1. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 10.12.2011:-

The NDAC (Oncology and Hematology) deliberated the proposals on 10.12.2011 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
Global Clinical Trials			
1	**Afatinib**		Recommended for giving permission for clinical trial subject to condition that trasuzumab naive patient arm should be excluded from the study, as patients cannot be left untreated of trastuzumab therapy / or treated with only investigational drug. Patients aged 18 to 65 years should be included in the study.
2	**Netupitant/ Palonosetron**		Recommended for giving permission for clinical trial subject to the following conditions:- ICD is very extensive and too technical for the patient to understand. It should be simplified. Definite statistical tests for the comparison of primary and secondary endpoints should be incorporated in the protocol.
3	**Crizotinib**		Recommended for giving permission for clinical trial subject to the following conditions:- Periodic ophthalmic examination should be performed at every visit as the drug is reported to have ophthalmological side effects in 53 % cases in phase 2 study. Patients aged 18 to 65 years should be included in the protocol. Method for causality assessment by the investigator should be included in the protocol.
New Drugs			
4.	**Crizotinib**		Approved with the condition that structured post marketing trial (Phase 4) should be conducted in Indian population. Report of post marketing trials ongoing in other countries when completed should be submitted.
5.	**Abiraterone**		Approved with condition of conducting Post

	Acetate		Marketing trial (Phase IV) in Indian population to monitor the adverse effects. Report of post marketing trials ongoing in other countries when completed should be submitted. For change in prescribing information/package insert based on clinical trial being conducted as per condition of US FDA approval should be communicated to the office of DCG (I).
6.	**Disodium Clodronate**		In view of lack of robust evidence to claim superiority over other Biphosphonates, randomized comparative clinical trial should be conducted in Indian population. The data submitted is very old, when the biophosphonate like Zoledronic acid etc. were not available.
7.	**Fosaprepitant Dimeglumine**		Approved with condition for conducting Phase IV trial in the country. Report of post marketing trials ongoing in other countries when completed should be submitted.
8.	**Degarelix**		Approved with the condition that data on survival rate of patients with advanced prostate cancer treated with Degarelix should be submitted to the office of DCG (I) before formal approval is granted. Also Post Marketing (Phase IV) trial should be conducted. Report of trials ongoing in other countries when completed should be submitted.
9.	**Pegaspargase**		Approved in patients with acute lymphoblastic leukemia hypersensitive to L-asparginase subject to following conditions. i) Supportive literature showing superiority or at least non inferiority of pegaspargase over L-asparginase should be submitted to the office of DCG(I) before formal approval. ii) Post marketing (Phase-IV trial) comparative trial of the firm's product vis-à-vis innovator's product should be conducted.

2. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 21.01.2012:-

The NDAC (Oncology and Haematology) deliberated the proposals on 21.01.2012 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
New Drugs			
1	**Nelarabine injection**		Experts opined that currently there is no recommended 3rd line therapy for the treatment of patients with T-cell lymphoblastic lymphoma. Therefore there is an unmet need for this drug for this subset of patients. Local clinical trial can be waived off. However the firm should submit detailed comparative evaluation of Chemical and Pharmaceutical data of Nelarabine bulk and formulation of the firm vis-à-vis that of Innovator's. The firm should also conduct single dose bioequivalence study in patients with T-cell lymphoblastic lymphoma with their formulation in comparison to that of Innovator's after getting protocol etc approved from the office of DCG(I). If above data is found satisfactory the product can be approved for marketing subject to Phase IV clinical trial.
2	**Mucotrol concentrated oral gel wafer**		As regards to the waiver of clinical trial requested by the firm, committee recommended for waiver of clinical trial in public interest in view of limited therapeutic medication. Recommended for marketing approval subject to condition that an open label Phase IV clinical trial on 400 patients should be conducted. Protocol etc. for the Phase IV clinical trial should be submitted to the office of DCG(I) within 1 month of approval and enrolment of patients should be initiated within 3 months of approval. The study should be completed within 6 months of launching the product in the market.
3	**Eribulin mesylate solution for injection**		Recommended for approval subject to condition that Phase IV clinical trial on 200 patients should be conducted. Protocol etc. for the Phase IV clinical trial should be submitted to the office of DCG(I) within 1 month of approval and enrolment of patients should be initiated within 3 months of approval. The study should be completed within 2 years of launching the product in the market.

4	**Plerixafor solution for subcutaneous injection**		Recommended for approval subject to condition that Phase IV clinical trial on 50 patients (as it is a rare disease) should be conducted. Protocol etc. for the Phase IV clinical trial should be submitted to the office of DCG(I) within 1 month of approval and enrolment of patients should be initiated within 3 months of approval. The study should be completed as early as possible. During the Phase IV trial, subjects should be given free medication.
Global Clinical Trials			
5	**PF-00299804**		Recommended for approval subject to the following conditions:- i) During the study, patients should be monitored for ophthalmological parameters in view of reports of ophthalmological problems in phase II studies. ii) The statement in the ICD "What are the possible benefits of being in this study?" should be modified. iii) Patients aged ≥ 18 yrs and ≤ 65 yrs should be included in the study. iv) Ethics Committee should be from same area where the sites are located.
6	**Tasquinimod**		Recommended for approval subject to the following conditions:- i) Patients aged ≥ 18 yrs and ≤ 80 yrs should be included in the study. ii) Patients who are on watchful criteria as per decision of the Investigator will be included. Inclusion criteria should be amended accordingly.
7	**Palifosfamide-tris**		Recommended for approval subject to condition that patients aged ≥ 18 yrs and ≤ 65 yrs should be included in the study
8	**AZD4547**		Recommended for approval subject to condition that patients aged ≥ 25 yrs and ≤ 80 yrs should be included in the study
9	**CT/89/11 Nilotinib**		Recommended for approval subject to condition that patients aged ≥ 18 yrs and ≤ 80 yrs should be included in the study
10	**Panitumumab**		Recommended for approval subject to condition that patients aged ≥ 18 yrs and ≤ 80 yrs should be included in the study

11	**Tamibarotene**		Recommended for approval subject to the following conditions: i) Patients aged ≥ 18 yrs and ≤ 80 yrs should be included in the study. ii) Inclusion criteria should be amended to include the following :- AST should be less than 2.5 × institutional ULN.
12	**Lucanthone**		Recommended for approval subject to condition that the firm will submit legal evidence to show that M/s Spectrum is also conducting the same study in USA and the data of M/s Spectrum can be extrapolated to the OncoRx study in India.
13	**AZT-011**		In an earlier conducted study, the benefit/risk ratio of the study drug was inferior to placebo. Also documentary evidence to show that the study has been approved by US FDA is not submitted. In view of above the committee did not recommend for approval of the study.
14	**SeeMore (EVP1001-1 injection)**		Protocol should be amended to assess the safety and efficacy of EVP 1001-1 in comparison to the existing contrast media. The firm should give undertaking that they have proposed the study in India with a plan to bring this drug into the country.

3. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 03.04.2012:-

The NDAC (Oncology and Haematology) deliberated the proposals on 03.04.2012 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
Global Clinical Trial (New Drugs)			
1	**Temsirolimus**		As per the protocol, all subjects will receive desipramine as prior therapy in the study. However desipramine is not approved in India. Committee recommended for giving permission to conduct the study subject to the following conditions:- i) The title of the study should be mentioned as Phase III instead of Phase IV. ii) Upper age limit of the subjects should be 65 years. iii) Promethazine should be used instead of desipramine as prior therapy. Amended protocol as above should be submitted to DCGI before giving formal permission to conduct the study by DCGI.
2	**AX-3**		There is inadequate preclinical and clinical data in support of use of the product in breast cancer patients. Moreover the study is proposed to be conducted only in India. In view of above, committee did not recommend for giving permission to conduct the study.
3	**Eltrombopag**		Recommended for giving permission to conduct the study.
4	**Vemurafenib**		Recommended for giving permission to conduct the study subject to the following conditions:- i) The title of the study should be mentioned as

			Phase III. ii) Lower age limit of the subjects to be included in the study should be 18 years.
5	**Masitinib**		The applicant did not turn up for presentation, hence it was not considered for approval
6	**TC-3**		Preclinical data is grossly inadequate. No clinical data of mitomycin C mixed with TC3 gel has been submitted. In view of above, committee did not recommend for giving permission to conduct the study.
7	**Sativex Oromucosal Spray**		Recommended for giving permission to conduct the study.
Global Clinical Trial (Biologicals)			
8	**EN3348(MCC)**		Committee recommended for giving permission to conduct the study in patients aged 18 to 65 years subject to submission of following data to DCGI:- i) Detailed data on characterization of components of the product. ii) Characterization specifying the active and inactive ingredients of the product.
9	**GP2013 plus CVP**		Recommended for giving permission to conduct the study subject to condition that the study should be conducted in patients aged 18 to 65 years.
10	**Velaglucerase alfa enzyme**		Recommended for giving permission to conduct the study subject to the following conditions:- i) The number of subjects to be enrolled from India in the study should not be more than 50% out of total number of subjects to be enrolled globally. ii) The applicant should come out with a policy to provide post trial benefit of medicine to the trial subjects.
11	**TDM 1**		Recommended for giving permission to conduct the study.

12	**Kedrion Factor VIII Concentrate (EMOCLOT)**		Recommended for giving permission to conduct the study subject to the condition that the applicant should come out with a policy to provide post trial benefit of medicine to the trial subjects.
13	**Denosumab**		Recommended for giving permission to conduct the study subject to condition that the upper age limit of patients to be included in the study should be 80 years.
14	**Recombinant Coagulation Factor IX Fc Fusion Protein, BIIB029**		Recommended for giving permission to conduct the study.
15	**Human Coagulation Factor IX Fusion Protein (rFIXFc)**		Recommended for giving permission to conduct the study subject to condition that the study should be conducted in subjects aged 6 to 12 years.
16	**Ofatumumab**		Recommended for giving permission to conduct the study subject to condition that upper age limit of the patients to be included in the study should be 55 years.
Marketing Authorisation (Biologicals)			
17	**Denosumab**		The firm has conducted clinical trials on 163 patients from India in three Phase III studies as part of global clinical trials. Committee in principle agreed for giving marketing permission of the drug. However before formal approval by DCGI, the firm should submit India specific subset analysis of clinical data specifically with respect to safety of the drug for consideration for approval.

4. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 05.05.2012:-

The NDAC (Oncology and Hematology) deliberated the proposals on 05.05.2012 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
New Drugs Proposals			
1	**(Hydroxyurea and Hyper hydration)**		Committee recommended for giving permission to conduct the study subject to condition that the study should be initiated on 10 patients aged 6-12 years. If the interim analysis of results on the 10 subjects shows positive results, the study may be continued in patients of lower age group of 1-6years. However, before initiation of the study in this group the interim results should be submitted to the office of DCG(I) and the ethics committee. If the results is not found satisfactory in Acute Lymphoblastic Leukemia subjects the study should be continued further only in Acute Myeloid Leukemia. The formulation of Hydroxyurea available in the country should be used as Investigational Product for the study.
2	**(Vemurafenib 240 mg tablet)**		The drug is indicated for treatment of unresectable or metastatic melanoma patients with BRAF V600 mutation which is a very rare disease in India. There is an unmet medical need of the medicine for such conditions. Therefore, the committee recommended for grant of permission to market the drug sucject to condition that the firm should generate data on at least 12 Indian patients under the global clinical trial which is already been permitted to be conducted in the country. The drug should be got tested from IPC, Ghaziabad before launching the product in the country.

3	**(Docetaxel Injection Concentrate for nanodispersion)**		Safety data generated from Phase I data was considered by the committee. The incidence of neutropenia (Grade 3 or Grade 4) observed in the Phase I study was stated by the firm to be transient in nature. The committee recommended for granting permission for the proposed clinical trial.
4	**(Lipidoluf)**		The committee opined that there is an unmet medical need for the product for diagnosis of various disease conditions and the drug is already being used in the country through personal permit also. Therefore there is no need for local clinical trials. The committee recommended for giving permission to market the product subject to condition that Phase IV clinical trial should be conducted on atleast 100 Indian subjects. The protocol for the Phase IV study should be submitted to the office of DCG(I) within 1 month of permission and the study should be initiated within the period of 3 months.
5	**(Valproate)**		Committee observed that there is adequate supportive data for conducting trial in both adult and children. Therefore, the committee recommended for giving permission for the proposed study.
6	**(Leoprolide Acitate for depot suspension- 3.75 mg)**		Committee recommended for granting permission for the study.
Recombinant Proposals			
7.	**(BioMab EFFR)**		The committee representatives did not turn up for the presentation. However, the committee deliberated the proposal and observed that the data with the drug has only been generated in Cuban subjects. The committee therefore recommended that firm should be asked to

			conduct an open label study in 200 Indian subjects with squamous cell carcinoma.
8.	**4-109/usv/11-BD** **(Filgrastim)**		The committee recommended for giving permission for the study subject to the following conditions: 1. Only one dose of Dexamethasone per cycle should be used in the study. Other alternative anti-emetics may be used. 2. The study should be conducted on atleast 100 completed subjects.
9.	**(Rituximab)**		Committee recommended for giving permission for the proposed study.
10.	**(Vectibix)**		Committee observed that there is an unmet need of this drug as it is indicated for life threatening disease, the treatment of patients with EGFR expressing metastatic colorectal carcinoma with non-mutated (wild -type) KRAS after failure of prior therapies. Therefore, the committee considered the waiver of local clinical trial and recommended for giving permission for import and market of the drug subject to condition that Phase IV study with the drug should be conducted in 50 Indian patients. The protocol for the Phase IV study should be submitted to the office of DCG(I) within 1 month of permission and the study should be initiated within the period of 3 months.
11.	**{r-EGFR (GLIOMA)}**		The committee representatives did not turn up for the presentation. However, the committee deliberated the proposal and recommended that the firm should be asked to conduct an active comparator controlled Phase III study to demonstrate the safety and efficacy of nimatuzumab in combination with radiotherapy plus chemotherapy in Indian patients with glioblastoma multiforme.

Bacterial Proposal			
12.	**(Mycobacterium W)**		The firm presented the Phase II clinical trial data generated in India and requested for considering proposal to market the drug in new indication - in combination with paclitaxel and cispalstin in advanced Non Small Cell Lung Cancer (NSCLC) patients. Committee considered the data and opined that the clinical data generated is adequate for considering approval for the said indication subject to condition that firm should conduct Phase IV clinical trial in at least 300 Indian subjects, as adjuvant therapy of Mycobacterium W in combination with Paclitaxel and cisplatin has shown a median increase in survival by 2 months. The protocol for the Phase IV study should be submitted to the office of DCG(I) within 1 month of permission and the study should be initiated within the period of 3 months. However, before granting the formal approval the firm should submit formal New Drug Application in CTD format alongwith PMS Data of Mycobacterium W generated so far for consideration and approval of DCG(I).
New Drugs			
13	**(denosumab)**		Committee recommended for giving permission for the proposed study.
14	**(Pertuzumab)**		Committee recommended for giving permission for the study subject to the following conditions: 1. The upper age limit of the subjects to enrolled in the study should be restricted to 75 years. 2. Regulatory approvals obtained from other participating countries should be submitted to the office of DCG (I).
15	**(Recombinant Human**		Committee recommended for giving permission for the proposed study. However the firm should submit interim results of the core study.

	Coagulation Factor VIII Fusion Protein (rFVIIIFc)		
16	**{Globo H-KLH(OPT-822)}**		Committee recommended for giving permission for the study subject to condition that the upper age limit of the subjects should be 75 years.
17	**(BAX326)**		Committee recommended for giving permission for the proposed study subject to condition that the firm will come up with a post trial access of the medicines for the subjects who benefits from the trial.
18	**(Rindopepimut / GM-CSF)**		Committee recommended for giving permission to for the proposed study subject to condition that the upper age limit of the subjects should be 75 years. The clinical trial batches are to be tested at CDL, Kasauli.

5. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 17.08.2012:-

The NDAC (Oncology and Hematology) deliberated the proposals on 17.08.2012 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
1	**Clofarabine Injection**		Committee opined that the drug Clofarabine is marketed in more than 40 countries. The drug has been approved in other countries based on CT data on 62 patients only. The drug is indicated for a rare disease, for which currently there is no therapy. Therefore committee opined that the request for the waiver of Clinical Trial/ Pharmacokinetic study in Indian patients can be considered for this drug. However before recommended for import and market of Clofarabine, the firm should submit the PMS data generated so far with the drug which should be provided to the members for examinations and final recommendation on the proposal.
2	**Lactobacillus Brevis Lozenges CD2 400 mg**		The firm presented the CT data generated with Lactobacillus Brevis Lozenges CD2 400 mg in Indian subjects in periodontitis as well as in subjects with chemotherapy induced mucostitis. The product is marketed in other country as food supplement. Committee opined that the clinical data generated is not adequate for approval of the product as a drug for the said indications and recommended that multicentric statistically powered Phase III clinical trials in the proposed indications are required to be conducted in sites geographically distributed in the country. Accordingly the protocol, name of sites etc., should be submitted for examination of the committee.
			The drug is already approved in the country for various indications. The firm presented

3	**Pemetrexed Disodium Powder for Solution for Injection**		the phase III clinical trial data conducted in India as a part of global trial in the proposed indication in 939 patients globally. In the study there are 54 patients from India in induction phase which reduced to 21 patients in maintenance phase. The drug is approved in proposed indication in many countries in EU. However it is under review by USFDA. Therefore the committee recommended for approval of the drug for proposed additional indication.
4	**Ondansetron Oral Spray (2 mg/ Spray)**		The firm presented the reports of Bioequivalent study conducted with the Ondansetron Oral Spray with Ondansetron mouth dissolving tablet. The result shows that both are bioequivalence. Hence, no other clinical trial is required. The oral spray of Ondansetron is advantageous over Ondansetron tablet as in some patients who cannot swallow the tablet, the drug can be administered in proposed form of oral spray. Therefore the committee recommended for giving permission to manufacture and market Ondansetron Oral Spray.
5	**Megestrol Acetate USP Oral Suspension 400 mg/10 ml**		Committee opined that the drug Megestrol is very old drug marketed in the country as tablet. The proposed new dosage form is already marketed in many country therefore the committee recommended for giving permission to market the Megestrol Acetate USP Oral Suspension 400 mg/10 ml.
6	**Axitinib**		The firm presented the data before the committee. The study is already approved in countries like Japan, Korea, Hong-Kong. The committee recommended for giving the permission to conduct the proposed clinical trial subject to condition that the upper age limit should be 65 years of age.
7	**Radotinib**		The applicant intimated on 09.08.2012 that the sponsor has decided not to include India in this global study due to the delay in its review and approval. Hence the proposal may be treated as withdrawn.

8	**Vandetanib**		The drug is already approved by USFDA on 06.04.2011 for the same indication. The proposed study is already approved in many countries including USA and UK. The committee recommended for giving the permission to conduct the proposed clinical trial subject to condition that the upper age limit should be 65 years of age.
9	**Afatinib**		The firm presented the data before the committee. The study is already approved in many countries including USA & UK. The committee recommended for giving the permission to conduct the proposed clinical trial subject to condition that the upper age limit should be 65 years of age.
10	**Doxorubicin-EMCH**		As per the protocol patients with locally advanced soft tissue sarcoma will also be included in the study. However the standard therapy for locally advanced soft tissue sarcoma is Iofosfamide with adriomycin. Since the proposed study include use of single agent of Doxorubicin EMCH Vs Doxorubicin, the committee recommended that locally advanced soft tissue sarcoma patients should be excluded from the study. The committee recommended for giving the permission subject to above condition and age limit of the subjects should be 18-65 years of age. Further the firm should submit the copy of protocol approved in USA.
11	**Somatuline Depot/Lanretide**		The committee recommended for extension of the study with further two years of therapy.
12	**Lapatinib plus an aromatase (AI)**		Lapatinib under brand name TYKERB/TYBERB has been approved in over 90 countries worldwide including USA and UK. The committee recommended for giving the permission for the proposed study.
13	**BCD-020 (rituximab)**		Rituximab is marketed in USA, Canada European Union and also in India. The study is approved in Russia and Ukraine. The committee recommended for giving the

			permission for the proposed study.
14	**LA-EP2006**		The study is approved in USA, Russia and Malaysia. The committee recommended for giving the permission for the proposed study.
15	**LA-EP2006**		The study is approved in Russia and Ukraine. The committee recommended for giving the permission for the proposed study.
16	**r-human Interleukin-11**		Committee opined that the marketed authorization cannot be granted on the basis of the data provided by firm. Therefore committee recommended that a new study with proper design should be initiated for effective assessment of safety and efficacy of this new drug in prevention of treatment of chemotherapy induced thrombocytopenia in adult cancer patients. The number of study centre should be adequate and geographically distributed in the country.
17	**Peg G-CSF**		Committee opined that study should be done first in healthy subjects and the data generated should be submitted before consideration of proposed study in patients.
18	**r-rasburicase Injection (TULY)**		The firm presented the data before the committee. The committee recommended for giving permission to market the drug r-rasburicase Injection in children and adults.

6. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 19.09.2012:-

The NDAC (Oncology and Hematology) deliberated the proposals on 19.09.2012 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
1	**Axitinib 1mg/5mg tablets**		The firm made detailed presentation of non-clinical and clinical data including two clinical trials conducted on Indian subjects (24 + 35) as part of global clinical trials. Committee recommended for giving permission to market the drug subject to condition that India specific subset analysis of the clinical data generated in two global clinical trials should be submitted to DCG(I) before approval of the drug. The firm should also generate additional data on safety and efficacy on 132 Indian patients as part of global clinical trial for which permission has already been granted by CDSCO and submit the same as post marketing data.
2	**Aspirin (Acetylsalicylic acid) 100mg tablet**		Committee recommended for giving permission to the proposed clinical trial.
3	**Clinical trial with Paclitaxel in combination with carboplatin**		The committee recommended for giving permission subject to condition that one medical oncologist or a physician having experience in treating lung cancer should be part of the study team.
4	**Gemcitabine HCl Conc. for Injection 38mg/ml**		Committee recommended for giving permission to manufacture and market the new dosage form of Gemcitabine HCl concentrate for injection 38mg/ml subject to submission of updated stability data to DCG(I) before grant of permission.
5	**Docetaxel Injection 160mg/8ml & 180mg/9 ml**		Committee recommended for giving permission to manufacture and market the new pack size of Docetaxel injection concentrate 20 mg/ml in pack size of

			160mg/8ml & 180mg/9ml injection subject to submission of updated stability data to DCG(I) before grant of permission.
6	**NKTR-102 (PEG-Irinotecan) (Protocol Amendment)**		The applicant has withdrawn their proposal.
7	**Sunitinib**		Sunitinib is already approved in India. The proposed protocol is already approved in US, France and Netherlands. Committee recommended for giving permission to conduct the proposed Phase IV clinical trial.
8	**BPL's High Purity factor X**		Committee recommended that the applicant should submit the report of Phase II clinical trial which is ongoing in other countries for further consideration of the committee.
9	**Trastuzumab**		The proposal was deferred.
10	**FIX**		Committee recommended for giving permission to the proposed clinical trial.
11	**BAX326 (Recombinant Factor IX)**		Committee recommended for giving permission to the proposed clinical trial.
12	**R-TPR-016 (Trastuzumab) Herceptin®**		Committee recommended for giving permission to conduct the proposed clinical trial subject to the following conditions:- i) The Pharmacokinetic part of the study should be conducted and based on DSMB reports, the second part of the study can be continued on the same subjects included in the Pharmacokinetic study. However before inclusion of additional subjects

			in the second part of the study, the PK data should be submitted to CDSCO for consideration to continue the study. ii) Age limit of subjects to be included in the study should be 18 to 65 years. iii) The study should be conducted on at least 100 evaluable subjects.
13	**R-TPR-023 (BEVACIZUMAB) AVASTIN**		Committee recommended for giving permission to conduct the proposed clinical trial subject to the following conditions:- i) The Pharmacokinetic part of the study should be conducted and based on DSMB reports, the second part of the study can be continued on the same subjects included in the Pharmacokinetic study. However before inclusion of additional subjects in the second part of the study, the PK data should be submitted to CDSCO for consideration to continue the study. ii) Age limit of subjects to be included in the study should be 18 to 65 years. iii) The study should be conducted on at least 100 evaluable subjects.
14	**Cetuximab**		The case was deferred.
15	**Rituximab**		The firm presented detailed data on characterization of the molecule along with a comparative Phase III trial conducted with their Rituximab vs the innovator's product, Mabthera. The results of clinical trial meet the endpoints of the study. Committee recommended for giving permission to manufacture and market the product.
16	**Rituximab**		Committee recommended for giving permission to conduct the proposed clinical trial subject to the following conditions:- i) Age limit of subjects to be included in

			the study should be 18 to 65 years. ii) The primary objective should be retained as it is in version 3 of the protocol. iii) The study should be conducted on at least 100 evaluable subjects.
17	**Rituximab**		The firm presented detailed data on characterization of the molecule along with the Phase III trial conducted on 50 patients. Although the clinical trial results meet the primary endpoint i.e. objective response rate (ORR), the results do not meet the secondary endpoint i.e. progression free survival (PFS). Committee recommended that the clinical trial should be extended to generate data to meet the secondary endpoint in 50 patients.
18	**Ofatumumab**		The clinical trial is ongoing in India as a part of global clinical trial. Committee recommended that the results of the ongoing global clinical trial with India specific subset analysis should be submitted to the committee for further examination.
19	**Trastuzumab**		Committee recommended for giving permission to conduct the proposed clinical trial subject to the following conditions:- i) The study should be conducted on at least 100 evaluable subjects. ii) Age limit of subjects to be included in the study should be 18 to 65 years.
20	**(For re-examination)** **Seemore (EVP1001-1 Injection)**		The applicant clarified the amendments. Committee recommended for giving permission to conduct the proposed clinical trial

7. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 08.12.2012:-

The NDAC (Oncology and Haematology) deliberated the proposals on 08.12.2012 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
1	**Ruxolitinib 5mg/15mg/20mg tablets**		Committee noted that myelofibrosis is a serious life threatening and very rare disease for which currently there is no approved therapy. The drug Ruxolitinib is approved and marketed in USA, EU etc. The drug has been designated as orphan drug by various authorities like EU, US, Swiss and Japan. Therefore committee observed that there is an unmet need of the drug for Indian patients and requirement of local clinical trial can be exempted in public interest. Committee recommended for giving permission to import and market the Ruxolitinib 5mg, 15mg and 20mg tablet for the treatment of patients with myelofibrosis including primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis subject to condition that the firm should capture all adverse reactions including unexpected serious risk of myelosuppression with long term exposure through intense prescription based monitoring of patients and submit the data to DCG(I). The safety data shall be reviewed after two years.
2	**Vorinostat 100mg capsules**		T-cell lymphoma is a serious and life threatening disease for which currently there is no satisfactory therapy. Therefore Committee opined that local clinical trial of the drug can be exempted in public interest. However a single dose bioequivalence study comparing Hetero's product with the innovator's product in patients with refractory cancer should be conducted getting protocol etc. approved from DCG (I). If B/E result is satisfactory, permission can be granted by DCG (I).
3	**Pegaspargase**		Lymphoblastic leukemia is a serious and life

	Injection		threatening disease for which currently there is no satisfactory therapy. Therefore Committee opined that local clinical trial of the drug can be exempted in public interest. The firm did not present supportive literature showing superiority or at least non-inferiority of pegaspergase over L-asparaginase. Committee recommended that a single dose bioequivalence study comparing Genova's product with the innovator's product in patients with refractory cancer should be conducted getting protocol etc. approved from DCG (I). If B/E result is satisfactory, permission can be granted by DCG (I).
4	**Temsirolimus Conc. For Injection with Diluent - 25mg/ml**		The firm has withdrawn their application.
5	**Docetaxel lipid suspension for injection 20mg/vial**		Committee examined the supporting data including reports of clinical trial conducted with this new dosage form of docetaxel lipid suspension for injection and recommended for giving permission to manufacture and market the product subject to condition that Post marketing safety data should be captured through intense monitoring of patients and submit data as part of PSUR etc.
6	**Palonosetron Melt in Mouth Tablets 0.5mg**		Palonosetron oral capsule 0.5mg is already approved in the country. Based on the B/E study data, committee recommended for giving permission to manufacture the new dosage form of Palonosetron Melt in Mouth tablets 0.5mg.
7	**Ondansetron SR Tablet 16/8mg**		Committee recommended for giving permission to conduct the proposed B/E trial and clinical trial subject to condition that the study sites should be multispecialty hospitals including Govt. medical colleges/institutions and the sites should be geographically distributed across the country.
8	**Everoliumus 2.5/5/10 mg tablet**		Committee examined the clinical data and other supportive information in support of use of everolimus in the proposed additional indications. The said indications are approved in USA and

			EU. Committee recommended for giving permission to market everolimus for the proposed two additional indications.
9	**Episil**		Chemotherapy/radiotherapy induced mucositis is a disease for which there is no satisfactory therapy. There is an unmet need of therapy for such condition. The product is marketed in many countries including USA, UK etc. The committee examined the supportive data and recommended for giving permission to import and market the product in the country without local clinical trial in public interest subject to condition that Phase IV trial is required to be conducted in atleast 400 patients after getting protocol etc. approved from DCG(I). The study should be completed within 1 year and report should be submitted to the committee for review.
10	**RAD001**		Committee recommended for giving permission to conduct the proposed global clinical trial subject to condition that upper age limit of the subjects should be 70 years.
11	**Trastuzumab**		Committee recommended for giving permission to conduct the proposed global clinical trial subject to condition that upper age limit of the subjects should be 70 years.
12	**Human-cl rhFVIII**		It is necessary to conduct such study in previously untreated patients with severe haemophilia. Hence inclusion of subjects of all age groups is justified. Committee recommended for giving permission to conduct the proposed clinical trial subject to submission of copy of approval of the study from MHRA UK and undertaking that US FDA has not raised any objection for conducting the proposed study in USA to DCG(I) for consideration and his approval. The firm should also submit Phase II interim analysis report and undertaking that the patients with positive response in the trial will be given free therapy under post trial access program to DCG(I).
13	**Octafibrin**		Committee recommended for giving permission to conduct the proposed global clinical trial

			subject to submission of undertaking that the patients with positive response will be given free therapy under post trial access program to DCG(I) for his consideration and approval.
14	**Filgrastim (USV)**		Committee feels that if the firm wants to use the dose of dexamethasone proposed initially, the secondary objective with respect to measurement of antibody should be removed from the protocol and amended protocol should be submitted to DCG(I) for approval. However the results of the study with respect to immunogenicity should be submitted to DCG(I) alongwith the reports of the clinical trial.
15	**Rituximab**		The committee noted that the firm has been asked earlier by another NDAC committee to conduct PK/PD study with the drug. Therefore committee recommended that the firm should submit the PK/PD study data for considering their proposal of conducting the Phase III clinical trial.
16	**Filgrastim (rh GCSF) Concentrated solution (Drug Substance) & Filgrastim Injection (Drug product)**		Committee examined the data including report of clinical trial conducted in Indian patients and recommended for giving permission to manufacture and market the drug for the indication for which clinical trial was conducted by the firm.
17	**(100mg/10ml & 500 mg/50ml vials)** **(Brand- Mabzen)**		The committee recommended that the data should be evaluated by Mr. R. M. Pandey, Prof and Head, Dept of Biostatistics, AIIMS, New Delhi from statistical view point and based on recommendation of the biostatistician; further decision can be taken by the committee on the proposal.

8. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 09.03.2013:-

The NDAC (Oncology and Haematology) deliberated the proposals on 09.03.2013 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
Special agenda 1 to 13			
1to 13	**Carmustine (polifeprosan 20 with carmustine Implant (wafer)** **Doxifluridine Caps. 100mg / 200mg** **Ixabepilone lyophilized powder inj. 15mg/45mg per vial** **Trabectedin powder for concentrate for solution for infusion 1 mg/vial** **Decitabine Lyophilized powder for injection 50mg/20ml vial** **Bendamustine Hydrochloride Lyophilized powder injection 100mg/vial** **Yttrium -90 Microspheres Injection (Yttrium – 90.. 3GBq (at the time of calibration) per vial)** **Nilotinib Capsules 200mg** **EltrombopagOlamine Tablets 25/50mg** **Pazopanib Hydrochloride Tablets 200/400mg** **Rasburicase injection**		The Committee was apprised that the Parliamentary Standing Committee (PSC) for the Ministry of Health & Family Welfare had presented its 59th report to the Parliament on 08.05.2012 on the functioning of the CDSCO. The report has made various recommendations and observation on various aspects such as approval of New Drugs, Pharmacovigilance, approval of clinical trials etc. The Ministry of Health & Family Welfare has submitted final action taken report on the observation/recommendations contained in the 59th report of the Hon'ble Parliamentary Standing Committee. As per the action taken report, it has been decided by the Ministry that 73 drugs including Fixed Dose Combinations, on approval of which the Hon'ble PSC has made various observations, would be referred to the NDACs for examination and review related to continued marketing of these drugs and updating of their product monographs in light of recent knowledge and regulatory changes overseas. Out of these 73 drugs, 13 drugs are in the category of Oncology and Hematologywhich are given below:-

	(1.5mg/ml, 7.5mg/ml powder and solvent for solution for infusion) (SanofiSynthelabo Ltd, Mumbai) **Exemestane(initial approval),** **Pemetrexed (initial approval).**		1. Carmustine (polifeprosan 20 with carmustine Implant (wafer) 2. Doxifluridine Caps. 100mg / 200mg 3. Ixabepilone lyophilized powder inj. 15mg/45mg per vial 4. Trabectedin powder for concentrate for solution for infusion 1 mg/vial 5. Decitabine Lyophilized powder for injection 50mg/20ml vial 6. Bendamustine Hydrochloride Lyophilized powder injection 100mg/vial 7. Yttrium -90 Microspheres Injection (Yttrium – 90.. 3GBq (at the time of calibration) per vial) 8. Nilotinib Capsules 200mg 9. EltrombopagOlamine Tablets 25/50mg 10. Pazopanib Hydrochloride Tablets 200/400mg 11. Rasburicase injection (1.5mg/ml, 7.5mg/ml powder and solvent for solution for infusion) (SanofiSynthelabo Ltd, Mumbai) 12. Exemestane(initial approval), 13. Pemetrexed (initial approval). The NDAC (Oncology and Hematology) discussed the issue and noted that Ministry of Health & Family Welfare has already constituted a Committee to formulate policy guidelines and SOPs for a) approval of new drugs. clinical trials, and banning of drugs under the Chairmanship of Dr. Ranjit Roy

			Chaudhury and b) for approval of the Fixed Dose Combinations under the Chairmanship Dr. C.K. Kokate. Therefore, the Committee opined that the above five drugs related to continued marketing and updating of the product monograph in the light of recent knowledge and regulatory changes overseas could be examined as per policies, guidelines and SOPs being prepared by the Dr. Ranjit Roy Chaudhury Committee and Dr. C.K. Kokate Committee. However, in the meantime the data/information on safety, efficacy of these five drugs including published data, PMS/PSUR, PSUR data especially on Indian patient required to be prepared in the Form of Dossier. Such data should be prepared from three different sources viz. i) by CDSCO ii) by PharmacovigilanceProgramme of India (PvPI) and iii) the firm concerned. The Dossier shall be circulated to all the experts of the NDAC(Oncology and Hematology) for their further review. If needed manufacturer may be requested to make their Presentation before the NDAC on safety and efficacy of the drugs.
14	**PazopanibHCl Tablets 200 mg/ 400 mg**		Pazopanib is been already approved in India in 2010.As per the presentation made by the firm, 1300 patients has already been exposed to the drug and no additional safetyconcern has been observed. After deliberation the committee opined that the clinical trial waiver for approval of the drug for the proposed indication can be considered provided the firms submits the Pharmacokinetic (PK) data on Indian population and the PK profile of the

			Drug is found to be comparable to that of Caucasian patients. The above PK data should be submitted to the office of DCG(I) for review and taking final decision by DCG(I). The drug Pazopanibwas initially approved for RCC in 2010 and the drug itself is also under examination by the Committeealongwith the list of 13 anti-cancer drugs.
15	**Trastuzumab**		The proposal is for approval of new indication for Trastuzumab Powder for Concentrate for Solution for Infusion i.e. “Trastuzumab is indicated for the treatment of patients with HER2 positive early breast cancer in combination with neoadjuvant chemotherapy followed by adjuvant Herceptin therapy, for locally advanced (including inflammatory) disease or tumors> 2cm in diameter”. The drug is already approved for other indication in the country. The proposed indication is already approved by EMA and swiss medic health authourity. Committee after reviewing the clinical data, recommended for approval of the drug for the proposed indication.
16	**Bevacizumab**		The proposal is for approval of new indication for Bevacizumab concentrate for solution for infusion i.e. “Bevacizumab in combination with Capecitabine is indicated for first-line treatment of patients with metastatic breast cancer in whom treatment with other chemotherapy options including taxanes or anthracyclines is not considered appropriate”. Bevacizumab has been withdrawn from USA for the Indication metastatic breast cancer. DCG(I) has also withdrawn the marketing permission of the drug for the same indication. There is no data on

			Indian patients for the proposed indication. Therefore the Committee did not recommend for approval of Bevacizumab for the proposed indication.
17	**Pegfilgrastim**		The drug is already approved in the country. The committee recommended for giving permission to conduct the proposed Bioequivalence study.
18	**Aflibercept**		This proposal is to import and market the drug in combination with irinotecan-fluoropyrimidine-based chemotherapy for patients with metastaic colorectal cancer (MCRC) previously treated with an oxiplatin containing regimen in chemotherapy.The Committee opined as under 1. There is an unmet need as a second-line therapy. 2. The firm has conducted clinical trial in other indications as part of Global clinical trial which showed no difference in the pharmacokinetic parameters in 14 Indian patients and there was no safety issue. 3. Pharmacokinetic data in Indian patients shows that there is no pharmacokinetic difference when compared to Caucasians. 4. The Drug has been found to be effective for the proposed indication as per the data generated in other countries. The committee considered the request for local clinical trial waiver and recommended for approval of the drug subject to the condition that the firm should submit the post marketing surveillance data for review of the marketing approval aftertwo years.
			Clofarabine is indicated for relapse or refractory ALL , after atleast two lines of

19	**Clofarabine concentrate 1mg/1ml**		therapy. The firm presented PSUR data along with other clinical trial data generated abroad. The committee considered the request for waiver of local clinical trial and recommended for approval of the drugsubject to the condition that the firm should follow up all the patients treated with the drug as part of post marketing surveillance. The PMS data should be submitted for review of the marketing approval after one year.

9. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 17.04.2013:-

The NDAC (Oncology and Haematology) deliberated the proposals on 17.04.2013 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
1	**Clinical Trial-Metronomic Therapy**		Committee recommended for giving permission to conduct the study subject to condition that placebo to be used in the study should be got manufactured under GMP facility.
2	**OndansetronHCl Orally Disintegrating Thin Strip 2mg**		Committee recommended for giving permission to market the product.
3	**Heparin Sodium Topical Solution 1000 IU/ml**		Committee recommended for giving permission to market the product subject to condition that prescribing information should clearly mention the number of dose applied at a time.
4	**Fulvestrant**		Committee recommended for giving permission to conduct the study with Protocol Amendment 1 submitted to the office of DCG(I) on 02-Apr-2013.
5	**LY2228820**		The proposed study is a Phase 1b/2 study. Phase 1b part is ongoing in other countries. The firm has proposed to conduct the Phase 2 part in India. Committee recommended that results of the Phase 1b study should be submitted which would be evaluated by the Committee before granting permission for the Phase 2 part of the study in India.
6	**Ozarelix (Protocol Amendment)**		The committee agreed to the inclusion of additional subjects in India for the proposed increase in maintenance dose from 65 mg sc to 100mg sc since the lower dose previously permitted i.e. 65 mg sc had no safety issues.

7	**BEZ235**		Committee recommended for giving permission to conduct the study.
8	**Fosaprepitant**		Committee recommended for giving permission to conduct the study subject to condition that the firm should include one additional site which should be a Govt Hospital. Information of the same should be submitted to the office of DCGI.
9	**Trastuzumab**		The firm has withdrawn their proposal.
10	**Hercules versus Herceptin®**		The committee has not recommended the study as the regulatory approvals from India and from RCGM to manufacture the Investigational Product are not furnished.
11	**Bevacizumab**		Committee recommended that the firm should submit PMS data and Phase IV data of Indian origin generated with Bevacizumab in the earlier approved indication for evaluation by the committee before the proposal is considered.
12	**Pegfilgrastim**		Committee recommended for giving permission to conduct the study.
13	**Cetuximab**		Committee recommended that the firm should submit PMS data and Phase IV data of Indian origin generated with Cetuximab in the earlier approved indication for evaluation by the committee before the proposal is considered.
14	**Filgrastim**		Committee recommended for giving permission to market the product for the indication on which clinical trial was conducted subject to condition that the firm should submit the query response on CMC part.
15	**Rituximab**		Committee recommended for giving permission to conduct the study.
16	**Rituximab**		Committee recommended for giving permission to conduct the study subject to condition that the firm should submit satisfactory PK data of rituximab carried out in healthy volunteers as per the protocol approved by this office in RA cases.
17			The committee recommended for conducting the

	Plerixafor Solution for Injection **(Re-examination)**		proposed Phase IV trial subject to the submission of a letter of access/undertaking from M/s Sandor stating that M/s SanofiSynthelabo will conduct the Phase IV clinical trial.
18	**Hydroxyprogesterone**		Committee recommended for giving permission to conduct the study subject to the following conditions:- i) Nerve conduction studies should be conducted on half of the sample size. ii) The study should be comparative and blinded. iii) Informed consent of the subjects should be taken prior to their screening. iv) Undertaking by the Sponsor for providing compensation in case of trial related injury or death of the subjects should be submitted to DCG(I). v) Patient Information Sheet should be modified as per gazette notification GSR 53(E)dated 30.01.13 and submitted to DCG(I).

10. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 02.08.2013:-

The NDAC (Oncology and Haematology) deliberated the proposals on 02.08.2013 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
1	**Non-pegylated Liposomal Doxorubicin Liposome injection 2 mg/ml**		The committee has opined to Include stoppage rules in case of toxicity occurring during the conduct of NEST study and PRONEST study
2	**Deferasirox dispersible tablet 100 mg/ 400 mg**		The committee opined that the drug is already approved and the safety and efficacy of the drug is already established. The committee recommended that clinical trial wavier can be granted. However the final decision in this regard will be based on guidelines being prepared Dr. Ranjitroychoudhary
3	**Paclitaxel protein bound particle for injectable suspension 100 mg**		The committee opined that the design of the protocol is not phase IV clinical trial and it is a Bioequivalence study. However the committee has recommended for conducting the BE study with the condition that the sponsor should provide the drug for complete treatment cycle.
4	**Imatinibmesilate 100 mg/ 400 mg tablets & 100 mg capsules**		The committee opined that the drug is already approved and the safety and efficacy of the drug is already established and clinical trial wavier can be granted after the recommendation made by Dr. Ranjit Roy Choudhary guidelines.
5	**Capecitabine 300mg/600mg + Cyclophosphamide 20mg/40mg tablets**		The combination has some potential for use in patients with metastatic breast cancer as metronomic therapy. The Committee opined that the firm initially should conduct phase-II dose ranging studies. Accordingly firm should submit the protocol to the committee for further consideration.
6	**PEGylated Recombinant Factor VIII (BAX 855)**		Firm is not coming for the presentation hence the proposal has been deferred to the next NDAC meeting.

7	**AZT-011**		In the previous application, the firm presented the data that showed the molecule produced increased toxicity for which it was not recommended for trial. In the current presentation given by the firm, no new data was presented to address the issue. Additionally, sites selected were not medical colleges. Hence the Committee did not recommend.
8	**Dinaclinib**		Firm has withdrawn the proposal
9	**Volasertib**		The committee recommended for giving permission to conduct the study.
10	**Crizotinib 200 mg and 250 mg capsule**		The prevalence of ALK positive –NSCLC patients is very low. So far 18 patients have been treated with Crizotinib on name patient basis as informed by the firm. The Firm should submit the compiled data in respect of the 18 patients to the committee before consideration of the waiver of conducting Phase IV study.
11	**Pegfilgrastim**		The firm presented the results of Clinical trial in Indian patients. The Committee recommended for granting of Marketing authorization. The indication granted is “For reduction in the duration of neutropenia and the incidence of febrile neutropenia in myeloid malignancy (equivalent to that of Neulastim).
12	**Trastuzumab**		The committee recommended the following: • The newly diagnosed patients shall not be included in the study. • The study should be conducted first in 5 patients to determine the infusional toxicities which will be reviewed by DSMB and then the randomization to be started. • The sample size is to be justified by statistical evaluation to an independent Biostatistician. Accordingly, the proposal shall be send to an independent Biostatistician for evaluation of suitability of sample size. • The firm should also submit NOC for Form 29 & Form 29 to manufacture

			clinical trial batches. The firm should submit the amended protocol with sample size justification to the experts for review.
13	**Bevacizumab**		The committee recommended the following: • The newly diagnosed patients shall not be included in the study. • The study should be conducted first in 5 patients to determine the infusional toxicities which will be reviewed by DSMB and then the randomization to be started. • The sample size is to be justified by statistical evaluation to an independent Biostatistician. Accordingly, the proposal shall be send to an independent Biostatistician for evaluation of suitability of sample size. • The firm should also submit NOC for Form 29 & Form 29 to manufacture clinical trial batches. The firm should submit the amended protocol with sample size justification to the experts for review.
14	**Pertuzumab**		The committee recommended for the waiver from local clinical trial. However, as the data on the clinical study 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 Indian population for the generation of toxicity/ safety data. The protocol shall be submitted by the firm to be reviewed by NDAC members and discussed in the subsequent meeting of Oncology & Hematology.
15	**Pegfilgrastim**		The committee recommended for conducting Phase III clinical trial.
16	**Rituximab**		The committee recommended that the study report is acceptable from the safety point.

17	**Bevacizumab**		The committee recommended for conducting the clinical trial with following inclusions in the protocol: • The newly diagnosed patients shall not be included in the study. • The study should be conducted first in 10 patients to determine the infusional toxicities/safety studies which will be reviewed by DSMB and then the randomization to be started. The revised protocol to be submitted for DCG (I) approval.

11. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 26.08.2013:-

The NDAC (Oncology and Hematology) deliberated the proposals on 26.08.2013 and recommended the following:-

AGENDA NO.	DRUG NAME		RECOMMENDATIONS
1	**Regorafenib 40 mg tablets**		The committee opined that proposed drug is for treatment of colorectal cancer which is unmet need. The firm presented the international phase III clinical trial data in which Indian population was not enrolled. The firm requested for the grant of clinical trial wavier. The committee recommended for grant of import and marketing permission of Regorafenib 40 mg tablets for following conditions to conduct phase IV clinical trial and submit the protocol before the NDAC. However Prof. Dr. Ranjit Roy Chaudhary committee recommendations should be referred for grant of clinical trial wavier.
2	**Pemetrexed Disodium**		The applicant did not turn up. Hence proposal has been deferred.
3	**Ondansetron CR Powder for Suspension 24mg**		The committee recommended the granting of permission for bio-availability (Phase1) study in healthy voluntaries as per the submitted protocol.
4	**Nanosomal Paclitaxel Lipid Suspension for injection 30mg/vial, 60mg/vial**		The firm presented the phase II clinical trial data. The committee recommended conducting the phase III clinical trial in statically significant population in geographically distributed clinical trial sites in medical college and multispecialty hospitals with emergency facilities. The firm should submit the protocol before NDAC committee for approval.
5	**Decitabine**		The committee recommended for grant of import

	Iyophilzed Powder for Injection 50mg		and marketing permission of Decitabine Iyophilzed Powder for Injection 50mg.
6	**Bortezomib Injection 3.5mg**		The committee recommended for grant of permission for changing the route of administration to Subcutaneous route of administration which is also approved in US and Europe.
7	**MK517**		The committee recommended the study subject to condition that the data emerging from the age group 2-17 yrs is to be submitted to cdsco for further review and approval for the lower age group ie infants and children's up to 2 yrs. The study should be conducted at multiple sites geographically distributed across the country including academic institutes/multispecialty centers/ and 50%govt sites having emergency facility with institutional ethics committee.
8	**Aprepitant**		The committee recommended the study subject to condition with age group for the study subject should be 2 to 17 yrs. And data emerging from this age group has to be submitted from the review and approval of the lower age group ie infants and children's up to 2 yrs. The study should be conducted at multiple site geographically distributed across the country including academic institute/multispecialty center/ govt institute. The 50% site must be govt hospital and 50% multispecialty private hospitals having multispecialty emergency facility with institutional ethics committee.
9	**Nimorazole**		The committee opined that trial was already approved by IRB of Tata Memorial Hospital and is on- going internationally and committee recommended granting of permission for conducting clinical trial as per submitted protocol.
10	**Afatinib**		The committee recommended the study subject to the condition that 50% of the sites must be

			govt hospitals and multispecialty hospitals having emergency facility with institutional ethics committee.
11	**Leucostin**		The committee did not recommend the study as the protocol submitted does not meet the primary objective of the study. The disease model is inappropriate for the trial protocol submitted to the CDSCO.
12	**Everolimus** **Protocol No. CRAD00IJIC06**		The committee recommended the study as per the protocol submitted to this directorate Subject to the condition that 50% of the sites are in govt hospital and other multispeciality sites with emergency and institutional ethics committees
13	**Everolimus** **Protocol No. CRAD001Y2201**		The committee recommended the study as per the protocol submitted to this directorate Subject to the condition that 50% of the sites are in govt hospital and other multispeciality sites with emergency and institutional ethics committees
14	**BAX 855 (Pegylated Recombinant Factor)**		The committee recommended the study subject to the condition that 50% of the sites are in govt hospitals and other multispecialty sites with emergency and institutional ethics committees. The trial participants should be provided post trial access.
15	**Glycerol+ Lecithin+ Ethanol+ Propylene Glycol+ Polysorbate 80+**		The firm made presentation of data /information to support their claims that the product is medical device. The firm also presented safety and efficacy data. Considering all aspect the committee opined that the product is a new drug not a medical device in Indian scenario. As regards to waiver of clinical trial the committee

	Pepermint Oil		recommended that the firm may wait till the recommendation of Prof. Ranjit Roy Chaudhary committee in this regards is consider by the government. Alternatively firm may conduct clinical trial after getting protocol etc. approved from CDSCO.
16	**Gamunex-C (IVIG)**		The firm has to give the undertaking that drug will be not marketed by sub cutaneous route and to resubmitted the dossier for the registration of drug product
17	**PegGCSF**		The committee opined that this is local treatment with a local immune modulator effect and as a part of standard care of bladder cancer treatment. Hence the firm may be granted for import and marketing permission.
18	**Rituximab**		The committee recommended the propose addition indication in line with the innovative product along with the condition to generate the PMS data
19	**BCG-medac**		The committee recommended the propose addition indication in line with the innovative product along with the condition to generate the PMS data
20	**Institutional**		The committee recommended that applicant should submit justification for enrolling 15 patients in each arm and also use of 5 mg dose for Zoledronic acid. The committee also recommended that DCG(I) may consider policies decision as to whether such institutional academies studies some time for thesis purpose are required to be regulated similar to the trial proposed for marketing by sponsor companies.

12. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 18.10.2013:-

The NDAC (Oncology and Hematology) deliberated the proposals on 18.10.2013 and recommended the following:-

AGENDA NO.	DRUG NAME		RECOMMENDATIONS
1	**Azacitidine for Injection 100mg/vial**		The committee noted the following, • Azacitidine Injectable suspension was approved by USFDA on 19.05.2004 for the treatment of all subtypes of Myelodysplastic syndrome (MDS) based on review of safety and efficacy results from clinical trial conducted on 191 patients only. • MDS is a disease primarily of the elderly with median age between 60 and 80 years. Treatment and outcome of MDS currently is unsatisfactory. • Azacitidine has been categorized a Orphan drug by USFDA. • In India MDS is also a rare disease and hence Azacitidine can be considered as an orphan drug for rare diseases. • It is the only drug found to be effective for intermittent and high risk MDS. • There is an unmet need for the drug in the country . • Earlier M/s Natco was permitted to conduct clinical trial on 60 patients in 2010 however firm could conduct this trial on 7 patients

2	**Azacitidine injection 100mg/vial**		only The results was presented by the firm before the committee.. • M/s Intas has requested for waiver of local clinical trial. • As per USFDA draft guidance on Azacitidine In-vitro evidence can demonstrate bioequivalence for generic Azacitidine In USA. In View of the above committee recommended for giving waiver of local clinical trial and recommended for giving permission to manufacture and market the drug in the country to the firms.
3	**Valrubicin Intravesical solution USP 40mg/ml**		The committee opined that the drug is indicted for the disease which is neither a rare disease nor a disease for which there is no therapy. However after BCG the only option remains surgical removal. Hence the committee did not recommend for waiver of local clinical trial before grant of Market Authorization. Protocol etc. for the local clinical trial should be submitted for examination of the committee.
4	**Afatinib 20/30/40/50mg in NSCLC**		Committee recommended that India specific subset analysis report from the ongoing clinical trial being carried out in India as part of global clinical trial and these data is required to be submitted from at least 40 subjects to the committee before considering the proposal for the grant of marketing authorization.

5	**Cabazitaxel**		The committee noted that Cabazitaxel is indicated for the third line treatment i.e. hormone refractory metastatic prostate cancer previously treated with Docetaxel-containing treatment regimen and recommended for the conduct of proposed phase IV study subject to condition that the firm should collate all the safety data from Indian subjects.
6	**Abiraterone Acetate**		Earlier the drug is approved for the treatment in combination with prednisone for the treatment of patients with metastatic castration resistant prostate cancer who have received prior chemotherapy containing docetaxel. Now the firm has proposed In the treatment of metastatic castration resistant prostate cancer in adult men who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated, with prednisone or prednisolone. Since the previous and the proposed indication are similar except prior orr post chemotherapy, the committee recommended for grant of permission for the marketing authorization in the proposed indication of Abiraterone Acetate Tablet 250 mg with the condition that the post marketing trial (Phase IV) in Indian population is required to be conducted. Accordingly protocols should be submitted within three months to the office of DCGI.
7	**Lipidol Ultra Fluid**		The firm presented Indian published data on proposed indication and based on published clinical data the committee recommended to grant the additional Indication for Interventional radiology in chemo-Embolization.

8	**Methylcobalamine Nasal Spray 500 mcg**		The committee opined that firm is required to submit Phase I data. After submitting the same the Phase III clinical trial permission will be considered since the proposed methyl cobalamine nasal spray is a new route of administration, which is not approved in any other country.
9	**Trastzumab**		The committee recommended to allow the manufacturing authorization with condition to submit the PSUR and proposed Risk management plan duly after seeking approval of NDAC the firm also submit CMC and Other Related Clarifications advised as per previous query letter issued by Office of DCGI. The drug shall be prescribed by registered Oncologist only.
10	**Panitunumab**		The committee recommended for giving permission for the proposed Phase IV trial initially the study shall be started in two centers viz.` BIBI memorial Hospital Hyderabad, And Central India Cancer Institute, Nagpur out of the 12 sites proposed. However Clinical trial study should be initiated in remaining sites after insuring that the total fifty percent sites are government institutions.
11	**Albumin Infusion**		The committee opined that Human Albumin is commercially available in India for the approved indication. Therefore, after the review of protocol the committee opined that such studies should not be considered in this forum since it is no longer a new drug.

12	**Emoclot** **of M/s Kedrion (Italy)**		The drug EMOCLOT is already approved for marketing in the country. The committee reviewed the protocol and recommended for conduct of the phase IV study with the drug which is a plasma derived product in Haemophilia –A patients. 50% site shall be government hospitals.
13	**Masitinib Tablets** **(for protocol version amendment)**		The committee reviewed the protocol and presentation made and recommended for the conduct of the Phase III protocol subject to the condition that 50% of the sites shall be government hospitals.
14	**Obinutuzumab**		The committee reviewed the protocol and presentation made and recommended for the conduct of the Phase III protocol subject to the condition that 50% of the sites shall be government hospitals. (Dr. Geetha Narayanan is not part of decision making as she is one of the investigator.)
15	**Pertuzumab**		The committee reviewed the protocol and presentation made and recommended for the conduct of the Phase III b protocol subject to the condition that 50% of the sites shall be government hospitals.
16	**Trastuzumab emtansine**		The committee reviewed the protocol and presentation made and recommended for the conduct of the Phase III protocol subject to the condition that 50% of the sites shall be government hospitals.

17	**Rituximab**		The committee reviewed the protocol and presentation made and recommended for the conduct of the Phase III with the biosimilar product subject to the condition that 50% of the sites shall be government hospitals.
18	**Afatinib** **in Head and neck Cancer**		The committee reviewed the protocol and presentation made and recommended for the conduct of the Phase III protocol subject to the condition that 50% of the sites shall be government hospitals.
19	**Afatinib** **(in NSCLC)**		The committee reviewed the protocol and presentation made and recommended for the conduct of the Phase III protocol subject to the condition that 50% of the sites shall be government hospitals.
20	**LDK378**		The committee reviewed the protocol and presentation made and recommended for the conduct of the Phase III protocol subject to the condition that 50% of the sites shall be government hospitals.

13. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 27.11.2013:-

The NDAC (Oncology & Hematology) deliberated the proposals on 27.11.2013 and recommended the following:-

AGENDA NO.	DRUG NAME		RECOMMENDATIONS
1.	**Bisphosphonates**		The Committee recommends grant of permission for the trial subject to submission of undertaking that the compensation will be provided to the patients as per Rule-122DAB as per GSR 53 (E) dated 30/1/2013 duly signed by the PI and endorsed by the Institutional Head.
2.	**Transarterial chemoembolization**		The Committee recommends grant of permission for the trial subject to submission of undertaking that the compensation will be provided to the patients as per Rule-122DAB as per GSR 53 (E) dated 30/1/2013 duly signed by the PI and endorsed by the Institutional Head.
3.	**Cyclophosphamide**		The Committee recommends grant of permission fot the trial subject to submission of undertaking that the compensation will be provided to the patients as per Rule-122DAB as per GSR 53 (E) dated 30/1/2013 duly signed by the PI and endorsed by the Institutional Head
4.	**SentiMag and Sienna**		The proposed product “Sentimag and Sienna” has yet not been approved anywhere in the world by the National Drug/Device Regulatory Authority. The preclinical and clinical data submitted are not adequate and not as per the requirements of the scheduled Y. Hence the Committee recommended to re-submit the data as per Schedule Y of Drugs and Cosmetics rules.
5.	**Paclitaxel Nanodisperison Concentrate for Injection**		The firm presented Phase-I clinical trial data conducted on 36 subjects and Phase-II / III data conducted on 180 subjects of their new Paclitaxel Nanodisperison Concentrate for Injection. After deliberation, committee recommended for grant of manufacturing and marketing permission of Paclitaxel Nanodispersion concentrate for injection for breast cancer. Further firm should also submit the detailed pharmacokinetic data developed with

			the proposed formulation for review by the office of DCG(I).
6.	**Capecitabine 300 mg/600 mg + Cyclophosphamide 20 mg/40 mg Tablets**		Firm presented the clinical trial protocol for phase II trial. However firm could not provide justification for the proposed dose schedule, statistical significance for the proposed no. of subjects. Further, committee also opined to re-examine the investigator sites by the firm. The revised protocol accordingly shall be submitted and place before the committee for approval.
7.	**Paclitaxel Injection concentrate for Nanodispersion 10% w/w (PICN)**		After deliberation, committee recommended for grant of BA/BE study of paclitaxel injection concentrate for nanodispersion 10% w/w (PICN).
8.	**(i) Paclitaxel Inj, (ii) carbplastin Inj. (iii)Cisplastin Inj.** **(GCT – Division)**		This is one institutional trial with the drugs which are already approved for marketing in the country. The phase –III (three) trial will be conducted at Tata Memorial hospital-I by the Principal Investiagtor Dr. Shyam kishor Srivastaav. The institutional IRB has granted approval for the same. The Sponsor will be Australia New Zealand Oncology Group. The committee recommends grant of permission for the trial.
9.	**(BKM 120) Buparlisib** **(GCT – Division)**		The drug, a P13 kinase inhibitor has under has undergone a Phse-I dose escalation study in Japanese Patients with advanced solid tumor. The drugs has demonstrated significant tumor growth inhibition in relevant tumor Xenografts in mice & Rats when administered orally, including models of renal cancer cell carcinoma. In GLP toxicological studies, Bupralisib exposure in terms of AUC $_{(0\text{-}24h)}$ and C_{max} increased in dose proportional manner in rat and dogs. Bupralisib 100 mg FC tablets developed by M/s Novartis Pharma AG has already been exposed to 500 subjects, mostly patients with advanced solid tumor as single agent and also in combination studies. Out of global 150 subjects in India 30 subjects will be enrolled in 3 centers as part of Phase-II global clinical development. The proposed study is planned in 18 countries including

			Germany, USA, UK and India. The committee recommends to permit the grant of permission of the trial.
10.	**Bosutinb** **(GCT – Division)**		Bosutinib the TK inhibitor is under treatment as second line to the Imatinib resistant / intolerant patients. This is an extension study of the already approved trial 2 subject in undergoing the trial in CMC (Vellore). 39 subjects discontinued from the basic trial as they did not meet the primary efficacy parameter. 5 SAEs also reported. The drug is already approved in UK, EMA, USA. M/s Icon, Bangalore is the CRO in this trial. The committee asks for the detailed data on safety and reasons for discontinuation of the subjects who will be switched over to one trail instead of the two protocols.
11.	**BCD-022 (Trastuzumab)**		The firm stated that they import the host cell line of CHO from USA and manufacture the DS in Russia. 46 patients of breast cancer participated in Phase –I study. The antibodies for the drug assay is also imported from USA based company. Total 206 patients will be recruited globally in India, Russia, Belarus. They have 3-tier of assessment of immunogenicity studies i.e at the screen, 3-cycle, 6-cycle and progressively followed even after 1-year.
12.	**BCD 021 (Bevacizumab)**		This biosimilar is produced in Russia and other CIS countries Viz. Belarus, Ukraine and Brazil. The Russian representative presented comparative certificates of structural and Physicochemical analysis of the presnt product with reference to Avastin. Tissue cross-reactivity studies and Stability study data, non-clinical PK data (Multiple dosing also) submitted. Phase I study done on 28 patients of NSCLC. The proposed phase-III comparative with Avastin trial protocol was discussed in details. Total 22 sites have been selected in India, out of this 11 will be in Govt. hospital.
13.	**Trastuzumab (Phase III Clinical trial)**		The proposal was earlier discussed in NDAC held on 02.08.2013 wherein experts have raised certain queries. Firm had responded to queries. Committee recommended for giving permission to conduct Phase III clinical trial with their indigenously developed Trastuzumab subject to condition that 50% clinical trial sites should be government

			hospital/medical college and 50% multispecialty hospital having emergency facility.
14.	**Pegfilgrastim Final Clinical Study Report**		Firm didn't turn up for the presentation. Deferred for next meeting.

14. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 28.01.2014:-

The NDAC (Oncology &Hematology) deliberated the proposals on 28.01.2014 and recommended the following:-

Agenda no.	Drug Name		Recommendations
1.	**Axitinib 1mg/5mg tablets**		The proposal of firm for import and marketing of Axitnib 1mg/5mg tablets was earlier deliberated in NDAC meeting held at 19.09.2012 and the committee had recommended to submit India specific subset analysis of the clinical data generated in two global clinical trials and also to generate additional data on safety and efficacy on 132 Indian patients as part of global clinical trial for which permission has already granted by CDSCO. The firm presented India specific safety subset analysis of the Clinical data generated in two global Phase 3 Studies clinical trial i.e. study A4061032 and study A4061051 where in a total of 57 patients participated in these global clinical trials in Renal Cell Carcinoma. The committee noted that the drug Axitinib has been approved in 33 countries including USA, EU, Japan and Australia. Further the drug has been given orphan drug status by European Union. After detailed deliberation and in view of above facts, the committee recommended for the grant of marketing authorisation of the drug. The committee also recommended to submit the results of the ongoing global clinical study i.e ATLAS after its completion.
2.	**Dabrafenib Mesylate capsule 50/75mg**		The firm presented clinical data along with safety and efficacy data on dabrafenib and requested for waiver off conduct of local clinical trial in Indian subjects in treatment of Metastatic Melanoma. Firm stated that there were 65 incidences of BRAF positive Melanoma in 2012 in India. The Committee noted that there was no scientific basis for data on incidence of BRAF V600 mutation in India. The need therefore for this drug in India and the justification for CT waiver cannot be assessed at present. Alternative options are available at present for patients in the country.

			After deliberation, the Committee recommended that this data be first obtained before marketing authorisation is considered.
3.			The committee was informed that the Parliametary Standing Committe of the Ministry of Health and Family Welfare The firm has presented safety data in respect of Doxifluridine in India and informed that out of 87 reports collected so far only 18 cases are of SAEs. The Committee noted that the firm has not been able to provide data in respect of patients exposed to the drug so far. Firm was granted permission for marketing authorisation in year 2008 based on clinical trial data generated in comparison with 5-fluorouracil in other country. Now the standard of care has been changed to Capacitibine. Further the firm has not be able to provide data on use of Doxifluridine in comparison to current standard of treatment i.e. Capacitabine. The committee recommended that a clinical trial be done showing non-inferiority of Doxifluridine in comparison to current standard of treatment Capacitabine is required to be carried out for its continued marketing in the country.
4.	**Pemetrexed Disodium**		The firm has presented safety data in respect of clinical trials conducted with Premetrexed sodium in India as well as the rest of world. The committee noted that more than 3000 patients in India have been exposed to the drug so far. The Committee recommended that the firm should submit the comparative safety data of the drug in Indian subjects vis-a-vis the globally reported AE/SAEs for further review by the committee.
5.	**Nilotinib**		The firm presented the safety data on Nilotinib in Indian subjects vis-a-vis the global clinical trials as part of the assistance programme. The committee noted that a total of 1064 patients have so far been exposed to the drug in India. At present 773 patients are currently on treatment of Nilotinib. The reported adverse events from clinical

			practices in India with Nilotinib is in line with the AEs reported world wide and no new safety signal has been seen. After detailed deliberation the Committee recommended for continued marketing of the drug in the country.
6.	**Eltrombopag Olamine**		The firm presented safety data on Eltrombopag. It was informed that the drug was launched in year 2011, and so far approximately 4400 patients have been exposed to this drug. The Spontaneous adverse events reported till date is 6 nos only and serious adverse events reported in 18 Indian patients as a part of Global Clinical Trial. No new safety signal has been generated After detailed deliberation the Committee recommended, in view of the above, for continued marketing of the drug in the country.
7.	**Decitabine**		The firm has presented safety data in respect of clinical trials conducted with Decitabine in India as well as the rest of world. The committee noted that more than 278 patients in India have been exposed to the drug so far. The Committee recommended that the firm should submit the comparative safety data of the drug in Indian subjects *vis-à-vis* the globally reported AE/SAEs for further review by the committee.
8.	**Trabectedin**		The firm has presented safety data in respect of clinical trials conducted with Trabectedin in India as well as the rest of world. The committee noted that more than 427 patients in India have been exposed to the drug so far and 17 AE reports received, with The Committee recommended that the firm should submit the comparative safety data of the drug in Indian subjects *vis-à-vis* the globally reported AE/SAEs for further review by the committee. And also to submit causality assessment of the cases of death reported in the studies.
9.	**Ixabepilone**		The firm has presented safety data in respect of clinical trials conducted with Ixabepilone in India as well as the rest of world.

			The committee noted that more than 26000 patients have been exposed to the drug globally and 1823 patients in India. After detailed deliberation the Committee recommended, in view of the above, for continued marketing of the drug in the country.
10.	**Bendamustine HCL**		The Committee was informed that the parliamentary (PSC) of the Ministry of Health & Family welfare had presented its 59th report to the parliament on the functioning of CDSCO. The Committee had made various recommendations and observations on approval of certain new drugs. Bendamustine Hydrochloride is one of such drug. This Directorate had approved the Bendamustine Hydrochloride lyophilized powder injection 100mg/ (Vial), for treatment of patients with chronic lymphocytic leukemia. As per action taken report, it was decided that the drug would be referred to NDAC for examination and review the issue related to continue marketing of the drug and updating of the product monograph in light of recent knowledge and regulatory changes overseas. The firm presented safety data in respect of Bendemustine and informed that approximately 200 patients in India have been exposed to the drug so far. The committee asked the company to submit a comparative analysis of published data on the Adverse events/Serious Adverse events reported from global literature vis-a-vis that which they have recorded from PSURs.
11.	**Pazopanib**		The Committee was informed that the parliamentary (PSC) of the Ministry of Health & Family welfare had presented its 59th report to the parliament on the functioning of CDSCO. The Committee had made various recommendations and observations on approval of certain new drugs. This Directorate had approved the Pazopanib Hydrochloride 200mg/400mg (Tablets) on 19th Oct. 2010, for the treatment of patients with advanced renal cell carcinoma. As per action taken report, it was decided that the drug would be referred to NDAC for examination

			and review the issue related to continue marketing of the drug and updating of the product monograph in light of recent knowledge and regulatory changes overseas. The firm presented safety data on Pazopanib. It was informed that the drug was launched in year 2011, and so far approximately 2350 patients have been exposed to this drug. The Spontaneous adverse events reported till date is 51 nos Which includes 42 serious cases and 37 cases were unexpected. No new safety signals identified. The Committee has recommended for continued marketing of the drug in the country.
12.	**Triptorelin for Injection 22.5mg**		Triptorelin (Lyophilized) 3.75 mg injection is approved by this directorate. Triptorelin 22.5 mg is already approved in many countries USA, UK, Australia. The committee recommended for grant import/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.
13.	**1. Leuprolide acetate injection, 10mg/ml, pen injector, 2.8ml Vs Sun** **2.Leuprolide acetate injection, 10mg/ml, pen injector, 2.8ml Vs innovator**		The synthetic nonapeptide Injection as Pen Injector SC Vs. IV administration will be done on healthy Indian subjects. 72 male subjects will be enrolled to achieve the power of 80% estimating the CV percentages of 27%. The NDAC recommends that the firm should submit undertaking that they will market the product in India and the methods of interim analysis statistical plan should be submitted before permission for BA/BE study is granted.
14.	**Rituximab**		The firm has applied for the grant of permission to conduct a Phase-IIIb clinical trial with rituximab, to investigate the efficacy of Subcutaneous (SC) Rituximab versus Intravenous (IV) Rituximab both in combination with CHOP (R-CHOP) in previously untreated patients with CD20 positive diffuse large B-cell lymphoma (DLBCL). Rituximab is an old drug and already approved for marketing in India. The firm has presented their proposal before the

			NDAC Experts and the committee has recommended for conduct of the trial.
15.	**Gencitabine and Capecitabine**		This is for grant of permission to conduct clinical trial , Phase-III open label in Pancreatic Cancer with combination therapy of Gemcitabine Ing. and Capecitabine Inj. in comparision to Gemcitabine Inj. alone . The indication of Pancreatic cancer is not yet approved for Gemcitabine Inj. The NDAC has recommended that the revised ICD as per GSR 53 (E) 30th Jan 2013 and undertaking for payment of compensation for research related injury/ death from the competent authority of the institute be submitted for consideration by NDAC.
16.	**Panitumumab (vecitibix)**		The firm presented the proposal. The committee opined that the import and marketing permission for Panitumumab for the treatment of first –line and second –line metastatic colorectal cancer can be permitted .However, since the drug is harmful /toxic if given to patients with RAS mutations, the NDAC recommended that permission should be given only for controlled marketing to patient after documentation of absence of RAS mutations.

15. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 04.03.2014:-

15th NDAC (Oncology & Hematology) deliberated the proposals on 04.03.2014 and recommended the following:-

AGENDA NO.	DRUG NAME		RECOMMENDATIONS
1.	**Vorinostat**		The Committee was informed that Vorinostat inhibits the enzyme activity of histone deacetylase HDAC1, HDAC2 and HDAC3 (Class I) and HDAC6 (Class II) at nonomolar concentrations (IC50<86 nM). These enzymes catalyze the removal of acetyl groups from the lysine residues of proteins, including histones and transcription factors. In some cancer cells, there is an over expression of HDACs, or an aberrant recruitment of HDACs to oncogenic transcription factors causing hypoacetylation of core nucleosomal histones. Hypoacetylation of histones is associated with a condensed chromatin structure and repression of gene transcription. Inhibition of HDAC activity allows for the association of acetyl group on the histone lysine residues in an open chromatin structure and transcriptional activation. The Proposal of the firm was placed earlier before the NDAC (Oncology & Haematology) Committee in its meeting held on 08.12.2012. The NDAC noted that T-cell lymphoma is a serious and life threatening disease for which currently there is no satisfactory therapy. Therefore NDAC opined that local clinical trial of the drug can be exempted in public interest. However a single dose bioequivalence study comparing Hetero's product with the innovator's product in patients with refractory cancer should be conducted. In view of this recommendation bioequivalence NOC was granted to the firm and the report of the same is awaited. If B/E result is satisfactory, permission can be granted. Accordingly, the proposal was deliberated in Technical Committee and Apex Committee in its meeting held on 15.01.2014 and 24.01.2014

			respectively. The Technical Committee recommended that the proposal should be forwarded to the NDAC for reconsideration of waiver of local clinical trial in public interest. The Apex Committee has also agreed to the recommendation of the Technical Committee After deliberation, the Committee noted that the drug is indicated for the treatment of cutaneous manifestation in patients with cutaneous T-cell Lymphoma(CTCL) who have progressive persistent or recurrent disease on or following two systematic therapies which is an unmet need and no effective alternative therapy is available for this rare condition. The drug also qualifies under the criteria of orphan drug as the drug is indicated for a rare disease. In view of this the Committee recommended for the waiver of requirement of local clinical trial as well as bioequivalence study in Indian subjects.
2.	**Gadoxetate**		The firm presented clinical data, efficacy and safety data of the drug Gadoxetate along with the pharmacological data, international regulatory status etc. The drug is already approved in USA and 54 other countries since nearly ten years. The firm requested for the waiver of clinical trial in Indian subjects. The Committee noted that the drug is a diagnostic product and does not fit the criteria for waiver of clinical trial in Indian subjects according to the action taken report on the recommendation of the expert Committee, as finalized by the Ministry of Health and Familly welfare. After deliberation, the Committee recommended for conduct of local clinical trial in Indian Subject before import and marketing approval of the drug.
3.	**Imatinib mesilate**		The firm presented the justification for clinical tria waiver. The committee recommended that clinica trial waiver may be considered as there are very few pediatric patients with Ph+ALL i.e. approx. 200 only in the country and therefore clinical trial is not

			feasible. Further this drug is labeled as an Orphan drug internationally. Further the drug is already approved for CML in pediatrics and therefore there is adequate experience with the drug in pediatric population. The committee opined that firm may be permitted to import and market the drug in the country for the treatment of paediatric patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ALL) integrated with chemotherapy.
4.	**Decitabine lyophilised powder for injection 50 mg**		The committee recommended for grant of import and marketing permission of decitabine lyophilised powder for injection 50 mg for the additional indication “in adult subjects aged 65 and above”.
5.	**Temsirolimus**		The applicant firm requests for permission to incorporate a protocol amendment in the existing phase-IIIb clinical trial with **Bevacizumab + temsirolimus** Vs. **Bevacizumab + Interferon Alfa** as First line treatment in Subjects with advanced renal cell carcinoma ” which was permitted on 07 Aug 2008. Now the firm has applied for protocol Amendment 4. The protocol was amended as a result of the primary analysis, which was conducted in Aug 2012. The NDAC recommends that the protocol amendment No. 4 is approved since there are no patients receiving active treatment at present and the IP (the combination) was not found to be superior to the existing drugs (Interferon-alfa + Bevacizumab.
6.	**Trastuzumab**		The firm did not present itself for the meeting.
7.	**Masitinib Mesylate**		The applicant CRO firm requests for permission to conduct Phase-III clinical trial to compare the efficacy and safety of Masitinib at 7.5mg/kg/day to

			dacarbazine in the treatment of patients with non-resectable or metastatic stage 3 or stage 4 melanoma carrying a mutation in the juxta membrane domain of c-kit. The proposed study is planned to be conducted in USA, France and India. 30 subjects are planned to be enrolled from India out of 200 globally. The undertaking for marketing submitted by the firm reveals that the firm will market the drug only if they get satisfactory results in India. This is not agreeable to the NDAC and the firm should submit the revised undertaking stating that they should market the drug in India if global results are satisfactory.
8.	**Pegfilgrastim**		Firm did not turn up for presentation.
9.	**Ofatumumab**		Committee examined the Indian specific subset analysis of OMB110911 study and results were found to be acceptable by the committee. Committee recommended for the Marketing Authorization of the Ofatumumab. The drug should be sold by the prescription of Oncologist & Hematologist only.
10.	**Cetuximab**		The firm presented the protocol for Phase III clinical trial with their indigenously developed Cetuximab. Committee noted the following observations: 1. Study should be re-designed to include an initial cohort to assess infusional safety, pharmacodynamic and pharmacokinetics variables. Accordingly, firm shall submit the revised protocol for Phase III study with their indigenously developed Cetuximab to this office for further consideration in next meeting.
11.	**Trastuzumab**		Committee recommended the continuation of the second part of the Phase III clinical trial study with their indigenously developed Trastuzumab.

12.	**Pegfilgrastim)**		Committee observed that the efficacy and safety data of the PK/PD study with Pegfilgrastim found to be incomplete in many aspects. Therefore, firm is required to present PK/PD study results and protocol for Phase III clinical trial for the next meeting.
13.	**Bevacizumab**		The firm presented the protocol for Phase III clinical trial with their indigenously developed Bevacizumab. Committee noted the following observations: 1. Justification for sample size need to be clarified. 2. Please submit the Statistical Analysis plan of the study. 3. Study site centers should be at least 50% Government hospitals/ Multispecialty hospitals. Accordingly, firm shall submit the revised protocol for Phase III study with their indigenously developed Bevacizumab to this office for further consideration in next meeting.

16. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 23.05.2014:-

The Committee while evaluating the following proposals, the Committee kept in view three following aspects

1. Risk versus benefit to the patients
2. Innovation viz a viz existing therapies
3. Unmet need in Indian population.

The NDAC (Oncology & Hematology) deliberated the proposals on 23.05.2014 and recommended the following:-

AGENDA NO.	DRUG NAME		RECOMMENDATIONS
1.	**Nanosomal Paclitaxel lipid suspension for injection 30mg/vial & 60mg/vial (25 ml)**		The NDAC had in its meeting on 26 Aug 2013 recommended a phase III study. However the firm requested that since Paclitaxel drug is being marketed for long time in market, requested that phase II study allowed to be extended in to Phase II/III Study. The previous data may be used for decision making because this drug has shown more efficacy and patients will be benefited with proposed formulation. The study already conducted shall be extended with the power of 80%; non-inferiority limit of 10%; and an alfa error of 5%. The data for progression free survival of the patients should be gathered for future. Accordingly the firm shall submit the extension study protocol as per above criteria for reviewing in subsequent NDAC.
2.	**Cabazitaxel Lipid suspension for injection 50mg/vial (25 ml).**		The NDAC has examined and opined that justification for dose selection has not been given. More animal experiments are required generating PK data to justify the dosage in comparison with innovator product of conventional dosage form in Dog or other suitable animal model. The firm should also revise the phase I trial protocol incorporating Neutrophil counts of ≤ 1500/ mm^2 and age more than 65 Years as exclusion criteria. Firm should clearly mention regarding what PK parameters will be studied in the study.
3.	**Gemcitabine**		Committee examined and recommended for

	Hydrochloride 10 mg/ml		manufacturing and marketing approval as these formulation is ready to use infusion bags for already approved formulation in Lyophilized formulation.
4.	**Human clrh F VIII**		The firm was granted NOC dated 03/09/2013 for conduct of a phase III clinical trial to evaluate Immunogenicity, efficacy and safety of treatment with Human cl rhFVIII- (a fourth –generation rhFVIII concentrate produced in genetically modified HEK 293F cells) in previously untreated patients with severe haemophilia A. The company reiterated that the subjects with positive response in the trial will be provided free therapy. However the company sought re-deliberation of the matter seeking clarification on treatment of study participants in case of inhibitor development . The NDAC has examined and opined that any patient who has inhibitor despite ITI, the firm will provide free medical management/standard care, for a period of 03 years post completion of the trial. Committee approved this amendment.
5.	**Octafibrin**		On 30 Aug 2013 the permission for Prospective, Controlled, Randomized, Cross-Over Study Investigating The Pharmacokinetic Properties, Surrogate Efficacy And Safety Of Octafibrin (a highly purified, lyophilised, human plasma fibrinogen concentrate, without added albumins) Compared To Haemocomplettan® P/Riastap™ In Subjects With Congenital Fibrinogen Deficiency was granted to M/s. Max Neeman International at the dose level of Single intravenous infusion of 70 mg/kg with Initial enrollment of 06 subjects out of 18 subjects globally. The company provided the interim safety analysis report which was found be satisfactory. Since there was no safety issue, the committee recommended the inclusion of two subjects as sought by the firm.
6.	**Coagulation Factor IX**		The committee recommended the protocol amendment i.e. use of polished product for all the subjects in India.

7.	**Rituximab**		This is a randomized, controlled double-blind phase III trial to compare the efficacy, safety and pharmacokinetics of GP2013 plus cyclophosphamide, vincristine, prednisone vs. MabThera® plus cyclophosphamide, vincristine, prednisone followed by GP2013 or MabThera® maintenance therapy in patients with previously untreated, advanced stage follicular lymphoma. GP2013 is a liquid formulation (Intravenous Infusion) based on rituximab as active ingredient at a concentration of 10 mg/mL provided in two strengths 100 mg and 500 mg / vial. Primary objective of this study is to demonstrate comparability of the overall response rate in patients with previously untreated, advanced stage follicular lymphoma, who receive GP2013-CVP combination treatments to patients who receive Mab Thera ® -CVP combination treatment. ORR will be determined during the combination treatment period using modified Response criteria for malignant lymphoma. Follicular Lymphoma is a disease of older age and there is as no safety related issues in this age group ,as observed from the global data in the elderly i.e. above 65 years of age.. Hence The NDAC recommends for age relaxation in India i.e inclusion of subjects above 65 years of age and the protocol amendment-3.
8.	**SB-3 (Trastuzumab Inj.)**		The applicant firm a CRO has applied for Permission to conduct a phase III randomized, double-blind, parallel-group, multicentre study to compare the efficacy, safety, pharmacokinetics and immunogenicity between SB3(a trastuzumab biosimilar, Mfgd. by M/s Samsung Bioepies South Korea) and Herceptin® in women with newly diagnosed HER2 positive or locally advanced breast cancer in neo adjuvant setting. The comparable clinical efficacy of SB3 and Herceptin® will be evaluated in terms of pathologic Complete Response (pCR) rate of the primary breast tumor in women with human

			epidermal growth factor receptor2 (HER2) positive early or locally advanced breast cancer (LABC). The NDAC examined and opined that the proposed trial may be approved as such.
9.	**PF-0580014+ Paclitaxel**		This is phase 03 clinical trial with the biosimilar Trastuzumab of Pifzer .The primary objective of this study is to compare the objective response rate (ORR) in patients with metastatic HER2-positive breast cancer who receive trastuzumab-Pfizer to those who receive trastuzumab-EU in combination with paclitaxel. The committee examined and recommended for the conduct of the trial.
10.	**Ruxolitinib**		This is phase randomized, open label, multicenter phase IIIb study evaluating the efficacy and safety of Ruxolitinib versus best available therapy in patients with polycythemia vera who are hydroxyurea resistant or intolerant (Response 2)". The primary objective is to compare the efficacy of ruxolitinib to BAT as assessed by Hct control at week 28. The drug is marketed in India for another indication and no major safety signal has so far been observed. The phase-2 studies in the indication: polycythemia vera is found to be encouraging. Ruxolitinib is a targetted therapy and there is no other therapy currently in this category for polycythemia vera other ttthhhan hydroxyurea. Therefore this clinical trial meets the genuine unmet need condition. NDAC therefore recommends approval of the clinical trial
11.	**Bevacizumab**		The applicant requests for permission to conduct an Open label randomized bioequivalence study to evaluate the pharmacokinetic (PK) and safety profile of **Bevacizumab** [mfgd. By M/s Mabaxience,

			Uruguay (DS at CMC Biologics, Denmark and DP at M/s Aptuit, UK)] VS. Bevacizumab **(AVASTIN®)** in combination with FOLFOX or FOLFIRI as first-line treatment in patients with **metastatic Colorectal Cancer**. The NDAC after review of the protocol and the presentation made by the firm, opined that since this is a first time used in human subjects, the trial may be approved with a condition that the interim analysis for safety be submitted after first cohort of six patients. Further approval may be granted based on the above results.
12.	**Pegfilgrastim**		Firm presented the data of PK/PD study with their indigenously developed Pegfilgrastim and Study Protocol of Phase III clinical trial with Pegfilgrastim. The NDAC after review of the study protocol # RLS/TP/2011/01, Version 05 dated 24th Mar 2014 and the presentation made by firm, recommended for the conduct of the study with the said protocol.
13.	**Cetuximab IV Injection**		The firms' proposal for conduct of Phase III clinical study with their indigenously developed Cetuximab was discussed in the NDAC (Oncology & Hematology) held on 04.03.2014 wherein committee noted that "Study should be re-designed to include an initial cohort to assess infusional safety, pharmacodynamic and pharmacokinetics variables". Firm has now presented the revised study protocol vide Protocol No. # RLS/ONC/2013/04, Version # 2.0 dated 24/03/2014 that includes an initial cohort to assess infusional safety, pharmacodynamic and pharmacokinetics variables. Committee after reviewing the revised protocol recommended for the conduct of the study with the said protocol.
14.	**Bevacizumab**		Committee reviewed the report presented by the firm of the first phase of the Phase III study with Bevacizumab. However there were significant data point missing including a detailed DSMB report was missing. Hence firm is asked to re-

			submit a detailed DSMB report alongwith the detailed review of all Adverse events including SAEs.

17. RECOMMENDATIONS OF THE NDAC (ONCOLOGY AND HEMATOLOGY) HELD ON 10.06.2014:-

The Committee while evaluating the following proposals, the Committee kept in view three following aspects

4. Risk versus benefit to the patients
5. Innovation viz a viz existing therapies
6. Unmet need in Indian population.

The NDAC (Oncology & Hematology) deliberated the proposals on 10.06.2014 and recommended the following:-

AGENDA NO.	DRUG NAME		RECOMMENDATIONS
1.	**Cabazitaxel**		The Committee noted that Cabazitaxel Injection 60mg / 1.5ml in combination with prednisone is approved by DCG(I) office for treatment of patients with hormone-refractory metastatic prostrate cancer previously treated with a docetaxel-containing treatment regimen. The proposed study is a hypothesis generating Investigator initiated Phase-II study for academic purpose. Further, there are not many options for patients suffering with resistant/recurrent Gastric Cancer. After detailed deliberation, the committee recommended for the conduct of the proposed study.
2.	**Crizotinib 200mg and 250 mg Capsules**		Crizotinib Capsule 200mg/250mg was approved by DCG(I) office on 16.12.2011 for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK) – positive as detected by an FDA-approved test. **The firm has requested to amend the approved indication to delete the words 'as detected by FDA-approved test' to CDSCO approved test.** **After deliberation, the committee recommended that the words 'as detected by FDA-approved test' to be replaced by "IHC/FISH test".**
3.	**Afatinib**		The committee was informed that in its

	20/30/40/50mg		earlier meeting it had asked the firm to present India specific subset analysis report from the ongoing clinical trial being carried out in India as part of global clinical trial before considering the proposal for the grant of marketing authorization. Now the firm presented the India specific subset analysis report from the ongoing clinical trial being carried out in India as part of global clinical trial on 47 Indian Patients. The Committee observed that the drug is Ethnically insensitive Found superior efficacy when compared to the comparators No new differential safety signal observed when compared to the global population The firm has been permitted to conduct another Phase-III trial with the same drug with 50 Indian patients. The incidence of EGFR mutation is only a fraction of NSC lung cancer The drug is approved by USFDA, EU, Canada, Australia, Japan etc including Asian Countries such as Taiwan, Singapore The Committee deliberated the matter in detail and noted that the data generated in Indian patients is adequate and the firm has also proposed to conduct another study with 50 patients. Hence, the Committee recommends for grant of permission for the import and marketing of **Afatinib 20/30/40/50mg Tablet** to be indicated for the treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) with Epidermal Growth Factor Receptor (EGFR) mutation(s) subject to the following conditions: Active monitoring of the patients for a period of 2 years and ADRs should be reported to Pharmacovigilance Programme of India. (PvPI).
4.	**Sorafenib tosylate 200mg**		The proposal was deferred as the firm did not turn up for presentation.

5.	**CD2 Lozenges**		The proposal was re-examined by the committee. In view of the additional national as well as international data presented by the firm on the efficacy of the product, the committee recommended for manufacturing and marketing of the CD2 Lozenzes with the condition that a Phase IV trial duly approved by CDSCO shall be conducted in a statistically significant number of patients distributed geographically across the country and after completion of the study, it shall be reviewed by the committee for further continued marketing of the drug in the country.
6.	**Paclitaxel injection 100mg/300 mg**		There was no justification provided by the firm for the selected doses in the proposed Phase I trial. Moreover there were no adequate animal studies to establish the proof of concept for the proposed Phase I trial. Hence the committee did not recommend for the trial in the present form.
7.	**Capecitabine +Cyclophosphamide**		The applicant requested for permission to manufacture and market the FDC of Capecitabine 300mg/600mg + Cyclophosphamide 20mg/40mg tablets which was earlier deliberated in the NDAC (Oncology & Hematology) meeting held on dated: 27.11.2013 wherein the committee observed that firm has presented the clinical trial protocol for Phase II trial. However, firm could not provide justification for the proposed dose schedule, statistical significance for the proposed no. of subjects. Now the firm has submitted the revised trial protocol for the prospective, randomized, open label, multicenter clinical trial to assess the efficacy and safety of the proposed FDC in metastatic breast cancer with failure of anthracycline and/ or taxane chemotherapy. Trial will be conducted as per submitted protocol NDAC opined permission may be granted for conducting clinical trial with a condition that independent DSMB should oversee the trial and Medical oncologist shall be included in the study team at each site.

8.	**CT-P10**		The application is for permission to conduct a Phase 1/3, randomized, parallel-group, active-controlled, double-blind study to demonstrate equivalence of pharmacokinetics and non-inferiority of efficacy for CT-P10 (Biosmiliar **Rituximab**, Concentrate for solution for intravenous infusion, Each vial is designed to deliver 500 mg of antibody per 50mL solution at a concentration of 10 mg/mL in comparison with **Rituxan,** each administered in combination with cyclophosphamide, vincristine and prednisolone (CVP) in patients with **advanced follicular lymphoma**. Globally 250 subjects and 60 subjects from India (at 14 centers) are planned to be enrolled. The test drug is not yet approved and The study is planned to be conducted in 20 countries including Bulgaria, Greece, Italy, Russia, USA, India. After deliberation the committee recommends the conduct the said trial with subjects of upper age limit up-to 75 yrs subject to submission of the MA /clinical trial approval from the country of origin.
9.	**CT-P6 and Herceptin Breast Cancer**		The applicant has applied for permission to conduct Phase 3, Double-Blind, Randomized, Parallel-Group, Active-Controlled Study to Compare the Efficacy and Safety of CT-P6 (**Trastuzumab**, Lyophillized and **Herceptin** in treatment of Patients with HER2-Positive Early Breast Cancer. The Primary objective of this study is to demonstrate equivalence of CT-P6 and Herceptin, both given in combination with docetaxel (Cycles 1-4) followed by FEC (cycles 5-8), in terms of efficacy as determined by Pcr, in patients with HER-2 positive operable early breast cancer. The drug is marketed in South Korea and Maldobva since Jan-14 and Oct-13. The trial will be overseen by DSMB.

			After deliberation the committee recommended permission for conduct of the trial.
10.	**Bosutinib**		The applicant requested for permission for the open label, Bosutinib (extension study in chronic myeloid leukemia (CML) who have previously participated in Bosutinib studies B1871006 or B1871008. The drug safety was assessed on single and repeat dose toxicity, genetic toxicity, reproductive and developmental toxicity, and phototoxicity Rats and doge in oral studies up to 6 and 9 months respectively. The drug was approved by US FDA in Sept 2012 and EU The proposed study is planned to be conducted in 32 countries are participating USA, Canada, UK, Germany, Japan and India. The proposal was discussed earlier at NDAC on 27/11/13 wherein committee after due deliberation asked for the detailed data on safety and reasons for discontinuation of the subjects who will be switched over to the open label study. NDAC has examined the safety data presented by the applicant and recommends the conduct of this open label clinical trial protocol WITH Bosutinib.
11.	**Factor VIII Concentrate**		The investigator has applied for permission to conduct the clinical trial entitled: an Assessment of the effectiveness of prophylactic replacement of lower than 'standard' doses of Coagulation Factor VIII Concentrates (EMOCLOT -1000 IU powder) for infusion in children with severe haemophilia and also to correlate this outcome with the dose of CFC used and evaluate if there is a dose response relationship at these doses. 100 subjects are planned to be enrolled. Patients will be classified into two categories according to age (3-5 and 5-7 years) and also into different groups according to the amount of factor replacement IU/kg/week (<20 iu/kg, 20-40 iu/kg and >40 iu/kg for >45

			weeks in a year) and IU/kg/year (500-1000 iu/kg; 1000-1500 iu/kg; 1500-2000 iu/kg; > 2000iu/kg). The study is planned to be conducted in 7 countries which includes Brazil, Malaysia, Iran, Egypt, South Africa, Venenzeula and India. The NDAC has examined the proposal and recommends approval of the trial subject to Fixation of the lower dose/dose range, for each of the groups of Emoclot (Factor-VIII) for the prophylactic treatment and that the trial is not observational but involves intervention . The revised protocol including the above changes are to be submitted to CDSCO for approval.
12.	**Trastuzumab Emtansine**		The proposal for the import and market the Trastuzumab Emtansine has been submitted for NDAC approval with Clinical Trial waiver. TDM 1 is a novel drug indicated for treatment of patients with HER2-Positive, unresectable locally advanced or metastatic breast cancer who have received prior treatment with Trastuzumab and a taxane" which is an unmet need. This drug is approved in 52 countries including countries such as US, Switzerland, Australia, Canada, Japan, Ecuador, Uruguay. Currently there is no standard of care for this condition and there is genuine unmet need. Overall 3000 patients have been exposed to the drug in various clinical trials globally. It shows significant improvement in overall survival. In addition to improving the Progression Free Survival, it also improves the overall survival based on the presentation made by firm. In view of the fact there is no therapy available for this condition and in the interest of public. Committee recommended for the permission to import and market for the subject drug may be given subject to conduct of

			adequately powdered phase IV clinical trial with a review of data in 2 years. The phase IV protocol should be duly approved by the CDSCO.
13.	**Bevacizumab**		Committee recommended for the conduct of the PMS study.
14.	**Recombinate Anti-haemophilic factor IX**		The proposal was deferred as the firm did not turn up for presentation.
15.	**Zaltrap (Aflibercept)**		Firm presented that there is an unmet need for this drug. The committee reviewed the presentation made in light of the Action taken report on Prof Ranjit Roy Committee Report and reiterate its previous observations which are as follows: ✓ There is an unmet need as a second-line therapy for metastatic colorectal cancer. ✓ The firm has conducted clinical trial in other indications as part of Global clinical trial which showed no difference in the pharmacokinetic parameters in 14 Indian patients and there was no safety issue. ✓ Pharmacokinetic data in Indian patients shows that there is no pharmacokinetic difference when compared to Caucasians. ✓ The Drug has been found to be effective for the proposed indication as per the data generated in other countries. Committee recommended for import and market subject to condition that firm should conduct a structured India specific Phase IV trial after getting approval by this office.
16.	**Bevacizumab**		The applicant requests for permission for carrying out the Phase III clinical trial with their indigenously developed Bevacizumab, the proposal was discussed in the NDAC (Oncology & Hematology) held on 04.03.2014

			wherein committee recommended for (i) Justification for sample size needs to be clarified (ii) to submit the statistical analysis plan of the study (iii) Study site centers should be at least 50 % Government hospitals/Multispecialty hospitals. The firm has presented the revised clinical trial protocol entitled “Prospective, comparative, Open label, randomized, Multicentric, Phase III study to compare the safety and efficacy of Bevacizumab of Intas Pharmaceuticals Ltd against Avastin in patients with Unresectable or Metastatic Non-Squamous Non-Small Cell Lung Cancer” Vide Protocol Number: 476-13,Version Number 02 Dated 10TH Mar, 2014 to comply with necessary suggested changes as per above said NDAC recommendation dated 04.03.2014. The NDAC examined the revised study protocol and opined that the permission may be granted for the conduct of the study.