MINUTES OF THE 27th MEETING OF THE APEX COMMITTEE HELD ON 06-04-2016 UNDER THE CHAIRMANSHIP OF SECRETARY, (HF&W) FOR SUPERVISING CLINICAL TRIALS ON NEW CHEMICAL ENTITIES

Present:

1. **SHRI B.P. SHARMA**
   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**
   DG, DGHS
4. **SHRI K.L. SHARMA**
   Joint Secretary
   Department of Health and Family Welfare

SPECIAL INVITEES:

1. **SHRI K.B.AGARWAL**
   Addl. Secretary (F&D)
   Ministry of Health and Family Welfare
2. **DR. G.N. SINGH**
   DCG(I), FDA Bhavan, New Delhi
3. **DR.S.ESWARA REDDY,**
   Joint Drugs Controller (I), CDSCO
4. **Dr. V.G.Somani**
   Joint Drugs Controller (I), CDSCO
5. **R.Chandrashekar,**
   Dy. Drugs Controller (I), CDSCO

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.1

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

1) **Proposal No.1**

A multicenter, randomized, double-blind, placebo controlled phase III study to evaluate the efficacy, safety and tolerability of Serelaxin when added to standard therapy in acute heart failure patients

The Apex 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).

2) **Proposal No.2**

Efficacy and Safety of Semaglutide versus Dulaglutide as add-on to Metformin in subject with type 2 diabetes

The Apex 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).

3) **Proposal No.3**

A 96-week, prospective, multicenter, randomised, double-blind, placebo-controlled, 2-parallel groups, phase 3 study to compare efficacy and safety of Masitinib 4.5 mg/kg/day versus placebo in the treatment of patients with primary progressive multiple sclerosis or relapse-free secondary progressive multiple sclerosis.

The Apex 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), with the observation that in future, where any recommendation is made for imposing any additional restriction including conduct of trials in the Government sites, the justification for that may be included in the minutes.

4) **Proposal No.4**

A Phase II Clinical Study to assess the efficacy and safety of the Genopep 1 (Issar 1) in a non-randomized, open-label, single-arm, multi-Centre design in Indian adult patients with Relapsed/Recurrent/Resistant Solid Tumours

The Apex 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). The Committee further observed that the IND Committee should be suitably strengthened and the IND proposals should be directly placed before the Apex committee and these need not be placed before the Technical Committee. The Committee also decided that DGHS may be co-opted in the IND Committee.

Item No.2
Proposals for Clinical Trial Waiver in Indian population for approval of new drugs and devices falling under the category of drugs, which have already been approved outside India

A. Agenda relating to local clinical trial waiver of medical devices in cases where it is approved by the regulators of ICH countries was postponed and will be taken up on 7-4-2016.

B. **Ten Proposals relating to local clinical trial waiver of new drugs and devices falling under the category of drugs, which have already been approved outside India**

Proposal No.1 Darunavir Ethanolate film coated tablet 800mg (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-III).

Proposal No.2 Deferasirox Film coated tablets 90/180/360 (Additional dosage form and strength)

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

Proposal No.3 Methadone Hydrochloride Oral Concentrate BP 5mg / 10 mg per ml &Methadone Tablets IP 5mg / 10 mg (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-III).

Proposal No.4 Tiotropium Bromide Inhalar 9 mcg and Tiotropium Bromide Rotacaps 18mcg (Additional indication).

The Apex Committee noted that no evidence is available regarding approval of the drug for Asthma and keeping this in view, did not approve the waiver of local clinical trial.

Proposal No.5 Triptorelin for injection 22.5mg (Lyophilized) (Additional strength)

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

Proposal No.6 Dengue tetravalent vaccine (live, attenuated)

The Apex Committee noted that clinical trial cited as evidence in the present case is not sufficient to waive conduct of clinical trial in the country.

Proposal No. 7 to 10:

- **Palbociclib Capsule 75mg/ 100mg/125mg.**
- **Trabecular Metal TM Ardis Interbody System Solid and Trabecular Metal TM Ardis Interbody System (Graft)**
- **Implantable Balloon**
- **Pulsecath Ivac3l**

Consideration of the above four proposals was postponed to the next meeting on 7.4.2016

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

Annexure-I 496

List of 04 cases of clinical trial of NCEs along with their evaluations and recommendations of the Technical Committee in its 31st Meeting.

Proposal No	Details of the proposal	Assessment of the Proposal *vis –a vis* specified Parameters	Recommendation 1. Technical Committee 2. Subject Expert Committee /IND Committee
1.	**Name of the Drug:** Serelaxin (RLX030) **Protocol No :** CRLX030A2302 **Phase of the Study:** Phase III **Name of the Applicant:** Novartis Healthcare Private Limited **Name of the Sponsor:** Same as above **Name of the Manufacturer:** Novartis Pharma Stein AG Schaffhauserstrasse CH-4332 Stein, Switzerland **Name of the countries where the study is ongoing:** Malaysia, Philippines, Singapore, Taiwan, Thailand **Title:** A multicenter, randomized, double-blind, placebo controlled phase III study to evaluate the efficacy, safety and tolerability of Serelaxin when added to standard therapy in acute heart failure patients.	**Risk vs. Benefit to the patients:** The safety profile of the study drug from preclinical pharmacology, single dose, repeat dose toxicity, reproductive toxicity and phase I, II clinical studies justify the conduct of the trial. **Innovation vis-à-vis Existing Therapeutic Option:** The purpose of the study is to evaluate the efficacy, safety and tolerability of Serelaxin when added to standard therapy in acute heart failure patients. **Unmet Medical Need in the country:** The test drug may potentially provide alternative treatment option in acute heart failure when added to standard therapy.	**1. Recommendation of SEC** After detailed deliberation the committee recommended conduct of the study as per protocol. The patients should be explicitly informed that the cost of standard treatment needed for chronic heart failure shall be borne by the patients. **2. Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended the conduct of the study as per the SEC recommendation.
2.	**Name of the Drug:** Semaglutide **Protocol No:** NN9535-4216 **Phase:** IIIb **Name of the Applicant:** Novo Nordisk India Private Ltd.	**Risk versus Benefit to the patients-** The safety profile of the test drug from preclinical studies including single dose toxicity, repeat dose toxicity, reproductive and developmental toxicity and Clinical Phase I, II & IIIa studies, justify the conduct of the study.	**1. Recommendation of the SEC:** After detailed deliberation the committee recommended conduct of the trial subject to the following conditions:- I. Dose titration with Dulaglutide in line with the approved prescribing

	Name of the Sponsor: Same as above **Name of the Manufacturer:** Novo Nordisk A/S, NovoAlle, Bagsvaerd Denmark **Name of the countries where the study is ongoing:** USA, UK, Finland and Ireland **Title:** Efficacy and Safety of Semaglutide versus Dulaglutide as add-on to Metformin in subject with type 2 diabetes.	**Innovation vis a vis existing therapeutic option-** The purpose of the study is to evaluate the efficacy and safety of semaglutide versus dulaglutide as add-on to metformin in subjects with type 2 diabetes. **Unmet need-** The test drug may be an alternative treatment option in subjects with type 2 diabetes.	information. Accordingly the protocol should be suitably modified. II. 50 % trial sites must be govt. sites. **2. Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended the conduct of the study as per the SEC recommendation.
III.	**Name of the Drug:** Masitinib Mesylate **Protocol No :** AB07002 **Phase of the Study:** Phase III **Name of the Applicant:** Maya Clinicals, Cyber Heights, Behind TDP Office, Flat No: 604, Road No: 2, Banjara Hills, Hyderabad - 500 034 **Name of the Sponsor:** AB Science, #3, Avenue George V – 75008, Paris – France. **Name of the Manufacturer:** Excella Gmbh, Nurnberger Street 12, Feucht -90537, Bavaria, Germany. **Name of the countries where the study is ongoing:** Germany, Greece, Morocco, Poland Romania, Spain etc **Title:** A 96-week, prospective,	**Risk versus Benefit to the patients-** The safety profile of the test drug from preclinical studies including single dose toxicity, repeat dose toxicity, reproductive & carcinogenicity and Clinical Phase I & Phase II studies, justify the conduct of the study. **Innovation vis a vis existing therapeutic option-** The purpose of the study is to compare efficacy and safety of Masitinib 4.5 mg/kg/day versus placebo in the treatment of patients with primary progressive or relapse-free secondary progressive multiple sclerosis **Unmet need-** The test drug may be alterative option in the treatment of patients with primary progressive or relapse-free secondary progressive multiple sclerosis	**1. Recommendation of the SEC Committee held on 14.07.2015:** The firm presented safety data from a phase II global trial. After detailed deliberation the committee opined that Masitinib has teratogenic and carcinogenic potentials in animal studies, several side effects, limited human experience hence the phase II study should be conducted in India before taking Phase III trial in India for the above indication. **2. Recommendation of the Technical Committee:** After detailed deliberation, the Committee noted the following:- I. The recommendation of the SEC II. The Phase III trial is ongoing in a number of countries III. There are significant number of patients with Multiple Sclerosis in India and Multiple Sclerosis is an area of great unmet medical need. Hence, the Committee

	multicenter, randomised, double-blind, placebo-controlled, 2-parallel groups, phase III study to compare efficacy and safety of Masitinib 4.5 mg/kg/day versus placebo in the treatment of patients with primary progressive multiple sclerosis or relapse-free secondary progressive multiple sclerosis.		recommended that permission may be granted to conduct phase III study in India based on the already available phase II clinical trial data done in France in 22 patients where 7 out of 22 patients showed significant improvement from this treatment.
IV.	**Name of the Drug:** Genopep -1 **Protocol No :** Issar/2012/01 **Phase of the Study:** Phase II **Name of the Applicant:** ISSAR Pharmaceuticals pvt.ltd Serene chambers,3rd floor , Road no.5, Banjara hills,Hyderabad-500 034,India **Name of the Sponsor:** Same as above **Name of the Manufacturer:** Same as above **Title:** A Phase II Clinical Study to assess the efficacy and safety of the Genopep 1 (Issar 1) in a non-randomized, open-label, single-arm, multi-Centre design in Indian adult patients with Relapsed/ Recurrent/Resistant Solid Tumours.	**Assessment of risk vs benefit to the patient:** There was minimal risk to any patient on the phase 1 study. Since the study group is advanced refractory or resistant cancers, any response to treatment or reduction in symptomatology will be of great benefit to the lives of cancer patients. **Innovation vis-à-vis existing therapeutic option:** There is no drug in this class of compounds in clinical use.Hence, it is truly innovative. The mechanism of action being different, the drug may have high activity in patients who have failed multiple lines of cancer therapy. **Unmet medical need in the country:** Relapsed refractory cancer patients often suffer emotionally and physically from severe symptoms from advanced cancer. Very few avenues of treatment except palliative and symptomatic treatment are presently available. A drug from a new class of agents (membrane lytic peptides), would therefore be a welcome addition to the treatment armamentarium.	**1. Recommendation of the IND Committee:** After detailed deliberation, the Committee recommended for giving permission for the proposed study subject to condition that haemolytic anemia should be monitored during the study. **2. Recommendation of the Technical Committee:** The Committee deliberated the proposal and opined that the firm may be asked to clarify the following for further deliberation: ➢ The firm shall specify the types of patients and the types of tumor. ➢ Whether the proposed treatment is post surgical, monotherapy or as an adjuvant therapy. ➢ Proof of efficacy of the drug in tumor reduction in animal model. Accordingly the firm has submitted response to the above query and the proposal was deliberated in the Technical Committee. **Recommendation of the Technical Committee:-** The Committee noted the explanation submitted by the firm and recommended the conduct of Phase II clinical trial as per the recommendation of the IND Committee.

Annexure-III

Recommendations of the 10 cases of Clinical trial waiver in Indian populations:

Sr. no.	Details of the proposals	Name of the Firm holding permission outside the country	Indication	1.Recommendation of the Technical Committee 2. Recommendation of the SEC
1.	Darunavir Ethanolate film coated tablet 800mg **(Additional strength).** **Name of the applicant:** M/s Cipla Limited **Regulatory status:** The drug is already approved in India.	M/s Janssen Pharmaceuticals, Inc, UK	Darunavir (800mg) co-administered with Ritonavir (Darunavir/Ritonavir) and with other anti-retroviral agents, is indicated for the treatment of HIV-1 infection in adult patients only.	**1. Recommendations of the SEC:** Firm also presented BE study report conducted fed as well as fasting state comparing their product vis-à-vis innovator product. This product is also approved by USFDA and EMA. The committee noted that Darunavir 300mg and 600mg tablet are already approved in the country. After detailed deliberation, the committee recommended for approval of the proposed strength. However the firm shall conduct phase IV trial and shall submit the Phase IV CT protocol before marketing of the product in the country. **2. Recommendations of the Technical Committee:** After detailed deliberation, the Committee recommended for waiver of local clinical trial as per SEC recommendation.
2.	Deferasirox Film Coated Tablets 90/180/360mg **(additional dosage form & strength)** **Name of the applicant:** M/s Novartis Healthcare Pvt Ltd. **Regulatory status:** The drug is already approved in India.	M/s Novartis Healthcare Pvt Ltd. Switzerland	Deferasirox film coated tablets indicated for:- •Treatment of chronic iron overload due to blood transfusion (Transfusion Haemosiderosis) in patients aged 2 years and above. •Treatment of chronic iron overload in patients with non-transfusion dependent thalassemia (NTDT) syndromes aged 10 years and older.	**1. Recommendations of the SEC** The committee noted that this drug is already in the market since 2007 for the same indications. The proposed new formulation has been shown to supra bioequivalent in three clinical studies conducted in USA. Subsequently this new formulation (Deferasirox Film coated tablet 90/180/360mg) has been approved by the USFDA in lower doses as proposed by the firm. The committee deliberated in details and recommends for approval of import and marketing of Deferasirox film coated tablet 90/180/360mg for the already approved indication. The CT

				waiver was also recommended as the Indication for the new formulation is same and adequate clinical data to show the bio- equivalence was presented for the new formulation. **2. Recommendations of the Technical Committee:** After detailed deliberation, the Committee recommended for waiver of local clinical trial as per SEC recommendation.
3.	Methadone Hydrochloride Oral Concentrate BP 5mg / 10 mg per ml &Methadone Tablets IP 5mg / 10 mg **(additional indication)** **Name of the Applicant:** M/s Rusan Pharma Limited. **Regulatory status:** The drug is already approved in India.	M/s Roxane Laboratories Inc, Columbus	Indicated for the treatment for Pain management and palliative care.	**1. Recommendations of the SEC:-** The committee noted that Methadone is approved by CDSCO for the treatment of opioid dependence and maintenance treatment for opioid dependence on 01-06-2009 with the condition that it is to be supplied to Govt. or Govt. approved de-addiction centers only. It is also listed in essential Narcotic drug list. Further both oral tablet and liquid formulation is already listed in IP 2010 under the category of opioid analgesic. This formulation is already approved in USA and UK for moderate to severe pain management. The committee deliberated the specific utility of this drug for chronic refractory severe pain. In view of the utility and the unmet need for management of chronic refractory severe pain, the committee recommended the use of Methadone Hydrochloride IP Oral Concentrate 5mg/10mgmL & Methadone Tablet IP 5mg/10mg for the following additional indication, that is, "Chronic refractory moderate to severe pain". This drug should be available as per GSR 359(E) dated 05-05-2015 of NDPS act, 1985 (Ministry of Finance). The drug should be prescribed by physicians trained and experienced in the management of chronic pain. The package insert should have the boxed warning for all serious toxicities

				of the drug. The committee also noted that the 1000 ml pack size should not be permitted for use in this additional indication. **2. Recommendations of the Technical Committee:** After detailed deliberation, the Committee recommended only for waiver of local clinical trial for the indication "Chronic refractory moderate to severe pain" as per SEC recommendation.
4.	Tiotropium Bromide Inhalar 9 mcg and Tiotropium Bromide Rotacaps 18mcg **(Additional indication).** **Name of the Applicant:** M/s Cipla Limited. **Regulatory status:** The drug is already approved in India.	M/s Cipla Limited.	Indicated for the treatment of an add-on maintenance bronchodilator treatment in adult patients with asthma who are currently treated with the maintenance combination of inhaled corticosteroids (≥800 mcg budesonide/day or equivalent) and long-acting β2 agonists and who experienced one or more severe exacerbations in the previous year.	**1. Recommendations of the SEC:-** The committee opined that, this drug is already in use for COPD since 2003 in India. It is already listed in guidelines of National and international professional bodies as add- on therapy for difficult to control asthma. The committee also opined that options of add-on therapy for difficult to control asthma is limited, hence the committee recommended this proposed indication can be considered for wavier of clinical trial. The committee felt that conducting additional clinical trial may not get any new information. Thus, the firm can be given permission to use this drug as an add-on therapy for difficult to control asthma in adult patients, which should be highlighted prominently in the label. Therefore the committee recommended for the following additional indication -Tiotropium is indicated as an add-on maintenance bronchodilator treatment in adult patients with asthma who are currently treated with the maintenance combination of inhaled corticosteroids (≥800 mcg budesonide/day or equivalent) and long-acting β2 agonists and who experienced one or more severe exacerbations in the previous year. The committee also opined that Phase IV clinical trial shall be conducted in significant number of Indian patients.

				2. Recommendations of the Technical Committee:-After detailed deliberation, the Committee recommended for waiver of local clinical trial as per SEC recommendation.
5.	Triptorelin for injection 22.5mg **(Lyophilized) (Additional strength)** **Name of the Applicant**: M/s Dr Reddys Laboratories Ltd **Regulatory status:** The drug is already approved in India.	M/s Debio Recherche SA Switzerland	Indicated for the treatment of locally advanced or metastatic, hormone dependent prostate cancer.	**1. Recommendations of the SEC:-** This proposal was deliberated in SEC (Oncology) and the committee noted that Triptorelin (Lyophilized) 3.75mg injection is approved by this Directorate. Triptorelin 22.5mg is already approved in many countries like USA, UK, and Australia. The committee recommended for grant import and marketing permission for Triptorelin injection 22.5mg (once in a 6 months dose) in view of safety and expected improved patient adherence to the drug. **2. Recommendations of the Technical Committee:-** After detailed deliberation, the Committee recommended for waiver of local clinical trial as per SEC recommendation.
6.	Dengue tetravalent vaccine (live, attenuated) **Name of the applicant**: M/s Sanofi Pasteur India Private Limited Regulatory status: Approved in Philiphins, Mexico and Brazil.	M/s Sanofi Pasteur India Private Limited	Dengue tetravalent vaccine (live, attenuated).	**1. Recommendations of the SEC:-** The committee deliberated the proposal of the firm in detail. 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, 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). **2. Recommendations of the Technical Committee:** After detailed deliberation, the Committee recommended for waiver of local clinical trial as per SEC recommendation.
7.	Palbociclib Capsule 75mg/ 100mg/125mg. **Name of the applicant:** M/s Pfizer Limited **Regulatory status:** Approved in US, Macau	M/s Pfizer Limited	Indicated in combination with letrazole for the treatment of postmenopausal women with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-Negative advanced breast cancer as initial endocrine- based therapy for their metastatic disease.	**1. Recommendations of the SEC:-** The firm has presented the clinical trial data conducted in other counties and requested for local clinical trial waiver. It is observed that the drug was approved by USFDA as breakthrough therapy for approved indication. It was also observed that the progression free survival is almost double to that of the comparator drug Letrozole. In view of the above, the Committee recommended for grant of marketing permission with waiver of local clinical trial subject to the condition that the firm should conduct a phase-IV clinical trial in not less than 100 patients and the firm should submit protocol etc., within 3 months of the approval. Further the firm should submit the data at12 months from the date of approval of the phase-IV protocol. **2. Recommendations of the Technical Committee:** After detailed deliberation, the Committee recommended for waiver of local clinical trial as per SEC recommendation.
8.	Trabecular Metal TM Ardis Interbody System Solid and Trabecular Metal TM Ardis Interbody System (Graft) **Name of the applicant:** M/s. Zimmer India Pvt.	M/s. Zimmer India Pvt	**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	**1. 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. **2. Recommendations of the**

	Ltd., Gurgaon **Regulatory status:** The proposed medical devices are approved for marketing in USA, Canada and Australia. **Composition**: Porous Tantalum		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 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.	**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. Accordingly the firm has submitted the data and was deliberated upon Technical Committee. **3. Recommendation of the Technical Committee:-** The Committee reviewed the published data submitted by the firm. After detailed deliberation, the committee recommended for the grant of import permission as per SEC recommendation. Committee deliberated the cases of clinical trial waivers for Medical Devices and opined that the Medical Devices which are already approved and used in ICH countries need not be insisted for local clinical trials unless there are justifiable safety concerns.
9.	Implantable Balloon **Name of the Applicant:** M/s. Encarta Pharma Pvt. Ltd **Regulatory status:** Approved by Israel and other European Union countries. **Brand Name:** OrthoSpace	M/s. Encarta Pharma Pvt. Ltd	The In Space biodegradable implantable balloon (spacer) is used as a spacer to reduce friction between the acromion and the humeral head or Rotator Cuff to allow smooth gliding of the humeral head against the acromion. The indications for the InSpace include: • Scarred or torn tendon	**1. Recommendations of the SEC:** The committee after deliberation opined that the applicant presented their case but failed to submit published data on efficacy of the product as desired by the committee. No randomized trials have been done so far. The Committee therefore, recommended that published data on randomized control trials need to be submitted for further review by the Committee.

	InSpace System **Composition:** The In Space Spacer is a single use, biodegradable, inflatable spacer (balloon) implant made of Poly(L-lactide-co-e-caprolactone).		due to trauma or degradation, • Absence of tendon /muscle or non-functional tendon/ muscle • Ruptured tendon	The firm has submitted the above asked data and deliberated by SEC – Orthopaedics in its meeting held on 05.11.2015. The Committee recommended that the firm shall conduct the clinical trial to generate data on Indian population; accordingly clinical trial protocol shall be submitted to the Committee for further review. **2. Recommendation of the Technical Committee:** The firm has represented to Directorate General of Health Services for consideration of their proposal for grant of import and marketing of the device in the country based on the Global clinical data generated on the product. The product is approved in European countries (the Netherland), Israel, South Africa and South Korea. After detailed deliberation, the Committee noted that the device is already approved and being used in European and other countries as mentioned above and as such there is no further requirement of conduct of clinical trial in Indian population for such medical device. Therefore, the Committee desired to call the subject expert in Orthopedics for deliberation in the next Technical Committee meeting and also desired to call the firm to present the proposal before the Committee. Accordingly the firm presented their proposal before the Technical Committee. **3. Recommendation of the Technical Committee:-** The firm presented before the Committee. The product is

				approved in European countries (The Netherland), Israel, South Africa and South Korea. The Technical committee deliberated with Orthopedic experts invited for the meeting and recommended for the grant of import permission with the condition that the firm shall carry out Phase-IV clinical trial on 100 subjects in the country.
10.	Pulsecath Ivac3l **Name of the Applicant:** M/s. Meril Life Sciences India Pvt. Ltd **Regulatory status:** Approved by The Netherlands, Austria, Germany, Russia. **Composition:** Medical grade stainless steel (316L), Medical grade stainless steel (316L) Polyurethane tube braided with nitinol, Poly urethane, Poly urethane /methyl methacrylate-acrylonitrile-butadiene-stryene-stryene polymer (MABS), with a polyurethane seal (gasket), Methylmethacrylate-acrylonitrile-butadiene-stryene-stryene polymer (MABS), Ployurethane	M/s. Pulse Cath B.V, Netherland	It is indicated for use in patients with impaired left ventricular function which require left ventricular mechanical circulatory support for upto 24 hours. It can be positioned in the left ventricular cavity through the subclavian/ axillary artery, or through the aortic wall during open-chest surgery. The iVAC3L-ST (Short Tip) has a shorter tip part and can only be used in case of direct insertion in the aortic arch, during open-chest surgery. The iVAC3L-ST is especially indicated in case the insertion site is located close to the aortic valve	**1. MDAC recommendation on 30/06/2014:** The Committee after deliberation recommended that the firm is need to conduct Clinical Trial on Indian Population on minimum of 30 patients as there is no latest human clinical data. Accordingly, this office has requested to the firm to submit the clinical trial protocol vide letter dated 14.07.2014 for MDAC further review. In response to that, the firm has requested to this office for clinical trial waiver of and the same has been again discussed in MDAC Cardiovascular held on 21.10.2014 . **2. Recommendation on 21.10.2014:** The committee deliberated and recommended that the firm's application for waiver of clinical trial of said product may not be considered and this office informed to the firm vide letter dated 03.11.2014 to submit the protocol as per letter dated 11.07.2014. The firm represented to Directorate General of Health Services vide letter dated 05.08.2015 for the clinical trial waive off based on the Unmet need and based on similar case of M/s. Edward Life Sciences

				Pvt Ltd., Mumbai discussed in the 19th Apex Committee held on 24.12.2014 and the same is placed before the Committee. **3. Recommendation of the Technical Committee:** After detailed deliberation, the Committee noted that the device is already approved and being used in countries like Netherland, Austria, Germany and as such there is no further requirement of conduct of clinical trial in Indian population for such medical device. Therefore, the Committee desired to call the subject expert in Cardiology for deliberation in the next Technical Committee meeting and also desired to call the firm to present the proposal before the Committee. Accordingly the firm presented their proposal before the Technical Committee. 4. **Recommendation of the Technical Committee:-** The firm presented before the Committee. The device is already approved and being used in countries like Netherland, Austria, Germany. The Technical committee deliberated with Cardiology invited for the meeting and recommended for the grant of import permission with the condition that the firm shall carry out Phase-IV Clinical trial on 100 subjects in the country.

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