

**MINUTES OF 31st MEETING OF THE TECHNICAL COMMITTEE HELD ON 01.02.2016
UNDER THE CHAIRMANSHIP OF DGHS FOR SUPERVISING CLINICAL TRIALS ON NEW
CHEMICAL ENTITIES IN THE LIGHT OF DIRECTIONS OF THE HON'BLE SUPREME
COURT OF INDIA ON 03.01.2013.**

Present:

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

From CDSCO:

1. Dr. S. Eswara Reddy,
Joint Drugs Controller (I)
2. Dr. V. G. Somani,
Joint Drugs Controller (I)
3. Mr. R. Chandrashekar,
Deputy Drugs Controller (I)
4. Mrs. Annam Visala,
Deputy Drugs Controller (I)
5. Mrs. Rubina Bose,
Deputy Drugs Controller (I),

The Chairman welcomed the members of the meeting and Dr. V. G. Somani, JDC (I) initiated the proceedings of the Committee. Thereafter, the Committee discussed the clinical trial proposals one by one as under:

The Committee deliberated 11 cases related to approval of clinical trials. Out of these 11 cases, 03 cases were related to clinical trials of NCEs, 01 case was related to global clinical trials (GCT) remaining 07 cases were related to clinical trials for approval of New Drugs and Biologicals.

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

The Committee evaluated the 03 cases related to clinical trial of NCEs and made recommendations considering all aspects of safety, efficacy especially in terms of the three parameters viz. risk versus benefit to the patients, innovation *vis-a-vis* existing therapeutic option and unmet medical need in the country. After detailed deliberation, the Committee recommended all 03 cases of NCEs. The recommendation of the Committee is enclosed as **Annexure-I**.

2. Proposal of Clinical Trials of GCT recommended by SECs.

Thereafter, the Committee evaluated 01 case related to global clinical trial. After detailed deliberation, the Committee recommended to conduct the clinical trial. The recommendation of the Committee is enclosed as **Annexure-II**.

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

The Committee evaluated the 07 cases of other than GCT/clinical trial of NCEs. After detailed deliberation, the Committee recommended all 07 cases, out of which for one case (S. No: 05 of the **Annexure-III**), the Committee recommended subject to certain condition. The recommendation of the Committee is enclosed as **Annexure-III**.

Thus, the Committee recommended all 11 cases of clinical trial proposals.

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

07 proposals from New Drug and Biological were placed before the Committee for consideration of permission for manufacture/ import for marketing in the country without local clinical trial. The details of recommendations of the Committee along with recommendation of the SEC is annexed as **Annexure-IV**.

5. Others:

Item No. 01:-

Appeal by M/s Novartis to waiver on the Clinical Trial condition imposed by Technical Committee in its 29th meeting dated 12-10-2015.

Study title: "A Phase III, randomized, double-blind, placebo controlled multi-centre study of subcutaneous Secukinumab (150 mg and 300 mg) in prefilled syringe to demonstrate efficacy (including inhibition of structural damage), safety, and tolerability up to 2 years in subjects with active psoriatic arthritis (FUTURE 5)"

It may please be informed that the proposal was deliberated in Technical Committee in its 29th meeting dated 12-10-2015 and CT NOC has been issued on 17-11-2015 as per the recommendations of Technical Committee meeting.

The details of the deliberations are given below:-

A. Deliberation of proposal by SEC held on 07.08.2015:-

The proposal was deliberated in the meeting of SEC held on 07-08-2015. The Committee after deliberation recommended as under:-

After the detailed deliberation the committee recommended the conduct of the study subject to the following condition:-

- i. If PPD skin test is negative Quantiferon TB Gold test should be done to rule out Latent TB.
- ii. The trial site should be geographically distributed across the country including representation from North and East part.

B. Deliberation of proposal in 29th Technical Committee held on 12.10.2015:-

The proposal was placed before the Technical Committee along with the recommendations of the SEC in the 29th Technical Committee meeting held on 12-10-2015.

The Committee after deliberation recommended as under:-

After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation with the condition that the patients with LV dysfunction (Ejection Fraction less than 40%) malnourishment and other immune compromised patients shall be excluded from the study & exclusion should specify the same.

C. Appeal by M/s Novartis for waiver on the condition imposed under CT NOC:-

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

Condition to have LV dysfunction as exclusion criteria in the protocol:

Patient with significant LV dysfunction such as New York heart association status of class III or IV are already considered to be excluded as per exclusion criteria 16 of study protocol.

Exclusion criteria no 16: Significant medical problems or disease, including but not limited to the following: uncontrolled hypertension ($\geq 160/95$ mmHg), Congestive heart failure (New York Heart Association Status of class III or IV) and uncontrolled diabetes.

Also exclusion criteria no 24 of study protocol has the provision to exclude subjects with current severe progressive or uncontrolled disease which in the judgment of the clinical investigator renders the subject unsuitable for the trial.

Exclusion criteria no. 24: Current severe progressive or uncontrolled disease which in the judgment of the clinical investigator renders the subject unsuitable for the trial.

Also we would like to highlight that as per approved SmPC for the study drug AIN457 (Secukinumab) based on EU approval dated 19/11/2015 for psoriatic arthritics indication, LV dysfunction is neither contraindicated nor there is any special warning for the same. However the current protocol still has the provision to exclude patients with LV dysfunction.

(II) Condition to exclude malnourished and other immune compromised patients:

In line with the condition any immune compromised subjects (HIV) or subjects at risk of low immunity such as malnourished are excluded from the study as per exclusion criteria 15 & 22 of study protocol.

Exclusion criteria no 15: Underlying metabolic, hematologic, renal, hepatic, pulmonary, neurologic, endocrine, cardiac, infectious or gastrointestinal condition which in the opinion of the investigator immune compromises the subject and / or places the subject at unacceptable risk for participation in an immune modulatory therapy.

Exclusion criteria no. 22: Known infection with human immunodeficiency virus (HIV), hepatitis B or hepatitis C at screening or randomization.

Based on the exclusion criteria mentioned above we would therefore ensure that the current protocol version itself would exclude patients with LV dysfunction (ejection fraction less than 40%), malnourishment and other immune compromised patients. Thus no additional amendments are really required.

The current study being a global study is already initiated in participating countries including key countries like US, UK and Spain. Hence, amending the protocol for condition “C” would be challenging. In case of delay in approval from your Directorate for Condition “C”, we may lose opportunity to include Indian patients in this global study. This will deprive patients suffering from Psoriatic arthritis to participate in the said global clinical trial.

Recommendation of the Technical Committee: After examining the justification furnished by the firm in detail the Committee recommended waiver of the CT NOC condition imposed in its 29th meeting.

Item No. 02:-

Appeal by M/s Novartis to waiver on the Clinical Trial condition imposed by Technical Committee in its 30th meeting dated 26-11-2015.

Study title: “A multicenter, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of LCZ696 compared to valsartan, on morbidity and mortality in heart failure patients (NYHA Class II-IV) with preserved ejection fraction”

It may please be informed that the proposal was deliberated in Technical Committee in its 28th meeting dated 21-08-2015 and CT NOC has been issued on 30-09-2015 as per the recommendations of Technical Committee meeting.

The details of the deliberations are given below:-

(A) Deliberation of proposal by SEC held on 16.07.2015:-

The proposal was deliberated in the meeting of SEC held on 16-07-2015. The Committee after deliberation recommended as under:-

After the detailed deliberation the committee recommended the conduct of the study subject to the following condition:-

1. Serum potassium levels should be assessed at 1 week post dose escalation to 160 mg BD.
2. Ejection fraction assessment should be performed by 2D volumetric methods.

(B) Deliberation of proposal in 28th Technical Committee held on 21.08.2015:-

The proposal was placed before the Technical Committee along with the recommendations of the SEC in the 28th Technical Committee meeting held on 21-08-2015.

The Committee after deliberation recommended as under:-

After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation with the condition that the patients who have eGFR less than 45 ml/min should be excluded from the study.

(C) Appeal by M/s Novartis for waiver on the CT NOC condition imposed by the Technical Committee in its 28th meeting dated 21-08-2015:-

There after the applicant represented the matter to DCG (I) for waiver on the condition imposed under CT NOC in 28th Technical Committee meeting.

(D) Deliberation in 30th Technical Committee held on 26.11.2015 on firm's appeal for CT NOC condition waiver:-

Based up on the firm's justification and clarification, the appeal for waiver of CT NOC condition i.e. "the patients who have eGFR less than 45 ml/min should be excluded from the study" was deliberated in 30th Technical Committee meeting dated 26-11-2015.

After examining the justification by the firm in detail, the committee opined that patients with severe diabetes, hypertension with diastolic blood pressure \geq 85 mmHg, patient on high dose of insulin should be excluded from the study. If e GFR decreases by \geq 25% from baseline, subject should not be randomised into the study.

(E) Appeal by M/s Novartis for waiver on the CT NOC condition imposed by 30th Technical Committee:-

As per the recommendation of 30th Technical Committee meeting dated 26-11-2015, waiver of CT NOC condition as imposed by 28th Technical Committee meeting has been granted subject to the condition that **"patients with severe diabetes, hypertension with diastolic blood pressure \geq 85 mmHg, patient on high dose of insulin should be excluded from the study. If e GFR decreases by \geq 25% from baseline, subject should not be randomised into the study"**.

There after the firm has appealed to the DGHS for the waiver of new condition i.e. **"patients with severe diabetes, hypertension with diastolic blood pressure \geq 85 mmHg, patient on high dose of insulin should be excluded from the study. If e GFR decreases by \geq 25% from baseline, subject should not be randomised into the study"** as imposed by the 30th Technical Committee based on the following justification;

However, additional clauses were introduced by the 30th Technical Committee that was not mentioned in the CT permission. We believe that recommending any additional clause once CT permission has been granted is not fair, also practically not implementable. Nevertheless, we would like to justify our case with regard to these additional recommendation related to diabetes and diastolic blood pressure.

Justification regarding clause of severe diabetics and patient`s on high dose of insulin.

- i. The study drug LCZ696 has been approved in US and EU for HF-rEF, Neither US FDA approved prescribing information (enclosure 3) nor EU approved summary of product characteristics (SPC) (enclosure \$) contradict the use of LCZ696 in patients with severe diabetes or in patients on high dose of insulin further, LCZ696 is not known to cause hyperglycemia or hypoglycaemia.
- ii. The approved prescribing information only contradicts use of LCZ696 with aliskrien in patient with diabetes and recommends periodic monitoring of serum potassium in diabetic patients to watch for hyperkalaemia. The current study protocol strictly prohibits concomitant use of any rennin inhibitor such as aliskrien while the patient is receiving the study drug. Similarly, serum potassium is being monitored at screening visit, during the run-in period, at randomization visit and at all site visits post randomization till the end of study.
- iii. Thus, the current protocol complies with the recommendations regarding diabetic patients and we do not foresee any undue risk to diabetic patients by virtue of their participation in the study. Further, irrespective of their diabetic status, patient`s blood glucose is also being monitored at periodic intervals during the study.

Justification regarding clause of hypertension with diastolic blood pressure \geq 85mmhg.

- I. Firstly, JNC 7 (seventh report of joint national committee on prevention, detection, evaluation and treatment of high blood pressure) and other university accepted hypertension guidelines classify patients as hypertensive only if the BP is \geq 140/90 mmhg. Thus patients with diastolic blood pressure $<$ 90 mmhg are not even considered to have hypertension.
- II. Secondly, LCZ696 is not known to cause hypertension. On the contrary, LCZ696 reduced blood pressure in hypertensive patients by causing vasodilatation and may cause hypotension. PARADIGM-HF data in patients with HF-rEF shows that approximately 18% patients on LCZ696 reported hypotension.
- III. The available dose formulations of LCZ696 50mg, 100mg and 200mg when taken twice daily provide Valsartan exposure equivalent to Valsartan 80mg, 160mg & 320mg respectively which are approved dosages for hypertension. Accordingly, the study protocol excludes subjects with SBP $<$ 110mmhg at screening visit or those with either SBP $<$ 100 or with symptomatic hypotension at the end of valsartan run in and at the end of LCZ696 run (i.e randomization visit.). The protocol also excludes patients with severe hypertension i.e SBP $>$ 180 mmhg and those with SBP between 150-180 mmhg unless they are receiving 3 or more antihypertensive drugs.
- IV. Further, Patient`s blood pressure is being monitored at all scheduled site visits during the study. Thus we do not really understand the rational for excluding patients with DBP \geq 85mmhg.

In addition, please note that the current study protocol has already been approved in 33 countries including key countries like US, UK, Switzerland, France, Germany, Canada and the study is currently recruiting. Approximately 1500 patients have been recruited globally till date.

In view of the above we believe that the current protocol complies with the approved prescribing information of LCZ696 and has adequate measures in place to monitor patient`s blood pressure and blood glucose levels. Further, LCZ696 is not known to cause hyperglycaemia or hypertension. Patients with severe hypertension and those are more prone to hypotension are being excluded from the protocol. Thus no additional measures are really required and we request your directorate to approve the study protocol in its current form.

Recommendation of the Committee: After examining the justification furnished by the firm in detail, the Committee recommended waiver of the CT NOC condition imposed in its 30th meeting subject to the condition that patients having eGFR between 30 to 45 ml post randomisation must be closely monitored for eGFR and serum potassium at every 15 days during the first 6 months.

Item No. 03:-

Application of M/s APAC Biotech Pvt. Ltd, Gurgaon for Marketing Authorization of APCEDENT™ [Dendritic Cell (DC) product].

The proposal of M/s APAC Biotech Pvt. Ltd, Gurgaon was deliberated in the meeting held on 03/02/2015 for clarification of MOM of 7th CBBTDEC meeting. The Committee studied the regulatory perspective of Pharmaceuticals & Medical Devices agency (PMDA), Japan and recommended that the company be given conditional approval. They should increase the number of patients to 439 to be conducted in period not exceeding two years before seeking marketing authorization.

Recommendation of the 28th Technical Committee held on 23.07.2015:- Further the proposal has been deliberated in the 27th Technical Committee meeting held on 23.07.2015 in which the committee opined that the data presented by the firm is more presumptive about approval. The recommendations of the CBBTDEC are not supported with the basis of approval as:-

1. In how many patients major improvement noted and in how many it is required in one particular indication;
2. What is the criteria for approval of indication in such “already in the practice” cell based product for “conditional approval” (either based on PMDA or CBBTDEC’s guidelines).

However, Committee acknowledged that if it is 19% improvement in the various tumors, it is considered as a major improvement. Therefore, the proposal may be referred back to CBBTDEC for review.

Similarly, a general comments or CBBTDEC’s view as what is meant by “Conditional approval” as per PMDA model and in how many patients it shall prove major/ significant improvements/ efficacy and what further condition shall be put with respect to further studies and charging the patients, may be obtained.

Recommendation of the CBBTDEC meeting held on 29.10.2015:- The CBBTDEC in their meeting held on 29/10/2015 has deliberated on the issues raised by the Technical Committee. The following clarification has been submitted by the CBBTDEC.

1. In how many patients major improvement noted and in how many it is required in one particular indication:

The committee was informed by the firm that improvement was noted on an average in 5 subjects in each condition of Ovarian, Prostrate, Colorectal, Lungs cancers.

As cancer is largely an unmet need, it was suggested to consider 15-20% improvement as substantial efficacy.

The committee opined that as a general principle, the significant and remarkable clinical improvement shall be observed in 5 to 10 patients in life threatening indication for consideration of conditional approval.

2. What are the criteria for approval of indication in such “already in the practice” cell based product for “conditional approval” (either based on PMDA or CBBTDEC’s guidelines).

PMDA Japan has implemented a new regulatory frame work in November 2014 for regenerative medicine products (RMP) considering the importance of earlier access of these products by the patients for unmet medical needs. PMDA has revised Pharmaceutical Affairs Law for RMP and the Japan’s parliament has enacted the Bill. The Bill allows the Japanese Government to give conditional approval to

such products if their safety is confirmed and expectable efficacy trends are demonstrated in early stage of clinical trials, as may occur on completion of Phase II.

Similarly, a general comments or CBBTDEC's view as what is meant by "Conditional approval" as per PMDA model and in how many patients it shall prove major/ significant improvements/ efficacy and what further condition shall be put with respect to further studies and charging the patients, may be obtained.

APAC need to include only those cancer conditions in which substantial safety and efficacy has been demonstrated. Hence, the committee recommended conditional approval for enhancing the number to 200 including 50 numbers in each of ovarian, Prostate, Lung and Colorectal Cancer patients. The company was advised to submit the data of 200 patients before seeking full marketing authorization. This should be completed within one year duration.

For rest of the cancer types, APAC needs to conduct well designed clinical trial including appropriate controls after obtaining approval from DCG(I)

The committee felt as per the PMDA model, the company may levy reasonable service charges during the conditional approval period. Since it is a new drug and the approval is being given at the earlier stage, the company may be recommended to supply the product at its cost. After negotiations, it was finalized as Rs 87500 per dose (of six dose treatment) excluding hospital charges and further breakup details need to be submitted by the firm. Accordingly, the proposal was discussed in the 30th Technical Committee meeting dated 26.11.2015.

Recommendation of the 30th Technical Committee held on 26.11.2015:-

The Committee deliberated the issue and required explanation and presentation from the applicant regarding the specific cancer condition that are to be considered as proven treatable indications based on result of clinical trials in general and specifically with regard to lung cancer. The Committee also sought the details of such product's approval status in other countries.

Recommendation of the Technical Committee:- After detailed deliberation, the Chairman requested the members to examine the documents submitted by the firm at the time of meeting and give their comments within 15 days.

Item No. 04:-

Clinical trial proposal of M/s Bio-Med (p) Ltd for evaluation of immunogenicity and safety of Rabies vaccine human (cell culture) IP in post exposure subjects.

The subject proposal was deliberated in Technical Committee meeting held on 21.08.2015, wherein the Committee has recommended for conduct of study subject to the condition that Immunogenicity of the subjects within 48 hours of Vaccination shall be measured and in case sufficient titre is not reached, rescue treatment (alternative vaccine) to be given to the subjects.

In response firm has replied that as per WHO TRS 941 "It is imperative to include a blood sample taken on day 0 and 7 in order to identify and exclude previously vaccinated subjects" It means that the firm shall be conducting immunological test on all samples to be taken on day 0 and 7 to identify volunteers who are already vaccinated or exposed. The Immunological test done on day 14 of vaccination shall be evaluated within 48 hours and the volunteers having titre ≤ 0.5 IU/ml shall be given rescue treatment.

The firm's amendment has a basic difference from Technical Committee recommendation i.e. wherein Technical Committee has recommended testing Immunogenicity within 48 hours the firm is intending to do the same at 14 days.

Hence, the same is submitted for deliberation, if the firm can be allowed for conducting Immunological test on day 14 of vaccination instead of within 48 hrs of vaccination as recommended by Technical Committee.

Recommendation of the Technical Committee:- The Committee examined the revised protocol and opined that firm may be asked to present before the Committee, the justification for proposing to test the immunogenicity of the proposed new Rabies vaccine in 14 days instead of 48 hrs as recommended by 30th Technical Committee.

Item No. 05:-

Clinical trial waiver proposal of M/s. Zimmer India Pvt. Ltd for the grant of registration certificate for the products i.e., Trabecular Metal TM Ardis Interbody System Solid and Trabecular Metal TM Artis Interbody 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.

Subject Expert Committee Recommendations: 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.

27th Technical Committee Recommendations: The case has been reviewed by 27th Technical Committee in its meeting held on 23/07/2015. The committee after deliberation recommended that the firm should submit more clinical trial data generated with new proposed indication of the device.

The firm has submitted the following updated Clinical Trial data on proposed Indication.

Annex No.	Further Clinical Trial data being submitted
A.	<p>Published Article – European Spine journal, Published 11.09.2015, Springer Authors: VandeKelft and Van Goethem. Trabecular Metal Spacers as standalone or with pedicle screw augmentation, in posterior lumbar Interbody fusion: a prospective, randomized controlled trial.</p> <hr/> <p>Summary</p> <p>Trabecular Metal spacers were found to provide a solid construct at more than 6-year follow up after posterior lumbar interbody fusion (PLIF) for Degenerative Disc disease (DDD) both with and without additional pedicle fixation.</p> <p>The clinical and radiological results were not significantly different. The results show that in well-selected patients with single-level DDD, PLIF yields good clinical results and very high rates of stable construct when using Trabecular Metal (TM) as an intervertebral spacer, even in a standalone fashion. <u>Therefore, Trabecular Metal Spacers may be suitable for standalone placement in well-selected cases without overt spinal instability.</u></p>

B.	<p>Published report – Global Spine Journal, 2015; 5: pages 322-328 A Randomized, Controlled Trial comparing Transforaminal Lumbar Interbody Fusion and Unistrumented Posterolateral fusion in the Degenerative Lumbar Spine.</p>
	<p>Summary</p> <p>Between 2001 and 2005, 135 patients were included in the study, 74 men and 61 women with a mean age of 44.5 years. Decompression and / or discectomy were performed if necessary in the standardized fashion. Trabecular Metal (tantalum) spacer was positioned in the inter body space, followed by compression over the pedicle screws on each side. The TM spacer is made of a porous material with the potential of bony ingrowth from the end plates. Clinical outcomes were measured preoperatively and at 12 and 24 months respectively. The results of current study showed improved clinical outcomes both in the TLIF & PLIF groups in mixed-patient selection with chronic lumbar pain.</p>
C.	<p>Clinical Investigation Report - Preliminary data report 2014 – 28.11.2014. A Prospective, Multicenter, post-market surveillance study to assess the clinical efficacy and fusion rates of the Zimmer TM-Ardis Interbody Fusion system.</p>
	<p>Summary</p> <p>Zimmer Spine is also in the process of conducting a multi-center post market surveillance study to assess the clinical efficacy and fusion rates of the Zimmer TM-Ardis Interbody Fusion system.</p> <p>Length of the study – 4 years (18 months Enrolment, 2 years) follow up and 6 months for analysis. Study Design – Multi-center, prospective, open, post-market surveillance study, n=80. Preliminary Report – The results of this report are descriptive in nature as the data of the 13 patients at the pre-operative visit, 9 patients at 3 months follow up visit, 4 patients at 6 months follow up visit and 1 patient at 12 months follow up visits cannot be appropriately analyzed and no conclusion drawn from this data.</p>

Zimmer Spine Post Market Surveillance for TM-Ardis – update – 30.09.2015: Enrollment of the 80 patients required by the protocol of the TM Ardis study has been completed and the patients will be followed up during the next 2 years.

The firm has submitted the Clinical Investigation Plan CIP ID: CME2013-01S. 21 patients have been enrolled in Canada, 59 patients in Europe. Zimmer Spine will be conducting an investigator meeting analyzing the preliminary results for patients who have reached one year.

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.

Item No. 06:-

Clinical trial waiver proposal of M/s. Eisai Pharmaceuticals India Pvt. Ltd. Mumbai for the grant of permission to import and market of new medical device “DC Bead Drug Delivery Embolization System”.

DC Bead is intended to be loaded with doxorubicin for the purpose of :

- Embolization of vessels supplying malignant hypervascular tumor(s).
- Delivery of a local controlled sustained dose of doxorubicin to the tumor(s).

SEC-Oncology Recommendations: The case has been reviewed by SEC – Oncology in its meeting held on 17.03.2015. The committee after deliberation recommended the grant of approval for import and marketing of the proposed product to be loaded with Doxorubicin for the purpose of embolization of blood vessels supplying hepatocellular carcinoma.

27th Technical committee Recommendations:- The case has been reviewed by 27th Technical committee in its meeting held on 23.07.2015. “After detailed deliberation, the Committee opined that there is no alternative therapy available and agreed with the SEC recommendations subject to the condition that the firm shall submit the detail of the conditions and hospital setting under which the device to be given”.

24th Apex Committee Recommendations:- The case has been deliberated by 24th Apex Committee meeting held on 19.08.2015. “Apex Committee noted the recommendations of Subject Expert Committee (SECs) and Technical Committee and after detailed deliberations, concurred with the recommendations of Technical Committee detailed in agenda notes annexed herewith as Annexure-II. The committee further desired that after the hospital settings and conditions under which product will be given is submitted by the firm, the Technical Committee may review it again prior to according approval”. Accordingly firm has submitted hospital setting.

Recommendation of the Technical Committee:-The Committee reviewed the documents submitted by the firm on Hospital settings and conditions under which product will be given, as per recommendations of the 24th Apex Committee. After detailed deliberation, the Committee recommended for the grant of import permission as per SEC recommendation with the condition that the hospital should have facilities for digital imaging, chemoembolization and tertiary care center supervised by radiologist.

Item No. 07:-Clinical trial waiver proposal of M/s. Encarta Pharma Pvt. Ltd., Bangalore for the grant of permission to import and market the medical device, “InSpace System, Implantable Balloon”

The InSpace 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 due to trauma or degradation,
- Absence of tendon/muscle or non-functional tendon/muscle
- Ruptured tendon

SEC-Orthopaedics Recommendations:- The case has been reviewed by SEC – Orthopaedics in its meeting held on 17.08.2015 whereby 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.

In SEC-Orthopaedics meeting held on 17.08.2015, committee recommended that the firm shall submit the published data on randomized control trials on its outcomes (safety and efficacy). The proposal was again deliberated on 05.11.2015 and the firm did not submit the desired data as asked earlier. 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.

30th Technical Committee Recommendation:- 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.

The case has been reviewed by Technical Committee meeting held on 26.11.2015. 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 orthopaedics for deliberation in the next Technical Committee meeting and also desired to call the firm to present the proposal before the committee.

Accordingly the proposal is placed as per recommendation of the 30th Technical Committee.

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.

Item No. 08:-

Clinical trial waiver proposal of M/s. Meril Life Sciences India Pvt. Ltd., for registration of PULSECATH iVAC3L and PULSECATH iVAC3L-ST (21 Fr.) manufactured by M/s. PulseCath B.V. having manufacturing premises at Third Floor, Orlyplein 85, 1043 DS Amsterdam, The Netherlands.

(1)Product name: PULSECATH iVAC3L

Description:- The iVAC is designed to provide circulatory support to patients with impaired left ventricular function. At heart rates from 60 to 120 beats per minute, the circulatory support provided by the iVAC is 2-3 L/min. the iVAC functions in combination with an Intra Aortic Balloon Pump (IABP) driving console.

a) Components / Accessories (If any):

- LV21 catheter with insertion set (iVAC3L) or LV21-ST catheter with insertion set (iVAC3L-ST)
- Single pump Membrane pump
- Catheter protector

b) Composition/ Material of Construction:

S.No.	Part Name	Material of Construction	Body Contact
1	The Tip	Medical grade stainless steel (316L)	Direct human body contact
2	The two-way valve	Medical grade stainless steel (316L)	Direct human body contact
3	The flexible parts	Polyurethane tube braided with nitinol	Direct human body

	of the LV21 catheter		contact
4	The Connector	Polyurethane	No body contact
5	The insertion set	Polyurethane/ methylmethacrylate-acrylonitrile-butadiene-stryene-stryene polymer (MABS), with a polyurethane seal (gasket)	Direct human body contact/ Indirect human body contact
6	Membrane Pump	methylmethacrylate-acrylonitrile-butadiene-stryene-stryene polymer (MABS)	Indirect human body contact
7	Catheter Protector	Ployurethane	No body contact

c) Indication: 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.

d) Approval of device(s) in different Countries: - The Netherlands, Austria, Germany, Russia.

(2) Product name: PULSECATH iVAC3L-ST (21 Fr.)

Description:- The iVAC is designed to provide circulatory support to patients with impaired left ventricular function. At heart rates from 60 to 120 beats per minute, the circulatory support provided by the iVAC is 2-3 L/min. the iVAC functions in combination with an Intra Aortic Balloon Pump (IABP) driving console.

a) Components / Accessories (If any):

- LV21 catheter with insertion set (iVAC3L) or LV21-ST catheter with insertion set (iVAC3L-ST)
- Single pump Membrane pump
- Catheter protector

b) Composition/ Material of Construction:

S.No.	Part Name	Material of Construction	Body Contact
1	The Tip	Medical grade stainless steel (316L)	Direct human body contact
2	The two-way valve	Medical grade stainless steel (316L)	Direct human body contact
3	The flexible parts of the LV21 catheter	Polyurethane tube braided with nitinol	Direct human body contact
4	The Connector	Polyurethane	No body contact
5	The insertion set	Polyurethane/ methylmethacrylate-acrylonitrile-butadiene-stryene-stryene polymer (MABS), with a polyurethane seal (gasket)	Direct human body contact/ Indirect human body contact

6	Membrane Pump	methylmethacrylate-acrylonitrile-butadiene-styrene-styrene polymer (MABS)	Indirect human body contact
7	Catheter Protector	Ployurethane	No body contact

c) Indication: 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.

MDAC Recommendations:- The said proposal has been deliberated in the MDAC-Cardiovascular meeting held on 30/06/2014 and 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 wherein the committee deliberated and recommended that the firms 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.

Note: The firm represented to DGHS vide letter dated 05.08.2015 for the clinical trial waiver 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.

30th Technical Committee Recommendation:- The case has been reviewed by Technical Committee meeting held on 26.11.2015. 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.

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.

Item No. 09:-

Phase-III clinical trial proposal of M/s Vascular Concepts Ltd., No. 19, GR Floor, S.V Complex, Bellary Road, Hebbal, Bangalore - 560 024.

29th Technical Committee Recommendations:- The case has been reviewed by SEC – Cardiology in its meeting held on 25.08.2015 and subsequent deliberation in 29th Technical Committee meeting on 12.10.2015. After deliberation, the Committee observed that the objective of the study is to assess the safety and performance of the HYDRA TAVI system in the treatment of severe aortic stenosis in high risk patients. Therefore the Committee opined that high risk patients need to be defined and to be monitored by team comprising of Cardiologist, Cardiac surgeon and Anesthetist for further review by the Technical Committee.

The firm has submitted the Revised Study Protocol No. VCL-HYDRA-01/2014, Version No. 3.0 Dated 20.11.2015 duly signed by the National Coordinator and Principal Investigator with the following changes.

- Definition for High Risk Patients.
 - a. STS score > 8%.
 - b. One clinical site cardiac surgeon, one interventional cardiologist and anaesthetist to determine patient eligibility.
 - c. Any patient that is over 70 years of age.
 - d. Has other co-morbidities with aortic stenosis (Renal dysfunction, COPD, lung disease etc.,)
- Addition of following two (2) other study Centers.
 - a. Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Dr. Ajit Kumar Valaparambil Kumar, Dr. Harikrishnan Sivadasan Pillai, Dr. Sanjay Ganapathi as Investigators.
 - b. Lisie Hospital, Cochin, Dr. Rony Matthew as the Investigator.
- Inclusion of acronyms “STS” and “COPD” in Appendix II.

Recommendation of the Technical Committee:-The Committee reviewed the documents submitted by the firm regarding the criteria of High Risk Patients. The Committee accepted the explanation submitted by the firm and recommended for conduct of Phase III clinical trial as per SEC recommendation.

Item No. 10:-

Proposal of M/s Alcon Laboratories (India) Pvt. Limited for grant of permission to import and marketing of FDC of Brinzolamide 10 mg/ ml + Brimonidine 2 mg/ml Eye Drops.

M/s Alcon Laboratories (India) Pvt. Limited, Bangalore has applied for grant of permission to Import and Marketing of FDC of Brinzolamide 10 mg/ ml + Brimonidine 2 mg/ml Eye Drops.

Recommendation of the SEC meeting dated 11.09.2015:- During the meeting the firm presented subset analysis of 69 Indian patients (i.e. 138 eyes) which were included in the study as a part of global clinical trial. Firm also presented justification showing that the said sample size is statistically significant. The result of the subset analysis shows a statistically significant reduction in intraocular pressure using the FDC which was comparable to the individual drugs given together. Further the Committee noted that the FDC is also approved in USA, Australia, UK etc. Hence the Committee recommended for Import and Marketing of the FDC. Firm had conducted above trial in 69 Indian patients (i.e. 138 eyes) as a part of global clinical trial.

Recommendation of the Technical Committee:- The Committee recommended for import and marketing permission of the FDC of **Brinzolamide 10 mg/ ml + Brimonidine 2 mg/ml Eye Drops** as per SEC recommendation.

Item No. 11:-

Proposal of M/s Issar Pharmaceuticals Pvt. Ltd. to conduct Phase II clinical trial entitled, “A Phase II Clinical Study to Assess the Efficacy and Safety of the Genoep 1 (Issar 1) in a Non-Randomized, Open-Label, Single-Arm, Multi-Centre Design in Indian Adult Patients with Relapsed/ Recurrent/ Resistant Solid Tumours”.

Recommendation of IND Committee meeting dated 21.08.2013:-

The proposal was deliberated in IND Committee meeting held on 21.08.2013. 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. The proposal was deliberated in the 30th Technical Committee meeting held on 26.11.2015.

Recommendation of the 30th Technical Committee meeting dated 26.11.2015:- The Committee deliberated the proposal and opined that the firm may be asked to clarify the following for further deliberation:-

- 1) The firm shall specify the types of patients and the types of tumor.
- 2) Whether the proposed treatment is post-surgical, monotherapy or as an adjuvant therapy.
- 3) Proof of efficacy of the drug in tumor reduction in animal model.

In response:-

1) The firm has specified the type of patients and types of tumors as follows:-

- Type of patients:- Relapsed/ recurrent/ resistant solid tumor cancer patients who have exhausted all standard cancer treatment.
- Type of tumors:- Breast, lung, stomach, colorectal, head and neck, pancreas, soft tissue sarcoma, prostate, cervix, bladder, endometrium.

2) The firm has informed that it is not adjuvant therapy. Patients may have undergone surgery and or adjuvant or palliative chemotherapy or radiotherapy for their tumors, either for their primary tumor or for the relapse.

3) In respect of proof of efficacy firm has submitted study summary conducted at Tata Memorial Center, Advanced Center for Treatment Research and Education in Cancer (ACTREC) in nude mice.

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.

List of 03 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 <i>vis –a vis</i> 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>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 SECA 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>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</p>	<p>1. Recommendation of the SEC: After detailed deliberation the committee recommended conduct of the trial subject to the following</p>

	<p>Phase: III</p> <p>Name of the Applicant: Novo Nordisk India Private Ltd.</p> <p>Name of the Sponsor: Same as above</p> <p>Name of the Manufacturer: Novo Nordisk A/S, NovoAlle, Bagsvaerd Denmark</p> <p>Title: Efficacy and Safety of Semaglutide versus Dulaglutide as add-on to Metformin in subject with type 2 diabetes.</p>	<p>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 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>conditions:-</p> <p>I. Dose titration with dulaglutide in line with the approved prescribing information. Accordingly the protocol should be suitably modified.</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>III.</p>	<p>Name of the Drug: Masitinib Mesylate</p> <p>Protocol No : AB07002</p> <p>Phase of the Study: Phase II</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,</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:</p> <p>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:</p> <p>After detailed deliberation, the Committee noted the following:-</p> <p>I. The recommendation of the SEC</p> <p>II. The Phase III trial is ongoing in a number of countries</p>

	<p>Feucht -90537, Bavaria, Germany.</p> <p>Title: 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.</p>		<p>III. There are significant number of patients with Multiple Sclerosis in India and Multiple Sclerosis is an area of great unmet medical need.</p> <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 improvement from this treatment.</p>
--	--	--	--

List of 01 case of Clinical Trial proposal of GCT along with evaluations and recommendations of the Technical Committee in 31st Meeting.

Proposal No.	Details of the proposal	Assessment of the Proposal <i>vis –a vis</i> specifiedParameters	Recommendation 1. Subject Expert Committee 2. Technical Committee
1.	<p>Name of the Drug: Insulin degludec/Insulin Aspart</p> <p>Protocol No : NN5401-4243</p> <p>Phase of the Study: Phase III</p> <p>Name of the Applicant:Novo Nordisk India Private Limited.</p> <p>Name of the Sponsor: Novo Nordisk India Private Limited.</p> <p>Name of the Manufacturer: Novo Nordisk A/S, Novo Allé DK-2880, Bagsværd, Denmark</p> <p>Title: A trial comparing efficacy and safety of insulin degludec/insulin aspart twice daily and biphasic insulin aspart twice daily in subjects with type 2 diabetes mellitus before, during and after Ramadan.</p>	<p>Assessment of Risk vs. Benefit to the patients: In light of the fact that the test drug is already approved and marketed in India, the safety profile of the test drug justify the conduct of the trial.</p> <p>Innovation vis-à-vis Existing-Therapeutic Option: The purpose of the study is to compare the efficacy and safety of insulin degludec/insulin aspart twice daily and biphasic insulin aspart twice daily in subjects with type 2 diabetes mellitus before, during and after Ramadan.</p> <p>Unmet Medical Need in the country: The data generated from the study may provide optimal second line therapy when first line therapy fails to provide adequate glycaemia control.</p>	<p>1. Recommendation of the SEC Committee held on 01.09.2015</p> <p>As per Technical Committee advice, SEC reviewed its previous recommendation of having at-least minimum of 8 hrs gap between each injection which is to be given before each meal and the committee again opined that its recommendation was appropriate.</p> <p>The firm presented the revised protocol after incorporating the suggestions of last SEC dated 01/09/2015. The committee was satisfied and recommended the modified protocol for approval.</p> <p>2. Recommendation of the Technical Committee:</p> <p>After detailed deliberation, the Committee recommended the conduct of the study as per the SEC recommendation.</p>

Annexure III

List of 07 cases of clinical trial proposals other than GCT/NCEs along with evaluations and recommendations of the Technical Committee in 31st Meeting.

SI No	Name of the Drug	Firm Name	Recommendations: 1. Subject Expert Committee 2. Technical Committee
1.	Apremilast Tablets 10 mg, 20 mg and 30 mg	M/s Glenmark Pharmaceuticals Limited	<p>1. Recommendation of the SEC : After detailed deliberation the committee recommended for approval of protocol subject to following conditions:-</p> <ol style="list-style-type: none"> 1. The patient withdrawn from the study from either arm should be provided standard of care treatment, including patients with suicidal tendencies. 2. The proposed sample size is less and it should be suitably increased based on statistical calculations. 3. The number of sites should be reduced. The Government Institutes / Medical colleges should not be reduced from the proposed sites. <p>2. Recommendation of the Technical Committee: After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.</p>
2.	Anagliptin Tablet 100 mg	M/s Intas Pharmaceuticals Limited	<p>1. Recommendation of the SEC Revised clinical trial protocol was deliberated in SEC (Endocrinology) held on 22.12.2015. After detailed deliberation the Committee recommended the revised clinical trial protocol.</p> <p>2. Recommendation of the Technical Committee: After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.</p>
3.	Chlorthalidone, Metoprolol and Telmisartan	M/s Sun Pharma Laboratories Limited	<p>1. Recommendation of the SEC: The committee recommended for conducting clinical trial with following conditions:</p> <ol style="list-style-type: none"> 1. Only patients who are on Metoprolol + Telmisartan combination should be enrolled in the study. 2. Patients with stable CAD and Essential Hypertension shall be enrolled.

			<p>3. Clinical monitoring should be conducted weekly for initial one month followed by monthly.</p> <p>4. If the Blood Pressure is not adequately controlled appropriate therapeutic measures must be ensured and such patient should be given rescue medicine and excluded from the study. Accordingly, firm shall submit the revised protocol for consideration by CDSCO.</p> <p>2. Recommendation of the Technical Committee: After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.</p>
4.	Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis B (rDNA) and Haemophilus Type B Conjugate Vaccine (Adsorbed) I.P	M/s Cadila Healthcare Limited	<p>1. Recommendation of the SEC: The committee examined the preclinical data of multiple dose toxicity as per Schedule Y and recommended for conduct of Phase I trial as per the submitted protocol.</p> <p>2. Recommendation of the Technical Committee: After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.</p>
5.	PCV 13 (Pevnar): Pneumococcal 13-valent conjugate vaccine (Diphtheria CRM ₁₉₇ Protein) containing polysaccharides of the capsular antigens of <i>S. pneumoniae</i> serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F	Dr. Ashish Bavdekar, Associate Professor, Consultant in Pediatric Research, Department of Pediatrics, KEM Hospital Research Centre, Rasta Peth, Pune	<p>1. Recommendation of the SEC: The committee deliberated the academic clinical trial proposal in detail. This is a trial evaluating 50% reduction in the nasopharyngeal carriage in the subjects compared to control group and committee recommended the proposal for conduct of study.</p> <p>2. Recommendation of the Technical Committee: After detailed deliberation, the Committee recommended that as the investigator initiated phase IV study proposes 2 doses of the vaccine instead of the regular 3 doses, therefore the investigator should determine the immunogenicity in first 20 subjects via nasopharyngeal route and submit the report to the Committee for evaluation.</p>

6.	Meningococcal Polysaccharide Vaccine	M/s Prosper channel Lifescience India pvt.ltd. B-244, Ramphal Chowk, Sector -7, Dwarka, New Delhi-110077, India	<p>1. Recommendation of the SEC: The committee deliberated the study protocol in detail and recommended for conduct of Phase III study trial.</p> <p>2. Recommendation of the Technical Committee: After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.</p>
7.	Influenza Vaccine (Split Virion), Inactivated	M/s Wockhardt Limited	<p>1. Recommendation of the SEC: The committee deliberated the study protocol in detail and recommended for conduct of Phase III study subject to the condition that the firm shall include more number of geographically representative study sites.</p> <p>2. Recommendation of the Technical Committee: After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.</p>

Recommendations of the 07 cases of Clinical trial waiver in Indian populations:

Sr. no.	Drug Name	Name of the Firm	Indication	1. Recommendations of the SEC. 2. Recommendations of the Technical Committee
1.	Darunavir Ethanolate film coated tablet 800mg (Additional strength).	M/s Cipla Limited	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.	<p>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.</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.	Deferasirox Film Coated Tablets 90/180/360mg (additional dosage form & strength)	M/s Novartis Healthcare Pvt Ltd.	<p>Deferasirox film coated tablets indicated for:-</p> <ul style="list-style-type: none"> • 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 	<p>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.</p>

			with non-transfusion dependent thalassemia (NTDT) syndromes aged 10 years and older.	<p>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.</p> <p>2. Recommendations of the Technical Committee:</p> <p>After detailed deliberation, the Committee recommended for waiver of local clinical trial as per SEC recommendation.</p>
3.	Methadone Hydrochloride Oral Concentrate BP 5mg / 10 mg per ml & Methadone Tablets IP 5mg / 10 mg (additional indication)	M/s Rusan Pharma Limited.	Indicated for the treatment for Pain management and palliative care.	<p>1. Recommendations of the SEC:-</p> <p>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</p>

				<p>Oral Concentrate 5mg/10mg/mL & 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.</p> <p>2. Recommendations of the Technical Committee:</p> <p>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.</p>
4.	Tiotropium Bromide Inhaler 9 mcg and Tiotropium Bromide Rotacaps 18mcg (Additional indication).	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 β_2 agonists and who experienced one or more severe exacerbations in the previous year.	<p>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</p>

				<p>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 $\beta 2$ 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.</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>
5.	Triptorelin for injection 22.5mg (Lyophilized) (Additional strength)	M/s Dr Reddys Laboratories Ltd	Indicated for the treatment of locally advanced or metastatic, hormone dependent prostate cancer.	<p>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.</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>
6.	Dengue tetravalent vaccine (live, attenuated)	M/s Sanofi Pasteur India Private Limited	Dengue tetravalent vaccine (live, attenuated).	<p>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).</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>

7.	Palbociclib Capsule 75mg/100mg/125 mg.	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 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 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>
----	--	--------------------	--	--
