MINUTES OF 27th MEETING OF THE TECHNICAL COMMITTEE HELD ON 23.07.2015 UNDER THE CHAIRMANSHIP OF DGHS FOR SUPERVISING CLINICAL TRIALS ON NEW CHEMICAL ENTITIES IN THE LIGHT OF DIRECTIONS OF THE HON'BLE SUPREME COURT OF INDIA ON 03.01.2013.

Present:

1.	Dr. Jagdish Prasad, Director General of Health Services, Nirman Bhawan, New Delhi	Chairman
2.	Dr.Rajutitus Chacko, Prof. & Head, Dept. of Medical Oncology, CMC, Vellore	Member
3.	Dr. Ashok Kumar Das, Professor of Medicine & Professor and Head of Endocrinology, Pondicherry Institute of Medical Sciences, Pondicherry – 605014	Member
4.	Dr. Yash Paul, Prof. & Head, Dept. of Cardiology, PGIMER, Chandigarh.	Member
5.	Dr. Kamlakar Tripathi, Prof., Dept. of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi – 221005	Member

Special Invitee:

1. Dr. S.S. Kothari, AIIMS, New Delhi
2. Prof. S.C. Kundu, IIT, Kharagpur, West Bengal
3. Dr. Kameswar Prasad, Prof & Head, Neurology, AIIMS, New Delhi
4. Dr. Sujata Mohanty, Associate Professor, AIIMS, NEw Delhi.
5. Dr. B. Dinesh Kumar, (Deputy Director) & Group Leader- PCT Scientist E, National Institute of Nutrition, Hyderabad
6. Dr. S. Varma, PGIMER, Chandigarh
7. Prof. Varsha Gupta, Govt. Medical College, Sec-32, Chandigarh

From CDSCO:

1. Dr. G. N. Singh
   Drugs Controller General of India
2. Dr. V. G. Somani,
   Joint Drugs Controller (I)
3. R. Chandrashekar
   Deputy Drugs Controller (India), CDSCO HQ
4. Mrs. Annam Visala
   Deputy Drugs Controller (I)
5. Mrs. Rubina Bose
   Deputy Drugs Controller (I)
6. Dr. A. Ramkishan
   Deputy Drugs Controller (I)

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

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

The Committee deliberated 23 cases related to approval of clinical trials. Out of these 23 cases, 03 cases were related to clinical trials of NCEs, 05 cases were related to global clinical trials (GCT). Remaining 15 cases were related to clinical trials for approval of New Drugs and biologicals.

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

The Committee evaluated the 03 cases related to clinical trial 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 deliberation, the Committee recommended all the three cases. The recommendation of the Committee is enclosed as **Annexure-I.**

2. <u>Proposals of Clinical Trials of GCT recommended by SECs / IND.</u>

Thereafter, the Committee evaluated 05 cases related to global clinical trial. After detailed deliberation, the Committee recommended all the five cases. The recommendation of the Committee is enclosed as **Annexure-II.**

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

The Committee also evaluated the remaining 15 cases of other than GCT/clinical trial of NCEs. After detailed deliberation, the Committee recommended for approval of 13 cases out of 15 cases. Out of 13 approved cases, in 01 case (S. No.12 of **Annexure-III**), the Committee recommended for approval subject to condition which is annexed at **Annexure-III.** The remaining 02 cases (S. No. 02 & 13 of **Annexure-III**) Committee referred back for seeking further clarification. The recommendations of the Committee in respect of these 15 cases are enclosed as **Annexure-III.**

Thus, the Committee recommended for approval of 21 cases, out of total 23 cases of clinical trial proposals.

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

The Committee deliberated the 08 proposals (07 from Medical Device and 01 from Biological) which have been recommended by the SECs for their approval for manufacture/ import for marketing in the country without local clinical trial. The recommendations of the Committee along with recommendations of SEC are annexed at **Annexure- IV**.

5. Others:

a) Re-deliberation of the proposals based on the recommendation of the Committee

I. Name of the Drug : Neutrogen (GCSF) (Filgrastim)
Name and Address of the Applicant: M/s QPS Bioserve India Pvt. Limited, # 6-56/6/1A, Opp: IDPL Factory, Balanagar, Hyderabad – 500 037, Telangana, India**.**

M/s QPS Bioserve India has submitted an application to conduct pk-pd study of Neutrogen subcutaneous injection 5mcg/Kg of M/s Virchow Biotech, India comparing with that of Neupogen (Filgratsim) of M/s Roche India Pvt. Ltd.

Protocol Title: An open-label, balanced, randomized, two-treatment, two-period, two-sequence, single dose, crossover study comparing Pharmacokinetic and Pharmacodynamic effects of Neutrogen (Filgrastim) of Virchow Biotech, India with that of Neupogen (Filgrastim) of Roche following 5mcg/kg subcutaneous injection in healthy adult human subjects.

The proposal was deliberated in the SEC wherein the Committee reviewed the protocol in depth and recommended for the proposed PK/PD study in healthy volunteers.

Thereafter, the proposal of the firm was discussed in the Technical Committee meeting held on 28.05.2015. After detailed deliberation the Committee observed that the study is proposed to be carried out in healthy volunteers. Therefore, the Committee opined that the firm shall submit published report of PK/PD and safety studies carried out in healthy human volunteers with these drugs for further deliberation by the Technical Committee. The recommendation of the Committee was communicated to the firm.

Accordingly the firm has submitted the published report of PK/PD and safety studies carried out in healthy human volunteers.

Recommendation of the Technical Committee:
The Committee opined that as the study is proposed to be carried out in healthy volunteers and administration of the study drug may increase the CBC count leading to pulmonary oedema, hypertension and other untoward reactions, therefore, the study should be conducted at hospital settings with emergency care and ICU facilities under monitoring.

II. Name of the Drug : Peg-Neutrogen (GCSF) (Peg-Filgrastim)
Name and Address of the Applicant:M/s QPS Bioserve India Pvt. Limited,

M/s QPS Bioserve India has submitted an application to conduct pk-pd study of PEG-Neutrogen subcutaneous injection of M/s Virchow Biotech, India comparing with that of Neulastim (PEG-Filgrastim) of M/s Roche India Pvt. Ltd. following 6mg subcutaneous injection in healthy, adult human subjects.
Protocol Title: An open-label, balanced, randomized, two-treatment, two-period, two-sequence, single dose, crossover, study comparing Pharmacokinetic and Pharmacodynamic effects of PEG-Neutrogen (PEG-Filgrastim) of Virchow Biotech, India with that of Neulastim (PEG-Filgrastim) of Roche following 6mg subcutaneous injection in healthy, adult human subjects.
The proposal was deliberated in the SEC wherein the Committee reviewed the protocol in depth and recommended for the proposed PK/PD study in healthy volunteer, with a condition that, there should be wash out period of 28 days. Accordingly revised protocol should be submitted to this office after which final approval may be granted.
Thereafter, the proposal of the firm was deliberated on the Technical Committee meeting held on 28.05.2015. After detailed deliberation the committee observed that the study is proposed to be carried out in healthy volunteers. Therefore, the committee opined that the firm shall submit published report of PK/PD and safety studies carried out in healthy human volunteers with these drugs for further deliberation by the technical committee. The recommendation of the TC was communicated to the firm.
Accordingly the firm has submitted the published report of PK/PD and safety studies carried out in healthy human volunteers.

Recommendation of the Technical Committee:
The Committee opined that as the study is proposed to be carried out in healthy volunteers and administration of the study drug may increase the CBC count leading to pulmonary oedema, hypertension and other untoward reactions, therefore, the study should be conducted at hospital settings with emergency care and ICU facilities under monitoring.

III. Name of the Drug : Darbepoetin Alfa

Name and Address of the Applicant: M/s Hetero Drugs Limited, Hetero Corporate, 7-2-A2, Industrial Estates, Sanath Nagar, Hyderabad- 500018, India.

M/s Hetero Drugs Limited has submitted an application to conduct Phase-I Pharmacokinetic and Pharmacodynamic Study of Darbepoetin alfa Injection, Hetero and 'ARANESP®' (Darbepoetin alfa Injection, Amgen) in healthy adult human subjects.

Accordingly, the proposal was deliberated in SEC wherein the Committee recommended for the conduct of the study as per approved study protocol for phase I, single dose, PK and PD study of Darbepeoitin alfa injection in healthy adult human subject.

Thereafter, the proposal was deliberated in the Technical Committee held on 11.02.2015. The Committee after deliberation observed that the study is proposed to be carried out in healthy volunteers. Therefore, the Committee opined that the firm shall submit the details of relevant studies (published in index journals such as LANCET etc. carried out with Darbepoetin in healthy human volunteers which will be discussed in the next Technical Committee meeting).

As the firm had submitted the published literature of Studies carried out with the drug Darbepoetin alfa, the proposal was again forwarded to the Technical Committee held on 28.05.2015. After review of the submitted published report of Pharmacokinetics studies of Darbepoetin Alfa in healthy volunteers published in international journal, the Committee noted that there was no safety report in healthy volunteers in the submitted published report. Therefore, the Committee recommended that the firm should submit published safety report in healthy human volunteers before the Committee for further deliberation.

Accordingly the firm has submitted the published report of PK/PD and safety studies carried out in healthy human volunteers.

Recommendation of the Technical Committee:

The Committee opined that as the study is proposed to be carried out in healthy volunteers and administration of the study drug may increase the CBC count leading to pulmonary oedema, hypertension and other untoward reactions, therefore, the study should be conducted at hospital settings with emergency care and ICU facilities under monitoring.

IV. Name of the Drug: GCSF (Filgrastim)

Name and Address of the Applicant: M/s Bio Genomics Limited, 1st Floor, Kothari compound, Opp. Tikuji-ni-wadi, Thane (W) 400 610, Maharashtra, India.

M/s Bio Genomics Limited has submitted an application to conduct Phase-I, Pharmacokinetic and Pharmacodynamic Study and study to Compare Safety and Tolerability of Granulocyte Colony Stimulating Factor (BioGenomics Limited) and Neupogen® (Roche Limited) Administered via Subcutaneous Route as Multiple Consecutive Doses in Healthy Adult Human Volunteers.

The proposal was deliberated in the SEC (Oncology) meeting. After detailed deliberation the Committee recommended for the conduct of the study, subject to the condition that the IV route group in the study should be deleted from the protocol.

Also it is observed that you have proposed Independent Ethics Committee namely: Independent Ethics Committee, Ethica Norma No. 19/11, Gandhi Street, Vanuampet, Chennai-600091. However, your proposed study is PK/PD trial as part of Marketing Authorization. Therefore, you are required to appoint a suitable Institutional Ethics Committee.

Thereafter, the proposal was deliberated on the technical Committee meeting held on 28.05.2015. After detailed deliberation the Committee observed that the study is proposed to be carried out in healthy volunteers. Therefore, the committee opined that the firm shall submit published report of PK/PD and safety studies carried out in healthy human volunteers with these drugs for further deliberation by the technical committee. The recommendation of the Technical Committee was communicated to the firm.

Accordingly the firm has submitted the published report of PK/PD and safety studies carried out in healthy human volunteers.

Recommendation of the Technical Committee:

The Committee opined that as the study is proposed to be carried out in healthy volunteers and administration of the study drug may increase the CBC count leading to pulmonary oedema, hypertension and other untoward reactions, therefore, the study should be conducted at hospital settings with emergency care and ICU facilities under monitoring.

V. **Drug Name and Strength:** Ebastine Oral Suspension 5mg/ml

Applicant: M/s Micro labs Limited

Subject: Approval of study protocol of Ebastine Oral Suspension 5mg/ml of Allergic Rhinitis in age 6-12 Years.

M/s Microlab applied for manufacturing and marketing permission of Ebastine oral suspension 5mg/ml indicated for use in Allergic rhinitis in children aged 6-12years.

The firm submitted the Phase III clinical trial protocol for conducting Clinical Trial. The proposal was deliberated in SEC (Antimicrobial) held on 08-05-2015 and the Committee recommended to conduct the Clinical Trial.

The proposal was deliberated in the Technical Committee meeting held on 28-05-2015. The Committee opined that opinion of Pulmonary/ENT may be taken to decide further.

As per the Technical Committee Recommendation, the proposal was deliberated in SEC (Pulmonary) held on 30-06-2015.The recommendation of the Committee is as under.

SEC (Pulmonary) recommendation: The Committee recommended the proposed clinical trial with the following suggestions.

1. There should be standard wash out period of one week for previous medication if any taken by the patients before enrolling into the study.
2. Patients with viral rhinitis should be excluded.
3. Additional ECG shall be performed at one week also.

Recommendation of the Technical Committee:
The Committee deliberated the proposal and recommended for conduct of the study as per SEC recommendation.

b) Representation from Research Society for the Study of Diabetes in India(RSSDI), Delhi to discuss the issue related to the labeling instruction of the approved drug Dulaglutide "to be prescribed only by endocrinologist"

A representation has been received from Research Society for the Study of Diabetes in India (RSSDI) wherein the following matter has been stated:
This office has recently approved the drug Dulaglutide label with the instruction that "it is to be prescribed only by endocrinologist, not by diabetologists".
India has more than 65 millions diabetics, out of which 90% are being treated by Internists and physicians or trained diabetologists only. Endocrinologists alone probably can't cater to even 10% patients on India, that too also only in metro or cities.
Trained internists or diabetologists have been serving to the needs of the patients by prescribing all the best options available in the interest of the patients whether it is DPP-4 inhibitors of GLP-1 analogues likes Exenatide or even Liraglutide etc. Internist, trained diabetologists and largely family physicians are competent to treat diabetes patients.
Hence, limiting the prescription of Dulaglutide only to endocrinologist will deprive large majority of patients of this good drug, so shall not be in the larger interest of Diabetic population. The applicant regrets this decision of DCGI which is not in the interest of patients and shall send a wrong signal to all physicians of India and will set wrong precedence.
Accordingly, the applicant requested to DCGI/ Health Ministry of India to immediately review their decision &issue a notification to this effect explicitly stating that physicians and diabetologist should also allowed to prescribe the drug.

Recommendation of the Technical Committee: After deliberation the Committee recommended to amend the labeling requirements as "To be sold by retail on the prescription of a registered MD (Internal Medicine) treating diabetic patients besides endocrinologist"

c) Re-appeal by M/s INC Research, Gurgaon, to waiver on the Clinical Trial condition imposed by Technical Committee and Apex Committee in its 23rd and 22nd meeting respectively.

Study title "A Randomized, Double-Blind, Placebo- and Active-Controlled Study of DS-5565 in subjects with Pain Associated with Fibromyalgia"

It may please be informed that the proposal was re-deliberated in Technical Committee and Apex Committee in its 23rd and 22nd meeting respectively.

The details of the deliberations by these Committees are given below:-

1. **Deliberation of proposal by SEC:-**

   The proposal was deliberated in the meeting of SEC (Neurology and Psychiatry) held on 28.08.2014. The Committee after deliberation recommended as under:-

After detailed deliberation the Committee recommended to conduct the trial subject to the condition that-

1. The investigator should be orthopaedics or rheumatologist. The team include clinical psychiatric/psychologist for the assessment of inclusion and exclusion criteria.
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.
3. The pk rationale for trying the drug OD or BD should be provided.

2. **Deliberation of proposal in 21st Technical Committee (TC):-**

   The proposal was placed before the Technical Committee along with the recommendations of the SEC in the 21st Technical Committee meeting held on 21-01-2015. The Committee after deliberation recommended as under:-

"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 only with complete cardiac monitoring for duration of one month. If AEs are not reported after the period of one month, trial can be conducted on OPD setup."

3. **Deliberation of proposal by 20th Apex Committee:-**

The proposal was deliberated in 20th Apex Committee meeting held on 30.01.2015, wherein Committee agreed with the recommendations of Technical Committee.

4. **Appeal by M/s INC Research for waiver on the condition imposed under CT NOC:-**

There after the applicant represented the matter to DCG (I) for waiver on the condition imposed under CT NOC.

5. **Deliberation of appeal made by firm in 23rd Technical Committee (TC):-**

The appeal by firm was placed before the Technical Committee along with the justification furnished by firm.

The Committee after deliberation recommended as under:-

"All the 105 subjects should be treated in hospitalized settings only, with complete cardic monitoring for duration of one week as various adverse events including acute

transmuralinferon-lateral myocardial infarction was reported in the phase-I study. If AEs are not reported after the period of one week, trial can be conducted on OPD setup."

6. Deliberation of proposal by 22nd Apex Committee:-

The proposal was then deliberated in 22nd Apex Committee meeting held on 23.04.2015, wherein Committee agreed with the recommendations of Technical Committee.

7. Re-appeal by M/s INC Research for waiver on the condition imposed under CT NOC:-

There after the applicant represented the matter to DCG (I) for waiver on the condition imposed under CT NOC based upon following justifications;

- Clarification on the cardiac event "acute transmural-infero-lateral myocardial infarction" listed in the Investigator Brochure (referenced in the minutes of meeting of Technical Committee held on 19 March 2015): the fatal MI in the Phase I renal study DS5565-A-E106 involved a 68 years old male with past medical history relevant for severe chronic renal insufficiency and hypertension who experienced a fatal MI 11 days after a single 5mg dose of study medication. Autopsy showed presence of the above mentioned transmural infarction, severe atherosclerosis of the coronary arteries with a complete obstruction of the right coronary artery, findings whose pathophysiology is more chronic in nature and is not temporally plausible within just 11 days. The mentioned cardiac event was not related to the study drug DS-5565 as assessed by the Medical Monitor and the "Investigator causality assessment" was also not related to the study medication.
- In the current Fibromyalgia Phase 3 Clinical trial program globally, across the three ongoing double-blind studies, 622 subjects have been randomized as of 25 May 2015, of which 80 patients have completed the 13 week double-blind treatment period. All these subjects have been treated as per protocol specified visits in an outpatient setting.
- The Clinical study protocol has adequate measures for the purpose for cardiac monitoring. Please refer section 6 and section 9.8 of the enclosed protocol. The exclusion criteria mentioned in the current protocol (section 4.1.2.) also takes proper care to monitor the cardiac condition of the subject during screening and excludes patients with cardiac abnormalities.
- The protocol for the study also refers to a thorough QT study done in the past to look at the effects of DS-5565 on the cardiac function (section 1.1.1.5. of the protocol). In this study, there were no clinically significant changes in 12-lead electrocardiogram (ECG) parameters; neither the therapeutic dose (15mg of DS-5565) nor the supratherapeutic dose (50mg of DS-5565) effected cardiac repolarisation.
- The current conditionality will affect the data collected in first week post randomization from Indian subjects as compared to that of the rest of the world subject's data. Frequent testing of subset of patients may introduce bias into the primary endpoint as there is a possibility of altered perception by the subject in severity of pain due to daily visits and due to treatment in hospitalized distress.

- The conditionality is not practical to be implemented by the site investigators as Fibromyalgia is an indication treated in routine clinical practice in an out-patients setup would inconvenience the patients and cause more psychological distress.
- No cardiac events/no SAEs were observed in the twenty one (21) subjects phase 1 study (DS5565-A-E114) conducted in India.

Recommendation of the Technical Committee: After detailed deliberation, the Committee agreed with the justification presented by the firm as the myocardial infarction was not related but patient himself was having problem and waived off the condition of conducting the trial in hospital and ICU setup for one week subject to the condition that diabetic patients should be excluded and accordingly inclusion and exclusion criteria shall be suitably amended and submitted to DCGI.

d) Re-deliberation of Phase III trial permission proposal with LCZ696 as per the recommendation of the 26th Technical Committee.

M/s Novartis Ltd had applied for the grant of phase III clinical trial permission with LCZ696 titled **"A multicenter study to evaluate safety and tolerability in patients with chronic heart failure and reduced ejection fraction from PARADIGM-HF receiving open label LCZ696"**

The proposal was examined by the Subject Expert Committee (SEC) and Technical Committee, details of deliberation are placed below:

- **SEC recommendation dated 26-02-2015:**

  After detailed deliberation the Committee opined that the protocol should include base line data of patient, CRF should include Echo Cardiographic assessment at base line and all follow up. Accordingly revised CRF and protocol should be submitted to this office for further review.

- **SEC recommendation dated 01-05-2015:**

  The firm expressed their inability to conduct ECHO cardiography assessment at base line and at follow up, as more than 150 patients have already been recruited in the study and it is difficult to amend global protocol. After detailed deliberation the Committee approves the existing protocol.

- **25th Technical Committee recommendation dated 28-05-2015:**

  After detailed deliberation, the Committee recommended that the applicant shall make detailed presentation before the Committee.

- **26th Technical Committee recommendations dated 26.06.2015**

  As per the recommendation of 25th Technical Committee the applicant made detailed presentation to the Committee. After detailed deliberation the Committee recommended that the experts in the field of cardiology be invited for further review of the proposal in forthcoming meeting.

Recommendation of the Technical Committee: After detailed deliberation, the Committee recommended the conduct of trial as per the SEC recommendation dated 01-05-2015.

e) To deliberate on the representation from M/s Venus Remedies Ltd, Panchkula with regard to clinical trial for manufacturing and marketing of New Drug "Etimicin Sulphate Injection"

M/s Venus Remedies Ltd had submitted an application for granting permission for manufacturing and marketing of Etimicin Sulphate Injection with the proposal to conduct a clinical study entitled "An open labeled, randomized, comparative study to evaluate the efficacy and safety of Etimicin Sulphate v/s Amikacin in patients suffering from various bacterial infections" to be indicated for the treatment of Lower Respiratory Tract infections, Urinary tract infection, Skin infection, and Post-surgical bacterial infection.

Based on the opinion of five experts as per the practice prevailing at that time, clinical trial permission was granted to the firm to conduct phase III clinical trial as per approved protocol. Accordingly, the firm conducted clinical trial and submitted the clinical trial report and the proposal was placed in NDAC (now renamed as SEC) meeting held on 16.03.2013.

1st Recommendation of NDAC (now renamed as SEC) meeting held on 16.03.2013

The committee asked for the submission of detailed Phase III clinical trial reported and the rationale of taking only 50 subjects for each indication i.e. RTI, UTI, Skin & postsurgical bacterial infection. Committee further stated that in LRTI aminoglycoside is not standard treatment and rationale of taking Amikacin for this indication as comparator needed to be justified and similarly in case of skin & postsurgical bacterial infection. PSUR data from China should be provided to the committee for review.

Based on the NDAC (now renamed as SEC) recommendation, the firm submitted the reply and the proposal was again deliberated in the NDAC (now renamed as SEC) meeting held on 22.11.2013.

2nd Recommendation of NDAC (now renamed as SEC) meeting held on 22.11.2013

The committee after deliberation recommended that the firm should present the safety data separately for each indication i.e. RTI, UTI, Skin & post-surgical bacterial infection in 50 patients along with microbiological culture data for further review by the Committee.

Accordingly, the firm has submitted the reply as per the SEC recommendation and the proposal was again deliberated in the NDAC in its meeting held on 28.02.2014.

3rd Recommendation of NDAC (now renamed as SEC) meeting held on 28.02.2014

The Committee noted that Amikacin is not used as monotherapy but as an add-on therapy except in UTI. Hence, Amikacin as comparator to the investigational drug is not appropriate. There were several queries on the data. The explanations provided by the firm were not

convincing, for example the efficacy of Amikacin in UTI was much below the expected level whereas none of the subjects on Amikacin showed nephrotoxicity and ototoxicity, known adverse effect of the drug. This is particularly surprising as many of the subjects were above 50 years of age. In patients of respiratory tract infections, the choice of Amikacin is not a standard practice. After deliberation, the Committee recommended that the firm has to conduct another phase-III clinical trial with proper design and in statistically significant number of subjects and the sites should be geographically distributed across the country. Accordingly clinical trial protocol etc. is required to be submitted before the Committee for further review.

Now this office has received the representation of the firm forwarded by the Ministry of Health and Family Welfare regarding the subject matter. As desired by DGHS, the matter is placed before the Committee and firm has been asked to represent their case before the Committee.

Recommendation of the Technical Committee:
After detailed deliberation, the Committee recommended that the firm shall be allowed to present their clinical study data in the forthcoming meeting after compilation and analysis of all clinical data in 200 patients with respect to efficacy in terms of microbiological culture and safety in terms of eGFR and nephrotoxicities. The firm shall also present non-inferiority with respect to Amikacin with statistical analysis and confidence interval.

The meeting ended with vote of thanks to the Chair.

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Annexure-I

List of 03 cases of clinical trial of NCEs along with their evaluations and recommendations of the Technical Committee in its 27th Meeting.

Proposal No	Details of the proposal	Assessment of the Proposal *vis –a vis* specified Parameters	Recommendation 1. Technical Committee 2. Subject Expert Committee
1.	**Name of the Drug:** QGE031 **Protocol No** : CQGE031B2201E1 **Phase of the Study:** Phase II **Name of the Applicant :** Novartis Healthcare Private Limited, Sandoz House , Dr. Annie Besant Road, Worli, Mumbai – 400 018 **Name of the Sponsor:** Same as above **Name of the Manufacturer:** Novartis Pharma AG, Lichtstrasse 35, CH-4056 Basel, Switzerland. **Title:** An open-label, multi-center, extension study to evaluate the long-term safety of subcutaneous 240 mg QGE031 given every 4 weeks for 52 weeks in allergic asthma patients who completed study CQGE031B2201	**Risk versus benefit to the patients**- The safety profile of the test drug from various pre clinical studies including repeat dose, reproductive and development toxicity, juvenile toxicity, immunogenicity study and clinical phase I, II studies justify the conduct of the study. **Innovation vis-a-vis existing therapeutic option** The purpose of study is to evaluate the long-term safety and tolerability of test drug given every 4 weeks for 52 weeks in allergic asthma patients who completed the core study CQGE031B2201 **Unmet need in the country**- The test drug may be an alternative treatment option in asthma patients.	**Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation. **SEC Recommendation on 30-06-15:** After detailed deliberation the committee recommended the conduct of the extension protocol no: CQGE031B2201E1 version 01 dated 22-04-2015 in its presented form.
2.	**Name of the Drug:** Roxadustat **Protocol no:** D5740C00002 **Phase of the Study:** Phase- III **Name of the Applicant:**	**Risk versus benefit to the patients** The safety profile of the test drug from various pre clinical studies including repeat dose toxicity study, embryo fetal development study, carcinogenicity and phase I, II clinical study justify the conduct of this study. **Innovation vis-a-vis existing therapeutic**	**Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.

	AstraZeneca Pharma India Ltd. **Name of the Sponsor:** AstraZeneca Pharma India Ltd. **Name of the manufacturer:** AstraZeneca Pharma India Ltd. **Title:** A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of Roxadustat for the Treatment of Anemia in Chronic Kidney Disease Patients not on Dialysis	**option** The purpose of study is to assess the Safety and Efficacy of Roxadustat for the Treatment of Anemia in Chronic Kidney Disease Patients not on Dialysis **Unmet medical need in the country:** The study drug may provide additional treatment option in patients with anemia.	**SEC Recommendation** : After detailed deliberation the committee observed that the detailed preclinical carcinogenicity study data is not available. The committee opined the firm should submit preclinical carcinogenicity data and initiates the study with primary objective i.e. to evaluate the cardiovascular Safety of Roxadustat for the treatment of Anaemia in Chronic Kidney Disease Patients in non dialysis, the firm may submit revised protocol accordingly.
3.	**Name of the Drug:** Roxadustat **Protocol no:** D5740C00001 **Phase of the Study:** Phase III **Name of the Applicant:** AstraZeneca Pharma India Ltd. **Name of the Sponsor:** AstraZeneca Pharma India Ltd. **Name of the manufacturer:** AstraZeneca Pharma India Ltd. **Title:** A Phase 3, Multicenter, Randomized, Open-Label, Active-Controlled Study of the Safety and Efficacy of Roxadustat in the Treatment of Anemia in Dialysis Patients	**Risk versus benefit to the patients** The safety profile of the test drug from various pre clinical studies including repeat dose toxicity study, embryo fetal development study, carcinogenicity and phase I, II clinical study justify the conduct of this study. **Innovation vis-a-vis existing therapeutic option** The purpose of study is to assess Safety and Efficacy of Roxadustat in the Treatment of Anemia in Dialysis Patients **Unmet medical need in the country:** The study drug may provide additional treatment option in patients with anemia.	**Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation. **SEC Recommendation** : After detailed deliberation the committee observed that the detailed carcinogenicity study data is not available. The committee opined the firm should submit preclinical carcinogenicity data and initiates the study with primary objective i.e. to evaluate the cardiovascular Safety of Roxadustat for the treatment of Anaemia in Chronic Kidney Disease Patients in dialysis, the firm may submit revised protocol accordingly.

Annexure-II

List of 05 cases of Clinical Trial proposals of GCT along with evaluations and recommendations of the Technical Committee in 27th Meeting.

Proposal No.	Details of the proposal	Assessment of the Proposal *vis –a vis* specified Parameters	Recommendation 1. Technical Committee 2. Subject Expert Committee
1.	**Name of the Drug: Canagliflozin** **Protocol No**: 28431754DNE3001 **Phase of the study: Phase III** **Applicant Name and Address**: Johnson & Johnson Private Limited, Arena Space, Off JVLR, Behind Majas Depot, Jogeshwari (East), Mumbai **Sponsor Name and Address**: Janssen Research and Development, LLC, 920 Route 202, P.O. Box 300, Raritan NJ08869. **Manufacturer Name and Address**: Janssen Ortho L.L.C. State Road 933, Km 0.1, Mamey Ward, Gurabo, PR 00778-9629, USA **Title**: A Randomized, Double-blind, Event-driven, Placebo-controlled, Multicenter Study of the Effects of Canagliflozin on Renal and Cardiovascular Outcomes in Subjects with Type 2 Diabetes Mellitus and Diabetic Nephropathy.	**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 conduct of the study is justified. **Innovation vis-à-vis Existing Therapeutic Option:** The purpose of the study is to assess the efficacy of canagliflozin relative to placebo in reducing the composite endpoint of end stage kidney disease, doubling of serum creatinine and renal or cardiovascular death. **Unmet Medical Need in the country:** The test drug may provide an alternative treatment option for diabetic nephropathic patient.	**Recommendation of the Technical Committee** After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation. **SEC recommendation dated 01-05-2015:** After detailed deliberation the committee recommended the trial subject to condition that: 1. The patient information sheet should contain information regarding risk of urinary tract infection and elevation of lipid profile. 2. There should be measurement of other parameters for measuring blood sugar other than urinary sugar i.e. blood sugar should be measured rather than urinary sugar. The urinary sugar measurement will not be reliable when patient on the test drug.
2.	**Name of the Drug:** Biphasic insulin aspart (BIAsp) **Protocol No**: **BIAsp 4157** **Phase of the Study: Phase-IV** **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	**Risk versus Benefit to the patients-** In light of the fact that the test drugs are old drug 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 compare the effect of intensification with BIAsp 30 versus intensification with basal bolus insulin analogues (insulin glargine and insulin aspart) on glycaemic	**Recommendation of the Technical Committee** After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation. **SEC recommendation:** After detailed deliberation the committee recommended the conduct of the study subject to the following conditions: 1. The investigators for this trial shall

	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 32-week randomised, multinational, treat-to-target, open label, parallel group comparison of stepwise insulin intensification of biphasic insulin aspart (BIAsp) 30 and basal-bolus therapy with insulin glargine and insulin aspart in insulin naïve type 2 diabetic patients inadequately controlled on oral anti-diabetic therapy.	control. **Unmet need-** The test drug BIAsp 30 may provide adequate basal insulin coverage without increasing the risk for hypoglyceamic episodes that may be beneficial to the T2DM Patients.	posses MD qualification 2. Impaired Renal function should be defined, patient with GFR less than 30ml/min/1.73sqM should be excluded from the study.
3.	**Name of the Drug:** Ranibizumab **Protocol No:** CRFB002H2301 **Phase of the study**: Phase-III **Applicant Name and Address:** Novartis Healthcare Private Limited, Sandoz House, Dr. Annie Besant Road, Worli, Mumbai – 400 018 **Sponsor Name and Address**: Novartis Healthcare Private Limited, **Manufacturer Name and Address:** Novartis Pharma AG, Lichtstrasse 35, CH-4056 Basel, Switzerland. **Title:** RAINBOW study: a randomized, controlled study evaluating the efficacy and safety of RAnibizumab compared with laser therapy for the treatment of Infants Born prematurely With retinopathy of prematurity.	**Risk versus Benefit to the patients**- In light of the fact that the study drug is already approved and marketed in India, the conduct of the study is justified. **Innovation vis a vis existing therapeutic option**- The purpose of the study is to demonstrate that intravitreal ranibizumab 0.2mg has superior efficacy to laser therapy in the treatment of retinopathy of prematurity. **Unmet need**: The test drug my provide an additional treatment option in patients with retinopathy of prematurity.	**Recommendation of the Technical Committee** After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation. **Recommendation of the SEC:** After detailed deliberation the committee recommended the conduct of the study.

4.	**Name of the Drug:** QVA149 (Indacaterol maleate + Glycopyrronium bromide) **Protocol No: CQVA149A3405** **Phase of the Study: III** **Sponsor Name and Address**: Novartis Healthcare Private Limited, Sandoz House , Dr. Annie Besant Road, Worli, Mumbai – 400 018 **Manufacturer Name and Address**: Novartis Pharma AG, Lichtstrasse 35, CH-4056 Basel, Switzerland. **Title:** A 12-week treatment, multi-center, randomized, double-blind, double-dummy, parallel group study to assess the efficacy and safety of switching from salmeterol/ fluticasone to QVA149 (indacaterol maleate/glycol pyrroniumbromide) in symptomatic COPD patients	**Risk versus benefit to the patients** The safety profile of the test drug from various pre clinical studies including repeat dose inhalation toxicity study, embryo fetal development study, and phase I, II, III clinical study justify the conduct of this study. **Innovation vis-a-vis existing therapeutic option** The purpose of study is to assess the efficacy and safety of switching from salmeterol/fluticasone to QVA149 (Indacaterol Maleate/Glycopyrronium Bromide) in symptomatic chronic obstructive pulmonary disease patients. **Unmet medical need in the country** This fix dose combination may potentially improve broncho dilation in chronic obstructive pulmonary disease and may provide more convenient dosing as compared to taking two compounds as separate agents.	**Recommendation of the Technical Committee** After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation. **SEC Recommendation on 30-06-15:** After detailed deliberation the committee recommended the conduct of the study in its presented form
5.	**Name of the Drugs:** Moroctocogalfa [AF-CC] **Phase of the Trial**: Phase III **Protocol No**: **B1831001** **Applicant Name and Address:** Pfizer Limited **Sponsor Name and Address**: Pfizer Limited **Manufacturer Name and Address**: Wyeth Farma, S.A. Autovia del Norte A1, Km 23, Desvio Algete, Km 128700 San Sebastian de los Reyes, Madrid, Spain	**Risk versus Benefit to the patients**- The safety profile of the test drug from various pre-clinical studies including repeat dose toxicity, immunogenicity toxicity and clinical phase I, II studies justify the conduct of the study. **Innovation vis a vis existing therapeutic option**: The purpose of the study is to evaluate prophylaxis treatment, and to characterize the efficacy, safety, and pharmacokinetics of BDomain Deleted Recombinant Factor VIII Albumin Free (Moroctocog alfa [AF-CC]) in Children With Hemophilia A. **Unmet need**- The test drug may be an alternative treatment option in	**Recommendation of the Technical Committee** After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation. **SEC Recommendation on 25-06-2015:** After detailed deliberation the committee recommended the study with the condition that the sponsor will provide post trial access of the IMP to the trial subjects till IMP is marketed in India

	Title: An Open-Label Study to Evaluate Prophylaxis Treatment, and to Characterize the Efficacy, Safety, and Pharmacokinetics of B-Domain Deleted Recombinant Factor VIII Albumin Free (Moroctocogalfa [AF-CC]) in Children With Hemophilia A	Children with Hemophilia A.	

Annexure III

List of 15 cases of clinical trial proposals other than GCT/NCE along with evaluations and recommendations of the Technical Committee in 27th Meeting.

Sl No	Name of the Drug	Firm Name	Recommendation of the Technical Committee
1.	Nepafenac 0.3% Suspension	M/s Micro Labs Limited	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
2.	Glibenclamide, Metformin Hydrochloride and Voglibose tablets	M/s Sun Pharma Laboratories Limited	After detailed deliberation, the Committee was not convinced about the 3 drugs combination. The Committee opined that the firm may be requested to make a detailed presentation before the Committee for further consideration.
3.	Adalimumab	M/s Hetero Drugs Limited	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
4.	Romiplostim Powder and Solvent for Solution for injection 250 mcg/0.5 mL and 500 mcg/1.0 mL vial.	M/s Intas Pharmaceuticals, Ltd	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
5.	Verapamil	Dr. Soumya Swaminathan, National Institute for Research in Tuberculosis, Chennai	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
6.	Alcaftadine Eye drops of 0.25 % w/v	M/s Ajanta Pharma Limited	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
7.	Piperaquine Tetraphosphate (PQP) and Dihydroartemisinin (DHA) (320/40 mg & 160/20 mg)	M/s Sigma Tau India Private Limited	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
8.	Tacrolimus Lipid Tablets	M/s Intas Pharmaceuticals Ltd.,	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
9.	Inactivated Tetravalent Influenza vaccine (Split Virion) I.P.	M/s Cadila Healthcare Ltd	After detailed deliberation, the Committee recommended to conduct the study as per

			the SEC recommendation.
10.	Inactivated Trivalent Influenza Vaccine (Split Virion) I.P. Single dose	M/s Cadila Healthcare Ltd	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
11.	Human Normal Immunoglobulin for Intravenous Administration BP 5% solution	M/s Reliance Life Sciences	The Committee recommended the conduct of study as per the SEC recommendation subject to the condition that the phase IV trial shall be conducted in minimum 100 subjects.
12.	Allogenic Mesenchymal Stromal Cells	M/s Stempeutics Research Private Limited	The Committee opined that the firm's proposal for marketing authorization without further clinical trials on larger number of patients based on CBBTDEC recommendation and considering the therapeutic option in this condition as unmet need, can be considered after the basis and guidelines in this regard including for fast track approval or conditional approval are finalized. Since the firm has presented reasonable pre-clinical, Phase-I and Phase-II data after due approval of clinical trial protocol from DCG (I), the proposal need not be referred back to CBBTDEC for re-evaluation. However, a general comments or CBBTDEC's view as what is meant by "Conditional approval" as per PMDA model and in how many patients it shall prove major/significant improvements efficacy and what further condition shall be put with respect to further studies and charging the patients, may be obtained.
13.	Autologous Dendritic Cell Product	M/s Apac Biotech Pvt. Ltd,	The Committee opined that the data presented by the firm is more presumptive about approval. The recommendations of the CBBTDEC are not supported with the basis of approval as: 1. In how many patients major improvement noted and in how many it is required in one particular indication; 2. What is the criteria for approval of

			indication in such "already in the practice" cell based product for "conditional approval"(either based on PMDA or CBBTDEC's guidelines). However, Committee acknowledged that if it is 19% improvement in the various tumors, it is considered as a major improvement. Therefore, the proposal may be referred back to CBBTDEC for review. Similarly, a general comments or CBBTDEC's view as what is meant by "Conditional approval" as per PMDA model and in how many patients it shall prove major/significant improvements efficacy and what further condition shall be put with respect to further studies and charging the patients, may be obtained. Since the firm had informed the office of DCG(I) on 29th June 2011 and subsequently in 31st Oct 2012 and has been in communication with CDSCO for obtaining acknowledgement or approval of their clinical trial and found to be compliant to rules with respect to facilities and practices, the ban on them shall be revoked as per the recommendation of CBBTDEC. However, they shall be permitted for this product for using in particular indication only after the basis of approval and future conditions for further studies and prices to be recovered from patients are clarified by CBBTDEC.
14.	Ulipristal acetate tablets 5 mg	M/s Intas Pharmaceuticals Ltd	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
15.	Bivalirudin	Dr Suruchi Hasija, AIIMS, New Delhi	After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.

Annexure-IV

Recommendation of the SEC and Technical Committee of the 08 proposals of Clinical trial waiver in Indian population:

Sr. no.	Drug Name	Name of the Firm	Indication	1. Recommendation of the Technical Committee 2. Recommendation of the SEC
1.	Bone Cement	M/s. Heraeus Technologies India Pvt. Ltd.,	Indicated for stable anchoring of all suitable joint prosthesis in primary arthroplasty operations, with added protection against infection. It is also used in revision operations resulting from the aseptic loosening of the prosthesis and infection of the prosthesis by organisms sensitive to Gentamicin and/or-Clindamycin.	**Recommendation of the Technical Committee** After detailed deliberation, the Committee noted that the product is globally marketed since many years and as such there is no requirement of clinical trial for such product. Therefore, the Committee agreed with SEC recommendations. **Recommendations of the SEC:** The committee **Orthopaedics** after detailed examination came to the conclusion that the firm may be granted permission for import & marketing of the product under Rule-122A of D & C Act & Rules as new Medical device with a condition to submit PMS data in Indian Population to the O/o DCG(I) every 6 months for the next 3 years.
2.	Bone Cement	M/s. Heraeus Technologies India Pvt. Ltd.,	It is indicated for filling, stabilizing or permanently fixing revision joint endoprostheses in surgically cleaned bone cavities which were previously infected by pathogens sensitive to Vancomycin and when solely Gentamicin containing cement is considered inadequate or undesirable during single-stage and two-stage replacement	**Recommendation of the Technical Committee** After detailed deliberation, the Committee noted that the product is globally marketed since many years and as such there is no requirement of clinical trial for such product. Therefore, the Committee agreed with SEC recommendations. **Recommendations of the SEC:** The case has been reviewed by SEC – **Orthopaedics** in its meeting held on 28.01.2015. The Committee after detailed examination came to the

			procedures.	conclusion that the firm may be granted permission for import & marketing of the product under Rule-122A of D & C Act & Rules as new Medical device with a condition to submit PMS data in Indian Population to the O/o DCG(I) every 6 months for the next 3 years.
3.	Cadexomer	M/s. Smith & Nephew Healthcare Pvt. Ltd.,	For the treatment of chronic exudating wounds including leg ulcers, pressure ulcers and diabetic ulcers. •Moderate to high exudates. • Where slough, infection or the risk of infection is an issue.	**Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended that the firm should conduct phase-III clinical trial in the Indian population. **Recommendations of the SEC:** The case has been reviewed by SEC – Dermatology in its meeting held on 30.04.2015. The Committee after deliberation recommended that based on the available clinical data the product may be permitted for import & marketing in India.
4.	Trabecular Metal TM Ardis Interbody System Solid and Trabecular Metal TM Ardis Interbody System (Graft)	M/s. Zimmer India Pvt. Ltd., Gurgaon	**System Solid:** It is indicated for use as an intervertebral body fusion device at one or two contiguous levels in the lumbosacral region (L2-S1) in the treatment of Degenerative Disc Disease with up to Grade 1 spondylolisthesis or retrolisthesis at the involved levels. It is implanted using a posterior or transforaminal approach and is intended to be used singly or in pairs with supplemental fixation. **System (Graft):** It is indicated for use with autogenous bone graft as an intervertebral body fusion device at one or two contiguous	**Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended that the firm should submit more clinical trial data generated with new proposed indication of the device. **Recommendations of the SEC:** The case has been reviewed by SEC–Orthopaedics in its meeting held on 28.01.2015. The Committee after deliberation recommended the firm may be granted permission for import and marketing of the product under Rule –122A of Drugs & Cosmetics Act & Rules as new Medical Device with a condition to submit PMS data in Indian population to the O/o DCG (I) every 6-months for the next 3 years.

			levels in the lumbosacral region (L2-S1) in the treatment of Degenerative Disc Disease with upto Grade 1 spondylolisthesis or retrolisthesis at the involved levels. It is implanted using a posterior or transforaminal approach and is intended to be used singly or in pairs with supplemental fixation.	
5.	Orthopaedic Implant	M/s. Johnson & Johnson Ltd	Total Hip Arthroplasty is intended to provide increased patient mobility and reduce pain by replacing the damaged hip joint articulation in patients where there is evidence of sufficient sound bone to seat and support the components.	**Recommendation of the Technical Committee:** After detailed deliberation, the Committee noted that the product is globally marketed since many years and as such there is no requirement of clinical trial for such product. Therefore, the Committee agreed with SEC recommendations. **Recommendations of the SEC:** The case has been reviewed by SEC – **Orthopaedics** in its meeting held on 28.01.2015. The committee after deliberation recommended the firm may be granted permission for import and marketing of the product under Rule – 122A of Drugs & Cosmetics Act & Rules as new Medical Device with a condition to submit PMS data in Indian population to the O/o DCG (I) every 6-months for the next 3 years.
6.	Bone Void Filler	M/s. Surya Surgical Industries	Intended Use: 1) It is a Ceramic Bone void filler intended only for orthopaedic applications as filler for gaps and voids that are not intrinsic to the stability of the bony structure. CERAMENT Bone Void Filler is indicated to be	**Recommendation of the Technical Committee:** After detailed deliberation, the Committee noted that the product is globally marketed since many years and as such there is no requirement of clinical trial for such product. Therefore, the Committee agreed with SEC recommendations.

			injected into bony voids or gaps in the skeletal system. These defects may be surgically created osseous defects or osseous defects from traumatic injury to the bone. It provides bone void filler that resorbs and is replaced by bone during the healing process. 2. It is resorbable ceramic bone graft substitute intended to fill gaps and voids in the skeleton system to promote bone healing. It provides void/gap filler that during the surgical procedure can augment hardware and bone alignments. Gentamicin is included in CERAMENT G to prevent colonization of Gentamicin sensible micro-organisms in order to protect bone healing.	**Recommendations of the SEC:** The case has been reviewed by SEC – **orthopaedics** in its meeting held on 28.01.2015. The Committee after deliberation recommended the firm may be granted permission for import and marketing of the product under Rule – 122A of Drugs & Cosmetics Act & Rules as new Medical Device with a condition to submit PMS data in Indian population to the O/o DCG (I) every 6-months for the next 3 years.
7.	DC Bead Drug Delivery Embolization System	M/s. Eisai Pharmaceuticals India Pvt. Ltd., Mumbai	DC Bead is intended to be loaded with doxorubicin for the purpose of : • Embolization of vessels supplying malignant hyper vascular tumor (s). • Delivery of a local controlled sustained dose of doxorubicin to the tumor(s).	**Recommendation of the Technical Committee:** After detailed deliberation, the Committee opined that there is no alternative therapy available and agreed with the SEC recommendations subject to the condition that the firm shall submit the detail of the conditions and hospital setting under which the device to be given. **Recommendations of the SEC:** The case has been reviewed by SEC – **Oncology** in its meeting held on 17.03.2015. The Committee after deliberation recommended the grant of approval for import and marketing of the proposed product to be loaded with Doxorubicin for the purpose of

				embolization of blood vessels supplying hepatocellular carcinoma.
8.	Recombinant Factor VIII (Turoctocog)	M/s Novo Nordisk India Private Ltd	Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency).	**Recommendation of the Technical Committee:** The Committee recommended waiver of Phase III clinical trial as per the SEC recommendation. Further, the Committee opined that it is not a typical orphan drug but there is limited availability of the drug for the patients. Therefore, the waiver of the conduct of Phase III Clinical Trial is considered as the subject drug is to be used in life threatening disease and not available in the market in the present situation to fulfill the present requirements in the country. **SEC recommendation on 28.01. 2015** The Committee observed that the drug has been shortly marketed in EU and Japan with patients exposure of 100 each (Approx.) and not yet launched in USA. No clinical data in Indian patients available. Therefore the committee is of the opinion that the firm should conduct phase III trial in Indian patients. **SEC recommendation on 25.06. 2015** After detail discussion, Committee opined that, being a drug to be used for rare and life threatening disease and moreover, as on date drug has been already marketed in USA, EU, Japan etc. therefore a requirement of clinical trial may be waived and the firm may be granted marketing authorization subject to condition that, firm shall carry out Phase IV study for assessment of safety and development of inhibitors on at least 50 Indian Subjects. The protocol for the same shall be submitted before initiation of marketing the product in India

Additionally following proposal was deliberated in the meeting:

Sr. no.	Drug Name	Name of the Firm	Recommendation
1	Rotavirus Vaccine (Rotateq®)	M/s MSD	The Technical Committee opined that the rotavirus vaccine manufactured by the firm is presently marketed in 92 countries with temperature variations in those countries and as on date no product quality issues reported in any part of globe. Further EMA has also relaxed the thermal stability testing for the vaccine. The product Rotateq® was used to be imported and approved by CDL even after inclusion of thermal stability test in IP (from July 2014 to till June 2015) since the product is being supplied from C & F agent of the firm directly to the physician in their own cold chain. Further, as the product is being imported in India for last five years with same specification, therefore the Committee opined that the firm may be given relaxation for the time being with respect to testing of thermal stability by the firm and CDL may release the lot at present as per lot release procedure. However it shall be clearly mentioned in the release certificate that the product is not for supply outside the cold chain of MSD. The firm should submit cold chain data on the supplies to India.

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