MINUTES OF THE 18th MEETING OF THE APEX COMMITTEE HELD ON 25-11-2014 UNDER THE CHAIRMANSHIP OF SECRETARY, HEALTH AND FAMILY WELFARE FOR SUPERVISING CLINICAL TRIALS ON NEW CHEMICAL ENTITIES.

Present:

1. Shri Lov Verma,
   Secretary,
   Department of Health and Family Welfare,
   Ministry of Health and Family Welfare, New Delhi
   & Chairman, Apex Committee

2. Dr. V. M. Katoch,
   Secretary, DHR & DG ICMR,
   New Delhi

3. Dr. Jagdish Prasad,
   Director General of Health Services,
   New Delhi

4. Shri K.L. Sharma,
   Joint Secretary,
   Ministry of Health and Family Welfare, New Delhi

Special Invitee:

1. Shri N.S.Kang,
   Addl. Secretary & DG (CGHS),
   Ministry of Health and Family Welfare, New Delhi

2. Dr. G. N. Singh,
   DCG (I), FDA Bhawan, New Delhi

Initiating the discussion, Chairman, Apex Committee welcomed the members of the Committee and special invitees to the meeting. Thereafter, the agenda items and recommendations of the 19th Technical Committee were taken up for consideration. The decisions taken by the Apex Committee on each agenda items are as below:

1. Adoption of minutes of the 17th Meeting of the Apex Committee

The Committee adopted the minutes of the 17th Apex Committee meeting held on 15.10.2014.

2. Proposals of Clinical Trials recommended by Technical Committee

2.1 The Apex Committee noted that the Technical Committee had deliberated 31 cases relating to approval of clinical trials/ protocol amendments. Out of these 31 cases, 10 cases related to global clinical trials (GCT) and remaining 21 cases concerned clinical trials for approval of New Drugs including fixed dose combination, subsequent new drugs and biologicals. Out of the 10 GCT cases, six cases related to approval of clinical trials and the remaining four concerned protocol amendments. Out of six proposals, one case of GCT of Rifampitine involved fresh examination based on new facts brought out during the presentation by the applicant.

2.2 The Apex Committee noted that the Technical Committee had evaluated the 10 cases relating to global clinical trials and made recommendations after due consideration of all aspects of safety and 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 needs in the country. The Technical Committee had recommended approval of 03 out of 05 cases of global clinical trials (Sr. No 1,2,3, of **Annexure-I**) and all 04 cases of protocol amendments as per details in **Annexure-I.**

2.3 As decided by the Technical Committee in its 18th meeting, in one case of global clinical trial, M/s B J Medical College made presentation before the Technical Committee on further details of the study A5279. The Technical Committee has, after deliberations, asked further information on the safety aspects and deferred the case **(Annexure-III).**

2.4 The Technical Committee also evaluated the remaining 21 cases other than GCT/clinical trials of NCEs. After detailed deliberations, the Technical Committee had recommended approval of all 21 cases except in respect of case at Sl.No 12 in **Annexure-II.** In case of proposal at Sl. No. 12, of Annexure II, the Technical Committee recommended conduct of study with certain conditions as specified in that Annexure.

2.5 The recommendations of the Technical Committee in respect of other 21 cases are enclosed as **Annexure-II.**

2.6 Out of the total 31 clinical trial proposals, the Technical Committee had recommended approval of 28 cases. In the remaining two cases (Sr. No 4 & 5 in the Annexure-I), the Technical Committee did not recommend approval of proposal for conduct of the clinical trials and one case of re-examination was deferred seeking additional information on safety **(Annexure-III).**

Recommendation:

The Apex Committee deliberated upon the proposals and agreed with the recommendations of the Technical Committee. The Committee also made an observation that evaluation of three criteria may not be written as "not applicable", as was done in respect of proposal No. 4 and 5 of **Annexure-I.** The Committee noted that the content of evaluation and reasons for refusal are already brought out in the recommendations, which could have also been reflected in the aforesaid column. It advised that the comments in the column pertaining to three criteria of evaluation be indicated in such cases in future.

3. Fresh proposal of Clinical Trial Waiver in Indian population for approval of new drugs, which have already been approved outside India.

3.1 As per the D&C Rules, for new drugs substances approved in other countries, phase III clinical trial is required to be carried out before granting permission to manufacture / import the finished formulation of the new drug. However, requirements of local Clinical Trial may be waived / relaxed under certain conditions as per Drugs & Cosmetics Rules (122 A (2),122 B (3) and clause 1 (3) of schedule Y depending on the nature of drugs and diseases for which it is indicated.

3.2 Under Rule-122A(2) & Rule-122B(3) of Drugs & Cosmetics Rules, the requirement of submitting the results of local clinical trials may not be necessary if the drug is of such a nature that the licensing authority may, in public interest, decide to grant such permission on the basis of data available from other countries. Further, the submission of requirements relating to animal toxicology data may also be modified or relaxed under the same Rules in case of new drugs approved and marketed for several years in other countries and adequate published evidence regarding the safety of the drug is available.

3.3 As per Clause 1 (3) of Schedule Y of the Drugs & Cosmetics Rules, for drugs indicated in life threatening / serious diseases or diseases of special relevance to the Indian health scenario, the toxicological and clinical data requirements may be abbreviated, deferred or omitted, as deemed appropriate by the Licensing Authority.

3.4 There are, as such, certain conditions specified in the Drugs & Cosmetics Rules under which the licensing authority may grant permission to manufacture / import new drugs without local clinical trials.

3.5 However, the Parliamentary Standing Committee in its 59th report had raised concerns on approval of certain new drugs in the country without local clinical trials. In the light of the same, the Ministry constituted a Committee under chairmanship of Prof. Ranjit Roy Chaudhury. The action to be taken on the recommendations of the Expert Committee has been finalized by the Ministry of Health & Family Welfare. Accordingly, "The waiver of Clinical Trial in Indian population for approval of new drugs, which have already been approved outside India, can be considered only in cases of **national emergency, extreme urgency, epidemic and orphan drugs for rare diseases and drugs indicated for conditions/diseases for which there is no therapy.**

3.7 The Apex Committee in its meeting held on 24.01.2014, recommended that waiver of local clinical trial of such cases should be granted only under the criteria as already decided by the Ministry viz national emergency, extreme urgency, epidemic and orphan drugs for rare diseases and drugs indicated for conditions/diseases for which there is no therapy. In case, the local clinical trial waiver is required for any other category, the matter should be brought before the Apex Committee for consideration along with the recommendations of the Technical Committee. In other cases, decision to waive may be taken by the Licencing Authority.

3.8 Three proposals (two from biologicals and one from New Drug) have been recommended by the SECs for their approval for manufacture/ import for marketing in the country without local clinical trial. The details of the same alongwith recommendations of the SEC were placed before the Technical Committee for perusal and comments:

3.9 The Technical Committee had after detailed deliberations, recommended local clinical trial waiver of all the three drugs namely Obinutuzumab Injection, Pertuzumab and Afatinib, as they qualify for such waiver based on the criteria laid down for the same, as per details given in the following table:

Sr. no.	Drug Name	Indication	Recommendations
1.	Obinutuzumab Injection	"Obinutuzumab in combination with chlorambucil is indicated for the treatment of patients with previously Untreated chronic	The Technical Committee agreed to the recommendation of the SEC and the drug comes under the category of "the drugs indicated for conditions / diseases for which there is no therapy" as one of the categories laid down by the Ministry for waiver of clinical trial. **SEC Recommendation:** The proposal is for approval for the import and market the Obinutuzumab with Clinical Trial waiver. Obinutuzumab injection (1000mg/40ml) has been approved in the US, Australia, Switzerland&

			lymphocytic leukemia (CLL).	Ecuador. Based on the fact that the drug got an orphan drug status in US and Europe and it is a rare disease, therefore clinical trial waiver can be granted. Committee after detailed deliberation recommended for the marketing authorization of the subject drug for the indication "Obinutuzumab in combination with chlorambucil is indicated for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL)" with the condition that "the safety data of the subject drug with respect to Indian patients shall be examined by the experts of SEC-Oncology after 1 year of marketing and the continuation of marketing authorization of the subject drug shall be considered after satisfactory evaluation of the PMS data by the experts". The drug is to be sold by the prescription of the "Oncologist & Haematology".
2.	Pertuzumab	Indicated for the treatment of positive metastatic or locally recurrent unresectable breast cancer, who have not received previously treatment or whose disease has relapse after adjuvant therapy.	The combination of Pertuzumab and Trastuzumab with Chemotherapy has shown unprecedented survival benefit in first line therapy of HER2+ metastatic breast cancer. There is no therapy existing with such benefits. In view of this fact the Technical Committee recommends that Pertuzumab Inj. may be allowed for import & marketing for the claimed indication without further clinical trial in India subject to condition as stipulated by SEC. **SEC Recommendations** The Committee recommended for the waiver from local clinical trial. However, as the data on the clinical studies presented by the firm did not give any significant results on Indian Population, the firm shall first submit structured phase IV study protocol to be conducted on the Indian population for the generation of toxicity/safety data. The protocol shall be submitted by the firm to be reviewed by the NDAC members and discussed in the subsequent meeting of oncology & Hematology.
3.	Afatinib	Indicated for treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) with Epidermal Growth Factor Receptor (ECFR) mutation.	The Technical Committee noted that the SEC (Oncology and Hematology) has recommended for local clinical trial waiver stating that it is an orphan drug for the proposed indication (for treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) with Epidermal Growth Factor Receptor (EGFR) mutation). The Committee deliberated the matter in detail. The Committee stated that Orphan drug for rare diseases is one of the criteria laid down by the Ministry of Health and Family Welfare for waiver of local clinical trial in the country and hence, recommended for the waiver of local clinical trial in the country . **SEC Recommendation:** The firm has applied for import and marketing of Afatinib film coated tablet 20/30/40/50 mg to be indicated for treatment of locally

			advanced or metastatic non-small cell lung cancer (NSCLC) with Epidermal Growth Factor Receptor (EGFR) mutation. The proposal was deliberated in SEC (Oncology and Hematology) held on 10.06.2014 and the Committee deliberated the matter in detail and noted that the data generated in Indian Patients are adequate and the firm has also proposed to conduct another study with 50 patients. The Committee recommended for grant of Permission for Afatinib film coated tablet 20/30/40/50 mg with indication for treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) with Epidermal Growth Factor Receptor mutation. The proposal was referred to the Committee for re-examination in light of the recommendations on the waiver of Clinical trial in Indian population for approval of New Drugs. After detailed deliberation the committee reconfirmed that waiver of clinical trial may be granted because this is an orphan drug for the proposed indication. The safety data available on 47 Indian patients (including 10 of the same indication) are adequate The efficacy data provided from global studies are adequate. Active monitoring of patients receiving the drug post marketing should be done for a period of 2 years and the ADRs reported in PVPI.

Recommendation: The Committee, after detailed deliberations, agreed with the recommendations of the Technical Committee.

4. Proposal of Clinical Trial Waiver after re-examination

4.1 The Technical Committee in its 18th meeting held on **13.10.2014** had recommended approval of following 03 drugs without clinical trials in India based on recommendations of the SEC.

4.2 The Apex Committee in its meeting held on 15.10.2014, recommended that the Technical Committee should mention if these three cases fall under the five laid down criteria as already decided by the Ministry for waiver of local clinical trial in Indian populations for approval of new drugs viz. **national emergency, extreme urgency, epidemic and for orphan drugs for rare diseases and drugs indicated for conditions/diseases for which there is no therapy.**

4.3 The Technical Committee after re-examination of these cases had mentioned the criteria under which they had recommended for local clinical trial waiver as per details given in the following table.

Sr. no.	Drug Name	Indication	Technical Committee Recommendations for mention of CT waiver criteria
1.	Aflibercept	For patients with metastatic colorectal cancer (MCRC) previously treated with an Oxaliplatin containing regimen.	Based on the recommendation of the Apex Committee the present case was re-deliberated in the Technical committee and in continuation of earlier SEC and Technical Committee recommendations, it was opined that Aflibercept in combination with FOLFIRI is safer and more effective therapy in **second line metastatic colon cancer which is an unmet need and where there is no such effective therapy**. Therefore the Technical Committee recommended for grant of permission to import and marketing of this drug subject to the condition of adequately powered Phase–IV clinical trial with review of data in two years, the phase-IV trial protocol should be approved by CDSCO.
2.	Trastuzumab emtansine	For the treatment of patients with HER2-Positive, unresectable locally advanced or metastatic breast cancer who have received prior treatment with Trastuzumab and a Taxane	Based on the recommendation of the Apex Committee the present case was re-deliberated in the Technical committee and in continuation of earlier SEC and Technical Committee recommendations, it was opined that in patients with HER2 new positive metastatic breast cancer that have failed treatment with Trastuzumab and chemotherapy, Trastuzumab Emtansine offers 6-months extra survival and also significantly more patients responded to the treatment. **The committee reiterated it's earlier stand that there is no such therapy available for these conditions and recommended it in public interest** for permission to import the drug for marketing subject to the condition of adequately powered Phase –IV clinical trial with review of data in two years, the phase- IV trial protocol should be approved by CDSCO.

Sr. no.	Drug Name	Indication	Technical Committee Recommendations for mention of CT waiver criteria
3.	Medroxyprogesterone Acetate (MPA) 104mg in 0.65mL suspension for injection	For long term female contraception and management of endometriosis associated pain.	Based on the recommendation of the Apex Committee the present case was re-deliberated in the Technical committee and in continuation of earlier SEC and Technical Committee recommendations, the Committee after detailed deliberation recommended for waiver of clinical trial of Medroxyprogesterone 104mg in 0.65 ml suspension (for Subcutaneous Injection) based on the fact that for the treatment of Endometriosis, **no satisfactory subcutaneous product or therapy is yet available in the country**, which is being provided by the said drug in SC route and as such Medroxyprogesterone is very old drug used for Endometriosis by IM route. Therefore clinical trial is not necessary as such for such slightly modified preparation of drug of already known safety and efficacy in given indication.

Recommendation:

The Apex Committee after considering the aforesaid facts, agreed with the recommendations of the Technical Committee. Further, the Committee desired that the Technical Committee will re-examine the criteria for waiver of local clinical trials in Indian population for approval of new drugs, which have already been approved outside India. Recalling the Supreme Court direction whereunder Secretary, MoHFW was to supervise the clinical trial related to N.C.E., the Committee directed that other cases that do not fall within the scope of the aforesaid directions of the Supreme Court but were being placed before the Technical and Apex Committee to ensure the consistency in decision making, now need not be placed before them in all cases. However, in specific cases, Licencing Authority may place the matter before DGHS for Technical advice.

5. **Re-examination of condition imposed on the applicant to manufacture the Drug Pasireotide in India, while granting local clinical trial waiver**

5.1 The Technical Committee in its 11th meeting had examined the proposal of M/s Novartis for waiver of local clinical trial for Pasireotide. The Technical Committee had after detailed deliberations recommended that waiver of local clinical trial may

be granted subject to the condition that drug should be manufactured in the country alongwith PMS study as recommended by the NDAC.

5.2 DCG(I) received a representation from M/s. Novartis India, wherein the firm mentioned that Pasireotide has been granted Orphan Drug status by major regulators world over including the USFDA and EMA and it is indicated primarily for use in patients of Cushing's disease which fails both surgical intervention as well as radiation therapy. The overall incidence of Cushing's disease is low (approx. 3/million.) Considering factors like healthcare access, diagnostic rates and patients willing to undergo surgery, etc., the ultimate number of patients who would qualify for use of Pasireotide would be very small.

5.3 Based on the preliminary market research conducted in India, the firm anticipates that only around 1500 patients per year would be eligible for treatment with Pasireotide Disparate. Considering this, it may not be practically feasible to set up a manufacturing site in India for this product where the overall expected patient population which would require the drug is abysmally low.

5.4 The Technical Committee had deliberated upon the issue in detail and opined that the condition to manufacture in India, while agreeing for waiver of local clinical trial, was a suggestive condition. However, as the number of patients in India would be very small i.e., around 1500 per year, as informed by the firm, this orphan drug (Paseriotide) used in Cushing's disease may be allowed to be imported and marketed. As far as its manufacturing in India is concerned, it shall be left to the applicant firm.

Recommendation:

The Apex Committee deliberated the issue and agreed with the recommendations of the Technical Committee.

6. **Re-examination of condition regarding clinical Trial study of Quark-Biocon on the basis of representation/ appeal by the applicant.**

6.1 M/s Manipal Accunova was granted permission for conduct of clinical trials for the protocol "A Pivotal Phase II/III, Randomized, Double-Masked, Sham-Controlled Trial of QPI-1007 Delivered By Multi-Dose Intravitreal Injections to Subjects With

Acute Non Arteritic Anterior Ischemic Optic Neuropathy (NAION)." on 10/11/2014 as per 17th Apex and 18th Technical Committee recommendations dated 15.10.2014 and 13.10.2014 respectively.

6.2 The Technical Committee had recommended that only severe cases of **NAION** should be included in the study i.e. the Subjects with visual acuity of finger counting close to face to 6/36, field defects on perimetry, retinal fibre thinning on OCT machine and FFA changes should be included. It also recommended that before phase III is initiated, the phase II trial data from all the centers should be submitted to CDSCO for further review by the experts. The committee had also opined that all the investigators must possess MS degree or alternate such as DNB".

6.3 Subsequently, the firm appealed against the conditions imposed on the conduct of clinical trial and requested to reconsider the matter in the Technical Committee, in the light of their previous request as following:

Parameters	CT NOC Conditions	Firm's Request/Appeal for Reconsideration
Visual Acuity	6/36	6/18 to 6/12
Field Defects on perimetry	Yes	Acceptable
Retinal thinning on OCT machine	Yes	Not mandatory to have retinal nerve fiber thinning as protocol criteria
FFA changes	Yes	Not required

6.4 The Technical Committee while reviewing its earlier recommendation on the basis of appeal/representation regarding the conditions of trial, recommended that the subjects with visual acuity 6/18 (as upper limit) may be recruited, the retinal thinning on OCT machine as part of inclusion criteria can be waived if regular monitoring of this parameter is already a part of protocol. Similarly the Technical Committee opined that the inclusion of FFA changes also can be waived as it may not provide any additional beneficial information.

Recommendation:

The Committee deliberated on the related the issues and agreed to the recommendations of the Technical Committee subject to the condition that the applicant be asked to submit monthly follow-up reports to DCG(I) about the progress of trial and the cases of deterioration of the condition of patients, if any, will be immediately brought to the notice of DCG(I). It decided that this practice be followed initially for a period of three months.

The meeting ended with the vote of thanks to the chair.

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Annexure-I

List of 09 cases of global clinical trials/ clinical trials of NCEs along with their evaluations and recommendations of the Technical Committee in its 19th Meeting.

Sr No.	IP	Protocol	Firm	Parameters 1. risk versus benefit to the patients 2. innovation vis-a-vis existing therapeutic option 3. unmet medical need in the country	Recommendation:
1	Rifabutin, Ritonavir, Lopinavir/ Ritonavir, Raltegravir	A5290	B J Medical College	**Risk Versus Benefit To The Patients** In light of the fact that the test drugs are already marketed in India, the conduct of the study is justified. **Innovation *vis-a-vis* Existing Therapeutic Option** The objective of the study is to compare rates of virologic suppression to < 400 copies/ml at 48 weeks for the two standard dose lopinavir/ Ritonavir and Rifabutin arm vs the double dose Lopinavir/ Ritonavir and Rifabutin arm. **Unmet Medical Need In The Country** The data generated from this study may provide a new approach in treatment of HIV related tuberculosis.	**Recommendation:** Recommended for approval as per the recommendation of SEC **NDAC Recommendation:** The applicant has presented the protocol before Committee. After detailed deliberation the Committee recommended the conduct of the study subject to the condition that the number of patients should be 60 (20 in each of the arms). The applicant should submit the HMSC approval to CDSCO and also there shall be a DSMB to the monitoring the patients safety.
2	Sunitinib Malate (SUTENT®)	A6181196	Pfizer Inc.	**Risk Vs Benefit to the Patients** The risk vs benefit profile of the test drug from Pre clinical single dose, repeated dose toxicity, reproductive toxicity, carcinogenicity studies, phase I, II, III clinical study justify the conduct of study. **Innovation vis-à-vis Existing Therapeutic option** The purpose of the study is to characterize the plasma pharmacokinetic profile of Sunitinib and its active metabolite SU012662 in children and young adult (6 to 18	**Recommendation:** Recommended for approval as per the recommendation of SEC **NDAC Recommendation:** After detailed deliberation the Committee recommended for conduct of the study with present protocol.

				Yrs of age) with advanced, unresectable gas gastrointestinal stromal tumour. **Unmet Medical Need In the Country** The data generated from this study may provide a therapy/treatment of pediatric gastrointestinal stromal tumour.	
3	Choline chloride	FCG-CNS-001	Prof S N Gaur, V.P. Chest Institute	**Risk Versus Benefit To The Patients** The safety profile of the test drug from various pre clinical and clinical studies justify the conduct of the trial. **Innovation Vis-A-Vis Existing Therapeutic Option** The purpose of the study is evaluation of choline chloride as an anti Inflammatory agent for the treatment of asthma and rhinitis through oral route. **Unmet Medical Need In The Country** The study drug may provide an alternate therapy for the treatment of asthma and rhinitis.	**Recommendation:** Recommended for approval as per the recommendation of SEC **NDAC Recommendation:** NDAC recommended the conduct of the proposed phase 3 trial in Asthma (with or without Rhinitis) and allergic alone, in 50 X 4 groups = 200 patients , subject to the submission of stability and other quality data of the test products to CDSCO
4	BenzaClin® Gel, (Clindamycin phosphate 1% and Benzoyl peroxide 5%, topical gel)	CRL/CT/05/12 -13	Clantha Research Ltd	Not applicable	**Recommendation:** The Committee agreed with the recommendations of the SEC and has not recommended the conduct of trial. **NDAC Recommendation:** The Committee reviewed the proposal and opined that for a blo-equivalence study placebo arm is not required. But the company claims that to market the drug in USA it is required to fulfill the condition of placebo arm, hence placebo arm is required; if it is so then trial should be conducted in USA only.

					The committee opined that the rationale of combination of two antibiotics still could not be explained by the applicant. Hence the Committee did not recommend the conduct of the study in India.
5	Isoniazid 300mg and Placebo for Isoniazid	P1078	B J Medical College	Not applicable	**Recommendation:** The Committee agreed with the recommendations of the SEC and has not recommended the conduct of trial. **NDAC** **Recommendation:** The Committee did not recommend for the conduct of the study. Small numbers of patients are proposed to be recruited in India, out of whom some may receive placebo. The data generated out of this study would be of no benefit in Indian context. The study design of this trial is not inconcurrence with the current guidelines of NACO and RNTCP.
6	MasitinibMesylate	AB07015	Maya Clinicals	**Risk Versus Benefit To The Patients** The risk vs benefit profile of the study drug from preclinical pharmacology, general toxicity, Reproductive toxicity, Genotoxicity and phase I, II and III clinical trials justify the conduct of this study. **Innovation Vis-A-Vis Existing Therapeutic Option** The purpose of the study is to compare the efficacy and the safety of study drug *versus* placebo in the treatment of patients with Severe Persistent Asthma treated with oral corticosteroids	**Recommendation:** Recommended for approval as per the recommendation of SEC **NDAC** **Recommendation:** The study is already under going. The applicant made presentation on the proposed protocol amendments regarding the monitoring of safety and efficacy. The committee after detailed deliberation

				Unmet Medical Need In The Country The test drug may potentially provide alternative treatment for patients with Severe Persistent Asthma.	recommended the protocol amendments 09 dt. 20-01-2013 and amendment 10 dt. 22-05-2014
7	Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine (Menactra)	**MTA-70**	Sanofy	**Risk Versus Benefit To The Patients** The risk vs benefit profile of the test drug from pharmacological toxicity, immunogenicity studies and clinical trials in the 2-55 years age groups justify the conduct of the study. The product is approved in India for the age group 2-55 years and the proposed trial is in the lower age group. **Innovation Vis-A-Vis Existing Therapeutic Option** The primary objective of the study is to assess the seroprotection rate after the second of the 02 doses of Menactra administered three to six months apart. **Unmet Medical Need In The Country** There is no licensed vaccine for the age group 9-23 months currently in India.	**Recommendation:** Recommended for approval as per the recommendation of SEC **NDAC Recommendation:** The Committee reviewed the presentation made regarding protocol amendment version 05 dt. 7th Feb 2014 and recommended the amended protocol for inclusion of additional subjects in India.
8	DE-109 Injectable (Sirolimus)	32-007	Excel Life Sciences	**Risk Versus Benefit To The Patients** The risk vs benefit profile of the study drug from preclinical pharmacology, general toxicity, Single dose toxicity, repeated dose toxicity and phase I, II and III clinical trials justify the conduct of this study. **Innovation Vis-A-Vis Existing Therapeutic Option** The purpose of the study is to assess safety and efficacy of Intravitreal injection of Sirolimus for the treatment of Active,non-Infectious uveitis of the Posterior Segment of the eye. **Unmet Medical Need In The Country** The test drug may potentially provide alternative treatment for	**Recommendation:** Recommended for approval as per the recommendation of SEC. **NDAC Recommendation:** Firm presented the clinical trial protocol amendment 05 version 06 dt. 313 Mar 2014. The Committee after review of the presentation made, recommended that the proposed additional patients must be recruited in the existing or Gov. teaching

				patients with non-infectious uveitis affecting the posterior segment of the eye.	Hospitals from Eastern and north-eastern part of the country
9	Fluocinolone Acetonide Intravitreal Insert (FAI insert)	PSV-FAI-001	Excel Life Sciences	**Risk Versus Benefit To The Patients** The risk vs benefit profile of the study drug from preclinical pharmacology, general toxicity, Single dose toxicity, repeated dose toxicity and phase I, II and III clinical trials justify the conduct of this study. **Innovation Vis-A-Vis Existing Therapeutic Option** The purpose of the study is to assess safely and efficacy study of a Fluocinolone Acetonide Intravitreal (FAI Insert) in subjects with Chronic Non-Infectious Uveitis affecting the posterior segment of the eye. **Unmet Medical Need In The Country** The test drug may potentially provide alternative treatment for patients with non-infectious uveitis affecting the posterior segment of the eye.	**Recommendation:** Recommended for approval as per the recommendation of SEC **NDAC Recommendation:** The Committee reviewed the presentation made for protocol amendment version 5 dt. 12 Dec 2013 and recommended for approval of the same.

List of 21 cases of clinical trial proposals other than GCT/NCE along with evaluations and recommendations of the Technical Committee in 19th Meeting.

Sl No	Name of the Drug	Firm Name	Recommendation
1.	Live attenuated Monovalent Rotavirus vaccine	M/s Bharat Biotech International Ltd., Hyderabad.	The Technical Committee has recommended to conduct the clinical trial as per recommendation of the SEC.
2.	Poliomyelitis Vaccine Live (Oral) I.P. (Trivalent)	M/s Bio-Med (P) Ltd., Ghaziabad	The Technical Committee has recommended to conduct the clinical trial as per the recommendation of the SEC.
3.	Recombinant Hepatitis B Vaccine 10g (0.5ml) & 20g(1ml)	M/s Wockhardt Ltd	The Technical Committee has recommended to conduct the clinical trial as per the recommendation of the SEC.
4.	Varicella vaccine (VR 795 Varicella Oka strain)	M/s Wockhardt Ltd	The Technical Committee has recommended to conduct the clinical trial as per the recommendation of the SEC.
5.	Fully Liquid Pentavalent Diphtheria, Tetanus, whole cell Pertussis, Hepatitis b and Haemophilus type b vaccine, (DTwP-HepB-Hib Vaccine) (My Five™)	M/s Panacea Biotech Limited	The Technical Committee has recommended to conduct the clinical trial as per the recommendation of the SEC.
6.	Acotiamide	M/s Lupin Ltd.	The Technical Committee has recommended to conduct the clinical trial as per the recommendation of the SEC.
7.	Arbekacin 200mg (Protocol Amendment)	Alkem Laboratories Limited	The Technical Committee has recommended to conduct the clinical trial as per the recommendation of the SEC.
8.	Paracetamol	Dr Bharathi B	The Technical Committee has recommended to conduct the clinical trial as per the recommendation of the SEC.
9.	Telmisartan + Chlorthalidone	M/s Ipca Laboratories Limited	The Technical Committee has recommended to conduct the clinical trial as per recommendation of the SEC.
10.	Cephalexin + Clavulanate Potassium Tablets	M/s Ranbaxy Laboratories Limited	The Technical Committee has recommended to conduct the clinical trial as per recommendation of the SEC.

11.	Teriparatide	M/s Sun Pharma	The Technical Committee has recommended to conduct the clinical trial as per recommendation of the SEC.
12.	Recombinant Human Growth Hormone (r-hGH)	Accutest Research Laboratories (I) Pvt. Ltd	The Technical Committee recommended as per the recommendation of the SEC subject to additional condition that insulin resistance and new onset of diabetes or other metabolic disorder should be monitored during the study.
13.	Teriparatide [Recombinant human parathyroid hormone (1-34)]	Intas Pharma Limited	The Technical Committee has recommended to conduct the clinical trial as per recommendation of the SEC.
14.	Teriparatide [Recombinant human parathyroid hormone (1-34)]	Intas Pharma Limited	The Technical Committee has recommended to conduct the clinical trial as per recommendation of the SEC.
15.	Rituximab concentrate for solution for infusion 500 mg/50 mL vial	Intas Pharma Limited	The Technical Committee has recommended to conduct the clinical trial as per recommendation of the SEC.
16.	Rituximab concentrate for solution for infusion 100 mg/10 mL and 500 mg/50 mL vial	Intas Pharma Limited	The Technical Committee has recommended to conduct the clinical trial as per recommendation of the SEC.
17.	Pegfilgrastim	Intas Pharma Limited	The Technical Committee has recommended to conduct the clinical trial as per recommendation of the SEC.
18.	Poly(2-hydroxy ethyl metha crylate	STEF Medical Care India	The Technical Committee has recommended to conduct the clinical trial as per recommendation of the SEC.
19.	Octenidine Dihydrochloride 0.3% Hand & Body Wash Gel	M/S. Dishman Pharmaceuticals & Chemicals Ltd	The Technical Committee has recommended to conduct the clinical trial as per recommendation of the SEC.
20.	Vitamin-D Supplement	Dr. Kana Ram Jat, GMCH, Chandigarh	The Technical Committee has recommended to conduct the clinical trial as per recommendation of the SEC.
21.	Vitamin-D Supplement	Dr. SK Sharma, AIIMS, New Delhi	The Technical Committee has recommended to conduct the clinical trial as per recommendation of the SEC.

List of 01 case of re-examination of global clinical trial (A5279) of Rifapentine and Isoniazid, based on presentation alongwith the evaluations and recommendations of the Technical Committee in its 19th Meeting.

Rifapentine, Isoniazid (*)	BJ Med, YRG, NARI	A5279	**Risk Versus Benefit To The Patients** In light of the fact that the test drugs are already approved for treatment of tuberculosis, the risk vs benefit profiles of the drugs justify the conduct of the study. **Innovation Vis-A-Vis Existing Therapeutic Option** The purpose of the study is to assess ultra-short-course rifapentine/isoniazid for the prevention of active tuberculosis in HIV-infected individuals with latent tuberculosis infection. **Unmet Medical Need In The Country** The study will potentially provide new regimen for treatment of latent tuberculosis infection in HIV-infected individuals.	**Recommendation dated 17-11-2014** After detailed deliberation committee recommended that 1. The safety profile of Rifapentine on the proposed dosing regimen of daily dosing for a period of 1 month shall be provided and presented to committee. 2. The steps/procedures taken for safety monitoring in USA on Rifapentine therapy as a (part of the protocol) be presented to the technical committee along with DSMB report. **NDAC/SEC Recommendation dated 11.02.2012:-** Proposed study is to compare 4 weeks daily Rifapentine/Isoniazid regimen to a standard 9 months daily Isoniazid for prevention of TB in HIV infected patients without active TB. Committee desires sound justification for the proposed regimen of Rifapentine/Isoniazid in view of recently published articles in NEJM showing efficacy of weekly Rifapentine/INH 900mg doses equivalent to 9 months efficacy of daily dose of INH. Compliance issue and post trial cost implementation should

				also be submitted. **NDAC/SEC Recommendation dated 28.092012:-** Data submitted is not adequate to address the following issues:- i) The possibility of increased serious adverse effects of daily dose of Rifapentine vs. once weekly use. ii) PK study has shown that peak conc. of rifapentine is associated with better efficacy than increased AUC in daily dose schedule. This also raises doubt about the efficacy of daily dose. Hence committee did not recommend for giving permission to conduct the proposed study. **18th Technical Committee Recommendation :** The Committee opined that the applicant should make a presentation on the proposal in the presence of HIV and TB experts in the next meeting.

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