhance magnetic resonance imaging. The potential to distinguish healthy tissue from unhealthy tissue based on a specific sustained pattern of enhancement provides a basis for evaluating the performance of SeeMore^{TM} in oncology patients.
9	**Tenofovir + Emtricitabine + Efavirenz**	**M/s YRG**	**ENCORE- 1**	**Risk versus benefit to the patients-** In light of the fact that this fix dose combination ofTenofovirDisoproxilFumarate300mg + Emtricitabin 200mg + Efavirenz 600mg tablets is approved in India, the risk vs. benefit profile of this combination justifies the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** By reducing the dosage of Efavirenz to 400mg the central nervous system adverse effects may be minimal. The purpose of the study is to compare the safety and efficacy of standard (600 mg) versus reduced dose (400

				mg qd) efavirenz as part of initial combination antiviral therapy. **Unmet medical need in the country-** The outcome of this study may potentially lead to the usage of reduced dosage of Efavirenz from the standard 600mg. This may reduce the adverse effects and the cost.
10	**Gentian Violet**	**B. J. Medical College/NARI**	**A 5265**	**Risk versus benefit to the patients-** In light of the fact that the drug is approved , the risk vs. benefit profile of the test drug justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The purpose of this study is to see which one of two medicines (topical gentian violet or nystatin oral suspension) is better than the other drugs in treating oral candidiasis in HIV 1 infected Patients. **Unmet medical need in the country-**This test drug may offer benefit to the HIV infected population suffering from oral candidiasis.
11	**THR-18**	**M/s Infinitus clinical research**	**THR-2010-01**	**Risk versus benefit to the patients-** The risk vs benefit profile of the test drug from preclinical studies including single dose , repeated dose, phase I, IIa clinical trials etc, justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The purpose of the study is to assess the safety and efficacy of the test drug(THR -18) when administered to patients suffering acute ischemic stroke and treated with tissue plasminogen activator (tPA) **Unmet medical need in the country-** The test drug (THR -18) is developed as an adjunct to tissue plasminogen activator tPA thrombolytic therapy that may be useful in treatment of acute ischemic stroke.

12	**Sativexoromucosal spray(Nabiximols)**	**M/s PRA**	**GWCA0999**	**Risk versus benefit to the patients-** The risk vs benefit profile of the test drug from preclinical studies including single dose repeated dose, genotoxicity, local tolerance toxicity studies, phase I, IIa clinical trials etc, justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** The Test drug acts via specific cannabinoid(CB) receptor for treatment of persistent chronic pain in advanced cancer. **Unmet medical need in the country-**The study will provide safety information on long term use of test drug by patients with advanced cancer.
13	**MK-0431A(Sitagliptin + Metformin)**	**M/s MSD Pharma**	**MK-0431A-170**	**Risk versus benefit to the patients-** In light of the fact that this fixes dose combinations is approved , the risk vs. benefit profile of the test drug justifies the conduct of study in lower age group. **Innovation *vis-a-vis* existing therapeutic option-** The purpose of this study is to **a**ssess safety and efficacy of test drug (MK-0431A) in Pediatric patients with type 2 diabetes. **Unmet medical need in the country-** The study will generate data **f**or potential use of this combination in pediatric patients with type 2 diabetes who have inadequate glycemic control on metformin mono-therapy.

Annexure-II

List of 18 cases of global clinical trials/ clinical trials of NCEs along with their evaluations and recommendations of the Technical Committee in its 16th Meeting.

Sr. No.	Drug	Applicant Name	Protocol No	Evaluations in respect of 1. risk versus benefit to the patients 2. innovation vis-a-vis existing therapeutic option 3. unmet medical need in the country	Recommendations
1.	Darunavir, Ertavirine,Emtricitabine, Raltegravir, Ritonavir	YRG Care	A5288	**Risk versus benefit to the patients** In light of the fact the all the study drugs are approved for treatment of HIV , there risk vs benefit profile justifies the conduct of this study. **Innovation vis-a-vis existing therapeutic option** The study is to establish the third line anti retroviral regimen for those patient who failed those patients who failed 1st and 2nd line ART treatment The study will use resistance test to choose anti HIV drugs and text messages to improve subject's adherence for anti HIV drug taking behavior in order to achieve a ≥ 65% rate of virologic control. The study will provide information to **optimize** the third line HIV treatment regimens for those failing 1st and 2nd line HIV regimens. **Unmet medical need in the country** The study will potentially provide a 3rd line ART regimen for HIV patient who failed on 1st and 2nd line HIV regimens **.**	**Recommended for approval as per recommendations of NDAC.**

2.	Darunavir, Ertavirine,EmtricitabineRaltegravir,itonavir	B J Medical College	A5288	**Risk versus benefit to the patients** All the study drugs are approved. Therefore the risk vs benefit profile justifies the conduct of this study. **Innovation vis-a-vis existing therapeutic option** The study is to establish the third line anti retroviral regimen for those patient who failed those patients who failed 1st and 2nd line ART treatment The study will use resistance test to choose anti HIV drugs and text messages to improve subject's adherence for anti HIV drug taking behavior in order to achieve a ≥ 65% rate of virologic control. The study will provide information to **optimize** the third line HIV treatment regimens for those failing 1st and 2nd line HIV regimens. **Unmet medical need in the country** The study will potentially provide a 3rd line ART regimen for HIV patient who failed on 1st and 2nd line HIV regimens.	**Recommended for approval as per recommendations of NDAC.**

3.	Escitalopram, Bupropion	Prof. Y.C. Janardhan Reddy	NA	**Risk versus benefit to the patients-** In light of the fact that the study drugs are already approved and are in use as anti depressants, mood stabilizers ,the risk vs. benefit profile of these drugs justify the conduct of the study. **Innovation vis-a-vis existing therapeutic option-** Antidepressants are widely prescribed as adjuncts to mood stabilizers for the treatment of bipolar depression. Systematic studies to assess the long term utility of antidepressants in preventing depressive relapses in bipolar patients are limited**.** The purpose of this study is to assess whether antidepressant treatment for 12 months reduces the risk of relapse into any mood episodes, including depression ,mania and hypomania compared to discontinuing the antidepressant and substituting it with placebo after 2 months. **Unmet medical need in the country-** This study will provide data on the effectiveness of long term use of antidepressants along with mood stabilizers or atypical antipsychotics in preventing depression without increasing the risk of mania.	**Recommended for approval as per recommendations of NDAC.**

4.	Idarucizumab	Boehringer	1321.3	**Risk versus benefit to the patients** The risk vs benefit profile of the test drug in preclinical toxicity studies including single and repeated dose intravenous studies in rats and monkeys and phase I trials, justify the conduct of this study **Innovation vis-a-vis existing therapeutic option** The test drug is for the reversal of the anticoagulant effects of dabigatrin. (Dabigatran is approved for prevention of stroke, systemic embolism and reduction of vascular mortality in adult patients with atrial fibrillation (SPAF) and prevention of venous thromboembolic (PVTE) events.) **Unmet medical need in the country** The test drug may potentially provide an alternative option for the management of serious bleeding in patients on dabigatran, including life-threatening or fatal bleeding episodes. Currently available options for such bleeds is limited to supportive care i.e. administration of blood or blood products and the possibility of dialysis to remove the drug Dabigatran.	**Recommended for approval as per recommendations of NDAC.**

5.	Pregabalin	Pfizer	A0081041	**Risk versus benefit to the patients** The risk vs benefit profile of the test drug from preclinical toxicity studies including acute oral and intravenous studies in rat and multiple dose in rats and monkey, fertility and pre-post natal toxicity in rat, embryo fetal development study in mice, rats and rabbits and phase I, II/III clinical trials in pediatric subjects 1 to 16 years age and adults respectively justify the conduct of the study. **Innovation vis-a-vis existing therapeutic option-** The purpose of the study is to assess the efficacy and safety of pregabalin as adjunctive therapy in children 4 -16 years of age with partial onset seizures. **Unmet medical need in the country-** Pregabalin has a different mode of action, pharmacokinetic and adverse event profile, as compared to the existing class of drugs, in the treatment of partial onset seizures. The study may potentially provide an alternative /adjunctive therapy, for the treatment of partial onset seizures in children.	**The committee Recommended to obtain opinion of the pediatrician. Based on positive opinion the proposal can be approved as per the recommendation of the NDAC, without refering to Technical Committee.**

6.	Pregabalin	Pfizer	A0081106	**Risk versus benefit to the patients** The risk vs benefit profile of the test drug from preclinical toxicity studies including acute oral and intravenous studies in rat and multiple dose in rats and monkey, fertility and pre-post natal toxicity in rat, embryo fetal development study in mice, rats and rabbits and phase I, II/III clinical trials in pediatric subjects 1 to 16 years age and adults respectively justify the conduct of the study. **Innovation vis-a-vis existing therapeutic option** The purpose of this extension study is to gather the safety and tolerability of pregabalin as adjunctive therapy in pediatric subjects 1 month to 16 years of age with partial onset seizures and pediatric and adult subjects 5 to 65 **years** of age with primary generalized tonic-clonic seizures. **Unmet medical need in the country** Pregabalin has a different mode of action, pharmacokinetic and adverse event profile, as compared to the existing class of drugs, in the treatment of partial onset seizures. The study will provide more data on the safety of pregabalin as an alternative /adjunctive therapy, in the treatment of partial onset seizures in children and adults with primary generalized tonic-clonic seizures.	**The committee Recommended to obtain opinion of the pediatrician. Based on positive opinion the proposal can be approved as per the recommendation of the NDAC, without refereeing to Technical Committee.**

7.	Mipomersen	SANOFI	MIPO3801011/EFC12875	**Risk versus benefit to the patients** The risk vs benefit profile of the test drug from preclinical single dose and repeat dose toxicity studies , phase I, II and III clinical trials, justify the conduct of this study with the sustained release dosage formulation. **Innovation vis-a-vis existing therapeutic option** Mipomersen is an oligonucleotide with a unique mechanism of action that prevents the synthesis and hepatic export of apolipoprotein B, the key lipoprotein in atherogenic particles including LDL. The purpose of the study is to assess the Safety and Efficacy of Two Different Regimens of Mipomersen in Patients with Familial Hypercholesterolemia and Inadequately Controlled Low-Density Lipoprotein Cholesterol **Unmet medical need in the country** The study may potentially provide a therapy for the treatment of Familial Hypercholesterolemia and inadequately Controlled Low-Density Lipoprotein Cholesterol, an inherited genetic defect. These patients remain at extremely high risk of coronary heart disease despite all current therapies and need other therapeutic options.	**The committee recommended approval as per the recommendation of NDAC subject to condition that if the subjects in the placebo arm are found refractory to standard of care after 3 months they should be withdrawn.**

8.	DAC HYP (Daclizumab High Yield Processed	Biogen Idec	205MS301	**Risk versus benefit to the patients** The risk vs benefit profile of the test drug from preclinical toxicity studies including single (acute) and repeated –dose, reproductive and developmental toxicity studies in monkeys and phase I, III trials justify the conduct of this study. **Innovation vis-a-vis existing therapeutic option** The test drug is a new class of treatment characterized by NK cell expansion through selective augmentation of IL-2 signalling • Not T-cell / B-cell depletion • Selective targeting of activated T-cells The purpose of the study is to determine the efficacy and safety of test drug Daclizumab- high yield process) Vs interferon β-1a **in patients with relapsing remitting multiple sclerosis.** **Unmet medical need in the country-** The study may potentially provide a Daclizumab formulation (manufactured via a high yield process) for the treatment of Multiple sclerosis.	**Recommended for approval as per recommendations of NDAC.**

9.	Selexipag	PharmaLeaf	AC-065A303	**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 phaseI, II and III clinical trials justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** Selexipag is a selective IP-receptor agonist which is administered orally and could represent a significant improvement over parenterally administered prostacyclin derivatives by virtue of its convenience of dosing,handling and absence of catheter-associated complications. The purpose of the study is to assess the safety and tolerability of Selexipag in patients with pulmonary arterial hypertension **Unmet medical need in the country-** The study may potentially provide an alternative/additional therapeutic option for the treatment of Pulmonary arterial hypertension patients.	**Recommended for approval as per recommendations of NDAC.**

10.	Myozyme® (alglucosidasealfa)	SANOFI-SYNTHELABO (INDIA) LTD.	AGLU07710/ MSC12790	**Risk versus benefit to the patients** The risk vs benefit profile of the test drug from preclinical pharmacology, 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-** **Alglucosidasealfa is the only approved therapy worldwide for the treatment of Pompe disease**. The purpose of the study is to characterize the pharmacokinetics of Alglucosidealfa in patients aged 8-18 years of age. **Unmet medical need in the country-** The study will provide data on the pharmacokinetics of Alglucosidealfa in the patient age group 8-18 years and may potentially benefit patients with pompes disease , a genetic disorder.	**Recommended for approval as per recommendations of NDAC.**

11.	Rituximab	Cliantha Research Limited	RTXM83-AC-01-11	**Risk versus benefit to the patients-** In vitro physicochemical characterization of test drug, pharmacokinetic/Pharmacodynamic studies and single dose toxicity studies in Cynomolgous monkeys with three different doses , in comparison with the reference product , justify the conduct of this study **Innovation *vis-a-vis* existing therapeutic option-** The purpose of this clinical Study is to compare (RTXM83), the test drug Plus CHOP Chemotherapy Versus a Reference Rituximab Plus CHOP (R-CHOP) in Patients With Diffuse Large B-cell Lymphoma (DLBCL) as first line therapy. **Unmet medical need in the country-** Availability of rituximab from multisource may potentially benefit the patients.	**Recommended for approval as per recommendations of NDAC.**

12.	Afatinib (BIBW 2992)	Boehringer	1200.161	**Risk versus benefit to the patients** The risk vs benefit profile of the test drug from Pre-clinical Safety pharmacology in rats and minipigs, single dose ,and repeat dose toxicity in rats,minipigs, reprodutive ,developmental toxicity studies etc several Phase I,II,III studies justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** Afatinib is a selective and potent low molecular weight irreversible inhibitor of the ErbB-family TKI receptors and HER2. The purpose of this study is to evaluate the safety and efficacy of the test drug vs methotrexate in patients with recurrent and or metastatic head and neck squamous cell carcinoma who have progressed after platinum-based therapy. **Unmet medical need in the country-** .Afatinib may potentially provide an alternative therapy for patients with recurrent/ metastatic HNSCC,in addition to offering an oral option as against IV infusion therapies with taxenes and other monoclonal antibodies.	**Recommended for approval as per recommendations of NDAC.**

13.	Afatinib (BIBW 2992)		1200.66	**Risk versus benefit to the patients** Pre-clinical Safety pharmacology in rats and minipigs, single dose ,and repeat dose toxicity in rats,minipigs,reprodutive ,developmental toxicity studies etc several Phase I,II,III studies with the test drug, justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** Afatinib is a selective and potent low molecular weight irreversible inhibitor of the ErbB-family TKI receptors and HER2. The purpose of the study is to assess the safety of afatinib for patients with locally advanced or metastatic non-small cell lung cancer **Unmet medical need in the country-** This trial will obtain additional data on clinical benefits of afatinib in patients with locally advanced or metastatic non-small cell lung cancer harboring EGFR mutations and have never been treated with EGFR/TKI	**Recommended for approval as per recommendations of NDAC.**

14.	Ranibizumab	Novartis	CRFB002 G2301	**Risk versus benefit to the patients** **The risk vs benefit profile of the test drug from** Pre-Clinical Pharmacology study in cynomolgus monkeys, single dose toxicity in rabbits, multidose toxicity in cynomolgus monkeys, and several clinical phase I, I/II, II and III studies with the test drug, justify the conduct of the proposed study. **Innovation *vis-a-vis* existing therapeutic option-** The Test drug is already approved for treating Age Related Macular Degeneration (AMD), Diabetic Macular Edema (DME) and Retinal Vein Occlusion (RVO). The purpose of this study is to evaluate the safety and efficacy **of Ranibizumab in patients with visual impairment due to vascular endothelial growth factor (VEGFR) driven Choroidal neovascularization (CNV).** **Unmet medical need in the country-** The trial may potentially provide alternative therapeutic options for the treatment of Choroidal neovascularization (CNV).	**Recommended for approval as per recommendations of NDAC.**

15.	Ranibizumab	Novartis	CRFB002 E2302	**Risk versus benefit to the patients** The risk vs benefit profile of the test drug from Pre-Clinical Pharmacology study in cynomolgus monkeys, single dose toxicity in rabbits, multidose toxicity in cynomolgus monkeys, and several clinical phase I, I/II, II and III studies with the test drug, justify the conduct of the proposed study **Innovation *vis-a-vis* existing therapeutic option-** Ranibizumab/test drug is approved in India for treating Age Related Macular Degeneration (AMD), Diabetic Macular Edema (DME) and Retinal Vein Occlusion (RVO). The purpose of this study is to evaluate the safety and efficacy **of Ranibizumab used as individualized dosing regimen in patients with visual impairment due to macular edema (ME) secondary to Central Retinal Vein Occlusion (CRVO)** **Unmet medical need in the country-** The trial may potentially provide alternative therapeutic options for **patients with visual impairment due to macular edema (ME) secondary to Central Retinal Vein Occlusion (CRVO)**)	**Recommended for approval as per recommendations of NDAC.**

16.	Ranibizumab	Novartis	CRFB002 F2302	**Risk versus benefit to the patients-** **The risk vs benefit profile of the test drug from** Pre-Clinical Pharmacology study in cynomolgus monkeys, single dose toxicity in rabbits, multidose toxicity in cynomolgus monkeys, and several clinical phase I, I/II, II and III studies with the test drug, justify the conduct of the proposed study **Innovation *vis-a-vis* existing therapeutic option-** The Test drug/Ranibizumab is approved in India for treating Age Related Macular Degeneration (AMD), Diabetic Macular Edema (DME) and Retinal Vein Occlusion (RVO). The purpose if the study is to evaluate the safety and efficacy of two individualized regimens of ranibizumab in comparison to verteporfinPDT (vPDT) in patients with visual impairment due to choroidal neovascularization (CNV) secondary to Pathologic Myopia (PM). **Unmet medical need in the country-** The trial may potentially provide alternative therapeutic options for patients with visual impairment due to choroidal neovascularization (CNV) secondary to Pathologic Myopia (PM).	**Recommended for approval as per recommendations of NDAC.**

17.	SB3(proposedtrastuzumabbiosimilar)	SIROClinpharmPvtLtd	SB3-G31-BC	**Risk versus benefit to the patients** The risk vs benefit profile of the test drug from preclinical pharmacology, repeat dose toxicity studies and phase I clinical trials justify the conduct of this study. **Innovation *vis-a-vis* existing therapeutic option-** Trastuzumab is a high-end monoclonal antibody**. The purpose of the study is to demonstrate comparable clinical efficacy of the test drug with that of the innovator product in Her2 + MBC in neo- adjuvant setting.** **Unmet medical need in the country- Multisource availability of trastuzumab may benefit Indian patients**	**Recommended for approval as per recommendations of NDAC.**
18.	Methylglyoxal Formulation	Lifecare Innovations Pvt Ltd	LC-ONCO-1/PH II	**Risk versus benefit to the patients:** The proposal is for the conduct of the Phase-II clinical study. Patients included in the trial are different types of recurrent advance cancers and the drug is reported to not having significant side effects as observed in experimental animals and in patients. This justify the conduct of the study. **Innovation vis-a-vis existing therapeutic option:** It is a new chemical entity as anti cancer with broad soectrum, good tolerance and insignificant side effects that makes it very promissing drug for cancer therapy **Unmet medical need in the country:** At present there is no drug available for cancer therapy that is broad spectrum effective and without side effect, in India or any -where in world	**Recommended for approval as per recommendations of IND.**

Annexure-III

A. List of 25 cases of clinical trial proposals other than GCT/NCE along with evaluations and recommendations of the Technical Committee in 16th Meeting.

Sl No	Drug	Applicant Name	Protocol No	Recommendation
1.	Biochaperone PDGF-BB	M/s Virchow Biotech Pvt. Ltd	BC1-CT4, V1,	**Recommended for approval as per recommendations of NDAC.**
2.	Rituximab	M/s Lupin Limited	LRP/RTX/2013/002	**Recommended for approval as per recommendations of NDAC.**
3.	Cetuximab	M/s Reliance Life Sciences Pvt. Ltd	RLS/ONC/2013/04	**Recommended for approval as per recommendations of NDAC.**
4.	Pegfilgrastim	M/s Reliance Life Sciences Pvt. Ltd	RLS/TP/2011/01	**Recommended for approval as per recommendations of NDAC.**
5.	Minodronic acid Tablets 1 mg & 50 mg.	M/s. MSN Laboratories Private Limited		**The committee recommended to obtain opinion of the pharmacologist. Based on positive opinion the proposal can be approved as per the recommendation of the NDAC, without referring to Technical Committee.**
6.	Azelnidipine	Precise Chemipharma Pvt. Ltd	CMI-PRE/AZEL-AMLO/CT-III/161012	**Recommended for approval as per recommendations of NDAC.**
7.	Capecitabine + Cyclophosphorine	M/s Intas Pharmaceuticals Ltd.		**Recommended for approval as per recommendations of NDAC.**

8.	Vero-cell culture derived Inactivated Japanese Encephalitis Vaccine	Biological E. Limited,	BECT027/JEV-PIV/CTP-01	**Recommended for approval as per recommendations of NDAC.**
9.	ENGERIX-B [Hepatitis B vaccine (Recombinant)	M/s Calcutta School of Tropical Medicine,		**Recommended for approval as per recommendations of NDAC.**
10.	Live Attenuated Tetravalent (G1-G4) Bovine-Human Reassortant Rotavirus Vaccine [BRV-TV]	ShanthaBiotechnics Limited,	BRV07	**Recommended for approval as per recommendations of NDAC.**
11.	Cabazitaxel	Dr. Raju Titus Chacko		**Recommended for approval as per recommendations of NDAC. Dr. Raju Titus Chacko did not participate in deliberation of Technical Committee for the proposal.**
12.	FUNGISOME – Liposomal Amphotericin B	Life Care Innovation		**Recommended for approval as per recommendations of NDAC.**
13.	Saroglitazar (Phase-III)	Cadila Healthcare Limited		**The committee recommended to obtain opinion of the Endocrinologist. Based on positive opinion the proposal can be approved as per the recommendation of the NDAC, without referring to Technical Committee.**
14.	Saroglitazar(Phase-IV)	Cadila Healthcare Limited		**Recommended for approval as per recommendations of IND.**

15.	Bioactive ceramic composite (Synthetic bone graft material) loaded with Autologous Bone marrow derived mesenchymal stem cells (MSCs).	M/s Christian Medical College, Vellore, Tamil Nadu		**Recommended for approval as per recommendations of NDAC.**
16.	Hydroxychloroquine Sulfate Tablets	Ipca Laboratories Limited	IPCA/LHCQ/PII-12,	**Recommended for approval as per recommendations of NDAC.**
17.	Everolimus/RAD 001	M/s Novartis India Limited	CRAD001AIN03T	**Recommended for approval as per recommendations of NDAC.**
18.	Foligraf	M/s Bharat Serums And Vaccines Limited,	BSV/r-FSH-IMG-2012	**Recommended for approval as per recommendations of NDAC.**
19.	BVX 20	M/s. Biocon Limited	BVX20-CT1-001-10	**Recommended for approval as per recommendations of NDAC.**
20.	Bevacizumab	M/s Intas Biopharmaceuticals Ltd	476-13	**Recommended for approval as per recommendations of NDAC.**
21.	Ranibizumab	M/s. Novartis Healthcare Private Limited	CRFB002EIN01	**Recommended for approval as per recommendations of NDAC.**
22.	Bevacizumab	M/s. Roche Products (India) Pvt Ltd	ML28446	**Recommended for approval as per recommendations of NDAC.**
23.	Choline chloride	Prof S N Gaur		**Recommended that the protocol etc. for the conduct of the study by oral route should be reviewed and recommended by the SEC (NDAC). Dr. S. N Gaur did not participate in deliberation of Technical Committee for the proposal.**

24.	Amphoteracin B Emulsion 15mg/Kg, 20mg/kg	M/s Bharat serums and Vaccine Ltd		**Recommended for approval as per recommendations of NDAC.**
25.	BepotastineBesilate Ophthalmic Solution 1.5% w/v	M/s Ajanta Pharma Ltd.		**Recommended for approval as per recommendations of NDAC.**