MINUTES OF THE 32nd MEETING OF THE APEX COMMITTEE HELD ON 03.11.2016 UNDER THE CHAIRMANSHIP OF SECRETARY, (H&FW) FOR SUPERVISING CLINICAL TRIALS ON NEW CHEMICAL ENTITIES

Present:

1. **SHRI C.K. MISHRA**
   Secretary
   Department of Health and Family Welfare
   Ministry of Health and Family Welfare &
   Chairman, Apex Committee
2. **Dr. SOUMYA SWAMINATHAN**
   Secretary, DHR & DG ICMR
3. **Dr. JAGDISH PRASAD**
   DGHS
4. **SHRI K. L. SHARMA**
   Joint Secretary
   Department of Health and Family Welfare

Special Invitees:

1. **SHRI K. B. AGGARWAL**
   Addl. Secretary (F&D)
   Ministry of Health and Family Welfare
2. **Dr. G. N. SINGH**
   DCG (I), FDA Bhavan, New Delhi

Initiating the discussion, Chairman, Apex Committee welcomed the members of the Committee and special invitees to the meeting. Thereafter, the Committee deliberated upon each of the agenda items and recommended as following:

ITEM No. 01

Proposals of Clinical Trials related to New Chemical Entities (NCEs) recommended by Technical Committee:

Proposal No.01:

A trial investigating the cardiovascular safety of oral Semaglutide in subjects with Type 2 diabetes

The Committee, after detailed deliberations, concurred with the recommendations of the Technical Committee for approval of clinical trial protocol for conduct of the study subject to verification of conduct of Phase II Clinical trial. (Details at **Annexure-I**).

Proposal No.02:

A Phase III, multicentre, multinational, randomized, open-label, parallel-arm study of Avelumab plus best supportive care versus best supportive care alone as a maintenance treatment in patients with locally advanced or metastatic urothelial cancer whose disease did not progress after completion of first line Platinum-containing chemotherapy.

The Committee, after detailed deliberations, concurred with the recommendations of the Technical Committee for approval of clinical trial protocol for conduct of the study subject to verification of conduct of Phase II Clinical trial. (Details at **Annexure-I**).

Proposal No.03:

A Randomized, Double-Blind, Placebo-Controlled, Six-Month Study to Evaluate the Efficacy, Safety and Tolerability of Sarizotan in Patients with Rett Syndrome with Respiratory Symptoms.

The Committee, after detailed deliberations, concurred with the recommendations of the Technical Committee for approval of clinical trial protocol for conduct of the study (Details at **Annexure-I**).

ITEM No. 02

Proposal No.04:

A Randomized, Double-Blind, Placebo-Controlled, Phase III Study to Compare NSAI plus Abemaciclib, a CDK4 and CDK6 Inhibitor, or plus Placebo and to Compare Fulvestrant plus Abemaciclib or plus Placebo in Postmenopausal Women with Hormone Receptor-Positive, HER2-Negative Loco regionally Recurrent or Metastatic Breast Cancer.

The Committee, after detailed deliberations, concurred with the recommendations of the Technical Committee for approval of clinical trial protocol for conduct of the study subject to verification of conduct of Phase II Clinical trial. (Details at **Annexure-I**).

Proposals of Clinical Trials related to IND's recommended by IND/CBBTDEC Committee:

Proposal No.01:

A multi-centre, non-randomized, open label, single arm trial to determine the efficacy, safety and tolerability of Tissue Engineered Xenografts (Bovine Pericardium, Bovine Jugular Vein and Porcein Pulmonary Artery) in patients with Structural Heart Disease and Pulmonary Stenosis" in patients of 100, 25, 25 respectively

The Committee, after detailed deliberations, concurred with the recommendations of the Technical Committee for approval of clinical trial protocol for conduct of the study.

Proposal No.02:

A Prospective, randomized, multi-centric, comparative, open label, double arm controlled clinical study to evaluate the safety and efficacy of UCMSCs in subjects with recently diagnostic Type I diabetes.

The Committee, after detailed deliberations, concurred with the recommendations of the Technical Committee for approval of clinical trial protocol for conduct of the study

Proposal No.03:

Prospective, randomized, open label, double arm, dose finding clinical study of R-HSC-008 as an adjunct cell based therapy as a prophylaxis for aGvHD after allogenic Hematopoietic stem cell Transplantation–Phase I/II".

The Committee, after detailed deliberations, concurred with the recommendations of the Technical Committee for approval of clinical trial protocol for conduct of the study subject to condition that outcome of Phase I shall be submitted to CBBTDEC.

Proposal No.04:

Prospective, multicentric, open label, two arm, parallel group, comparative dose escalation clinical study to evaluate the safety and efficacy of R-HSC-002(Autologous bone marrow derived MSCs) and R-HSC-003(Allogenic cord derived MSCs) dosage as an adjunct cell based therapy in the treatment of patients with ischemic limb disease.

The committee after detailed deliberations, concurred with the recommendations of the Technical Committee for approval of clinical trial protocol for conduct of the study subject to justification of two arm study to be verified by CDSCO.

ITEM No. 03

Proposals for Clinical Trial Waiver in Indian population for approval of new drugs falling under the category of drugs, which have already been approved outside India

Proposal No.01:

Hydralazine tablet 25 mg/50 mg.

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-II**).

Proposal No.02:

Dengue Tetravalent Vaccine (Live, Attenuated).

The proposal is deferred.

Secretary, DHR may take a presentation from the applicant along with DGHS and the outcome should be submitted to the Apex Committee for consideration.

Proposal No.03:

Idarucizumab (Praxiband).

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-II**).

Proposal No.04:

Riboflavin Ophthalmic Solution 0.1%

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-II**).

Proposal No.05:

Eliglustat 84 mg Capsules.

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-II**).

Proposal No.06:

Alectinib Capsules 150 mg.

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-II**).

Proposal No.07:

Tranexamic Acid Film Coated Tablet 1000mg (Additional Strength)

The Committee noted that proposed formulation is higher dose of approved drug which is within the recommended dose. After detailed deliberations, the Apex Committee concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-II**)

Proposal No.08:

Bendamustine Hydrochloride 100mg /vial (Additional Indication).

The Apex Committee, after detailed deliberations, concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-II**).

Proposal No.09:

Insulin Glargine solution for Injection 300 IU/mL [Additional Strength].

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-II**).

Proposal No.10:

Trametinib 0.5 mg & 2 mg Tablets and Trametinib in combination with Dabrafenib as 50mg/75mg Capsules.

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-II**).

Proposal No.11:

Daratumumab Concentrate for solution for infusion 100 mg and 400 mg.

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-II**).

Proposal No.12:

Bone allograft products derived from human donor musculo skeletal donor tissue - R-HSC-003(Allogenic cord derived MSCs) and R-HSC-003(Allogenic cord derived MSCs) Musculoskeletal Donor Tissue.

The Apex Committee, after detailed deliberations concurred with the recommendations of the Technical Committee for waiver of local clinical trial (Details at **Annexure-II**).

OTHERS:

ITEM NO. 01

1. Compliance report on the recommendation of the 30th Apex Committee regarding the clinical trial proposal of M/s Pharmazz.

The Committee noted that DG, ICMR has reviewed the revised protocol after incorporating amendments recommended by the IND Committee. The Apex Committee recommended for approval of clinical trial protocol for conduct of the study

2. Discussion on the proposal of M/s APAC Biotech Pvt. Ltd, Gurgaon for Marketing Authorization of APCEDEN™ [Dendritic Cell (DC) product].

The Committee recommended for the conduct of Phase III clinical trial on suitable number of subjects. Further, it was decided that DCG (I) may constitute an expert Committee for verifying the compliance of M/s APAC Biotech to the provisions of Drugs and Cosmetics Act, 1940 and Rules, 1945.

3. The Committee decided that the disposal of applications of Clinical Trials/New Drugs shall be carried out keeping in view the first in first out basis, the Committee also directed that the pendency of existing applications brought down so that all applications are disposed of within the prescribed timelines.

ITEM NO. 02

(i) The decision of the Apex Committee taken in its meeting held in first week of July 2016, that "the drugs (including Cosmetics and Medical Devices) approved by ICH regulators, with no adverse events, did not require Phase III ", may be implemented.

(ii) In future, cases of waivers need not be brought to Technical Committee and Apex Committee and these should be considered and disposed of by the Central Licencing Authority as per provisions of Drugs and Cosmetics Act, Rules and Guidelines issued by the Government from time to time and Technical Committee will act as Appellate Committee in cases of disputes.

The meeting ended with vote of thanks to and from the Chairman.

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Annexure-I

Proposal of clinical trial of NCEs along with their evaluations and recommendations of the Technical Committee in its 35th and 36th Meeting held on 21.09.2016 and 20.10.2016 respectively.

Proposal No	Details of the proposal	Assessment of the Proposal *vis – a vis* specified Parameters	Recommendation 1. Subject Expert Committee 2. Technical Committee
1.	**Name of the Drug:** Oral Semaglutide **Date of Application:** 19/04/2016 **Protocol No**: NN9924-4221 **Phase of the trial:** IIIa **Name of the Applicant:** Novo Nordisk India Private Ltd, Plot No. 32, 47 - 50, EPIP Area, Whitefield, Bangalore - 560 066, Karnataka, India **Name of the Sponsor:** Novo Nordisk India Private Ltd, Plot No. 32, 47 - 50, EPIP Area, Whitefield, Bangalore - 560 066, Karnataka, India. **Name of the Manufacturer:** Novo Nordisk A/S, Novo AlléDK-2880, Bagsværd, Denmark **Title:** A trial investigating the cardiovascular safety of	**Risk versus benefit to the patients-** The safety profile of the test drug from preclinical toxicity studies including repeat dose toxicity, genotoxicity, carcinogenicity 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 investigate the cardiovascular safety of oral Semaglutide in subjects with type 2 diabetes. **Unmet need in the country-** The test drug may be an alternative treatment option in subjects with type-2 diabetes at high risk of cardiovascular events.	**1. The proposal was deliberated in SEC (Endocrinology) held on 14/06/2016.** After the detailed deliberation the committee recommended the conduct of the trial subject to the following condition **i.** Primary responsibility for the Standard of Care should be with the trial investigator **ii.** The HbA1c at inclusion must be between 7 to 10 % **iii.** The hypoglycemic criteria and rescue medication should be clearly defined under the protocol. **iv.** The OADs be provided free of cost. **The proposal was Re-deliberated in SEC (Endocrinology) held on 22/08/2016.** After detailed deliberation the committee approved the study as the points raised earlier have been complied with. The firm further clarified that the

	Oral Semaglutide in subjects with Type 2 diabetes.		patients with Type 2 diabetes with HbA1C ≥10.0 % will receive standard of care along with Insulin and the study medication. **SEC Expert List:** 1. Dr. Rajesh Rajput, Senior Professor & Head, Dept. of Endocrinology, PGIMS, Medical Road, Rohtak-124001 2. Dr. Anil Bhansali, Additional Prof. & HOD, Endocrinology, PGIMER, Sector-12, Chandigarh. 3. Dr. Richa Dewan, Director and Professor, Dept. of Medicine, MAMC, New Delhi. 4. Dr. Lalit Kumar Gupta, Professor Dept. of Pharmacology, Lady Harding Medical College, New Delhi. **2. Recommendation of the Technical Committee on 21.09.2016:** After detailed deliberation, the committee agreed with the recommendation of the SEC and recommended the approval of the study.
02	**Name of the Drug:** Avelumab is the proposed International Non-proprietary Name (INN) for the anti-PD-L1 monoclonal antibody, MSB0010718C.	**Assessment of Risk vs. Benefit to the patients:** The safety profile of the study drugs from preclinical safety pharmacology and toxicology studies and clinical studies justify the conduct of the trial. **Innovation vis-avis Existing Therapeutic Option:** To	**1. The proposal was deliberated in SEC (Oncology) held on 27/09/2016.** After detailed deliberation the committee recommended the conduct of the study.

	Date of Application: 25/06/2016 **Protocol No**: B9991001 **Phase of the trial:** III **Name of the Applicant:** M/s Pfizer Limited, The Capital, 1802/1901, Plot No. C-70, G Block, Bandra Kurla Complex, Bandra (East), Mumbai 400051, Maharashtra, India **Name of the Sponsor:** M/s Pfizer Inc., 235 East 42nd Street, New York, NY 10017, USA **Name of the Manufacturer:** M/s Merck Serono S.A., Succursale d'Aubonne, Zone Industrielle del'Ouriettaz, CH-1170 Aubonne, Switzerland **Title:** A Phase 3, multicentre, multinational, randomized, open-label, parallel-arm study of avelumab plus best supportive care versus best supportive care alone as a maintenance treatment in patients with locally advanced or metastatic urothelial cancer whose disease	demonstrate the benefit of maintenance treatment with Avelumab plus BSC vs BSC alone in prolonging overall survival (OS) in patients with unresectable locally advanced or metastatic US whose disease did not progress on or following completion of first-line platinum-containing chemotherapy in each co-primary UC patient population: 1) patients determined to have PD-L1-positive tumors (including infiltrating immune cell) by a verified GMP PD-L1 1HC test, and 2) all randomized patients. **Unmet Medical Need in the Country:** The test drug may potentially provide alternative treatment of subjects with locally advanced or metastatic urothelial cancer.	**SEC Expert List:** **1.** Dr. Sameer Bakshi, Professor, dept. of Medical Oncology, AIIMS, New Delhi. **2.** Dr. C.K. Bose, Assistant Professor, Netaji Subhash Chandra Bose Cancer Research Institute, Kolkata. **3.** Dr. Sanjay Kumar Singh, Dept. of Medical Oncology, Gajara Raja Medical College, Veer Savarkar Marg, Gwalior-474009 Gwalior. **4.** Dr. Prantar Chakroborty, Dept. of Hematology, NRS Medical College, Kolkata 700014. **5.** Dr. Renu Saxena, Prof. and Head, Dept. of Hematology, AIIMS, New Delhi. **6.** Dr. Bikash Medhi, Pharmacology, PGIMER, Sector 12, Chandigarh. **7.** Dr. K.V. Anand, HOD, Dept. of Vascular Surgery, Army Hospital, R & R, New Delhi. **2. Recommendation of the Technical Committee on 20.10.2016:** After detailed deliberation, the committee agreed with the recommendation of the SEC and recommended the approval of the study.

	did not progress after completion of first line platinum-containing chemotherapy.		
03	**Name of the Drug:** Sarizotan Hydrochloride **Date of Application:** 21/04/2016 **Protocol No**: Sarizotan/001/II/2015 **Phase of the trial:** II **Name of the Applicant:** M/s CliniRx Tangent Research India Pvt Ltd Patriot House, 4th Floor, 3 BSZ Marg, New Delhi –110 002 **Name of the Sponsor:** Newron Pharmaceuticals S.p.A. Via Ludovico Ariosto 21 20091 Bresso (Milano) Italy **Name of the Manufacturer:** Merck KGaA **Address:** Frankfurter Str. 250, 64293 Darmstadt, Germany **Title** A Randomized, Double-Blind, Placebo-Controlled, Six-Month Study to Evaluate the Efficacy, Safety and Tolerability of	**Assessment of Risk vs. Benefit to the patients:** The safety profile of the study drug from preclinical pharmacology, single dose, repeat dose toxicity, carcinogenotoxicity, reproductive toxicity and Phase I clinical studies justify the conduct of the trial. **Primary objective:** To evaluate the effect of Sarizotan (5 to 10mg bid), compared to placebo, on reducing the number of apnea episodes, during awake time, in patients with RTT with respiratory abnormalities. **Unmet Medical Need in the country:** The test drug may provide alternate treatment option in in Patients with Rett Syndrome with Respiratory Symptoms.	**1. The proposal was deliberated in SEC (Neurology & Psychiatry) held on 26/08/2016.** After detailed deliberation the committee has recommended the following conditions: **1.** The title of the study should be phase II instead of phase II/III. **2.** Description and composition of placebo and the justification for use of placebo considering the RETT Syndrome to be a rare condition. **3.** Specify the exact number of the patients to be recruited from India **SEC Expert List:** **1.** Dr. Shruti Srivastava, Professor Department of Psychiatry, Uniersity College of Medical Sciences, New Delhi. **2.** Dr. M.V. Padma, Department of Neurology, AIIMS Hospital, New Delhi. **3.** Dr. Bikash Medhi, Dept. of Pharmacology, PGIMER, Sector 12, Chandigarh. **2. Recommendation of**

	Sarizotan in Patients with Rett Syndrome with Respiratory Symptoms		**the Technical Committee on 20.10.2016:** After detailed deliberation, the committee agreed with the recommendation of the SEC and recommended the approval of the study
04	**Name of the Drug:** LY2835219(Abemaciclib) **Date of Application:** 21/06/2016 **Protocol No**: 13Y-CR-JPBQ **Phase of the trial:** III **Name of the Applicant:** Eli Lilly and Company (India) Pvt. Ltd. Gurgaon – 122001, Haryana **Name of the Sponsor:** Eli Lilly and Company (India) Pvt. Ltd. Gurgaon – 122001, Haryana **Name of the Manufacturer: :** Eli Lilly and Company, Lilly Technology Center, Indianapolis, Indiana 46221, USA **Title** I3Y-CR-JPBQ: A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study to Compare NSAI plus	**Risk versus benefit to the patients** The safety profile of the test drug from pre-clinical toxicity including repeat dose toxicity, genotoxicity, carcinogenotoxicity studies 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 compare treatment with Abemaciclib plus NSAI(anastazole or letrozole) therapy versus placebo plus NSAI therapy with respect to PFS in post menopausal women with HR+ HER2 metastatic breast cancer. **Unmet need in the country-** The test drug may be an alternative treatment in subjects with metastatic breast cancer.	**1. The Proposal was deliberated in SEC (Oncology) held on 23/08/2016.** After detailed deliberation the committee recommended the conduct of phase III clinical trial. However, the committee raised the query regarding the rationale/justification of recruiting only 45 patients out of 450 patients recruiting globally. **SEC Expert List:** **1.** Dr. Sameer Bakshi, Prof. Dept. of Medical Oncology, AIIMS, New Delhi. **2.** Dr. H.P. Pati, Professor, Dept. of Hematology, AIIMS, New Delhi 110010. **3.** Dr. Prantar Chakra borty, Dept. of Hematology, NKS Medical College, Kolkata-700014. **4.** Dr. C.K. Bose, Assistant Professor, Netaji Subhash Chandra Bose Cancer Research Institute, Kolkata. **5.** Dr. H.S. Rehan, Professor and Head, Dept. of Pharmacology,

	Abemaciclib, a CDK4 and CDK6 Inhibitor, or plus Placebo and to Compare Fulvestrant plus Abemaciclib or plus Placebo in Postmenopausal Women with Hormone Receptor-Positive, HER2-Negative Locoregionally Recurrent or Metastatic Breast Cancer.		Lady Harding medical college, New Delhi. **6.** Dr. Renu Saxena, Professor and Head, Dept. of Hematology, AIIMS, New Delhi. **2. Recommendation of the Technical Committee on 20.10.2016:** After detailed deliberation, the committee agreed with the recommendation of the SEC and recommended the approval of the study

Annexure II

Recommendations of the 12 cases of Clinical trial waiver in Indian populations of the Technical Committee in its 35th and 36th Meeting held on 21.09.2016 and 20.10.2016 respectively.

S. No.	Drug Name	Indication	1. Recommendations of the SEC 2. Recommendation of Technical Committee
1.	**Name of the Drug:** Hydralazine tablet 25 mg/50 mg **Date of Application: 30.11.2015** **Name of the Firm:** M/s Cadila Pharmaceuticals **Regulatory status in India:** Approved as FDC (37.5 mg) **Regulatory status in other countries:** US and EU (for the proposed indication)	For the treatment of moderate to severe hypertension (essential hypertension) alone or as adjunct	**1. Recommendations of SEC:** The proposal was deliberated in **SEC (Cardiovascular) held at CDSCO (HQ) on 05.07.2016.** The firm presented the Bioequivalence study data with internationally approved product. The committee also noted that the product Hydralazine 25 mg/50 mg tablets is approved in USFDA and E.U, however the drug has not been in use in India, for last many years. Therefore the committee recommended for the manufacturing and marketing permission with the condition that Phase IV study is to be conducted and accordingly firm shall submit Phase IV protocol within 3 months. **SEC Expert List:** **1.** Dr. Shyam Sunder Kothari, Prof. Dept of Cardiology, AIIMS, New Delhi. **2.** Dr. D S Arya, Dept. of Pharmacology, AIIMS, New Delhi **3.** Dr. Sandeep Bansal HOD, Department of Cardiovascular, VMMC & Safdurjung Hospital, New Delhi **4.** Dr. S.K. Agrawal, Professor & Head of the department, Dept. Of Nephrology AIIMS, New Delhi. **5.** Dr. A.H.Ansari, Assistant Professor, Vardhman Mahavir Medical College, New Delhi-110029 **2. Recommendation of Technical Committee on 21.09.2016:** The committee opined that the said drug is approved in India as parenteral and also as an ingredient in and FDC. After detailed deliberation, the committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial with the condition that-

			1. The drug should not be used as first line therapy and the indication should be revises as "for moderate to severe hypertension (in conjunction with a β-adrenoreceptor blocking agent or diuretic) and hypertensive crisis". **2.** A systematic Phase IV study should be done for which protocol should be submitted to the office of CDSCO.
2.	**Name of the Drug:** Dengue Tetravalent Vaccine (Live, Attenuated) **Date of Application: 20.10.2015** **Name of the Firm:** M/s Sanofi Pasteur India Private Limited **Regulatory status in other countries:** Brazil, Philippines and Mexico	The vaccine is intended for the prevention of Dengue disease caused by dengue virus serotypes 1, 2, 3 and 4 in individuals 9 through 60 years of age living in endemic areas	**1. Recommendation of SEC:** The firm's proposal was earlier deliberated in **SEC dated 12.01.16** wherein the committee deliberated the proposal of the firm in detail and opined that the firm has conducted Phase II clinical trial in the age group of 18-45 years in India and the results were accepted by the SEC dated 08.04.15. Now, the firm has requested for Marketing Authorization of the vaccine without conduct of Phase III trial. The firm has submitted published data of Phase III trials from other Asian and Latin American countries (Thailand, Brazil, and Mexico etc.) based on which the vaccine has been approved in Mexico, Philippines and Brazil. Although, the vaccine does not qualify the requirements of waiver of clinical trial, considering the fact that Dengue is a health problem of major concern in the country and can be life threatening in certain cases, the committee recommends for Market Authorization of the vaccine in the age group of 18-45 years only with the condition to conduct Phase IV clinical trial in time bound manner (Protocol submission within 3 months of marketing of the product)." The proposal was further deliberated in the Technical committee dated 01.02.2016 wherein the committee after detailed deliberation, recommended for waiver of local clinical trial as per SEC recommendation. As per the procedure, the proposal was forwarded to **Apex committee dated 06.04.2016** for their opinion wherein the committee after due deliberation had noted that the evidence in the case is not sufficient to waive conduct of clinical trial. Accordingly, firm was informed about the decision of the committee. Now, the firm has requested for reconsideration of

			the same in public interest as it will delay the availability of vaccine to Indian patients. **SEC Expert List:** **1.** Dr. A.P. Dubey, Prof & Head, Paediatrics, MAMC, New Delhi **2.** Dr. Ramesh Aggarwal, Additional Professor, Vaccine & Neonatology, AIIMS, New Delhi **3.** Dr. Savita Verma, Professor, Pharmacology, PGIMS, Rohtak. **2. Recommendation of Technical Committee on 21.09.2016:** The Committee noted that there is no alternate treatment/ therapy available for Dengue and it is also a life threatening disease. Further, due to frequent outbreaks of Dengue and the vaccine being approved and marketed in other countries including Brazil, Mexico, Philippines etc., after detailed deliberations, the committee agreed with the recommendation of earlier SEC dated 12.01.2016 and recommended for waiver of local clinical trial.
3.	**Name of the Drug:** Idarucizumab (Praxiband) **Date of Application: 18.12.2015** **Name of the Firm:** M/s Boehringer Ingelheim India Private Limited **Regulatory status in India:** Not Approved **Regulatory status in other countries:** US	Idarucizumab is a specific reversal agent for Dabigatran and is indicated in patients treated with Dabigatran Etexilate capsules when rapid reversal of the anticoagulant effects of Dabigatran is required: **1.** For emergency surgery/urgent procedures **2.** In life-threatening or uncontrolled bleeding	**1. Recommendation of SEC:** The proposal was deliberated in 30th **SEC (Cardiovascular and Renal)_held at CDSCO (HQ) on 31.05.2016.** The committee after deliberation observed that this is a specific antidote used in emergent management of bleeding due to a specific drug i.e Dabigatran. The efficacy and safety data of Idarucizumab was deemed adequate. There is no other specific therapy available for this indication. Therefore, in view of this the committee recommended for grant of marketing authorization with waiver of Phase III clinical trial on Indian subjects. The firm also required to submit detailed PMS data of first 25 patients or data generated from the patients in two years, whichever is earlier. **SEC Expert List:** **1.** Dr. Shashi Mohan Sharma, Professor, Dept. of Cardiology, SMS Hospital Medical College & Attached hospitals, J.L.N. Marg, Jaipur-

			302004 **2.** Dr. Shyam Sundar Kothari, Prof. Dept of Cardiology, AIIMS, New Delhi **3.** Dr. Lalit Kumar Gupta. Professor Dept. of Pharmacology, LHMC, New Delhi **4.** Dr. Sandeep Bansal HOD, Department of Cardiovascular, VMMC & Safdurjung Hospital, New Delhi **5.** Dr. A.H.Ansari, Assistant Professor, Vardhman Mahavir Medical College, New Delhi-110029 **2. Recommendation of Technical Committee on 21.09.2016:** The committee opined that there is an unmet need in the country for the said drug and hence after detailed deliberation, the committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
4.	**Name of the Drug:** Riboflavin Ophthalmic Solution 0.1% **Date of Application: 28.12.2015** **Name of the Firm:** M/s. Sunways (India) Private Limited **Regulatory status in India:** Not approved **Regulatory status in other countries:** European Union, USA and Asian countries	To treat keratoconus and corneal ectasia pathologies. The treatment can prevent the necessity of corneal transplant. It is classified as class II	**1. Recommendation of SEC:** The proposal was deliberated in **SEC (Ophthalmology) held at CDSCO (HQ) on 09.06.2016.** After deliberation the committee opined that, the drug is being used in clinical practice worldwide and the safety proven globally. As per information provided the product is approved in USA as Orphan drug and also approved in European Union and few other Asian countries. The committee recommended the grant of permission to manufacture the product provided the firm shall submit PSUR data as per Schedule Y of Drugs and Cosmetics Act and Rules there under to the office of DCG (I) for the period of 04 years. **SEC Expert List:** **1.** Dr. Rohit Saxena , Additional Prof. AIIMs, New Delhi – 110029 **2.** Dr. R.K. Jain, Professor, Lady Harding Medical College, new Delhi. **3.** Dr. Kamalesh Khilnani, Professor SMS Medical College, New Delhi **4.** Dr. Bikash Medhi, Professor, Department of Pharmacology, PGIMER, Chandigarh

			2. Recommendation of Technical Committee on 21.09.2016: After detailed deliberation, the committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
5.	**Name of the Drug:** Eliglustat 84 mg Capsules **Date of Application: 28.03.2016** **Name of the Firm:** M/s Sanofi – Synthelabo (India) Private Limited **Regulatory status in India:** Not Approved **Regulatory status in other countries:** Europe, USA, Japan, Australia, South Korea and 30 other countries	It is indicated for the long term treatment of adult patients with Gaucher Disease Type I (GD1) who are CYP2D6 Poor Metabolisers (PM's), Intermediate Metabolisers (IM's) or Extensive Metabolisers (EM's).	**1. Recommendation of SEC:** The proposal was deliberated in 29th **SEC (Endocrinology) held at CDSCO (HQ) on 22.08.2016.** The firm has applied for the grant of permission to Import and market Eliglustat 84 mg Capsules which is indicated for the long term treatment of adult patients with Gaucher disease type 1 (GD1) who are CYP2D6 Poor Metabolizers (PM's), Intermediate Metabolizers (IM's), or Extensive Metabolizers (EM's). After detailed deliberation the committee opined that the adult Gaucher disease is a rare disorder and Eliglustat for its treatment has been approved as orphan drug in 36 countries including US, EU, Japan etc. Further, the Genotype analysis of the patient is mandatory prior to initiation of treatment and the company has agreed to bear the cost of this analysis. Therefore the Committee recommended import and marketing of Eligustat for above indication without local clinical trial. **SEC Expert List:** **1.** Dr. D. S Arya, Professor, Dept. Of Pharmacology, AIIMS, New Delhi **2.** Dr R K Arya, Dept. Of Orthopaedics, RML Hospital, New Delhi **3.** Dr Arunagshu Talukdar, MD, Professor, Rhuematology, Dept. Of Medicine, Medical College, Kolkata-700073 **4.** Dr Chandralekha, Professor and Head, Dept, of Anaesthesiology, AIIMS, New Delhi **5.** Dr Anjan Trikha, Professor and Head, Dept. of Anaesthesiology, AIIMS, New Delhi **6.** Dr Uma Kumar, Head, Professor, Rhuematology, Department of Medicine, AIIMS, New Delhi 110029 **2. Recommendation of Technical Committee on 21.09.2016:**

			After detailed deliberation, the committee opined that Gaucher's disease is a very rare disease, and therefore agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
6.	**Name of the Drug:** Alectinib Capsules 150 mg **Date of Application: 11.02.2016** **Name of the Firm:** M/s Roche Products (India) Private Limited **Regulatory status in India:** Not Approved **Regulatory status in other countries:** US and Japan (In patients with ALK-positive unresectable, recurrent or advanced NSCLC)	It is indicated for the treatment patients with Anaplastic Lymphoma Kinase ALK-positive, locally advanced or metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to Crizotinib	**1. Recommendation of SEC:** The proposal was deliberated in 42nd **SEC (Oncology) held at CDSCO (HQ) on 19.07.2016.** After detailed deliberation the committee opined the following. The firm has presented proposal for clinical trial waiver of Alectinib capsules 150 mg to be indicated for the treatment of patients with anaplastic lymphoma kinase (ALK) -positive, locally advanced or metastatic nonsmall cell lung cancer (NSCLC) who have progressed on or are intolerant to Crizotinib before the Committee. The Committee noted that the data presented is Phase II, and it was also informed by the firm that the Phase III study is ongoing. However, the drug has received breakthrough therapy designation, orphan drug designation in the US and the current indication was approved under FDA'S Accelerated approval program (based on Overall response rate). The application was granted priority review. The Committee also noted the drug is especially active for relapse of the disease in the brain, and that at present is an unmet need for ALK-positive, locally advanced or metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to Crizotinib. In view of this the Committee recommended the import and marketing permission with local clinical trial waiver along with the submission of the Phase-III report to the Committee for review and continued marketing of the drug**.** **SEC Expert List:** **1.** Dr Sameer Bakshi, Professor, Dept. Of Medical Oncology, AIIMS, New Delhi **2.** Dr C K Bose, Assistant Professor, Netaji Subhash Chandra Bose Cancer Research Institute, Kolkata **3.** Dr Sanjay Kumar Singh, Dept. of Medical Oncology, Gajara raja Medical College, Veer Savarkar Marg, Gwalior – 474009

			4. Dr Bikash Medhi, Dept. of Pharmacology, PGIMER, Chandigarh **2. Recommendation of Technical Committee on 21.09.2016:** After detailed deliberation the committee opined that Alectinib is indicated in patients with ALK Positive, locally advanced or metastatic Non-Small Cell Lung Cancer (NSCLC) who have progressed on or are intolerant to Crizotinib where the number of patients are very less, therefore the committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
07.	**Name of the Drug:** Tranexamic Acid Film Coated Tablet 1000mg **(Additional Strength)** **Date of Application:** 31.05.2016 **Name of the Firm:** M/s Akums Drugs & Pharmaceuticals Limited **Regulatory status in India:** Approved **Regulatory status in other countries:** Not Approved for the proposed strength	For the treatment if Mennorhagia	**1. Recommendation of SEC:** The proposal was deliberated **in 21st SEC (Reproductive and Urology) held on 30.08.2016.** "After detailed deliberation committee recommended as this is a BCS class III drug waiver of BE study may be considered. The molecule is already approved with the same indication and also the proposed strength is within the recommended dose range, therefore marketing permission can be granted without local CT". **SEC Expert List:** **1.** Dr. N.K. Mohanty, Prof & Head, Dept. of Urology, Vardhman Mahavir Medical College &Safdurjung Hospital, New Delhi. **2.** Dr. Rajeev Sood, Prof & Head Dr. RML Hospital & PGIMER, Baba Kharak Singh Marg, Type 3, President's Estate. **3.** Dr. Anup Kumar Kundu, Professor & Head, IPGMER & SSKM, Kolkata, West Bengal-700020 **4.** Dr. Seema Singhal, Assistant Professor, Department of Gynaecology AIIMS, New Delhi **5.** Dr. Pikee Saxena, Professor, Lady Harding College, New Delhi- 110001 **6.** Dr. Amlesh Seth, Professor & Head Department of Urology, AIIMS,New Delhi **7.** Dr.C.D.Tripathi, Professor and Head, Dept. of Pharmacology, VMMC, Safdurjung, New Delhi

			8. Dr. S. K. Singh, Professor, Department Urology, PGIMER, Chandigarh-160012 **2. Recommendation of Technical Committee on 21.09.2016:** After detailed deliberation, the committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
08	**Name of the Drug:** Bendamustine Hydrochloride 100mg /vial **(Additional Indication)** **Date of Application:** 18.03.2014 **Name of the Firm:** M/s Johnson & Johnson Limited **Regulatory status in India:** Approved (Chronic Lymphocytic leukaemia on 16-05-2009) **Regulatory status in other countries:** UK and Germany (for the proposed indication)	For the treatment of Front line treatment of multiple myeloma (Durie-Salmon stage II with progress or stage III) in combination with prednisone for patients older than 65 years who are not eligible for Autologous stem cell transplantation and who have clinical neuropathy at time of diagnosis precluding the use of thalidomide or bortezomib containing treatment	**1. Recommendation of SEC:** The proposal was deliberated **in SEC (Oncology& Hematology) held on 27.10.2015.** "The firm presented the proposal before the committee. The committee noted that the proposed indication fulfils the criteria for waiver of clinical trial under rare disease condition. The committee also noted that this drug is approved for the same indication in UK, Germany etc. Hence proposed additional indication is recommended with CT waiver". **SEC Expert List:** **1.** Dr. Sameer Bakshi, Professor, Dept. of Medical Oncology, AIIMS, New Delhi **2.** Dr. S.D. Banavali, Head, Dept. of Medical Oncology, Tata Memorial Hospital, Parel, Mumbai- 400 012 **3.** Dr. Hemant Malhotra, Head, Division of Medical Oncology, SMS Medical College, Jaipur. **4.** Dr. C. K. Bose, Assistant Professor, NetajiSubhash Chandra Bose Cancer Research Institute, Kolkata. **5.** Dr. Urmila Thatte, Prof. And Head, Dept. of Clinical Pharmacology, SGS Medical College, KEM Hospital, Mumbai **6.** Dr. Sanjay Kumar Singh, , Dept. of Medical Oncology, Gajara Raja Medical College, Veer SavarkarMarg, Gwalior – 474009 Gwalior **7.** Dr. (Brig.) Ajay Sharma, Professor, Dept of Hematology, Army Hospital (Research & Referral), Dhaula Kuan, New Delhi, Delhi 110010 **8.** Prof Dr. H.P. Pati, Dept of Hematology,

			AIIMS, Ansari Nagar Delhi-110029 **9.** Dr. B. Gupta ,Dept. of Medicine ,NDMC & Hindu Rao Hospital ,New Delhi **10.** Dr. R.K Arya, Professor and Head Dept of Orthopaedics, RML New Delhi **11.** Dr. Sushma Bhatnagar, Associate Professor and Head, Dept of Anesthesiology, AIIMS, New Delhi. **2. Recommendation of Technical Committee on 21.09.2016:** After detailed deliberation, the committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
09.	**Name of the Drug:** Insulin Glargine solution for Injection 300 IU/ml **[Additional Strength]** **Date of Application:** 16.02.2016 **Name of the Firm:** M/s Sanofi India Limited **Regulatory status in India:** Approved [100 IU/mL Strength] **Regulatory status in other countries:** EU, US and 16 other Countries	For the treatment of Insulin dependent Diabetes Mellitus Type I and Type II	**1.** The proposal was deliberated in **24th SEC (Endocrinology) held at CDSCO (HQ) on 22.03.2016**. The committee opined that proposed product falls under the definition of new drug. Firm have shown the clinical trial results of said product in USA where you have shown different PK/PD properties of this drug as compared to Glargine 100 IU/ml. Firm have not done any clinical trial (efficacy and safety studies) in Indian population. Therefore the **committee recommended for the conduct of local clinical trials** for consideration for the grant of Marketing Authorization of the product. The proposal was deliberated in the **35th Technical Committee Meeting held on 21.09.2016**. The committee opined that the firm shall give proper justification and presentation while representing the case for reconsideration in the Technical Committee. **SEC Expert List:** **1.** Dr. Rajesh Khadgawat, Associate Professor, Dept of Endocrinology, AIIMS, New Delhi – 110029 **2.** Dr. Rajesh Rajput, Senior Professor & Head Department Endocrinology & Medicine VI PGIMS, Medical Road, Rohtak – 124001 **3.** Dr. C. R. Jayanti, Professor & Head,

			Pharmacology, Bangalore medical College, Bangalore **4.** Dr. Deepak Khandelwal, Maharaja Agrasen Hospital, West Punjabi Bagh, New Delh9i – 110026 **5.** Dr. Richa Dewan, Department of Medicine, MAMC, New Delhi. **2. Recommendation of Technical Committee on 20.10.2016:** The drug Insulin Glargine100 U/mL is already approved in India. Further, Insulin Glargine 300 U/mL is approved in USA, EU, Canada, Australia, Japan and other countries (total of 66 countries) and is marketed since 3 years in those countries. The additional advantage of 300 U/mL is slow release leading to constant insulin supply with low variability and low risk of hypoglycemia. In patients requiring higher dose of insulin, the quantum/volume required is low. Therefore, it is beneficial for patients. Hence Insulin Glargine 300 U/mL is recommended by the committee.
10.	**Name of the Drug:** Trametinib 0.5 mg & 2 mg Tablets and Trametinib in combination with Dabrafenib as 50mg/75mg Capsules **Date of Application:** 02.02.2016 **Name of the Firm:** M/s. Novartis Healthcare Private Limited **Regulatory status in India:** Not Approved	As a monotherapy or in combination with Dabrafenib for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600 mutation	**1. Recommendation of the Subject Expert Committee (Oncology) 27.09.2016:** The firm has for the grant of permission to Import and market Trametinib 0.5 mg & 2 mg Tablets: • As a monotherapy or in combination with Dabrafenib for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600 mutation with waiver of local clinical trial. After detailed deliberation, the committee observed that metastatic melanoma is a rare disease and USFDA has granted orphan drug designation to Trametinib, Dabrafenib and combination therapy. In view of above, the committee recommended the waiver of local clinical trial as an orphan drug for the proposed indication. **SEC Expert List:**

	Regulatory status in other countries: USFDA, EMEA and Health Canada		**1.** Dr. Sameer Bakshi, Professor, dept. of Medical Oncology, AIIMS, New Delhi. **2.** Dr. C.K. Bose, Assistant Professor, Netaji Subhash Chandra Bose Cancer Research Institute, Kolkata. **3.** Dr. Sanjay Kumar Singh, Dept. of Medical Oncology, Gajara Raja Medical College, Veer Savarkar Marg, Gwalior-474009 Gwalior. **4.** Dr. Prantar Chakraborty, Dept. of Hematology, NRS Medical College, Kolkata 700014. **5.** Dr. Renu Saxena, Prof. and Head, Dept. of Hematology, AIIMS, New Delhi. **6.** Dr. Bikas Medhi, Pharmacology, PGIMER, Sector 12, Chandigarh. **7.** Dr. K.V. Anand, HOD, Dept. of Vascular Surgery, Army Hospital, R & R, New Delhi **2.Recommendation of Technical Committee on 20.10.2016:** After detailed deliberation, the committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
11.	**Name of the Drug:** Daratumumab Concentrate for solution for infusion 100 mg and 400 mg **Date of Application:** 04.05.2016 **Name of the Firm:** M/s Johnson & Johnson Pvt Ltd **Regulatory status in India:** Not Approved **Regulatory status in other countries:** USFDA and EU	Daratumumab is indicated for the treatment of patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent.	**1.** The proposal was discussed in the **SEC (Oncology)** committee meeting which was held on **27-09-2016**. The firm has presented the data as desired by the committee in the previous meeting dated 23-08-2016. After detailed deliberation, the committee recommended for marketing authorization of drug for the indication of relapsed and refractory multiple myeloma, whose prior therapy included proteasome inhibitor and immunomodulatory agent. The committee also accepted the request for waiver of phase III clinical trial in India, since the drug is conditionally approved in USA and EMA as orphan drug and there is no therapy for this indication. However the firm is required to conduct phase IV clinical trial as per the requirements of Indian GCP and schedule Y of Drugs and Cosmetics Rules and

			accordingly firm should submit protocol before marketing of the said drug in India. **SEC Expert List:** **1.** Dr. Sameer Bakshi, Professor, dept. of Medical Oncology, AIIMS, New Delhi. **2.** Dr. C.K. Bose, Assistant Professor, Netaji Subhash Chandra Bose Cancer Research Institute, Kolkata. **3.** Dr. Sanjay Kumar singh, Dept. of Medical Oncology, Gajara Raja Medical College, Veer Savarkar Marg, Gwalior-474009 Gwalior. **4.** Dr. Prantar Chakroborty, Dept. of Hematology, NRS Medical College, Kolkata 700014. **5.** Dr. Renu Saxena, Prof. and Head, Dept. of Hematology, AIIMS, New Delhi. **6.** Dr. Bikash Medhi, Pharmacology, PGIMER, Sector 12, Chandigarh. **7.** Dr. K.V. Anand, HOD, Dept. of Vascular Surgery, Army Hospital, R & R, New Delhi **2. Recommendation of Technical Committee on 20.10.2016:** After detailed deliberation, the committee agreed with the recommendation of the SEC and recommended for waiver of local clinical trial.
12.	**Name of the Drug:** Bone allograft products derived from human donor musculo skeletal donor tissue - R-HSC-003(Allogenic cord derived MSCs) and R-HSC-003(Allogenic cord derived MSCs) Musculoskeletal Donor Tissue **Name of the Applicant**: M/s Lakshmi Associates, Chennai	As scaffolding where there is a need for correcting, restructuring, filling, repairing, or rebuilding bone defects or deficiencies due to bone loss in dental (oral-maxillofacial) procedures.	**Recommendation of the CBBTDEC Committee:** **9th CBBTDEC dated 13.05.2016** **1.** The firm is required to submit aggregate data in a summary form with table on safety and efficacy. **2.** The marketing approvals by various countries and the conditions for post marketing commitments are to be studied. **3.** Committee felts that there is unmet need for such products as opined by the subject experts. **4.** The aggregate data and conditions of the market approval can be evaluated by circulation to the members. **Consideration by 10th Cellular Biology Based Therapeutic Drugs Evaluation Committee (CBBTDEC) dated 06.09.2016**

	Date of Application: 18.02.2015 **Regulatory status in India:** Not Approved **Regulatory status in other countries:** USA		As requested, the data was provided by the company. The 9th CBBTDEC committee has already mentioned that there is unmet need for such products as opined by the subject experts and the product is approved by US-FDA. The committee recommended for import and market authorization of bone allograft products derived from human donor musculoskeletal donor tissue with the condition to conduct Phase IV clinical trial in at least 200 subjects. The Apex committee in its 27th meeting dated 06.04.2016 has recommended that IND proposal or those proposals which are chaired by DG, ICMR shall be directly placed before the Apex Committee. Accordingly, the proposal is placed before the Committee. **Expert Committee Members:** **1.** Dr. Soumya Swaminathan, Chairperson of CBBTDEC, Secretary, Department of Health Research & Director General, ICMR, Ansari Nagar, Post Box No. 4911, New Delhi -110029. **2.** Dr. Alok Srivastava, Professor& Head, Dept. of Hematology, CMC, Vellore – 632004, Tamil Nadu. **3.** Prof. N. K. Mehra, National Chair & former Dean (Research) and ex Head Dept. of Transplant Immunology and Immunogentics, AIIMS, New Delhi. **4.** Dr. Rita Mulherkar, Former Sr. Scientist, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai, 410210.R/o. A-103, Park Dew, Sector-20 Kharghar, Navi Mumbai-410210. **5.** Dr. H.S.Chhabra,Medical Director, Indian Spinal Injury Centre,Vasantkunj,New Delhi.

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