MINUTES OF 32nd MEETING OF THE TECHNICAL COMMITTEE HELD ON 26.04.2016 UNDER THE CHAIRMANSHIP OF DGHS FOR SUPERVISING CLINICAL TRIALS ON NEW CHEMICAL ENTITIES IN THE LIGHT OF DIRECTIONS OF THE HON'BLE SUPREME COURT OF INDIA ON 03.01.2013.

Present:

1.	Dr. Jagdish Prasad, Director General of Health Services, Nirman Bhawan, New Delhi	Chairman
2.	Dr. Raju Titus Chacko, Prof. & Head, Dept. of Medical Oncology, CMC, Vellore	Member
3.	Dr. Yash Paul Sharma, Prof. & Head, Department of Cardiology, PGIMER, Chandigarh.	Member
4.	Dr. P. K. Dalal, Head of Department, Department of Psychiatry, KGMU Medical College, Lucknow.	Member
5.	Dr. B. L. Sherwal, Professor, Dept of Microbiology, RIMS, Ranchi.	Member

Special Invitees:

1. Dr. Sudha Prasad, Head, Dept. of Gynaecology, MAMC, New Delhi.
2. Dr. Alka Kriplani, Dept of Gynaecology, AIIMS, New Delhi,
3. Dr. Indu Chawla, Dept. of Gynaecology and Obstetrics in Dr. Ram Manohar Lohia Hospital (RML) Delhi

From CDSCO:

1. Dr. G. N. Singh,
   Drugs Controller General (India)
2. Dr. S. Eswara Reddy,
   Joint Drugs Controller (India)
3. Dr. V. G. Somani,
   Joint Drugs Controller (India)
4. Mr. R. Chandrashekar,
   Deputy Drugs Controller (India)
5. Mrs. Annam Visala,
   Deputy Drugs Controller (India)
6. Mrs. Rubina Bose,
   Deputy Drugs Controller (India)

The Chairman welcomed the members of the Committee for the 32nd meeting. Thereafter, the Committee discussed the clinical trial proposals and other agenda one after another as under:
The Committee deliberated 18 cases related to approval of clinical trials. Out of these 18 cases, 04 cases were related to clinical trials of NCEs, 08 cases were related to global clinical trials (GCT), remaining 06 cases were related to clinical trials for approval of New Drugs and Biologicals.

1. **Proposals of Clinical Trials of NCEs recommended by SECs.**

The Committee evaluated 04 cases related to clinical trials of NCEs and made recommendations considering all aspects of safety, efficacy especially in terms of the three parameters viz. risk versus benefit to the patients, innovation vis-a-vis existing therapeutic option and unmet medical need in the country. After detailed deliberations, the Committee recommended all 04 cases of NCEs. The recommendations of the Committee are enclosed at **Annexure-I.**
The Committee also opined that the cases for protocol amendment of NCEs need not be brought before the Technical Committee hereafter.

2. **Proposal of Clinical Trials of GCT recommended by SECs.**

The Committee evaluated 08 cases related to global clinical trials. After detailed deliberations, the Committee recommended conduct 06 clinical trials and deferred 02 proposals of GCT. The recommendations of the Committee are enclosed at **Annexure-II.**

3. **Proposals of Clinical Trials other than GCT/ NCEs recommended by SECs.**

The Committee evaluated 06 cases of other than GCT/clinical trial of NCEs. After detailed deliberations, the Committee recommended 05 cases, and deferred the remaining case for further clarification. The recommendation of the Committee is enclosed as **Annexure-III.**

Further, the Committee observed that its mandate is to review the proposals related to the clinical trials of GCT/NCEs only and therefore recommended that in future meetings only such proposals should be placed before it for deliberation.

Thus, the Committee recommended 15 out of 18 cases of clinical trial proposals and deferred 03 proposals.

4. **Waiver of Clinical Trial in Indian population for approval of New Drugs and Drugs falling under the category of Medical Devices which have already been approved outside India:**

05 proposals were placed before the Committee for consideration of permission for manufacture/ import for marketing in the country with waiver of local clinical trial. The details of recommendations of the Committee along with recommendation of the SEC are annexed as **Annexure-IV.**

5. Others:-

Item No. 01

Subject: Medroxyprogesterone Acetate (MPA) 104mg in 0.65mL suspension for injection for "long term female contraception" without local clinical trial

This Directorate has received an application from M/s. Pfizer Products India Pvt Ltd. for grant of permission to import and market of SAYANA® PRESS (Medroxyprogesterone Acetate) 104 mg in 0.65mL suspension for injection in pre filled syringe (new delivery system and new strength) and route of administration (subcutaneous) for long term female contraception and management of endometriosis associated pain**.**

MPA is a synthetic analogue of 17α hydroxyl progesterone which has anti-oestrogenic, anti-androgenic and anti-gonadotropic effects. It diffuses freely into target cells in the female reproductive tract, mammary gland, hypothalamus, and the pituitary and bind to the progesterone receptor. Once bound to the receptor, progestins slow the frequency of release of gonadotropin releasing hormone (GnRH) from the hypothalamus and blunt the pre-ovulatory LH surge. Medroxyprogesterone Acetate **(MPA) 150mg/mL** suspension for injection (I.M) was earlier approved by this directorate on 06-01-1998.

Now firm has submitted application for import and marketing of Medroxyprogesterone Acetate **104mg in 0.65mL** Suspension for Injection (subcutaneous route) **"for long term female contraception and management of endometriosis associated pain".**

1) The proposal of the firm was referred to NDAC (Reproductive and Urology) held on 23.01.2014.The committee opined that this particular formulation is being marketed in various countries and it is also recommended by WHO. The proposed formulation is a reduced dose than I.M dose. This delivery system is novel and it is convenient for use when compared to I.M. Drug (Medroxyprogesterone Acetate **(MPA) 150mg/mL** suspension for injection) and the safety and efficacy of the drug is already established. Therefore committee recommended for import and marketing of MPA 104mg in 0.65mL subject to submission of PSUR every six month to the office of DCG(I).

2) The proposal was deliberated in Technical Committee on 13-10-2014 where the Committee after detailed deliberation agreed to the recommendations of the SEC for marketing authorization of the drug without conducting local clinical trial.

3) The proposal was deliberated in Apex Committee on 15-10-2014 where the Committee recommended that the Technical Committee should specifically mention if this case falls under the five criteria laid down for waiver of local clinical trial in Indian populations for approval of

new drugs viz. national emergency, extreme urgency, epidemic and for orphan drugs for rare diseases and drugs indicated for conditions/diseases for which there is no therapy.

4) The proposal was re-deliberated in Technical Committee held on 17-11-2014 based on the recommendation of the Apex Committee. The Committee after detailed deliberation recommended for waiver of clinical trial of Medroxyprogesterone 104mg in 0.65 ml suspension (for Subcutaneous Injection) **based on the fact that for the treatment of Endometriosis, no satisfactory subcutaneous product or therapy is yet available in the country,** which is being provided by the said drug in SC route and as such Medroxyprogesterone is very old drug used for Endometriosis by IM route. Therefore clinical trial is not necessary as such for such slightly modified preparation of drug of already known safety & efficacy in given indication. The Technical Committee did not recommend the indication **"for long term female contraception".**

5) The proposal was also deliberated in the Apex Committee meeting held on 25-11-2014. After consideration of aforesaid facts, the Apex Committee agreed with the recommendation of Technical committee.

6) Accordingly the import and marketing permission for Medroxyprogesterone Acetate suspension for injection (Subcutaneous route) "**Indicated for the management of endometriosis associated pain"** was issued to firm on 18-12-2014.

7) The firm requested this Directorate vide letter REG/PPIPL/RC/14?SJ/546 dated 22 Dec 2014 for amendment in the Form -45 permission for intimation of addition of indication addition of "**for long term female contraception."**

8) The proposal for addition of indication (**for long term female contraception)** was deliberated in 11th SEC (Reproductive and urology) meeting held on 27-02-2015 for additional indication i.e long-term female contraception. The SEC noted that MPA, 104 mg in 0.65mL, SC is already approved for management of endometriosis. Firm has requested for additional indication for long term female contraception and informed that this product is already approved internationally (USA, UK etc.,) for the proposed indication. The committee recommended for approval of the indication i.e. for long term female contraception without conducting clinical trial as it is satisfactory subcutaneous therapy for the proposed indication which is not yet available in the country and further dose is also reduced with SC route when compared to IM route.

9) The proposal **for import and marketing of Medroxyprogesterone Acetate (MPA) 104mg in 0.65mL Suspension for Injection for long term female contraception** was deliberated in 24th technical committee on 06.05.2015 where committee noted that there are various alternatives available in respect of the proposed additional indication and being a sub-cutaneous route which is new for its use and operationalization for the purpose of contraception, the Committee recommended **that a phase III trial shall be conducted.**

10) As per the recommendation of technical committee this directorate has issued a letter stating firm has to conduct phase III study and protocol shall be submitted to this directorate for further action on dated 05-06-2015 and 18-09-2015

The firm has made a representation to DGHS for reconsideration. As desired by the Chairman, three subject experts have been invited to the meeting of the committee for giving their opinion on the proposal. The firm has been invited to present its proposal before the Committee.

Recommendation of the Technical Committee:- The firm has made a presentation before the Committee and the following three subject experts.:

1. Dr. Sudha Prasad, HOD, Dept. of Gynaecology, MAMC, New Delhi.
2. Dr. Alka Kriplani, HOD, Dept of Gynaecology, AIIMS, New Delhi.
3. Dr. Indu Chawla, Dept. of Gynaecology and Obstetrics in Dr. Ram Manohar Lohia Hospital (RML) Delhi.

The subject experts opined that subcutaneous route is a better option over the Intramuscular route as lower dose of the drug is required and also because of convenience for use. Further, the drug is approved for the applied indication through subcutaneous route in 38 countries. The Committee also noted that pivotal study for the same indication through subcutaneous route has been conducted in Asian countries like Bangladesh and Pakistan which has demonstrated the safety and efficacy of the drug. Therefore, the Committee agreed with the opinion of the subject experts and recommended for waiver of local clinical trial.

Item No. 02

Proposal of M/s. India Medtronic Pvt. Ltd.

Generic Name: Transcatheter Aortic Valve Implant System
Brand Name: CoreValve System and CoreValve Evolut R System

M/s. India Medtronic Pvt Ltd. has already obtained Import permission for the Medtronic Trans Catheter Aortic Valve Implant (TAV) [Import Permission no. Import-142/2015 dated 19.06.2015] with the following conditions:

- The product shall be used in the cases which are not fit for surgery and morbid condition on the advice of cardiac surgeon and cardiologists.
- The firm shall generate and submit systematic PMS data of first 100 patients along with the periodic safety update report.
- The device shall be allowed to be used by Cardiac Surgeons / Cardiologist in presence of Anesthesiologist in Hybrid Operation Theater.

The conditions in Import permission, under point # 5 is “As part of post marketing surveillance, the applicant shall submit “Periodic Safety Update Reports” every six months for the first two years. For subsequent two years, the Periodic Safety Update Reports shall be submitted annually. Further, it were mentioned at point # 10 “Systematic PMS data of the device in first 100 patients

shall be generated and submitted to this office along with the periodic safety update review" as per recommendation of 20th Technical Committee and 19th Apex Committee meeting.

The firm has made representation to the Directorate General of Health Services regarding waiver of the conditions no. 10 i.e. systematic PMS data of the device in first 100 patients shall be generated and submitted to this office along with the periodic safety update report and to allow them to comply to conditions no. 05 by which they will be submitting Periodic safety update reports every six months for first two years and for subsequently two years annually.

M/s. India Medtronic Pvt. Ltd and M/s. Edward Life sciences (India) Pvt. Ltd. made representation to DCG (I) on 28.10.2015 and it was decided that, the waiver of condition of systematic PMS data of first 100 patients cannot be considered as the same was recommended by Technical and Apex Committees and the same may be placed before the Committee.

Recommendation of the Technical Committee:- The Committee deliberated the proposal and recommended for waiver of condition No. 10 i.e.; systematic PMS data of the device in first 100 patients.

Item No. 03

Reconsideration of the waiver of local clinical trial waiver of Tiotropium Bromide Inhaler 9 mcg and Tiotropium Bromide Rotacaps 18mcg (Additional indication).

It may be noted that the proposal was deliberated in the Technical Committee and Apex Committee on 01.02.2016 and 06.04.2016 respectively. After detailed deliberation, the Technical Committee recommended for waiver of local clinical trial as per SEC recommendation.

Recommendations of the SEC:- The committee opined that, this drug is already in use for COPD since 2003 in India. It is already listed in guidelines of National and international professional bodies as add- on therapy for difficult to control asthma. The committee also opined that options of add-on therapy for difficult to control asthma is limited, hence the committee recommended this proposed indication can be considered for wavier of clinical trial. The committee felt that conducting additional clinical trial may not get any new information. Thus, the firm can be given permission to use this drug as an add-on therapy for difficult to control asthma in adult patients, which should be highlighted prominently in the label. Therefore the committee recommended for the following additional indication -Tiotropium is indicated as an add-on maintenance bronchodilator treatment in adult patients with asthma who are currently treated with the maintenance combination of inhaled corticosteroids (≥800 mcg budesonide/day or equivalent) and long-acting β2 agonists and who experienced one or more severe exacerbations in the previous year. The committee also opined that Phase IV clinical trial shall be conducted in significant number of Indian patients.

Recommendation of the Apex Committee: The Apex Committee noted that no evidence is available regarding approval of the drug for Asthma and keeping this in view, did not approve

the waiver of local clinical trial. The Committee suggested to place before it evidence of approval in other countries for re-examination of the proposal.

Approval status of the drug: In India, Tiotropium Bromide Inhaler 9mcg and Tiotropium Bromide Rotacaps 18mcg are approved for the maintenance treatment of chronic obstructive pulmonary disease (COPD) on 18.08.2003 and 16.04.2003 respectively to M/s. Cipla ltd.

Tiotropium Bromide Inhalation spray 2.5mcg/1.25mcg has been approved in USA and Tiotropium Bromide solution for inhalation 2.5mcg has been approved in EU for asthma.

Recommendation of the Technical Committee:- The Committee noted the following:-

1. Tiotropium Bromide Inhalation spray 2.5mcg/1.25mcg is approved for asthma in USA and UK.
2. Tiotropium Bromide 9mcg inhaler and 18mcg rotacaps are not approved anywhere in the world for the indication of asthma.

Therefore, the Committee has not recommended for the waiver of local clinical trial.

Item No. 04

Appeal by M/s Novartis for waiver of the Clinical Trial condition imposed by Technical Committee in its 30th meeting dated 26-11-2015.

Study title: "A multicenter, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of LCZ696 compared to Valsartan, on morbidity and mortality in heart failure patients (NYHA Class II-IV) with preserved ejection fraction"

It may please be informed that the proposal was deliberated in Technical Committee in its 28th meeting dated 21-08-2015 and CT NOC has been issued on 30-09-2015 as per the recommendations of Technical Committee meeting.

The details of the deliberations are given below:-

I. Deliberation of proposal by SEC dated 16.07.2015:-

The Committee after deliberation recommended as under:-

After the detailed deliberation the committee recommended the conduct of the study subject to the following condition:-

1. Serum potassium levels should be assessed at 1 week post dose escalation to 160 mg BD.
2. Ejection fraction assessment should be performed by 2D volumetric methods.

II. Deliberation of proposal in 28th Technical Committee dated 21.08.2015:-

The Committee after deliberation recommended as under:-

After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation with the condition that the patients who have eGFR less than 45 ml/min should be excluded from the study.

III. Appeal by M/s Novartis for waiver of the CT NOC condition imposed in the 28th Technical Committee meeting dated 21-08-2015:-

There after the applicant represented the matter to DCG (I) for waiver on the condition imposed under CT NOC in 28th Technical Committee meeting.

IV. Deliberation in 30th Technical Committee meeting dated 26.11.2015 on firms appeal for waiver of CT NOC condition :-

Based on the firm's justification and clarification, the appeal for waiver of CT NOC condition i.e. "the patients who have eGRF less than 45 ml/min should be excluded from the study" has been deliberated in 30th Technical Committee meeting dated 26-11-2015.

After examining the justification by the firm in detail, the committee opined that patients with severe diabetes, hypertension with diastolic blood pressure ≥ 85 mmHg, patient on high dose of insulin should be excluded from the study. If eGFR decreases by ≥ 25% from baseline, subject should not be randomised into the study.

V. Appeal by M/s Novartis for waiver on the CT NOC condition imposed in the 30th Technical Committee meeting dated 26-11-2015:-

As per the recommendation of 30th Technical Committee meeting dated 26-11-2015 waiver of CT NOC condition as imposed by 28th Technical Committee meeting was granted subject to the condition that "**patients with severe diabetes, hypertension with diastolic blood pressure ≥ 85 mmHg, patient on high dose of insulin should be excluded from the study. If eGFR decreases by ≥ 25% from baseline, subject should not be randomised into the study".**

There after the firm appealed to DGHS for the waiver of new condition i.e. "**patients with severe diabetes, hypertension with diastolic blood pressure ≥ 85 mmHg, patient on high dose of insulin should be excluded from the study. If eGFR decreases by ≥ 25% from baseline, subject should not be randomised into the study" as** imposed in its 30th Technical Committee meeting based on the following justifications;

VI. Appeal by M/s Novartis for waiver on the CT NOC condition imposed in the 31st Technical Committee meeting dated 01-012-2016:-

The firm appealed to DGHS for the waiver of additional CT condition imposed by the 30th Technical Committee in its 31st meeting dated 01-02-2016 along with justification for waiver. **After examining the justification furnished by the firm in detail, the Committee recommended waiver of the CT NOC condition imposed in its 30th meeting subject to the condition that patients having eGFR between 30 to 45 ml post randomisation must be closely monitored for eGFR and serum potassium at every 15 days during the first 6 months.**

Thereafter the firm re-appealed to DCG (I) for the waiver of the additional CT NOC condition i.e. **"patients having eGFR between 30 to 45 ml post randomisation must be closely monitored for eGFR and serum potassium at every 15 days during the first 6 months"** imposed by Technical Committee in its 31st meeting.

Justification for the waiver of clause as below;

Novartis acknowledges Indian HA's concerns over the importance of careful monitoring of potassium levels in patients with moderate to severe renal impairment. However, based on recent analyses of LCZ696 safety data, **Novartis believes the approved protocol provides for sufficient monitoring and additional lab assessments are not necessary**. We would like to furnish the following information to address these conditions.

1. As per the Technical Committee recommendation, 10 additional visits would be required in the first 6 months of double blind period. This would result in a total of 17-18 visits in the first 8 months of trial for patients with eGFR <45ml/min/1.73 m^2.
2. The relatively old(>50 years) target patient population of this study with moderate renal impairment will be less likely to participate due to excessive burden of the trial, resulting in de facto exclusion of these patients. Ultimately, the sample of patients from India will not be representative of the overall Indian HFpEF population. Patient who do agree to participate will be at a substantial risk for a missing clinic visits (and missing data), increased withdrawal of consent and loss to follow-up, thereby negatively impacting the quality of data of Indian sites and the overall trial. Novartis is seeking to ensure robust participating from Indian patients in the PARAGON-HF trial.
3. The PARADIGM-HF trial (CLCZ696B2314), which randomized 8442 patients including 637 patients from India, showed that LCZ696 was superior to enalapril (current standard of care) in reducing the risk of cardiovascular (CV) death or HF hospitalization (primary endpoint), CV death alone, HF hospitalization alone, and all cause death in patients with HF and reduced EF. The greater benefit of LCZ696 over enalapril was also evident in patients regardless of degree of renal impairment, including patients with moderate or severe impairments. Further, LCZ696 was associated with substantially lower rates of hyperkalemia and renal adverse events than enalapril in patients with eGFR<45 ml/min/1.73m^2. This trend was generally consistent among Indian patients as well subgroup analysis data along with detailed justification of waiver request is enclosed (Encl. 5).

4. LCZ696's safety profile in HFpEF patients is not expected to be significantly different from that in HFrEF patients. The GFR related exclusion criteria in the proposed PARAGON study are exactly similar to PARADIGM-HF trial. Also, US FDA approved prescribing information of LCZ969 recommends no dosage adjustments for patients with mild to moderate renal impairment i.e. eGFR 30-90mL/min/1.73m^2.
5. Currently approved protocol includes guidance to PIs on management of renal dysfunction and hyperkalemia. Further, protocol allows that the investigator may conduct unscheduled safety lab assessments, including assessing eGFR and serum potassium, in any patient based on his/her medical judgment which can be conducted at whatever frequency the investigator sees fit.
6. In addition, it may be noted that the current study protocol has already been approved in 40 countries including key countries like US, UK, Switzerland, France, Germany, Canada and the study is currently recruiting. Approximately 2,037 patients have been recruited globally till date.

In view of the above and based on the excellent renal safety profile of LCZ696 and its effect on potassium levels, the firm believe that the current protocol provides sufficient safety monitoring to safeguard patients with eGFR<45ml/min/1.73m2 and thus requested for the waiver of recent requirement for additional monitoring of eGFR and potassium in this subgroup of patients.

Recommendation of the Technical Committee:- After detailed deliberations on the justification furnished by the firm, the Committee recommended the waiver of the CT condition imposed in its 31st meeting subject to the condition that assurance is provided that standard of care treatment and safety monitoring shall be same as in other countries.

Item No. 05

Proposal of M/s Gennova Biopharmaceuticals Limited.

M/s Gennova Biopharmaceuticals Limited was asked to do clinical trials in India after getting the protocol (GBL/TNK-t-PA/AIS/0002) approved by this office. The firm complied with and conducted the clinical trial with 50 patients (Dy No. 47778, dated 8 Oct 2010). The firm was again asked to do clinical trial on another 50 patients as per Schedule Y of the Drugs & Cosmetic Act, 1940 and the protocol was approved by this office (F. No. 12/GEN-13/FNK/08-BD (Part-I). The firm generated safety and efficacy data on a total of 79 patients with Acute Ischemic Stroke and requested DCG (I) to approve the drug for the indication Acute Ischemic Stroke as alternative to Alteplase and has given a commitment that it will complete the 100 patient clinical trial.

However, it may be noted that a letter was received from Indian Stroke Association (FTS No-38271/2015, dated 20.07.2015) with some concerns related to the clinical trial protocol of Tenecteplase. The concerns raised were discussed in the **SEC (Cardiovascular and Renal) meeting held on 25.08.2015**, with following suggestions.

1. Currently, r-tPA is the only approved gold standard therapy worldwide. To test a new agent e.g. Tenecteplase, it should be tested:
   a. In a clinical trial preferably in a randomized, double blind fashion and compared to the gold standard i.e. r-tPA.
   b. The trial should be adequately powered to detect the difference.
   c. It should have valid end points, e.g. a dichotomized mRS (0-1 or 0-2) for good outcome at three months.
   d. At least, if it is open label, the end points should be tested in a blinded manner (e.g. PROBE design)
2. Clarification on the following points:
   a. The scientific robustness of this open label Phase III study with only 75 patients.
   b. The strength of clinical trial design: sample size, methodology, primary and secondary endpoints; duration of follow up: the trial is open labeled without a comparative arm and has NIHSS as primary end point. Moreover the secondary endpoints although mentioned as mRS but do not specify the dichotomization for outcomes.

After discussion, committee opined that, proposal is related with the treatment of stroke and preferably may be discussed in the SEC (Neurology). The proposal was forwarded to **SEC-Neurology meeting held on 30.09.2015** and following deliberation was made. With reference to the letter received from Indian Stroke Association, regarding the design of the already approved protocol, conduct of clinical Phase III trial for Tenecteplase for Acute Ischemic Stroke was discussed with the members of SEC. The committee opined that the concerns raised in the letter are valid. Therefore, the firm may be directed to present the protocol in the next SEC meeting with proper justification.

In the light of the presentation of the firm, the proposal is placed before the Technical Committee meeting for further deliberation.

Recommendation of the Technical Committee:- The Committee recommended that the proposal may be discussed in SEC while co-opting experts in the area from reputed institution.

Item No. 06

Re-deliberation of the proposal of M/s Bio-Med to conduct clinical trial for evaluation of immunogenicity and safety of Rabies vaccine human (cell culture) IP in post exposure subjects.

- The proposal was deliberated in Technical Committee meeting held on 21.08.2015, wherein the Committee has recommended for conduct of study subject to the condition that Immunogenicity of the subjects within 48 hours of Vaccination shall be measured and in case sufficient titre is not reached, rescue treatment (alternative vaccine) to be given to the subjects.

  In response firm has replied that as per WHO TRS 941 "It is imperative to include a blood sample taken on day 0 and 7 in order to identify and exclude previously vaccinated

subjects". It means that the firm shall be conducting immunogical test on all samples to be taken on day 0 and 7 to identify volunteers who are already vaccinated or exposed. The immunological test done on day 14 of vaccination shall be evaluated within 48 hours and the volunteers having titre $\leq$ 0.5 IU/ml shall be given rescue treatment.

The firm's amendment has a basic difference from Technical Committee recommendation i.e. wherein Technical Committee has recommended testing Immunogenicity within 48 hours; the firm is intending to do the same at 14 days.

Hence, the same is submitted for redeliberation, if the firm can be allowed for conducting Immunological test on day 14 of vaccination instead of within 48 hrs of vaccination as recommended by Technical Committee.

- The above mentioned concern of the firm was deliberated in the Technical Committee dated 01.02.2016, wherein the Committee examined the revised protocol and opined that firm may be asked to present before the Committee, the justification for proposing to test the immunogenicity of the proposed new Rabies vaccine in 14 days instead of 48 hrs as recommended by 30th Technical Committee.

  Hence, firm was invited to present its case.

  Recommendation of the Technical Committee:- The Committee accepted the justification to test the immunogenicity of the proposed new Rabies vaccine at day 14 instead of 48 hrs and recommended for conduct of the proposed study.

  The meeting ended with vote of thanks to the Chair.

Annexure-I

List of 04 cases of clinical trial of NCEs along with their evaluations and recommendations of the Technical Committee in its 32nd Meeting.

Proposal No	Details of the proposal	Assessment of the Proposal *vis –a vis* specified Parameters	1. Recommendation of the Subject Expert Committee /IND Committee 2. Recommendation of the Technical Committee
1.	**Name of the Drug:** NW-3509A (Evenamide) **Name of the Applicant**: CliniRx Tangent Research India Private Limited Patriot House, 4th Floor, 3 BSZ Marg, New Delhi –110 002 **Name of the Sponsor**: Newron Pharmaceuticals S.p.A. Via Ludovico Ariosto 21 20091 Bresso (Milano) Italy **Name of the Manufacturer :** Patheon/DSM Pharma Chemicals, Donaustaufer Strasse 378, 39055 Regensburg, Germany **Title:** A phase -IIa, prospective, randomized, double-blind, placebo controlled, multiple-dose study designed to determine the safety, tolerability and preliminary efficacy of an oral dose range of nw-3509a in patients with chronic schizophrenia not responding adequately to their current antipsychotic medication.	**Assessment of Risk vs. Benefit to the patients:** The safety profile of the study drug from preclinical pharmacology, single dose, repeat dose toxicity, genotoxicity and phase I clinical studies justify the conduct of the trial. **Innovation vis-à-vis Existing Therapeutic Option:** The purpose of the study is to evaluate the safety and tolerability of NW-3509A given as an oral dose range of 30 to 50 mg/day (15 to 25 mg, BID) in patients with schizophrenia on a stable dose of their current antipsychortic medication (aripiprazole or risperidone). **Unmet Medical Need in the country:** The test drug may provide alternate treatment option in schizophrenic patient, stable on their antipsychortic medication (aripiprazole or risperidone).	**1. Recommendation of the Subject Expert Committee** on 18-03-2016. After detailed deliberation the committee recommended the study with the following conditions 1. Subjects should be hospitalized for observation for a period of 24 hrs post dosing for change of all dose visits. 2. The trial sites should be multispecialty hospitals with emergency facilities. 3. All investigations including kidney function tests and serum electrolyte testing must be done. **2.Recommendation of the Technical Committee** After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of the study.

2.	**Name of the Drug:** QPI-1007 **Protocol No**: QRK207 **Name of the Applicant**: Manipal AcuNova Limited Mobius Towers, SJR i-Park Whitefield, EPIP Bangalore – 560066. Karnataka, India. **Name of the Sponsor**: Quark Pharmaceuticals, Inc, 6501 Dumbarton Circle, Fremont, CA 94555, USA. **Name of the Manufacturer**: Active pharmaceutical ingredient (API): **Agilent Technologies, Inc. 5555 Airport Road Boulder, CO 80301 USA** Finished Formulation: **Albany Molecular Research Inc (AMRI) Burlington: 20 Blanchard Rd Burlington, MA 01803 USA.** **Title:** A Phase 2/3, Randomized, Double-Masked, Sham-Controlled Trial of QPI-1007 Delivered By Single or Multi-Dose Intravitreal Injection(s) to Subjects with Acute Nonarteritic Anterior Ischemic Optic Neuropathy (NAION).	**Risk Vs Benefits to the patients:** The Risk Vs Benefits profile of the test drug from pre clinical single, repeated dose toxicity studies, genotoxicity and phase I clinical study justify the conduct of study. **Innovation vis a vis existing therapeutic option:** The purpose of the study is to assess the safety, efficacy and tolerability of QPI- 1007 administration as three bimonthly intravitreal injections on visual acuity in subjects with recent onset NAION. **Unmet Medical Need in the Country**: NAION is an unmet medical need. There are no therapeutic options currently approved for the disease.	**1. Recommendation of the SEC:** The initially approved protocol was version 02. The firm now requested for certain amendments vide protocol version 05 dt. 16.10.2015. After detailed deliberations the committee recommended approval of version 05. Further the firm made an oral request for increasing the number of patient from India from 120 to 160. However the committee felt that the increase in number of subjects, at this stage, is not called for. **(Dr. Rohit Saxena did not participate in the deliberations.)** **2. Recommendation of the Technical Committee** After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of the study.

3.	**Name of the Drug:** PvDBPII vaccine Recombinant Plasmodium vivax malaria vaccine **Protocol No** : MVDP/vivax/1/15/02/01 **Phase of the Study:** Phase I **Name of the Applicant:** International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi **Name of the Sponsor:** International Centre for Genetic Engineering and Biotechnology AND Malaria Vaccine Development Program (MVDP) International Centre for Genetic Engineering and Biotechnology (ICGEB) Campus, Aruna Asaf Ali Marg, New Delhi-110 067, India **Name of the Manufacturer**: **Manufacturer for Drug Product & Diluent**: Zydus Cadila, Plot Survey No.23,25/P, 37, 40/P, 42 SarkhejBavala, Highway 8-A, Opp. Ramdev Masala, Village Changodar, Tal: Sanand, Dist., Ahmedabad – 382213 (Gujarat), India. **Manufacturer for Drug Substance:** M/s Syngene International	**Benefit** This malaria Phase I vaccine study is not per se expected to provide any "direct" benefits to the study participants, especially for the subjects who are going to be randomized to receive PvDBPII/GLA-SE. However, the study has the potential to contribute towards public health gains on account of scientific advances in the field of P.vivax malaria vaccine development, a disease much prevalent in India. Based on the study results further clinical studies will be planned for PvDBPII/ GLA-SE. Subjects who will receive Hepatitis B vaccine will benefit by participating in the Phase I clinical trial because it is expected to provide protection against Hepatitis B. **Risk** This is the first human trial of a PvDBPII based vaccine. Based on the information gathered from human studies that have been conducted with GLA-SE, possible risks from administration of PvDBPII/GLA-SE malaria vaccine formulation have been mentioned above. Because PvDBPII/GLA-SE vaccine is an experimental vaccine being administered to humans for the first time, there may be unknown risks. During this study participants will undergo phlebotomy procedures for blood drawing. The procedure carries its own associated risks of infection, vascular damage, bruising and clot formation. In addition, there is always a theoretical risk associated with breach of confidentiality by participating in this study. However, every measure will be taken to assure the confidentiality of participants in	**1.Recommendation of the IND Committee held on 16.12.2015:** The committee deliberated the proposal in detail and recommended the proposed Phase-I study subject to condition that to submit justification on the difference in the Lymph node enlargement in acute toxicity study in mice and rat [IIiac (mice)/Popliteal (rat) Lymph nodes] **2.Recommendation of the Technical Committee** After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of the study.

	Ltd., Plot No 2& 3, Unit BPP, IV Phase, Bommasandra Jigani Link Road, Banglore 560099 **Manufacturer for Adjuvant GLA-SE:** M/s Gennova Biopharmaceuticals Ltd., Gennova Vaccine Formulation Centre & Research lab 2, Chrysalis Enclave, International Biotech Park, Phase II, Hinjewadi, Pune Maharashtra-411057 **Title:** Phase-I, randomised, controlled, dose escalating, single blind clinical trial to evaluate the safety and immunogenicity of PvDBPII vaccine (recombinant *Plasmodium vivax* malaria vaccine Region II) formulated with adjuvant GLA-SE in healthy Indian male subjects	this study. Following steps have been taken to ensure subject safety: • The study vaccines have been prepared according to current Good Manufacturing Practices (cGMP) and tested in animal toxicology studies under Good Laboratory Practices (GLP). •The vaccines will be administered in the Human Pharmacology Unit (HPU) under the supervision of experienced, trained and qualified clinicians, nurses and support staff; the HPU is a Phase I unit equipped with drugs and equipment to immediately and effectively treat any anaphylactic reactions and other adverse events. •All vaccine doses will be given by slow injection to minimize injection site reactions. Each immunization will be administered to alternate arms, with the first immunization in non-dominant arm, second in the dominant arm and third in the non-dominant arm. Prior to each immunization, the arm will be inspected for lesions, wounds or clinically evident physical findings that might interfere with post-immunization assessment of reactogenicity. If such a finding is discovered, the unaffected arm will be used, even if the alternate arm schedule is not preserved. •Each subject will be closely observed for around 4-5 hours in the facility following immunization and vitals will be recorded within 45 mins of immunization . •Each cohort enrollment will be staggered over 2-3 days so as to allow better monitoring of subjects •The subjects will be monitored and	

		treated for all safety events for their duration of participation in the study. In order to prevent or minimize all possible risks and hazards associated with this study, the site medical team will observe the subjects closely and offer standard medical care and treatment for any medical problem during the participation period. The study physicians will conduct physical examinations and laboratory tests as outlined in visit schedule. A study physician will always be available on phone for any untoward event. •Free medical management shall be given as long as required or till such time it is established that the injury is not related to the clinical trial, whichever is earlier.	
4.	**Name of the Drug:** Purified Chikungunya Viral Vaccine (Inactivated) **Protocol No.:** BBIL/CHKV/I/2014 **Phase of the Trial:** Phase-I **Name of the Applicant:** M/s Bharat Biotech International Ltd., Hyderabad **Name of the Sponsor:** M/s Bharat Biotech International Ltd., Hyderabad **Name of the Manufacturer**: Bharat Biotech International Limited Genome Valley, Shameerpet Hyderabad **Title**: Phase I open Label Label, dose-	**Vaccination with CHIKV vaccine, BBV87:** This is the first use of the vaccine in clinical trials and there are no known directly attributable risks associated with this vaccine. By participating in this study subject will learn about Chikungunya fever and how to treat it. Subject participation in this study will help in generating information about the effect of this novel vaccine and lead the direction for further development of the vaccine so that it can become available to general public. If successful, the vaccine will be able to prevent Chikungunya in treated subject and benefit a large population.	**1.Recommendation of the IND on 16.12.2015:** The committee deliberated the proposal in details and recommended for the proposed study as per the amended protocol. **2.Recommendation of the Technical Committee** After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of the study.

	escalation clinical trial to evaluate the safety, tolerability and immunogenicity of Chikungunya vaccine in healthy adults of 18 to 50 years age.		

Annexure-II

List of 08 case of Clinical Trial proposal of GCT along with evaluations and recommendations of the Technical Committee in 32nd Meeting.

Proposal No.	Details of the proposal	Assessment of the Proposal *vis – a vis* specified Parameters	Recommendation 1. Subject Expert Committee 2. Technical Committee
1.	**Name of the Drug:** Insulin degludec/liraglutide **Protocol No**: NN9068-4228 **Applicant Name and Address**: Novo Nordisk India Private Ltd, Plot No. 32, 47 - 50, EPIP Area, Whitefield, Bangalore -560 066, Karnataka, India. **Sponsor Name and Address**: Novo Nordisk India Private Ltd, Plot No. 32, 47 - 50, EPIP Area, Whitefield, Bangalore -560 066, Karnataka, India. **Manufacturer Name and Address**: Novo Nordisk A/S, Novo Allé, DK-2880, Bagsværd, Denmark **Title:** A 104 week clinical trial comparing long term glycaemic control of insulin degludec/ liraglutide (IDegLira) versus insulin glargine therapy in subjects with type 2 diabetes mellitus.	**Risk vs Benefit to the patients:** In light of the fact that the test drugs are already approved and marketed in India, justify the conduct of the study. **Innovation *vis a vis* against existing therapy:** The purpose of the study is to compare the long term glycaemic control of insulin degludec/liraglutide (IDegLira) versus insulin glargine therapy in subjects with type 2 diabetes mellitus. **Unmet need-** The test may provide alternate treatment option for insulin naïve subjects with T2DM inadequately controlled with oral antidiabetic drugs.	**1. Subject Expert Committee on 22-03-2016** After detailed deliberation the committee recommended the conduct of the study with the following condition 1. The doses of any OADs to be used during the trial needs to be clearly defined. Accordingly India specific Annexure to the protocol must be submitted to CDSCO. (Dr. Rajesh Rajput did not take part in decision making). **2.Recommendation of the Technical Committee** After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of the study.
2.	**Name of the Drug:** BIAsp 30 **Protocol No:** BI-ASP-4200	**Risk vs Benefit to the patients:** In light of the fact that the test drug is already approved and marketed in India, justify the conduct of the study.	**1. Recommendation of the SEC Committee 22.03.2016:** After detailed deliberation the committee recommended the conduct of the trial with the

	Phase of the study: Phase IV **Name of the Applicant:** Novo Nordisk India Private Ltd, Plot No. 32, 47 - 50, EPIP Area, Whitefield, Bangalore -560 066, Karnataka, India. **Name of the Sponsor:** Novo Nordisk India Private Ltd, Plot No. 32, 47 - 50, EPIP Area, Whitefield, Bangalore -560 066, Karnataka, India. **Name of the Manufacturer:** Novo Nordisk A/S, Novo Allé DK-2880, Bagsværd, Denmark **Title:** A 24-week, multinational, multicentre, randomised, open label, parallel-group treat-to-target trial to compare efficacy and safety of thrice daily versus twice daily NovoMix® 30 (Biphasic insulin aspart 30) in subjects with type 2 diabetes inadequately controlled with basal insulin.	**Innovation vis a vis against existing therapy:** The purpose of the study is to compare efficacy and safety of thrice daily versus twice daily NovoMix® 30 (Biphasic insulin aspart 30) in subjects with type 2 diabetes inadequately controlled with basal insulin. **Unmet need:** More safety data will be generated from this study.	condition that the ICF should be able to take three meals during the trial and any exception should be excluded from the trial. Subject with impaired Kidney function should be excluded from the study as subjects should be receiving OADs. **2.Recommendation of the Technical Committee** After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of the study.
3.	**Name of the Drug:** Levofloxacin,Ethionamide, Cycloserine, Ethambutol, etc. **Protocol No:** ISRCTN 78372190 **Phase of the study:** Phase IIIb **Name of the Applicant:** National Institute for Research in Tuberculosis ,	**Risk Versus Benefit to the Patients:** In light of the fact that the test drugs are old drugs and already marketed in the country, the safety profile of the test drugs justify the conduct of the trial. **Innovation vis-a-vis Existing Therapeutic Option:** The purpose of the study is the evaluation of a standard treatment regimen of antituberculosis drugs for patients with MDR-TB for	**1. Recommendation of the SEC Committee on 18.01.2016:** After detailed deliberation the committee noted that in a previous trial STREAM Stage 1, the applicant was asked to submit the safety data of moxifloxacin 800 mg. The applicant withdrew the proposal (STREAM Stage 1). Now the applicant presented the protocol for STREAM Stage 2.

	Chennai **Name of the Sponsor:** The International Union Against Tuberculosis and Lung Disease (The Union North America) **Title:** STREAM The evaluation of a standard treatment regimen of anti-tuberculosis drugs for patients with MDR-TB- for shortening of MDR-TB treatment.	shortening of MDR-TB treatment. **Unmet Medical Need in the Country:** The test drugs may potentially provide alternate treatment regimens/ option in patients with MDR-TB	During the presentation the applicant provided DSMB report which indicated that there is no major safety concern in STREAM Stage 1 trial wherein 154 patients are on 800 mg of moxifloxacin. After detailed deliberation the committee recommended conduct of the STREAM Stage 2 trial with following condition- 1. The no. of subject randomized to receive dose of 600 and 800 mg moxifloxacin should not exceed 10 for each dose. After 4 weeks of treatment with these doses, the applicant should present the safety data. After reviewing the data by the committee, decision for further enrolment in these doses will be considered while the treatment for already enrolled subject may be continued per protocol. **2.Recommendation of the Technical Committee** After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of the study.
4.	**Name of the Drug:** Lopinavir/ritonavir **Protocol No:** P1115 **Phase of the study:** Phase I/II **Name of the Applicant:** Dr.Sandhya Khadse,	**Risk Versus Benefit to the Patients:** In light of the fact that the test drugs are old drugs and already marketed in the country, the safety profile of the test drugs justify the conduct of the trial. **Innovation vis-a-vis Existing Therapeutic Option:** The primary objective of the study is to assess HIV remission among	**1. Recommendation of the SEC Committee 18.01.2016:** After detailed deliberation the committee recommended the conduct of the study with the following conditions- 1. Adverse events should be closely monitored. 2. Children permanently

	Professor & Head, Dept. of Pediatrics, B J Govt. Medical College & Sassoon General Hospitals, Pathology Museum, First Floor, Jai Prakash Narayan Road, Pune-411001. Maharashtra **Name of the Sponsor:** B J Government Medical College & Sassoon General Hospitals Clinical Research Site Pathology Museum First Floor, Jai Prakash Narayan Road, Pune-411001. Maharashtra **Name of the Manufacturer:** AbbVie Ltd, Barceloneta, PR 00617 for AbbVie Inc., North Chicago, IL 60064 USA **Title:** Very Early Intensive Treatment of HIV-Infected Infants to achieve HIV Remission: A Phase I/II Proof of Concept Study	HIV-infected neonates who initiate ART within 48 hours of birth. **Unmet Medical Need in the Country:** The study will provide essential data on whether early combination of antiretroviral therapy for high risk infants would achieve cure	discontinued from the study should be provided treatment/ referred to the NACO centre. **2. Recommendation of the Technical Committee** After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of the study.
5.	**Name of the Drug:** Sofosbuvir **Protocol No:** **GS-US-334-1112** **Phase of the study:** Phase II **Name of the Applicant:** Klinera Corporation India, 401 Hillview Industrial Estate, LBS Marg, Ghatkopar (West), Mumbai 400086.	**Assessment of Risk vs. Benefit to the patients:** In light of the fact that the test drug is already approved and marketed in India , the safety profile of the test drug justify the conduct of the trial. **Innovation vis-à-vis Existing Therapeutic Option:** The purpose of the study is to investigate the safety and efficacy of Sofosbuvir + Ribavirin in Chronic HCVinfected pediatric subjects. **Unmet Medical Need in the**	**1. Recommendation of the SEC Committee held on 06-11-2015** After detailed deliberation the committee opined the following- 1. Proposed sites should have pediatricians as principal investigator. 2. Data of PK studies in children, that have been already completed, should be made available, in particular of children age below 12 years. This is particularly because a fixed

	Name of the Sponsor: Gilead Sciences, Inc. 333 Lakeside Drive Foster City, CA 94404, USA. **Name of the Manufacturer:** Patheon, Inc. Mississauga, Ontario L5N 7K9, Canada. Metrics, Inc. 1240 Sugg Parkway, Greenville, 27834, USA. **Title:** A Phase 2, Open-Label, Multicenter, Multi-cohort, Single-Arm Study to Investigate the Safety and Efficacy of Sofosbuvir + Ribavirin in Adolescents and Children with Genotype 2 or 3 Chronic HCV Infection.	**country:** The test drug may potentially provide alternative treatment option in chronic HCV-infected pediatric subjects	dose is sought to be used for a large age range. Also, the presenter could not inform the dose that is to be used for 3 to < 6 years of age. The committee agreed to allow the trial in children aged 12 to <18 years of age using 400 mg per day of sofosbuvir.. **Recommendation of the SEC Committee held on 19-04-2016** After detailed deliberation the on the justification and data now furnished, the committee recommends the conduct of the trial in children aged 6-12 yrs (Cohort 2). However the committee did not recommended the conduct of the trial in children aged less than 6 yrs (Cohort 3) **2. Recommendation of the Technical Committee** After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of the study.
6.	**Name of the Drug:** BI 695502 **Protocol No:** 1302.5 **Phase of the study:** Phase III **Name of the Applicant:** Boehringer Ingelheim India Private Limited 1102, 11th Floor Hallmark Business Plaza, Gurunanak Hospital	**Assessment of Risk vs. Benefit to the patients:** The safety profile of the study drug from preclinical repeat dose toxicity and phase I clinical study justify the conduct of this study. **Innovation vis-à-vis Existing Therapeutic Option:** The purpose of the study is to evaluate efficacy and safety of BI 695502 plus chemotherapy versus Avastin® plus chemotherapy in patients with	**1. Recommendation of the SEC Committee on 15-03-2016:** After detailed deliberation the committee recommended the conduct of the protocol version no- 04 dt 19/02/16. The committee felt that it is appropriate for the applicant to submit data of at-least 100 subjects from India for consideration of MA at a later

	Road Near Gurunanak Hospital, Bandra East, Mumbai –400 051, INDIA **Name of the Sponsor:** Boehringer Ingelheim India Private Limited on behalf of Boehringer Ingelheim International GmbH **Name of the Manufacturer:** Boehringer Ingelheim Pharma GmbH & Co KG Birkendorfer Strasse 65, 88397 Biberach/Riss., Germany **Title:** A multicentre, randomized, double-blind Phase III trial to evaluate efficacy and safety of BI 695502 plus chemotherapy versus Avastin® plus chemotherapy in patients with advanced nonsquamous Non-Small Cell Lung Cancer (nsNSCLC)	advanced non squamous NonSmall Cell Lung Cancer (nsNSCLC). **Unmet medical need in the country** Multisource availability of Bevacizumab may benefit Indian patients	date. **2.Recommendation of the Technical Committee** After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of the study.
7.	**Name of the Drug:** Rifampicin, Levofloxacin, Ethambutol, Pyrazinamide, Isoniazid. **Protocol No:** IRB00051196 **Phase of the study:** Phase I/II **Name of the Applicant:** Dr. Bella D, National Institute for Research in Tuberculosis, Chennai **Name of the Sponsor:** National Institute for Research in Tuberculosis,	**Risk versus Benefit to the patients-** In light of the fact that the test drugs are old drugs and marketed in India, the safety profile of the test drugs justify the conduct of the trial. **Innovation vis a vis existing therapeutic option-** The purpose of the study is to evaluate the Pharmacokinetic, Safety and Treatment outcomes of multidrug Treatment including high dose Rifampicin with or without Levofloxacin versus standard treatment for Paediatric Tuberculous Meningitis. **Unmet need-** The test drug may be an alternative treatment option for Pediatric Tuberculous	**1. Recommendation of the SEC Committee on 26.10.2015:** The applicant presented justification for inclusion of Arm 2. After detailed deliberation, the committee did not agree with the justification presented for the following reasons-. 1. No study has been done in India in adults with high dose of Rifampicin + Levofloxacin or high dose of Rifampicin alone. 2. No literature in support of high dose of Rifampicin + Levofloxacin or high dose of Rifampicin alone was presented.

	Chennai **Name of the Manufacturer:** Macloeds Pharmaceuticals Limited, Plot No. 25-27, Survey No. 366, Premier Industrial Estate, Kachigam, Daman-396210 (U. T.), India. **Title:** A Phase I/II Randomized, Open-label Trial to Evaluate the Pharmacokinetics, Safety, and Treatment Outcomes of Multidrug Treatment Including High Dose Rifampicin with or without Levofloxacin versus Standard Treatment for Pediatric Tuberculous Meningitis	Meningitis.	3. No trial has been conducted with high dose of Rifampicin + Levofloxacin or high dose of Rifampicin alone so far in children anywhere. Hence the committee did not recommend to include ARM 2 at this stage. The study should be conducted with ARM 1 and ARM 3 of the proposed protocol as recommended by the committee on 22-06-2015. **2. Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended that the matter may be re-deliberated by SEC comprising of following additional experts: 1. Dr. Rohit Sarin, Department of TB & Respiratory Diseases, Delhi 2. Dr. K. S. Sachdeva, TB Division Nirman Bhawan Delhi. 3. Dr. S K Sharma, AIIMS Delhi 4. Dr. Behera, PGIMER, Chandigarh
8.	**Name of the Drug:** Rifampicin, Levofloxacin, Ethambutol, Pyrazinamide, Isoniazid. **Protocol No:** IRB00051196 **Phase of the study:** Phase I/II **Name of the Applicant:** Dr. Aarti Kinikar, MD ,Associate Professor, Pediatric Department, B J Government Medical College& Sassoon General	**Risk versus Benefit to the patients-** In light of the fact that the test drugs are old drugs and marketed in India, the safety profile of the test drugs justify the conduct of the trial. **Innovation vis a vis existing therapeutic option-** The purpose of the study is to evaluate the Pharmacokinetic, Safety and Treatment outcomes of multidrug Treatment including high dose Rifampicin with or without Levofloxacin versus standard treatment for Paediatric Tuberculous Meningitis.	**1. Recommendation of the SEC Committee on 26.10.2015:** The applicant presented justification for inclusion of Arm 2. After detailed deliberation, the committee did not agree with the justification presented for the following reasons-. 1. No study has been done in India in adults with high dose of Rifampicin + Levofloxacin or high dose of Rifampicin alone. 2. No literature in support of high dose of Rifampicin + Levofloxacin or high dose of

	Hospitals, Pune B J Government Medical College & Sassoon General Hospitals, Pathology Museum, First Floor, Jai Prakash Narayan Road, Pune - 411001, Maharashtra. **Name of the Sponsor:** B J Government Medical College & Sassoon General Hospitals Clinical Research Site B J Government Medical College & Sassoon General Hospitals, Pathology Museum, First Floor, Jai Prakash Narayan Road, Pune- 411001, Maharashtra **Name of the Manufacturer:** Macloeds Pharmaceuticals Limited, Plot No. 25-27, Survey No. 366, Premier Industrial Estate, Kachigam, Daman-396210 (U. T.), India. **Title:** A Phase I/II Randomized, Open-label Trial to Evaluate the Pharmacokinetics, Safety, and Treatment Outcomes of Multidrug Treatment Including High Dose Rifampicin with or without Levofloxacin versus Standard Treatment for Pediatric Tuberculous Meningitis.	**Unmet need-** The test drug may be an alternative treatment option for Pediatric Tuberculous Meningitis.	Rifampicin alone was presented. 3. No trial has been conducted with high dose of Rifampicin + Levofloxacin or high dose of Rifampicin alone so far in children anywhere. Hence the committee did not recommend to include ARM 2 at this stage. The study should be conducted with ARM 1 and ARM 3 of the proposed protocol as recommended by the committee on 22-06-2015. 2.**Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended that the matter may be re-deliberated by SEC comprising of following additional experts: 1. Dr. Rohit Sarin, Department of TB & Respiratory Diseases, Delhi 2. Dr. K. S. Sachdeva, TB Division Nirman Bhawan Delhi. 3. Dr. S K Sharma, AIIMS Delhi 4. Dr. Behera, PGIMER, Chandigarh

Annexure III

List of 06 cases of clinical trial proposals other than GCT/NCEs along with evaluations and recommendations of 32nd Meeting.

Sl No	Name of the Drug	Firm Name	Recommendations: 1. Subject Expert Committee 2. Technical Committee
1.	Typhoid Vi capsular polysaccharide tetanus toxoid conjugate vaccine.	M/s Cadila Healthcare Limited.	**1. Recommendation of the SEC dated 12.01.2016:** The Committee deliberated the proposal in detail and recommended it with the following conditions:- 1. Subjects will be equally divided in the two age groups i.e 6 months to 17 years and 18 to 45 years. 2. Enrollment for the younger age group (6 months to 17 years) will start only after full enrollment and also completion of 21 days follow up of adult cohort (18 to 45 years). Accordingly, the firm should submit the revised protocol. The firm submitted revised protocol incorporation the recommendation of SEC. **2. Recommendation of the Technical Committee** After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of the study.
2.	Pregabalin and Amitriptyline tablets	M/s Sun Pharma Laboratories Limited.	**1. Recommendation of the SEC dated 14.07.2015:** The Committee noted that firm has complied with all the recommendation of the committee as suggested on 29.11.2014. The Committee recommended for conducting clinical trial. The Committee also opined that Neurosurgeon in this study as a principle investigator shall be replaced appropriately as per the study requirement. However the report of the study shall be placed before the Committee. The firm submitted the revised data. **2. Recommendation of the Technical**

			Committee After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of the study.
3.	Azelnidipine 16mg and Metoprolol Succinate extended release 50mg capsules	M/s Glenmark Pharmaceuticals Limited.	**1. Recommendation of the SEC dated 26.02.2016:** The firm presented the revised protocol after incorporating the recommendation made by this Committee in its earlier meeting. The Committee deliberated the proposal in detail and observed that all the necessary changes have been made and therefore, recommended grant of permission for conduct of clinical trial as per the presented protocol. **2. Recommendation of the Technical Committee** After detailed deliberations, the Committee requested to place before it the approved indication for Azelnidipine and also clarification whether monotherapy is intended to be used in mild, moderate or severe hypertension for taking decision in this regard.
4.	Ranibizumab	M/s Lupin Limited.	**1. Recommendation of the SEC dated 18.02.2016:** Firm presented the Phase III clinical trial protocol, after detail deliberation the Committee approved the study protocol with following:- 1. The investigator will follow the guidelines framed by All India Ophthalmological Society and Vitero Retinal Society of India for the procedure of intra-vitreal administration of drug. **2. Recommendation of the Technical Committee** After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of the study.

5.	Clotrimazole Troche / Lozenges	M/s Thinq Pharma-CRO Limited.	**1. Recommendation of the SEC dated 21.03.2016:** M/s Thinq Pharma-CRO Limited on behalf of the sponsor M/s Unique Pharmaceutical Laboratories presented the protocol to conduct Phase III, a multicentre, randomized, double-blind, parallel group, comparative clinical trial to evaluate the safety and clinical equivalence to generic Clotrimazole Troche / Lozenges USP, 10mg (M/s Unique Pharmaceuticals Laboratories, India) to Clotrimazole Troche / Lozenges 10mg (Roxane Laboratories Inc., USA) in subjects with Oropharyngeal Candidiasis before the Committee. After detailed deliberation, committee approved the protocol with the following suggestion:- 1. Patients who are resistant to Clotrimazole after culture and sensitivity test have to be excluded from the study. **2. Recommendation of the Technical Committee** After detailed deliberation, the Committee agreed with the recommendation of the SEC and recommended for the approval of the study.
6.	Glycopyrronium 12.5 mcg and Formoterol Fumarate 12 mcg Powder for Inhalation.	M/s Glenmark Pharmaceuticals Limited.	**1. Recommendation of the SEC dated 29.03.2016 :** The firm has given presentation on the proposed CT protocol of the FDC. After detailed deliberation, the committee opined that both the individual drugs of the FDC is already approved. Therefore, the committee recommended to conduct the study with the conditions that the protocol should include ophthalmic assessment (IOT) and assessment of urinary retention at baseline, in the middle and lastly at the end visit. **2. Recommendation of the Technical Committee** After detailed deliberation, the Committee

			agreed with the recommendation of the SEC and recommended for the approval of the study.

Annexure-IV

Recommendations of the 05 cases of Clinical trial waiver in Indian populations of 32nd meeting:

Sr. no.	Drug Name	Name of the Firm	Indication	1. Recommendations of the SEC. 2. Recommendations of the Technical Committee
1.	Travoprost Ophthalmic Solution 0.003%w/v (IZBA) with preservative Polyquaternium 0.001 w/v.	M/s Alcon labs India Pvt. Ltd.	Decrease of elevated intraocular pressure in adult patients with ocular hypertension or open-angle glaucoma.	**1. Recommendation of SEC dated 14-01-2016:** The committee observed that in-view of the fact that Travoprost ophthalmic solution 40mcg/ml is already approved for use in India with good clinical safety and efficacy profile, and the earlier trial has showed a similar response in Indian subjects as compared to other subjects globally, and also that the reduced strength of 30mcg/ml may decrease the long term cumulative side effects of the drug, the committee recommended import and marketing of Travoprost ophthalmic solution 30mcg/ml with polyquaternium 0.001% w/v. Further the committee also noted that the said product is already approved in US and EU. This approval is subject to condition that a phase IV clinical trial in atleast 500 Indian subjects be carried out within one year of approval. 2. **Recommendations of the Technical Committee:** After detailed deliberations, the Committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
2.	Midodrine Hydrochloride 2.5 mg Tablet.	M/s Gurmail Brothers	For the treatment of Orthostatic dysregulation and Hypotension and	**1. Recommendation of SEC dated 26.02.2016** The firm has applied for permission to import and

			Neurogenic Hypotension	market Midodrine Hydrochloride 2.5 mg tablets for the indication of orthostatic dysregulation and hypotension, neurogenic hypotension and requested for waiver of local clinical trial. The firm presented the proposal in detail. The Committee observed that the drug is approved in several other countries including USFDA (as an Orphan drug in 1996). The firm presented that there is no satisfactory drug therapy available for proposed indication in the country. After detailed deliberation, the Committee recommended for granting permission for import and marketing of the drug with local clinical trial waiver subject to the condition that the firm shall conduct active surveillance as part of PMS of 200 patients and the data should be submitted to the office of DCG (I). **2. Recommendations of the Technical Committee:** After detailed deliberations, the Committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
3.	Nivolumab 10 mg/mL concentrate solution for infusion: 40 mg and 100 mg.	M/s Bristol-Myers Squibb India Private Limited,	For the treatment of Non Small Cell lung Cancer (NSCLC) and renal Cell Carcinoma (RCC).	**1. Recommendation of SEC dated 23.02.2016:** After detailed deliberation, committee recommended for the marketing authorization to import and market in India for the indications applied for, with waiver of local clinical trial, in view of non-availability of any standard effective treatment for the mentioned indications in

				India. The firm may be directed to conduct the phase IV clinical trial and shall submit the protocol for it within six months of marketing of drug in India. 2. **Recommendations of the Technical Committee:** After detailed deliberations, the Committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
4.	Ramucirumab, Concentrate for Solution for Infusion 10mg/mL (100mg/10mL vial and 500mg/50mL vial	M/s Eli Lilly and Company (India) Pvt. Ltd	For the treatment of gastric cancer and non-small cell lung cancer.	**1. Recommendation of SEC dated 19.01.2016:** The firm has presented the global clinical trial data of the studies of REGARD, RAINBOW and REVEL. After detailed deliberation the committee opined that the drug is indicated for second line therapy of Gastric Cancer and Non Small cell lung cancer. The drug has already been approved by USFDA & EMA for the indications of Gastric Cancer, and by USFDA for lung cancer. The firm also presented the detail safety data of 79 Indian patients who participated in REGARD and REVEL trial; no specific adverse safety signals were observed in Indian patients. Therefore the committee opined that marketing authorization for Ramucirumab may be granted for both indications. **2. Recommendations of the Technical Committee:-** After detailed deliberations, the Committee agreed with the

				recommendation of the SEC and recommended for waiver of local clinical trial.
5.	Pembrolizumab Injection (25mg/ml solution in a single use vial: 100mg/4ml).	M/s MSD Pharmaceuticals Pvt. Ltd.	For the treatment of patients with unresectable or metastatic melanoma.	**1. Recommendation of SEC dated 24.11.2015:** After detailed deliberation, committee opined that, Pembrolizumab is an orphan drug and it was approved in USA and some other countries. In view of the above, the SEC opined that the permission for import and marketing may be granted to the firm with the waiver of local clinical trial with the condition of conducting Phase IV study in Indian patients. Further the firm should submit the data at 12 months from the date of approval of the phase-IV protocol. **2. Recommendations of the Technical Committee:-** After detailed deliberations, the Committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.

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