**MINUTES OF 21st MEETING OF THE TECHNICAL COMMITTEE HELD ON 21.01.2015 UNDER THE CHAIRMANSHIP OF DGHS FOR SUPERVISING CLINICAL TRIALS ON NEW CHEMICAL ENTITIES IN THE LIGHT OF DIRECTIONS OF THE HON'BLE SUPREME COURT OF INDIA ON 03.01.2013.**

**Present:**

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| 1. | Dr. Jagdish Prasad,<br>Director General of Health Services | Chairman |
| 2. | Dr. Nandini Kumar,<br>Former Dy. Director (Sr. Grade)<br>National Institute of Epidemiology,<br>ICMR, New Delhi | Member |
| 3. | Dr. Kamlakar Tripathi,<br>Prof., Dept. of Medicine,<br>Institute of Medical Sciences,<br>Banaras Hindu University, Varanasi – 221005. | Member |
| 4. | Dr. Nikhil Tandon,<br>Professor, Dept. of Endocrinology<br>& Metabolism, AIIMS, New Delhi | Member |
| 5. | Dr. Yash Paul,<br>Prof. & Head, Dept. of Cardiology,<br>PGIMER, Chandigarh. | Member |
| 6. | Dr. B.L Shrerwal, Additional Medical Supdt.<br>Director-Professor, LHMC, Delhi | Member |

**Special Invitees:**

1. Dr. Rohit Sarin,
   LRS Instituted of Tuberculosis and Respiratory Disease, Sri Aurobindo Marg,New Delhi.

2. Dr. Niraj Kulsheshtra,
Addl. DDG(TB), DGHS, New Delhi
(For proposal of anti-TB drug)

3. Dr. Rohit Saxena,
Associate Professor of Ophthalmology, AIIMS, New Delhi
(For proposal of ophthalmology drug)

**From CDSCO:**

1. Dr. G.N Singh
Drugs Controller General of India

2. Dr.V.G.Somani,
Joint Drugs Controller (India)

3. Mrs. A Visala
Deputy Drugs Controller (India)

4. Mrs. Rubina Bose
Asst. Drugs Controller (India)

5. Mr. Sanjeev Kumar
Asst. Drugs Controller (India)

Dr. G.N Singh, DCG (I) welcomed the members of the meeting and thereafter, Dr. V.G. Somani, JDC (I) with the permission of the Chairman, initiated the proceeding of the Committee as per the agenda.

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

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

The Committee deliberated 29 cases related to approval of clinical trials. Out of these 29 cases, 03 cases (including 01 case of protocol amendment) were related to clinical trials of NCEs and 04 cases (including 02 cases of protocol amendment) were related to global clinical trials (GCT). Remaining 22 cases were related to clinical trials for approval of New Drugs including fixed dose combination, Medical Devices and biologicals. Out of these 22 cases, one case was for re-deliberation (S.No 04 of the Annexure-II).

The Committee evaluated the 03 cases related to NCEs and 04 cases related to global clinical trials one by one and made recommendations considering all aspects of safety, efficacy especially in terms of the three parameters viz. risk versus benefit to the patients, innovation *vis-a-vis* existing therapeutic option and unmet medical need in the country. After detailed deliberations, the Committee recommended approval of all 07

cases. The recommendations of the Committee in respect of these 07 cases are enclosed as **Annexure-I.**

The Committee also evaluated the remaining 22 cases which were other than GCT/clinical trial of NCEs. After detailed deliberation, the Committee recommended for approval of 21 out of 22 cases. Out of approved 21 cases, in one case (S.No 02 of Annexure-II), the Committee recommended the conduct of trial subject to certain condition. In case of S.No.04 of Annexure-II, the Committee has recommended to conduct additional preclinical study before considering the permission for clinical trial. The recommendations of the Committee in respect of these 22 cases are enclosed as **Annexure-II.**

Thus out of total 29 cases of clinical trial proposals, the Committee recommended for approval of 28 cases.

The Committee recommended that the cases of protocol amendment shall not be placed before the Committee except in cases of major protocol amendment of NCEs. The cases of major protocol amendment of NCEs shall be placed with the reasons and justification for placing it before the Committee.

Similarly, the cases of BA/BE studies of other than NCEs which are not for the purpose of new drug approval for marketing in India also shall not be placed before the Committee.

The Committee further recommended that the cases of phase-IV clinical trials which are not meant for purpose of approving new indication or new modification as per rule, shall usually not be placed before the Committee.

The CDSCO shall dispose off above mentioned cases (which are not required to be placed before the Committee) of protocol amendment, BA/BE studies, phase-IV trials at their level as per rules.

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

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

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

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

As per Clause 1(3) of Schedule Y to Drugs & Cosmetics Rules, for drugs indicated in life threatening / serious diseases or diseases of special relevance to the Indian health scenario, the toxicological and clinical data requirements may be abbreviated, deferred or omitted, as deemed appropriate by the Licensing Authority.

It would be thus observed that there are certain conditions specified in the Drugs & Cosmetics Rules under which the licensing authority may grant permission to manufacture / import of new drugs without local clinical trials.

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

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

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

Following proposal from New Drug has been recommended by the SECs for their approval for manufacture/ import for marketing in the country without local clinical trial. The details of the same alongwith recommendations of SEC are placed before the Committee for perusal and comments: The recommendation of the Technical Committee is as under:

| Sr. no. | Drug Name | Indication | Recommendations |
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| 1. | Treosulphan Injection 5g/vial | Indicated to treat ovarian cancer, bone-marrow ablation before stem-cell transplantation, to treat malignant melanoma, and breast cancer. | After detailed deliberation, the Committee recommended for waiver of local clinical trial as per recommendation of SEC for the indication "bone marrow ablation before stem cell transplantation" which is a rare indication.<br>**SEC Recommendation:** The application is for the grant of permission to manufacture and market of Treosulphan Injection 5g/vial indicated to treat ovarian cancer, bone marrow ablation before stem-cell transplantation, to treat malignant melanoma, and breast cancer. The drug is reported to have been approved in EU and was given orphan drug status "in the conditioning treatment prior to hematopoietic progenitor cell transplantation" by EMEA on 22.11.2004.<br>The firm has requested for the waiver of requirement |

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| | | | of conducting local clinical trial in Indian subjects.<br>The Committee deliberated the matter in detail. The Committee observed that there are alternative treatment options for other indications except for the indication "bone-marrow ablation before stem-cell transplantation". The Committee agreed that the bone marrow ablation before stem cell transplantation is rare indication and qualifies for orphan status. Hence, the Committee recommended for the local trial waiver subject to the condition that a Pharmacokinetic study in not less than 12 patients should be conducted and the results should be presented before the committee for evaluation |

## 3. Others:

**a) Proposal of Dr. P V Dave for grant of permission to conduct a study entitled " A clinical trial to study the efficacy safety and operational feasibility, of administration of single dose of Rifampicin as chemoprophylaxis in the contact of leprosy patients in the Union Territory of D & N Haveli,"**

Dr. P V Dave, Additional Director of Health Services, Gujarat submitted an application to conduct clinical study on "Operational feasibility of administration of single dose of Rifampicin as chemoprophylaxis in the contact of leprosy patients in the Union Territory of D & N Haveli, India" to the office of DCG (I),

This application alongwith protocol was deliberated in Subject Expert Committee meeting (Antimicrobial, Anti-parasitic & Antifungal, Antiviral) held on 08.12.2014 and it was opined by the SEC experts that the protocol of the study is not clear whether it is for chemoprophylaxis or treatment of latent leprosy. There is no follow up in this study to know the efficacy of drug and the adverse events. The revised protocol along with informed consent documents explaining clearly the purpose of the study should be submitted to SEC for examination.

Therefore, for further deliberation on grant of permission for this clinical study, as per directions of DGHS, a meeting was held on 23rd December, 2014 at 11:00 A.M. in the chamber of DGHS under the Chairmanship of DGHS where members of SEC (Antimicrobial, Anti-parasitic & Antifungal, Antiviral) along with invited experts from Government Medical Colleges/Institutes were present. (List of Experts is enclosed as Annexure A). The proposal was presented by Dr. M A Arif, Co-investigator of the clinical study, on behalf of Dr. P V Dave, Principal Investigator to the experts group and the following action points were summarised:-

- In response to the queries raised by the experts of SEC, it was clarified by the applicant that the primary objective of the clinical study is to study the use of

Rifampicin as Chemoprophylaxis in contacts of leprosy. This was also clarified that the study will be conducted as a study under the ongoing National Leprosy Eradication Programme.

- Therefore, it was considered as a clinical trial by this Committee and the protocol was revised, specifically to mention the following:-

1. To study the efficacy and safety in addition to operational feasibility as objective of this trial.
2. The control group in the study.
3. Follow up procedures of adverse events.

It was further mentioned that in India, use of single dose of Rifampicin as chemoprophylaxis in healthy contacts of leprosy patients is a new health intervention, of which the efficacy was already tested elsewhere e.g. Bangladesh and Indonesia. The primary objective of the clinical study is to ascertain the efficacy and safety of administration of single dose of Rifampicin as chemoprophylaxis in the healthy contacts of leprosy patients and the secondary objective of the study is to ascertain the operational feasibility of administration of single dose of Rifampicin as chemoprophylaxis in the contact of leprosy patients in Indian context. Based on the evaluation and detailed deliberation, all the members felt that the present clinical study for use single dose of Rifampicin as chemoprophylaxis in leprosy is useful in national interest as it is special health scenario in India, hence, recommended for grant of permission for this clinical study.

**Recommendation:** After deliberation, the Committee recommended the proposed clinical study of single use of Rifampicin as chemoprophylaxis in the contact of leprosy patients as the Committee observed that the study is useful in national interest in the context of special health scenario in India.

**b) "Request by M/s BJ Medical College to reconsider the study entitled "P 1078 – TB APPRISE, A Phase IV randomised double blind placebo controlled trial to evaluate the safety of immediate (antepartum initiated) versus deferred (post-partum initiated) Isoniazid preventive therapy among HIV infected women in high TB incidence settings"**

It may please be informed that the proposal was examined by the Subject Expert Committee (SEC), Technical Committee and Apex Committee and the trial was not recommended. The details of the deliberations by these Committees are given below:-

**(1) Consideration of proposal by Subject Expert Committee (SEC):-**

The proposal was deliberated in the meeting of 10th NDAC (since renamed as Subject Expert Committee) held on 28.02.2014 for consideration the applications for clinical trials relating to Antimicrobial, Antiparasitic, Antifungal and Antiviral. During the meeting to deliberate the clinical trial on anti-TB drugs the following experts were also invited

(1) Dr. Sach Deva, Central TB Division, MoHFW

(2) Dr. Mayank Ghedia, Central TB Division, MoHFW

(3) Dr. Lakshmana Bharathi, NACO, DAC, MoHFW

The Committee after deliberations recommended as under:-

***'M/s BJ Medical College, Pune (Dr. Ramesh A Bhosale) requested for permission to conduct a phase IV clinical trial with Isoniazid tablets as preventive therapy among HIV-infected women in high TB prevalence settings. There is a concern about treatment of latent TB infection in India as there is an increased load of active TB cases in India. Furthermore, patients with active TB may be mistakenly treated as LTBI and this will further amplify the problem of drug resistance. The NDAC after deliberation has not recommended for the conduct of the proposed clinical trial'.***

**(2) Further reconsideration of proposal by SEC:-**

Based on appeal by the applicant, the case was reconsidered in 12th SEC (NDAC) – Antimicrobial, Antiparasitic, Antifungal and Antiviral meeting held on 25.07.2014 wherein the Committee opined that

1) ***'Small number of patients is proposed to be recruited in India, out of which some may receive placebo. The data generated out of this study would be of no benefit in Indian context.***
2) ***This study design of this trial is not in concurrence with current guidelines of NACO and RNTCP. Therefore the committee did not recommend for the conduct of the study.'***

**(3) Consideration of proposal by Technical Committee:-**

The proposal was then placed before the Technical Committee along with the recommendations of the SEC in the **19th Technical Committee** meeting held on

17.11.2014, wherein the applicant and following experts were also invited for deliberation of the proposal along with the Technical Committee experts:

1. Dr. Rohit Sarin, Director, NITRD, MoHFW
2. Dr. Gupta, DDG(TB – Division), MoHFW
3. Dr. Rita Prasad, NACO, MoHFW

***The Committee agreed with the recommendations of the SEC and did not recommend the conduct of clinical trial.***

**(4) Consideration of proposal by Apex Committee:-**

The proposal was then deliberated in **18th Apex Committee** meeting held on 25.11.2014, wherein ***Committee agreed with the recommendations of Technical Committee***.

**(5) Request for Reconsideration by BJ Government Medical College,:**

Thereafter the Investigator has changed the protocol by increasing the sample size from 25 to more than 100 and also given the justification that how this study is useful for India by referring to NACO, TRG group meeting, RNTCP programme and screening Committee of Health Ministry's recommendations and represented the matter to DCG(I). DCG (I) referred the representation to DGHS, Chairman of Technical Committee, who in turn decided to call the experts of Tuberculosis division in the Technical Committee for consideration of the revised proposal.

Accordingly following experts have attended the meeting:

1. Dr. Rohit Sarin, LRS Instituted of Tuberculosis and Respiratory Disease, Sri Aurobindo Marg,New Delhi
2. Dr. Niraj Kulsheshtra, Addl. DDG(TB), DGHS, New Delhi

The revisions and justifications provided by the applicant are as following:

a. *"The study aims to find out what is the best time to start isoniazid preventive therapy (IPT) in HIV-infected women on anti-HIV medications during pregnancy and postpartum period.*
b. *The best time to start IPT among HIV-infected pregnant women is not known and is a recognised limitation in the WHO 2011 guidelines for INH in HIV-infected persons on page 7 (http://www.who.int/tb/challenges/hiv/ICF_IPTguidelines/en/).*

c. *NACO in its TRG review said that "the proposal is relevant to National Programme. IPT is proven to reduce incident TB among PLHIV and it acts in synergy with ART in decreasing incident TB to the extent of more than 90%. Both NACP and RNTCP have recently reviewed the evidence and WHO recommendations for IPT for prevention of TB among PLHIV, and is likely to implement the intervention across the country in near future. Hence information on safety of its use for TB prevention in HIV infected pregnant women would be of critical importance"*
d. *The Health ministry screening committee has already approved the study after obtaining clearance from NACO and the central TB division.*
e. *In P1078, all participants will receive IPT, half will get it during pregnancy women will receive IPT after 3 months of delivery for the women to return to baseline physiologic state after pregnancy.*
f. *We plan to enrol 100 or more Indian participants of the total 950 (at least 10% of sample) in the study and every participant will receive Isoniazid (INH) prophylactic therapy (IPT) which will generate sufficient India specific data.*

*The study will directly benefit both NACO and RNTCP as the best time to start IPT data for HIV-infected pregnant and postpartum women are currently not available anywhere in the world. This study will provide crucial data on safety, tolerability, effectiveness, and optimal timing for IPT among HIV-infected pregnant and postpartum women."*

**Recommendation:** The Committee observed that the applicant had provided adequate justification for the conduct of the study in 100 subjects and recommended for the conduct of the study.

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**Annexure-I**

**List of 07 cases of Global Clinical Trials/ clinical trials of NCEs along with their evaluations and recommendations of the Technical Committee in its 21st Meeting.**

| Sr No. | IP | Name of FIRM | PROTOCOL | Parameters<br>1. risk versus benefit to the patients<br>2. innovation vis-a-vis existing therapeutic option<br>3. unmet medical need in the country | Recommendation |
|---|---|---|---|---|---|
| 1 | Olodaterol + Tiotropium | M/s. Boehringer Ingelheim | 1237.19 | **Risk versus benefit to the patients-** The safety profile of the test drug from various pre- clinical studies including single dose, repeat dose, carcinogenicity, reproductive and development toxicity, genotoxicity and clinical phase I, II studies justify the conduct of the study.<br><br>**Innovation vis a vis existing therapeutic option-** The purpose of the study is to evaluate the effect of 52 weeks once daily treatment of orally inhaled tiotropium + olodaterol fixed dose combination compared with tiotropium in Chronic Obstructive Pulmonary Disease (COPD) exacerbation in patients with severe to very severe COPD.<br><br>**Unmet medical need in the Country-** The test drugs may provide an alternative treatment option for patients with chronic obstructive pulmonary disease. | **Recommendations**: The Committee recommended for approval as per the recommendation of the SEC<br><br>**SEC Recommendations:**<br><br>After detailed deliberation committee recommended for conduct for the trial. |
| 2. | DS-5565<br><br>**(NCE)** | M/s. INC Research | DS5565-A-E311 | **Risk versus benefit to the patients-**<br>Risk versus benefit of the test drug from various preclinical toxicity study including single dose, repeat dose, carcinogenicity, genotoxicity, reproductive and development toxicity studies, clinical phase I, II studies justify the conduct of this study.<br>**Innovation vis a vis existing therapeutic option-** The primary objective of the study is to compare change in weekly average daily pain score (ADPS) from baseline to week 13 in subjects receiving either dose of test drug versus placebo.<br>**Unmet medical need in the country -** The study drug may provide an alternative option for patients with pain associated with fibromyalgia | **Recommendations**: The Committee recommended for the conduct of trial as per the SEC recommendation subject to the condition that all the 105 subjects should be treated in hospitalized setting with complete cardiac monitoring for duration of one month. If AEs are not reported after the period of one month, trial can be |

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| | | | | | conducted on OPD basis.<br><br>**SEC Recommendations:**<br><br>After detailed deliberation the committee recommended to conduct the trial subject to the condition that-<br>1. The investigator should be Orthopaedics or rheumatologist. The team should include clinical psychiatric/psychologist for the assessment of inclusion and exclusion criteria.<br>2. The number of proposed subjects from India is 105. Considering drop out 50% as per protocol statistical analysis, therefore this cannot be applicable for marketing permission in India.<br>3. The pk rationale for trying the drug OD or BD should be provided.<br>(**Dr S K Das is the proposed PI in the subject trial hence did not take part in final decision making process)** |
| **3.** | Ticagrelor | M/s Astra Zeneca | D513BC00001 | **Risk versus benefit to the patients-** The single and repeate dose toxicity studies in mice, rats, and marmosets and clinical phase I, II and III studies justify the conduct of the proposed phase 3b study.<br><br>**Innovation vis a vis existing therapeutic option-** The objective of the study is to compare the effect of long term treatment with study drug vs placebo for the prevention | **Recommendations**: The Committee recommended for approval as per the recommendation of the SEC subject to the condition that the upper age limit should be 60 years and dose |

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| | | | | of major cardiovascular events in patients with Type 2 diabetes at high risk of cardiovascular events.<br><br>**Unmet need**- The test drug may provide benefit due to its anti-platelet action for prevention of cardiovascular events in patients with diabetes mellitus who has no medical history of previous MI or stroke. | of Aspirin should be 75 mg.<br><br>**SEC Recommendations:**<br><br>The committee opined that the unlimited age for recruitment may pose a potential risk since there is no evidence of safety in the older subject of the targeted diabetes population with the trial drug. Finally the Committee recommended to conduct the trial subject to the condition that there is an upper age limit for recruitment that is 75 yrs and the revised protocol should be submitted to CDSCO before permitting the trial. |
| **4.** | QGE031<br><br>Human monoclonal antibody against human IgE<br><br>(**NCE**) | M/s. Novartis | CQGE031B2201 | **Risk versus benefit to the patients-** The safety profile of the test drug from various preclinical studies including repeat dose, reproductive and developmental toxicity, juvenile toxicity and clinical phase I, II studies justify the conduct of the study<br><br>**Innovation vis a vis existing therapeutic option-** The purpose of the study is to investigate the efficacy and safety of 16 weeks treatment with subcutaneous QGE031 in asthma patients not adequately controlled with high dose acting beta 2 agonists.<br><br>**Unmet need-** The test drug may provide an alternate treatment option for asthma patients. | **Recommendations**:<br>The Committee recommended for approval as per the recommendation of the SEC subject to the condition that the study should be conducted only in hospitalized patients at centers with ICU setting. SAEs should be reported within statutory time lines.<br><br>**SEC Recommendations:**<br><br>After detailed deliberation committee recommended for conduct of the trial. |

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| **5.** | Idarucizumab<br><br>**(NCE)** | M/s. Boehringer Ingelheim | 1321.3 | **Risk versus benefit to the patients-** The risk vs benefit profile of test drug in preclinical toxicity studies including acute and multiple-dose intravenous studies in rats and monkeys and phase I trials justify the conduct of this study<br><br>**Innovation vis a vis existing therapeutic option-** The purpose of the study is to evaluate the reversal of the anticoagulant effects of Dabigatran by intravenous administration of 5.0 g Idarucizumab (BI 655075) in patients treated with Dabigatran etexilate who have uncontrolled bleeding or require emergency surgery or procedures.RE-VERSE-AD (A study of the RE-VERSal Effects Of idarucizumab on Active Dabigatran) trial.<br><br>**Unmet need**- The study drug may provide treatment option for the reversal of pharmacological effect of Dabigatran. | **Recommendations**: The Committee recommended for approval as per the recommendation of the SEC<br><br>**SEC Recommendations:**<br><br>The applicant has made presentation on the proposed amendments in consonance with the SEC recommendation Dt. 25.11.2014. After detailed deliberation the committee reiterated that the pregnant women and women who test positive for pregnancy should be excluded. The committee also opined that the primary objective should not be for the evaluation of "maximum reversal" but should be "reversal" of anticoagulant effect of dabigatran. Accordingly CDSCO will examine the India version protocol for consideration of approval. |
| **6.** | Treprostinil Diethanolamine | M/s Pharmaceutical Research Associates India Private Limited | TDE-PH-310 | **Risk versus benefit to the patients-** The risk vs benefit profile of the IMP from preclinical single dose and repeat dose toxicity studies and phase I, II and III clinical trials justify the conduct of this study with the sustained release dosage form.<br><br>**Innovation vis a vis existing therapeutic option-** The IMP is an innovative therapy, not because it originates from a new therapeutic class of drug, but rather due to the route of administration and the sustained release nature of the IMP.<br><br>The purpose of the study is to compare the | **Recommendations**:<br><br>The Committee recommended for approval as per the recommendation of the SEC<br><br>**SEC Recommendations:**<br><br>The committee recommended the protocol amendment. It was stressed that |

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| | | | | time to first clinical worsening of PAH in patients receiving IMP + ERA / PDE5-I therapy vs ERA/PDE5-I therapy alone.<br><br>**Unmet need**- Treprostenil SR(UT-15C) oral formulation may help pulmonary arterial hypertension patients due its once weekly dosing. | only those drugs approved in country for the treatment of PAH will be the part of the background monotherapy. |
| **7.** | Treprostinil Diethanolamine | M/s Pharmaceutical Research Associates India Private Limited | TDE-PH-311 | **Risk versus benefit to the patients-** The risk vs benefit profile of the IMP from preclinical single dose and repeat dose toxicity studies and phase I, II and III clinical trials justify the conduct of this study with the sustained release dosage form.<br><br>**Innovation vis a vis existing therapeutic option-** The IMP is an innovative therapy, not because it originates from a new therapeutic class of drug, but rather due to the route of administration and the sustained release nature of the IMP.<br><br>The purpose of the study is to compare the time to first clinical worsening of PAH in patients receiving IMP + ERA / PDE5-I therapy vs ERA/PDE5-I therapy alone.<br><br>**Unmet need**- Treprostenil SR(UT-15C) oral formulation may help pulmonary arterial hypertension patients due its once weekly dosing. | **Recommendations**:<br><br>The Committee recommended for approval as per the recommendation of the SEC<br><br>**SEC Recommendations:**<br><br>The committee recommended the protocol amendment it was stressed that only those drugs approved in country for the treatment of PAH will be the part of the background monotherapy. |

**Annexure-II**

**List of 22 cases of clinical trial proposals other than GCT/NCE along with evaluations and recommendations of the Technical Committee in 21st Meeting.**

| Sl No | Name of the Drug | Firm Name | Recommendation |
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| **1.** | Mirabegron MR tablets (50 mg) | M/s. Lupin Limited, Mumbai | The Committee recommended for proposal as per the recommendations of the SEC |
| **2.** | Prucalopride (as succinate) 1 mg and 2 mg | Torrent Pharmaceuticals Limited | The Committee recommended for conduct of the study subject to the condition that the firm shall specify the level of hemoglobin in the exclusion criteria for patients with history of anemia as not less than 12.5 gm percent for male and not less than 12 gm percent for female.<br>Accordingly, the firm shall submit revised protocol to the office of DCG (I), based on which permission may be granted for clinical trial. |
| **3.** | Investigational Device- PPIUCD inserter | Population Services International-India | The Committee recommended for the proposal as per the recommendations of the SEC. |
| **4.** | Poly Lactide-co-Glycolic Acid (PLGA) biodegradable, synthetic carrier membranes | M/s LV Prasad Eye Institute, Hyderabad, Andhra Pradesh | The committee recommended that the study should be conducted in one more animal species for duration of 6 weeks or till the duration for which the membrane under study is not visible or completely disintegrates. |
| **5.** | Dendritic Cell vaccine primed either with patient's own whole tumour lysate or using | M/s Cancer Institute (WIA) Annexe campus, 38, Sardar Patel | The Committee recommended for proposal as per the recommendations of the SEC. |
| **6.** | Autologous Adult Live Cultured Osteoblasts (OSSRON™) | M/s Regeneratie Medical Services Pvt. Ltd., Mumbai | The Committee recommended for proposal as per the recommendations of the SEC |

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| **7.** | Autologous Adult Live Cultured Chondrocytes (CHONDRON) | M/s Regeneratie Medical Services Pvt. Ltd., Mumbai | The Committee recommended for proposal as per the recommendations of the SEC. |
| **8.** | Follitropin alfa (r-hFSH) [Recombinant Human Follicle Stimulating Hormone Injection | Intas Pharmaceuticals Limited | The Committee recommended for proposal as per the recommendations of the SEC |
| **9.** | Follitropin alfa (r-hFSH) [Recombinant Human Follicle Stimulating Hormone Injection | Intas Pharmaceuticals | The Committee recommended for proposal as per the recommendations of the SEC |
| **10.** | Insulin Aspart Mix 70/30 [70% insulin aspart protamine suspension and 30% insulin aspart injection, (rDNA origin)] | Wockhardt Ltd. | The Committee recommended for proposal as per the recommendations of the SEC |
| **11.** | Insulin Aspart (recombinant DNA origin)] | Wockhardt Ltd. | The Committee recommended for proposal as per the recommendations of the SEC |
| **12.** | Wockhardt's long-acting basal insulin analog Glargine. 21A- Gly-30Ba-L-Arg-30Bb-L-Arg-human insulin | Wockhardt Ltd. | The Committee recommended for proposal as per the recommendations of the SEC |
| **13.** | Insulin Lispro Mix75/25 human insulin | Wockhardt Ltd. | The Committee recommended for proposal as per the recommendations of the SEC |
| **14.** | Insulin Lispro (rDNA origin) Lys(B28), Pro(B29) human insulin | Wockhardt Ltd. | The Committee recommended for proposal as per the recommendations of the SEC |
| **15.** | Insulin Analogue Glargine (Glaritus® ) | Wockhardt Limited | The Committee recommended for proposal as per the recommendations of the SEC. |
| **16.** | Wosulin 30 R/ 70 N [(30% Insulin Human Injection USP(r-DNA origin)/ 70% Isophane Insulin Human Suspension] | Wockhardt Ltd. | The Committee recommended for proposal as per the recommendations of the SEC |

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| **17.** | rDNA human regular Insulin (Wosulin R) 100 IU/mL, Vial 10.0 mL | Wockhardt Limited | The Committee recommended for proposal as per the recommendations of the SEC |
| **18.** | Darbepoetin alfa | Reliance Life Sciences Pvt. Ltd. | The Committee recommended for proposal as per the recommendations of the SEC |
| **19.** | Rituximab | Dr. Reddy's Laboratories Ltd. | The Committee recommended for proposal as per the recommendations of the SEC |
| **20.** | Trastuzumab for injection (intravenous [IV] administration) Recombinant humanized anti-HER2 monoclonal antibody. | Roche Products (India) Pvt Ltd | The Committee recommended for proposal as per the recommendations of the SEC |
| **21.** | SILDENAFIL + DAPOXETINE | M/s Hetero Labs Ltd. | The Committee recommended for proposal as per the recommendations of the SEC. |
| **22.** | Polyethylene Glycol 400 0.4% w/v & Propylene Glycol 0.3% w/v. | Alcon Laboratories (India) Pvt. Ltd. | The Committee recommended for proposal as per the recommendations of the SEC. |