

520

MINUTES OF THE 28th MEETING OF THE APEX COMMITTEE HELD ON 11-04-2016 UNDER THE CHAIRMANSHIP OF SECRETARY, (H&FW) 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. SHRI 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 which have been postponed from the 27th Apex Committee meeting held on 06.04.2016 and recommended as following:

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 as per recommendations of earlier Apex Committee and Technical Committee meeting for policy on waiver of local clinical trial waiver for medical devices.

The Committee deliberated in detail on the proposal for clinical trial waiver in Indian population for approval of new medical devices falling under the category of drugs, which have already been approved outside India. The Committee noted that in EU, medical devices are regulated by Conformity Assessment Bodies while in USA, the medical devices are regulated by USFDA itself.

The USFDA model for approval of medical devices requires the submission of clinical data as part of preapproval submission. Such data ensures safety and performance of the medical device in human population. After detailed deliberations, the Committee decided that in cases where medical devices, approved by USFDA are based on clinical data, DCG (I) may issue local clinical trial waiver after being satisfied about the merit of the proposal. However, in cases, where USFDA had issued a conditional approval for marketing of medical devices, such cases may continue to be brought before the Technical and Apex Committee for consideration of local clinical trial waiver.

B. Four 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.7 Palbociclib Capsule 75mg/ 100mg/125mg.

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.8 Trabecular Metal TM Ardis Interbody System Solid and Trabecular Metal TM Ardis Interbody System (Graft)

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.9 Implantable Balloon

The Apex Committee noted that the clinical study cited as evidence in the present case is not sufficient to waive conduct of clinical trial in the country (Details at Annexure-III) and accordingly, approved that phase-III clinical trials will be required.

Proposal No.10 Pulsecath Ivac3l

The Apex Committee noted that the clinical study cited as evidence in the present case is not sufficient to waive conduct of clinical trial in the country (Details at Annexure-III) and accordingly, approved that phase-III clinical trials will be required.

Other Items 1:

The Committee observed that the experts of the SEC need to be appraised about the regulatory requirements relating to the clinical trials for compliance of the provisions for securing uniformity in the recommendations of various expert Committees. It was decided that a few workshops may be conducted for this purpose.

Other Items 2:

The Committee also observed that the agenda presented before the Committee should also contain details of the date of application, date of referring the matter to the SEC and Technical Committee.

The Committee also decided that reasons including inadequacy of clinical evidence for rejecting a proposal by the SEC should be recorded and similarly when the Technical Committee overrules the SEC, the reasons for arriving at a decision to the contrary must also be recorded.

Other Items 3:

The Committee, had in its 27th meeting deliberated upon the waiver of local clinical trial for approval of additional indication for drug Tiotropium Bromide Inhaler 9 mcg and Tiotropium Bromide Rotacaps 18 mcg and had not approved the proposal as evidence regarding approval of this drug for the additional indication of asthma by USFDA was not available. DGHS brought out the fact that the drug had the approval of USFDA for asthma. The Committee decided that the matter may be re-examined in the light of facts available on file with CDSCO.

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

517

Annexure-I

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.	<p>Name of the Drug: Serelaxin (RLX030)</p> <p>Protocol No : CRLX030A2302</p> <p>Phase of the Study: Phase III</p> <p>Name of the Applicant: Novartis Healthcare Private Limited</p> <p>Name of the Sponsor: Same as above</p> <p>Name of the Manufacturer: Novartis Pharma Stein AG Schaffhauserstrasse CH-4332 Stein, Switzerland</p> <p>Name of the countries where the study is ongoing: Malaysia, Philippines, Singapore, Taiwan, Thailand</p> <p>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.</p>	<p>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.</p> <p>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.</p> <p>Unmet Medical Need in the country: The test drug may potentially provide alternative treatment option in acute heart failure when added to standard therapy.</p>	<p>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.</p> <p>2. Recommendation of the Technical Committee: After detailed deliberation, the Committee recommended the conduct of the study as per the SEC recommendation.</p>
2.	<p>Name of the Drug: Semaglutide</p> <p>Protocol No: NN9535-4216</p> <p>Phase: IIIb</p> <p>Name of the Applicant: Novo Nordisk India Private Ltd.</p> <p>Name of the Sponsor: Same as above</p>	<p>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.</p> <p>Innovation vis a vis existing therapeutic option- The purpose of the study is to evaluate the</p>	<p>1. Recommendation of the SEC: After detailed deliberation the committee recommended conduct of the trial subject to the following conditions:-</p> <p>1. Dose titration with Dulaglutide in line with the approved prescribing information. Accordingly the protocol should be suitably modified.</p>

	<p>Name of the Manufacturer: Novo Nordisk A/S, NovoAlle, Bagsvaerd Denmark</p> <p>Name of the countries where the study is ongoing: USA, UK, Finland and Ireland</p> <p>Title: Efficacy and Safety of Semaglutide versus Dulaglutide as add-on to Metformin in subject with type 2 diabetes.</p>	<p>efficacy and safety of semaglutide versus dulaglutide as add-on to metformin in subjects with type 2 diabetes.</p> <p>Unmet need- The test drug may be an alternative treatment option in subjects with type 2 diabetes.</p>	<p>II. 50 % trial sites must be govt. sites.</p> <p>2. Recommendation of the Technical Committee: After detailed deliberation, the Committee recommended the conduct of the study as per the SEC recommendation.</p>
<p>3.</p>	<p>Name of the Drug: Masitinib Mesylate</p> <p>Protocol No : AB07002</p> <p>Phase of the Study: Phase III</p> <p>Name of the Applicant: Maya Clinicals, Cyber Heights, Behind TDP Office, Flat No: 604, Road No: 2, Banjara Hills, Hyderabad - 500 034</p> <p>Name of the Sponsor: AB Science, #3, Avenue George V – 75008, Paris – France.</p> <p>Name of the Manufacturer: Excella GmbH, Nurnberger Street 12, Feucht -90537, Bavaria, Germany.</p> <p>Name of the countries where the study is ongoing: Germany, Greece, Morocco, Poland Romania, Spain etc</p> <p>Title: A 96-week, prospective, 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</p>	<p>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.</p> <p>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</p> <p>Unmet need- The test drug may be alterative option in the treatment of patients with primary progressive or relapse-free secondary progressive multiple sclerosis</p>	<p>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.</p> <p>2. Recommendation of the Technical Committee: After detailed deliberation, the Committee noted the following:-</p> <ol style="list-style-type: none"> I. The recommendallon 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. <p>Hence, the Committee 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</p>

	<p>in the treatment of patients with primary progressive multiple sclerosis or relapse-free secondary progressive multiple sclerosis.</p>		<p>improvement from this treatment.</p>
<p>4.</p>	<p>Name of the Drug: Genopep -1</p> <p>Protocol No : Issar/2012/01</p> <p>Phase of the Study: Phase II</p> <p>Name of the Applicant: ISSAR Pharmaceuticals pvt.ltd Serene chambers,3rd floor , Road no.5, Banjara hills,Hyderabad-500 034,India</p> <p>Name of the Sponsor: Same as above</p> <p>Name of the Manufacturer: Same as above</p> <p>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.</p>	<p>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.</p> <p>Innovation vis-à-vis existing therapeutic option: There is no drug in this class of compounds in clinical use.Hence, it is truly innovative.</p> <p>The mechanism of action being different, the drug may have high activity in patients who have failed multiple lines of cancer therapy.</p> <p>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.</p>	<p>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.</p> <p>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:</p> <ul style="list-style-type: none"> > 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. <p>Accordingly the firm has submitted response to the above query and the proposal was deliberated in the Technical Committee.</p> <p>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.</p>

514

Annexure-II

Agenda note for the upcoming Apex Committee Experts recommendations for the waiver of Clinical Trials for New Drug (Medical Device) - regarding.

This is with reference to the 26th Apex Committee meeting held on 10.12.2015, wherein the committee desired that the agenda note for giving waiver to medical devices approved by regulators of ICH with necessary safeguard be brought before the next Apex Committee meeting.

In this regard, the minutes of the 31st Technical Committee meeting held on 01.02.2016 may be referred wherein the committee deliberated the cases of clinical trial waiver 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.

CDSCO regulates the Safety, Efficacy (Performance) and Quality of 15 categories of notified medical devices as "Drugs" under the provisions of Drugs and Cosmetics Act, 1940 and Rules 1945 made thereunder.

As per existing procedures, for the device which is approved in other countries but not approved in India, the applications of clinical trials of New Medical Devices are preliminarily evaluated by CDSCO, the safety and performance of the devices are evaluated by Subject Expert Committee (SEC) and recommendations of the SEC are further reviewed by the Technical Committee (TC). In case of clinical Trial waiver, the same is evaluated by Apex Committee after recommendation of Technical committee. CDSCO grants approval of clinical Trial and New Drugs based on the recommendation of Technical Committee (TC) and Apex Committee.

As per the DCG (I) order dated 03.07.2014 regarding Waiver of Clinical Trial in Indian population for approval of New Drugs, it has been decided that waiver of Clinical Trial in Indian population for approval of new drugs, which have already been approved outside India, can presently be considered only in cases of National Emergency, Extreme urgency, and epidemic and for orphan drugs for rare disease and drugs indicated for conditions / disease for which there is no therapy.

Further, as per the DCG(I) order dated 03.07.2014 regarding Clinical Trial on Medical Device, the Clinical Trial of Medical Device is different in nature as compared to that of Drugs or vaccine. In case of Medical Device, there is no concept of conducting Phase I Clinical trial to assess safety, tolerability of the Medical Device. However, in pursuant to the decisions of the Ministry of Health & Family Welfare, it has been decided that the procedures for the Clinical Trials approval, accreditations of Investigators, sites, Ethics Committee and such other conditions would be similar to the Clinical Trial of New Drugs / Vaccines.

In case of Medical devices, there is no Phase-I, II, III & IV whereas Pilot and feasibility studies on medical devices are considered as first-in-man studies and for medical devices, the Clinical Investigation is carried out. The Clinical Investigation is not required for low risk medical devices and insisted only for High risk medical devices. The regulatory requirement for approval of New Medical devices is different among the countries which includes the ICH member countries like United States, Japan, Switzerland, Canada and European Union member States (Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania,

Luxembourg, Malta, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Sweden, The Netherlands, and United Kingdom).

For instances, in European Union, the medical devices are regulated by notified body. In USA, the devices are regulated by USFDA itself. For approval of devices in European Union, the clinical investigation on minimum number of approximately 5-30 patients are required. It may be stated that the data generated for approval in European Union is insufficient for approval of the same in USFDA.

Clinical data requirements in European Union

The need for clinical data in the CE marking process arises from the requirement to demonstrate that a device is safe, that it performs as intended by the manufacturer, and that any risks are acceptable when weighed against the benefits of the device. The term "clinical data" within the meaning of the EC Directives is a broad concept that includes everything from bench testing to clinical trials in human subjects. As stated in the MDD, the clinical data used for CE marking may be in one of two forms:

- Either a compilation of the relevant scientific literature currently available on the intended purpose of the device and the techniques employed, together with, if appropriate, a report containing a critical evaluation of the compilation
- The results and conclusions of a specifically designed clinical investigation.

Literature route:

The CE marking of low- to medium-risk devices (Class I, IIa and IIb) for which safety and performance can be adequately demonstrated by a combination of non-clinical data (i.e., bench testing and animal testing) and clinical data that already exists on the device (published or unpublished) or by analogy with published data generated on an equivalent device.

Clinical Investigation route

The majority of the trials are non-randomized, single arm, feasibility studies involving less than 100 patients for which the primary objective is to demonstrate safety.

The case for Trial Data on EU Devices: The need to furnish clinical data from prospective clinical investigation is especially necessary in the following cases:

1. When components, features, and/or method of action are previously unknown
2. When an existing device is modified in such a way that the clinical performance and/or safety may be significantly effected
3. When a device uses new materials for which there is no prior clinical experience
4. When an established device is proposed for a new indication.

Clinical data requirements In USA:

The U.S. approval process for medical devices is very different, especially in terms of the scope and size of clinical trials required for high-risk devices (Class-III). Class III devices require Premarket Approval (PMA) process which is more involved and comprises the submission of clinical data.

Clinical data requirements in Japan:

512

In Japan, medical devices are classified into Class I, II, III or IV according to their risk level. When the medical device is classified into Class IV under the Classification Notification, **clinical data must, in principle**, be submitted for each product, excluding medical devices that can be proved to be equivalent to already approved medical devices and those falling under the scope of medical devices for which the approval standard is specified. The foregoing shall not apply, however, if due to a valid reason, the clinical efficacy and safety of the product can be evaluated based on the data other than clinical data of the product.

In the case of a **new medical device**, the firm has to prepare and submit a survey plan (draft) on use results of the new medical device by referring to PAB/MDD (Yakuki) Notification No. 133 issued jointly by the Director of Medical Device Development Division and the Director of Safety Division, Pharmaceutical Affairs Bureau, dated July 26, 1995, "Use Results Survey of New Medical Devices."

In general, for new medical devices and improved medical devices, the Clinical Trial is mandatory as per PMDA Act.

In view of above, it is proposed that, the safety and performance of new medical devices which are critical in nature must be evaluated in Indian population before grant of permission in country in order to safeguard the patient health wherever required.

The Committee may deliberate the proposal and give its recommendations.

Recommendation of the Technical Committee and SEC of four 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

S. NO	Details of the Drugs	Name of the firm holding the permission outside the Country	Indication	1. Recommendation of the SEC 2. Recommendation of the Technical Committee
1.	<p>Palbociclib Capsule 75mg/100mg/125mg.</p> <p>Name of the applicant: M/s Pfizer Limited</p> <p>Regulatory status: Approved in US, Macau</p>	M/s Pfizer Limited	Indicated in combination with letrozole 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.	<p>1. Recommendations of the SEC:- The firm has presented the clinical trial data conducted in other countries 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 at 12 months from the date of approval of the phase-IV protocol.</p> <p>2. Recommendations of the Technical Committee: After detailed deliberation, the Committee recommended for waiver of local clinical trial as per SEC recommendation.</p>
2.	<p>Trabecular Metal TM Ardis Interbody System Solid and Trabecular Metal TM Ardis Interbody System (Graft)</p> <p>Name of the applicant: M/s. Zimmer India Pvt. Ltd., Gurgaon</p> <p>Regulatory status: The proposed medical</p>	M/s. Zimmer India Pvt	<p>System Solid:</p> <p>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</p>	<p>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.</p> <p>2. Recommendations of the SEC: The case has been reviewed by SEC--Orthopaedics in its meeting held on 28.01.2015.</p>

	<p>devices are approved for marketing in USA, Canada and Australia.</p> <p>Composition: Porous Tantalum</p>		<p>implanted using a posterior or transforaminal approach and is intended to be used singly or in pairs with supplemental fixation.</p> <p>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.</p>	<p>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.</p> <p>Accordingly the firm has submitted the data and was deliberated upon Technical Committee.</p> <p>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.</p> <p>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.</p>
<p>3.</p>	<p>Implantable Balloon Name of the Applicant:</p> <p>M/s. Encarta Pharma Pvt. Ltd</p> <p>Regulatory status: Approved by Israel and other European Union countries. Brand Name: OrthoSpace InSpace System</p> <p>Composition: The In Space Spacer is a single use, biodegradable, inflatable spacer (balloon) implant made of Poly(L-lactide-co-e-</p>	<p>M/s. Encarta Pharma Pvt. Ltd</p>	<p>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.</p> <p>The indications for the InSpace include:</p> <ul style="list-style-type: none"> • Scarred or torn tendon due to trauma or degradation, • Absence of tendon /muscle or non-functional tendon/muscle 	<p>1. Recommendations of the SEC:</p> <p>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.</p> <p>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</p>

	caprolactone).		<ul style="list-style-type: none"> • Ruptured tendon 	<p>population; accordingly clinical trial protocol shall be submitted to the Committee for further review.</p> <p>2. Recommendation of the Technical Committee:</p> <p>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.</p> <p>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.</p> <p>Accordingly the firm presented their proposal before the Technical Committee.</p> <p>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.</p>
--	----------------	--	---	---

<p>4.</p>	<p>Pulsecath Ivac3I</p> <p>Name of the Applicant: M/s. Meril Life Sciences India Pvt. Ltd</p> <p>Regulatory status: Approved by The Netherlands, Austria, Germany, Russia.</p> <p>Composition: Medical grade stainless steel (316L), Medical grade stainless steel (316L) Polyurethane tube braided with nitinol, Polyurethane, Polyurethane /methyl methacrylate-acrylonitrile-butadiene-stryene-stryene polymer (MABS), with a polyurethane seal (gasket), Methylmethacrylate-acrylonitrile-butadiene-stryene-stryene polymer (MABS), Ployurethane</p>	<p>M/s. Pulse Cath B.V, Netherland</p>	<p>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</p>	<p>1. MDAC recommendation on 30/06/2014:</p> <p>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 .</p> <p>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.</p> <p>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.</p> <p>3. Recommendation of the Technical Committee:</p> <p>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</p>
-----------	--	--	---	---

				<p>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.</p> <p>Accordingly the firm presented their proposal before the Technical Committee.</p> <p>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.</p>
--	--	--	--	---

	<p>Name of the applicant: M/s Sanofi Pasteur India Private Limited</p> <p>Regulatory status: Approved in Philipphins, Mexico and Brazil.</p>	<p>Private Limited</p>		<p>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).</p> <p>2. Recommendations of the Technical Committee: After detailed deliberation, the Committee recommended for waiver of local clinical trial as per SEC recommendation.</p>
<p>7.</p>	<p>Palbociclib Capsule 75mg/100mg/125mg.</p> <p>Name of the applicant: M/s Pfizer Limited</p> <p>Regulatory status: Approved in US, Macau</p>	<p>M/s Pfizer Limited</p>	<p>Indicated in combination with letrozole 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.</p>	<p>7. 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 at 12</p>

				months from the date of approval of the phase-IV protocol.
				<p>8. Recommendations of the Technical Committee:</p> <p>After detailed deliberation, the Committee recommended for waiver of local clinical trial as per SEC recommendation.</p>
8.	<p>Trabecular Metal TM Ardis Interbody System Solid and Trabecular Metal TM Ardis Interbody System (Graft)</p> <p>Name of the applicant: M/s. Zimmer India Pvt. Ltd., Gurgaon</p> <p>Regulatory status: The proposed medical devices are approved for marketing in USA, Canada and Australia.</p> <p>Composition: Porous Tantalum</p>	M/s. Zimmer India Pvt	<p>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.</p> <p>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.</p>	<p>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.</p> <p>2. 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. Accordingly the firm has submitted the data and was deliberated upon Technical Committee.</p> <p>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.</p> <p>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.</p>

9.	<p>Implantable Balloon Name of the Applicant:</p> <p>M/s. Encarta Pharma Pvt. Ltd</p> <p>Regulatory status: Approved by Israel and other European Union countries.</p> <p>Brand Name: OrthoSpace InSpace System</p> <p>Composition: The In Space Spacer is a single use, biodegradable, inflatable spacer (balloon) implant made of Poly(L-lactide-co-e-caprolactone).</p>	M/s. Encarta Pharma Pvt. Ltd	<p>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.</p> <p>The indications for the InSpace include:</p> <ul style="list-style-type: none"> • Scarred or torn tendon due to trauma or degradation, • Absence of tendon /muscle or non-functional tendon/ muscle • Ruptured tendon 	<p>1. Recommendations of the SEC:</p> <p>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.</p> <p>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.</p> <p>2. Recommendation of the Technical Committee:</p> <p>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.</p> <p>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</p>
----	--	------------------------------	---	--

				<p>for deliberation in the next Technical Committee meeting and also desired to call the firm to present the proposal before the Committee.</p> <p>Accordingly the firm presented their proposal before the Technical Committee.</p> <p>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.</p>
10.	<p>Pulsecath Ivac3I</p> <p>Name of the Applicant: M/s. Meril Life Sciences India Pvt. Ltd</p> <p>Regulatory status: Approved by The Netherlands, Austria, Germany, Russia.</p> <p>Composition: Medical grade stainless steel (316L), Medical grade stainless steel (316L) Polyurethane tube braided with nitinol, Polyurethane, Polyurethane /methyl methacrylate-acrylonitrile-butadiene-stryene-stryene polymer (MABS), with a polyurethane seal (gasket), Methylmethacrylate-acrylonitrile-butadiene-stryene-stryene polymer</p>	M/s. Pulse Cath B.V, Netherland	<p>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</p>	<p>1. MDAC recommendation on 30/06/2014:</p> <p>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 .</p> <p>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</p>

	(MABS), Ployurethane			<p>11.07.2014.</p> <p>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.</p> <p>3. Recommendation of the Technical Committee:</p> <p>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.</p> <p>Accordingly the firm presented their proposal before the Technical Committee.</p> <p>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.</p>
--	-------------------------	--	--	---