MINUTES OF THE 11th MEETING OF TECHNICAL COMMITTEE HELD ON 15-01-2014 & 16-01-2014 UNDER THE CHAIRMANSHIP OF DGHS FOR SUPERVISING CLINICAL TRIALS ON NEW CHEMICAL ENTITIES IN THE LIGHT OF DIRECTIONS OF THE HON'BLE SUPREME COURT OF INDIA ON 03.01.2013.

Present:

1. Dr. Jagdish Prasad, Chairman
   Director General of Health Services

2. Dr. Nandini Kumar, Member
   Former Dy. Director (Sr. Grade)
   National Institute of Epidemiology, ICMR, Delhi

3. Dr.Rajutitus Chacko, Member
   Prof. & Head, Dept. of Medical oncology,
   CMC, Vellore.

4. Dr. Nikhil Tandon Member
   Professor, Dept. of Endocrinology & Metabolism,
   AIIMS- New Delhi.

From CDSCO:

1. Dr. G.N. Singh,
   Drugs Controller General (India)

2. Sh. A.K. Pradhan,
   Deputy Drugs Controller (India)

3. Mrs. A Vishala
   Deputy Drugs Controller (India)

Dr. Jagdish Prasad, DGHS welcomed the members and briefed them about the outcome of the tenth meeting of the Technical Committee which was held on 28.11.13. The minutes of the tenth meeting approved by the Chairman were already circulated to the members.

Evaluation of 157 Global Clinical Trials as per order of Hon'ble Supreme Court of India

The Committee was again apprised the order of the Hon'ble Supreme Court of India, dated 21.10.2013 in the matter of W.P. (C) No. 33/2012 of Swasthya Adhikar Manch, Indore & Anr Vs. Ministry of Health and Family Welfare & Ors. with WP(C) No. 779/2012 regarding clinical trials. The operative part of the order in respect of 162 global clinical trials which were approved by DCG(I), since November 2011 to 31.8.3013 were also again placed before the Committee. The same is reproduced below:

> "Out of 285 applications which have been recommended for approval by NDACs include clinical trials for investigational products relating to Anti-AIDS, Oncology, Cardiology, Neurology, Psychiatry, Metabolism, Endocrinology, etc. NDACs have evaluated carefully pharmacological, toxicological data, clinical data and protocol for the clinical trials including the objective of the study, eligibility criteria of the subjects, treatment, safety and efficacy assessments, etc. Of these 285 applications, DCG(I) has given approval to conduct clinical trials in 162 cases till 31.08.2013.
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> Out of 162 approvals, 157 approvals were given by the DCG(I) before 31.12.2012 which were prior to directions of this Court on 03.01.2013. The DCG(I) has given the approval to conduct clinical trials in the remaining 5 cases from 01.01.2013 till 31.08.2013 after the approval of the Apex Committee assisted by the Technical Committee.
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> The above facts show that insofar as 5 cases out of 162 cases which were given approval by DCG(I) are concerned, these 5 cases had undergone the three-tier screening. First by NDACs, then by the Technical Committee and the Apex Committee and thereafter the approval has been given by the DCG(I).
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> However, as regards 157 approvals which were given by the DCG(I) before 03.01.2013, learned Additional Solicitor General fairly submits that these cases have not been evaluated by the Technical Committee and the Apex Committee. He submits that the Central Government is agreeable that these 157 cases may be evaluated by the Technical Committee and the Apex committee as well, as has been done for the 5 cases for which approval was given after 03.01.2013.
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> We accept the statement of the learned Additional Solicitor General. We, however, observe that the Technical committee and the Apex Committee while evaluating the above 157 cases shall keep in view all relevant aspects of safety and efficacy particularly in terms of assessment of risk versus benefit to the patients, innovation *vis-a-vis* existing therapeutic option and unmet medical need in the country.
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> In the light of the above, it is not possible to pass any order today with regard to 157 cases and the same will be considered after the reports of the Technical Committee and the Apex Committee in respect of 157 cases are submitted before this Court. As regards 5 cases for which approval has been

given by the DCG(I) after 03.01.2013, we record and accept the statement of Mr. Siddharth Luthra, learned Additional Solicitor General that before the clinical trials are conducted, appropriate provision shall be made or administrative direction shall be issued which ensures that audio-visual recording of the informed concerned process of the participants is done and the documentation preserved, adhering to the principals of confidentiality. In other words, the clinical trials in respect of five cases shall commence after proper framework is in place concerning audio-visual recording of the informed concerned process and the preservation of documents while adhering to the principals of confidentiality."

The Committee then discussed the issue of evaluation of 157 cases of Global Clinical Trials approved by DCGI based on NDACs recommendations, as per order of Hon'ble Supreme court dated 21.10.13.The Committee was informed that out of these 157 cases, 65 trials are ongoing,13 trials have not yet been initiated by the applicants and 39 already completed. Out of the remaining 40 cases, 25 trials have been withdrawn by the respective applicants without any patient enrolment while15 trials have been terminated /suspended by the respective applicants prematurely due to various reasons like administrative reasons, no beneficial effects observed, disease progression, lack of efficacy and failure to reach primary endpoint.

Out of the 157 cases, 50 cases of ongoing trials were evaluated by the Committee in its 10th meeting held on 28.11.13. The detailed information in respect of the remaining 107 cases were already forwarded to the members of the Committee through e-mail. List of these proposals is annexed as **Annexure-I.**

The Committee first evaluated the remaining 15 cases of the ongoing trials (Sr. No. 1 to 15 in the **Annexure-I**) in detail one by one and recommended that 14 of these 15 cases meet all the requirements of safety and efficacy aspects especially in terms of risk versus benefits to the patients, innovation *vis-a-vis* existing therapeutic options and unmet medical need in the country and these studies should continue. In respect of one case mentioned at Sr. No. 9 in the **Annexure-I,** the Committee opined that prophylactic anti TB treatment is acceptable. However, empiric treatment with anti TB drugs in HIV patients may not be justified given the risk *vs*. benefit to the patients. Therefore, the Committee recommended that the report of the Data Safety Monitoring Board (DSMB) for this trial shall be submitted to the Committee for evaluation. Till such time the DSMB report is evaluated by the Committee, there should be no further enrolment of any new subjects in this trial. However, the trial should continue with the subjects already recruited in the study.

Thereafter, the Committee evaluated the 13 cases one by one, which have not yet been initiated by the respective applicants (Cases mentioned at Sr. No. 70 to 82 of the **Annexure-I**) and recommended that except one case mentioned at Sr. No. 76, all other 12 cases meet all the requirements of safety and efficacy particularly in terms of assessment of risk versus benefit to the patients, innovation vis-a-vis

existing therapeutic option and unmet medical need in the country. The case at Sr. No. 76 is the same study as mentioned in Sr. No. 9 of annexure-I, permitted to different applicant. The recommendation made by the committee in respect case at Sr. No. 09 above is applicable for the case mentioned at Sr. No. 76.

The Committee then evaluated the remaining 79 cases, of which 39 are already completed, 15 are terminated/ suspended by the applicants and 25 cases are those which have been withdrawn by the respective applicants without any patient enrolment. No specific action was recommended by the Committee for these cases.

Thus, the Committee completed its evaluation of all the 157 cases of GCTs as per the order of the Hon'ble Supreme Court.

Evaluation of 36 cases of fresh proposals of clinical trials

Thirty six cases of fresh proposals of clinical trials details of which were forwarded through e-mail to the members were also evaluated by the Committee in the meeting keeping in view risk versus benefit to the patients, innovation *vis-a-vis* existing therapeutic option and unmet medical need in the country. These cases have already been recommended by the NDACs. The lists of these cases are annexed as **Annexure II.** The recommendations of the Committee in respect of these 36 proposals are as under:

- In cases of proposals at Sr. No. 1, 2, 7, 8, 9, 10, 12, 15, 17, 30, 31 & 36 the Committee observed that there was no Pharmacologist present during NDAC meetings when these proposals were evaluated. The Committee therefore recommended that these proposals should be evaluated by the NDACs in their meetings with proper representation of members including at least one Pharmacologist in each meeting.

- In case of the proposal at Sr. No. 14, the Committee noted that there is no Govt. clinical trial site included in the study. Therefore, the Committee recommended that there shall be at least 25% Govt. sites in the study.

- For proposal at Sr. No. 16, the Committee recommended that only the reference product should be provided to the patients under the compassionate use stage of the trial and not the test drug.

- In case of proposal at Sr. No. 27 the Committee observed that the trial is proposed to be conducted in children with cerebral palsy. However, there was neither any Pediatrician nor Neurologist, present during the NDAC deliberation. The Committee therefore recommended that this proposal shall be again deliberated by the NDAC in its meeting with a proper representation of its members alongwith Pediatrician and Neurologist.

- For remaining 21 cases mentioned at Sr. No. 3, 4, 5, 6, 11, 13, 18, 19, 20, 21, 22, 23, 24, 25, 26, 28, 29, 32, 33, 34 and 35, the Committee recommended for giving permission to conduct the trials.

Recommendations of the Committee on further strengthening of clinical trials

The Committee, while taking note of the various regulatory measures already taken to strengthen the approval and monitoring of clinical trials in the country, recommended for certain other actions as under to improve the transparency and accountability in clinical trials.

i) Number of NDACs should be increased from existing 12 to about 50 Committees.
ii) The number of cases that should be evaluated by NDACs in a meeting should not be more then 8 to 10.
iii) As and when required the Technical Committee shall invite the outside subject experts by the Chairman.
iv) The Sponsor/CRO should put all details of clinical trials being conducted in the public domain.
v) CDSCO should further strengthen the "clinical trial monitoring cell" in its headquarter as well as in Zonal offices.

Requirements of local clinical trials for approval of New Drugs already approved in other countries

The Committee was then requested to give advice in matters related to proposals of approval of new drugs (already approved in other countries) for their approval without local clinical trials in the country. In this regard the Committee was apprised about the regulatory requirements of approval of new drugs in the country.

It was informed that as per the Drugs & Cosmetics Rules, for new drugs substance approved in other countries, phase III clinical trial is required before granting permission to manufacture / import of finished formulation of the new drug.

However, requirements of local Clinical Trial may be waived off / relaxed under certain conditions as per Drugs & Cosmetics Rules (122 A (2) ,122 B (3) & clause 1 (3) of schedule-Y as mentioned above depending on nature of drugs and diseases for which it is indicated.

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

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

It was further informed that Parliamentary Standing Committee in its 59th report has raised concerns on approval of certain new drugs in the country without local clinical trials. In light of the same the Ministry constituted a Committee under Chairmanship of Prof. Ranjit Roy Chaudhury, the Committee submitted its report. The various actions to be taken on the recommendations of the Ranjit Roy Chaudhury Committee has been finalized by the Ministry of Health & Family Welfare and the same has already been posted in the CDSCO website.

With regard to the waiver of local clinical trial for approval of new drugs, which have already been approved outside India, the Ministry has decided that such waiver can be considered only in cases of national emergency, extreme urgency, epidemic and for orphan drugs for rare diseases and drugs indicated for conditions/diseases for which there is no therapy.

The Committee after detailed deliberation opined that waiver of local clinical trial for approval of new drugs which have already been approved in other countries can be considered under the four conditions as decided by the Ministry. However, such proposals should be evaluated carefully on case by case basis. If considered necessary by the expert committee in light of risk versus benefits to the patients, innovation *vis-a-vis* existing therapeutic options and unmet medical need in the country, such cases of new drugs may be considered for approval in the country without going through local clinical trials in larger interest of the patients as per three above criteria flagged by the Hon'ble Supreme Court of India, in its order dated 21.10.2013 in the matter of W.P. (C) No. 33/2012 of Swasthya Adhikar Manch, Indore & Anr *Vs*. Ministry of Health and Family Welfare & Ors. with WP(C) No. 779/2012 regarding clinical trials.

The Committee evaluated 10 such proposals of new drug approvals including one case of Fixed Dose Combination already recommended for approval by the NDACs. Details of the same along with the recommendations of the Technical Committee is annexed as **Annexure - III.**

Audio-visual recording of the informed consent process

As regards to audio-visual recording of the informed consent process, the Committee was informed that as per the observation / direction of the Hon'ble Supreme Court on 5 cases of Global Clinical Trials for which approvals were given by DCGI between 03.01.13 to 31.08.13, DCGI vide its order dated 19.11.13, with the approval of the Ministry of Health and Family Welfare, issued directions making audio-visual recording of the informed consent process mandatory in all clinical trials. As per the direction, in addition to the requirements of obtaining written informed consent, audio-visual recording of the informed consent process of each trial subjects, including the procedure of providing the information to the subjects & his/her understanding on such consent is required to be done while adhering to the principles of confidentiality. This is applicable to the new subjects to be enrolled in all

clinical trials including Global Clinical Trials. Such audio-visual recording and related documentation would be preserved.

The Apex Committee in its 10th meeting of the Committee recommended that DCG(I) should prepare detailed guidelines specifying procedures for such audio-visual recording of Informed Consent Process and adherence to the principles of confidentiality, preservation of the audio-visual recordings and other related documents.

Draft guidance document for Audio-visual recording of the informed consent process

Accordingly, a draft guidance document has been prepared and uploaded on CDSCO website for comments from the stakeholders. A copy of the draft guideline was also placed before the Committee. The members of the Committee were of the opinion that audio-visual recording of giving detailed information to the subjects as per the elements specified in Appendix-V of Schedule-Y may be a cumbersome procedure. Therefore, the members were of the opinion that, the patients understanding on the informed consent should be recorded through audio-visual means instead of recording the whole procedure of giving detailed information as well patients understanding on the informed consent. However, the Committee recommended that the guidelines should be finalized taking the suggestions/opinions of the stakeholders into consideration.

The meeting ended with the vote thanks to the Chair.

ANNEXURE- I

S. No.	Drug	Applicant
1.	FST-100 (0.1 %Dexamethasone and 0.6% PVP- Iodine)	Excel life sciences
2.	DE-109 (Sirolimusintraverial formulation)	Excel life sciences
3.	Valacyclovir hydrochloride	Smita N Despande
4.	Vandetanib	Quintiles
5.	BAX326 (Recombinant Factor IX)	Baxter
6.	Polycap [FDC of Simvastatin (40mg) + Ramipril (10mg) + Atenolol (100mg) + Hydrochlorothiazide (25mg) Capsule], low dose aspirin and vitamin D	Cadila
7.	Raltegravir+Lopinavir/Retinovir	YRG
8.	Riyataz+Stocrin+ Truvada+Combivir+Laetra/Aluvia+Norvir+Epzicom+Prezista	YRG
9.	Atripla+Truvada+Emtriva+Vierad+Stocrin	YRG
10.	AMG-785 (Anti-sclerostin monoclonal antibody)	Amgen Technology Pvt. Ltd
11.	CF101	Karmic
12.	Vemurafenib	Roche
13.	nabiximols	PRA
14.	Rindopepimut	Novotech
15.	MEDI-546	Kendle
16.	BUSPIRONE HYDROCHLORIDE TABLETS 5 MG AND 10 MG (App. In INDIA)	Accutest Research Lab
17.	RP5063	Sristek Clinical Research
18.	LA-EP2006 (Pegfilgrastim) and Neulasta	inVentiv
19.	LA-EP2006 (Pegfilgrastim) and Neulasta	inVentiv
20.	Netupitant and Palonosetron	PAREXEL
21.	Trastuzumabemtansine	Roche
22.	NVA237 (Glycopyrronium bromide)	Novartis
23.	NVA237 (Glycopyrronium bromide)	Novartis
24.	QAW039	Novartis
25.	MOMETASONE FUROATE	Novartis
26.	SAR153191(SARILUMAB)	SANOFI
27.	TenofovirDisoproxilFumarate (TDF)	Klinera
28.	AR-12286	MAX NEEMAN
29.	Glimepiride and Metformin	SANOFI
30.	LINAGLIPTIN	Boehringer
31.	Linagliptin and Metformin	Boehringer
32.	Bosentan	Clintec
33.	A-623 (Blisibimod)	Kendle

34.	Fluticasone Propionate/FormoterolFumarate	Kendle
35.	CXA-201 (Ceftolazone) and metronidazole	PRA
36.	Insulin deglutide/Liraglutide	Novonordisk
37.	Biphasic insulin aspart (BIAsp)	Novonordisk
38.	Insulin Degludec/Liraglutide	Novonordisk
39.	LIRAGLUTIDE (Approved in INDIA)	Novonordisk
40.	USL255 (Topiramateexetended release tablet)	PPD
41.	Sitagliptin	MSD
42.	Tafenoquine	GSK
43.	Macitentan	Clintec
44.	PF-04937319	Pfizer
45.	Fesoterodinefumarate (PF-00695838)	Pfizer
46.	PF-04937319	Pfizer
47.	PH 797804	Pfizer
48.	Ranolazine	Klinera
49.	BAX326 (recombinant factor IX)	Baxter
50.	Brinzolamide 10 mg/mL / Brimonidine 2 mg/mL Eye Drops, Suspension	Alcon lab
51.	Starplus^{TM}Starch acetate (high amylose maize starch 6% acetate)	Christian Medical College
52.	CD0271 (Adapalene)	CIPD
53.	AUS-131 (S –Equol)	Novotech
54.	BCD-020 (Rituximab)	SMO
55.	DEB025 (Alisporivir)	Novartis
56.	AZD4547	AstraZeneca
57.	Palifosfamide-tris	PPD
58.	Lucanthone	OncoRx Pharma Pvt. Ltd
59.	Lurasidone	Quintiles
60.	OPT-822	Clinigene
61.	Preladenant	Fulford
62.	Vernakalant Hydrochloride (MK-6621	MSD
63.	Extended Release Niacin/Laropiprant	Covance
64.	Niacin/Laropiprant	Covance
65.	Tamibarotene	Veeda
66.	BMS-820836 (Liafensine)	BMS
67.	BMS-820836 (Liafensine)	BMS
68.	Teriparatide	Eli Lilly
69.	YKP3089	Quintiles
70.	Kedrion Factor VIII concentrate (EMOCLOT)	MAX Neeman
71.	Sevuparin / DF02	MAX NEEMAN
72.	AR-12286 Ophthalmic Solution,0.5%	MAX NEEMAN
73.	EGT0001442	MAX NEEMAN
74.	Esmolol hydrochloride (Galnobax®)	SIRO
75.	BAX 326 (Recombinant Factor IX)	Baxter
76.	Atripla (r) Drug: EfavirenzDrug: Truvada Drug: Rifampin/isoniazid/pyrazinamide/ethambutol FDC Drug: Rifampin/isoniazid FDC	NARI

77.	SeeMoreTM(EVP 1001-1 Injection)	Kentron
78.	Tenofovir + Emtricitabine + Efavirenz	YRG
79.	Gentian Violet	BJ Medical college/NARI
80.	THR-18 (Tissue plasminogen activator)	Infinitus
81.	nabiximols	PRA
82.	Sitagliptin + Metformin	MSD
83.	CP690,550 F C (Tofacitinib) Tablet	Pizer
84.	CP,690,550 TOFACITINIB	Pizer
85.	Tofacitinib	Pizer
86.	CP-690,550	Pizer
87.	CP-690,550(Tofacitinib)	Pizer
88.	CP-690,550 (Tofacitinib)	Pizer
89.	Oxycodone/Naloxone	Kendle
90.	SOLIFENACIN (approved in INDIA)	PPD
91.	Eltrombopag	GSK
92.	Ofatumumab	GSK
93.	OPC-34712 (Brexspipraezole)	Quintiles
94.	EN3348 (Mycobacterial cell wall DNA complex)	Diagnosearch
95.	Armodafinil (CEP-10953)	inVentiv
96.	Armodafinil (CEP-10953) 50mg uncoated tablet	inVentiv
97.	Recombinant Human Coagulation Factor IX Fusion Protein (rFIXFc)	Biogen Idec
98.	Etanercept	Pfizer
99.	Teriparatide (rDNAorgin) Injection (LY333334)	Eli Lilly
100.	V212 Inactivated Varizella Zoster Virus Vaccine	MSD
101.	Aripiprazole	Covance
102.	Aripiprazole	Covance
103.	BA058 (Teriparatide) for injection 80µg	Pharmanet
104.	BIBW 2992(Afatinib)-20/30/40 mg	Boehringer
105.	BI10773 (Empagliflozin)	Boehringer
106.	DALCETRAPIB	Quintiles
107.	Eprotirome	MED PACE

Annexure-II

Sr. No.	Drug	Names of the Applicant	Division
1.	Treprostinil	PRA. India	GCT
2.	Treprostinil	PRA. India	GCT
3.	SB4 (Proposed Etanercptbiosimilar) or EU Sourced Enbrel	Quintiles Pvt. Ltd	GCT
4.	SB2 (PropsedBiosimilar of Remicade)	Quintiles Pvt. Ltd	GCT
5.	Belimumab	Quintiles Pvt. Ltd	GCT
6.	AIN457 (Secukinumab)	Novartis Healthcare	GCT
7.	Rituximab	Cliantha Research Limited,Ahmedabad	GCT
8.	Afatinib (BIBW 2992)	BoehringerIngelheim India Pvt Ltd.	GCT
9.	Afatinib	BoehringerIngelheim India Pvt Ltd.	GCT
10.	LDK378	Novartis Healthcare	GCT
11.	MasitinibMesylate	Maya Clinicals	GCT
12.	MasitinibMesylate	Maya Clinicals	GCT
13.	BCD-020	CJSC BIOCAD	GCT
14.	Linagliptin	ManipalAcunova limited	GCT
15.	Biochaperone	Virchow Biotech Pvt.	Biological (Recombinant)
16.	Trastuzumab	Cadila Healthcare Limited,	Biological (Recombinant)
17.	Ranibizumab	Novartis Healthcare	Biological (Recombinant)
18.	Albumin	Dr. Kapildevsoni	Biological
19.	Typhoid Vi Capsular polysaccharide- tetanus toxoid conjugative vaccine(TYPBAR-TCV)	Bharat biotech International Ltd.	Biological (Vaccine)
20.	Varicella Vaccine, Live (I.P.)	Bio-Med Private Limited	Biological (Vaccine)
21.	Monovalent Oral Poliovirus Vaccine type 3 (mOPV3) and Azithromycin	Christian Medical College	Biological (Vaccine)
22.	Cyclophosphamide	Dr. Lalit Kumar, AIIMS,	Institutional CT
23.	Bisphosphonate	Dr. SiddharthDubey, AIIMS	Institutional CT
24.	Transarterial Chemoembolization	Dr. Madhusudhan KS	Institutional CT

25.	Probiotic VSL#3	Dr. ArvindSaili, Lady Hardinge Medical College	Institutional CT
26.	Chlorhexidine	Dr. Vinod Kumar Paul, AIIMS	Institutional CT
27.	Tizanidine	Dr. Pratibha.D.Singhi, P.G.I.M.E.R.	Institutional CT
28.	Guaifenesin 600mg Extended Release Bi- layer Tablets.	ManipalAcunova Ltd	SND
29.	Clindamycin phosphate 1.2% and Benzoyl peroxide 5%, topical gel	Cliantha Research Limited	GCT
30.	BepotastineBesilate Ophthalmic Solution	Ajanta Pharma Limited	NDA
31.	Phentermine hydrochloride	Cadila Healthcare Ltd.	NDA
32.	On X Mechanical heart versus SJM Mechanical valve	IProcess Clinical Marketing process Pvt. Ltd	Medical Device
33.	BKM120	Novartis	GCT
34.	Trastuzumab	Biocad	GCT
35.	Bevacizumab	Biocad	GCT
36.	Cyclosporine Ophthalmic Emulsion 0.05 %	AurobindoPharma Ltd.	GCT

Annexure-III

Sr. no.	Drug Name	Recommendation(s) of the Committee
1.	Clofarabine	**Applicant: M/s Sandor** This Directorate has received an application for grant of permission to import and market Clofarabine concentrate 1mg/ml for solution for infusion. It is proposed to be indicated for the treatment in patient's ≤ 21 years old at initial diagnosis with relapsed or refractory acute lymphoblastic leukaemia (ALL) after at least 2 prior regimens. Clofarabine injection 1mg/ml, 20ml vial is reported to be approved for marketing in USA and EU. Earlier, the proposal of the firm was referred to five independent experts out of which four experts recommended foe giving marketing permission for the drug. Clofarabine was deliberated by the NDAC (Oncology & Haematology) in its meeting held on 17.08.2012 wherein the NDAC recommended that the firm should submit the PMS data generated so far with the drug which should be provided to the members for examination and final recommendation on the proposal. The firm submitted the data/information as recommendation above by NDAC meeting held on 09.03.2013 where in the NDAC considered the request for waiver of local clinical trial and recommended for approval of the drug subjects to condition that the firm should follow up all the patients treated with the drug as part of post marketing surveillance. The Committee recommended that the drug Clofarabine which is indicated for the treatment of patients with relapsed or refractory acute lymphoblastic leukaemia after atleast two prior regimen, could be appropriate current third line

		treatment for the indication. Therefore the Committee recommended for giving approval to market the drug in the country subject to the condition that the drug should be manufactured in the country.
2.	Vorinostat	**Applicant: M/s Hetero Labs** This Directorate has received an application for grant of permission to manufacture and market Vorinostat 100mg capsule indicated for the treatment of Cutaneous manifestation's in patients with cutaneous T-cells lymphoma. It is reported that the product is approved by USFDA since 2006. The Proposal of the firm was placed 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. The Committee recommended that the proposal should be forwarded to the NDAC for reconsideration of waiver of local clinical trial in public interest.
3.	Pegasparagase	**Applicant: M/s. Gennova Biopharmaceuticals Limited** This Directorate has received an application for grant of permission to for manufacture and market Pegaspargase 3750IU/5ml indicated for the component of a mult-agent chemotherapeutic regimen for the treatment of patients with:- 1. First line acute lymphoblastic leukemia. 2. Acute lymhoblastic leukemia and hypersensitivity to asparginase.

		The drug is reported to be approved and marketed in USA, Mexico, Canada etc. The Proposal of the firm was placed before the NDAC (Oncology & Haematology) committee in its meeting held on 10.12.2011. The NDAC recommended that 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. Further, post marketing (Phase-IV trial) comparative trial of the firm's product vis-à-vis innovator's product should be conducted. The Proposal of the firm was again placed before the NDAC (Oncology & Haematology) committee in its meeting held on 08.12.2012. The NDAC noted that Lymphoblastic leukemia 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. The firm did not present supportive literature showing superiority or at least non-inferiority of pegaspergase over L-asparaginase. NDAC recommended that a single dose bioequivalence study comparing Genova's product with the innovator's product in patients with refactory cancer should be conducted. If B/E result is satisfactory, permission can be granted. The Committee opined that in patients with acute lymphoblastic leukemia who are hypersensitive to asparaginase, presently there is no option. Therefore the Committee recommended for approval of manufacturing & marketing of Pegasparagase injection for the treatment of acute lymphoblastic leukemia who are hypersensitive to asparaginase. As regards to the proposal to market the drug as first line treatment in acute lymphoblastic leukemia, the Committee recommended that therapeutic drug monitoring study in patients should be conducted after getting protocol approved from DCGI for further consideration.
4.	Nelarabine	**Applicant:M/s. Natco Pharma** This Directorate has received an application for

		grant of permission to manufacture and market Nelarabine injection5mg/ml indicated for the treatment of T-cell Lymphoblastic Leukemia and Lymphoma(T-LBL) whose disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens The drug is reported to be approved and marketed in US and EU. The Proposal of the firm was placed before the NDAC (Oncology & Haematology) committee in its meeting held on 21.01.2012. The NDAC opined that 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 lympho blastic 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. After deliberation, the Committee opined that the drug is indicated for the treatment of T-cell Lymphoblastic Leukemia and Lymphoma whose disease has not responded or has relapsed following treatment with at least two chemotherapy regimens for which currently there is no therapy. Therefore the Committee recommended for giving permission to manufacture & market the drug subject to condition that phase-IV clinical trial should be conducted after getting protocol etc. approved from DCGI.
5.	Fomepizole	**Applicant: M/s Cadila Healthcare Limited** This Directorate has received an application for grant of permission to manufacture the bulk drug of Fomepizole and manufacture and market Fomepizole injection 1gm/ml indicated for the

		treatment of ethylene glycol or methanol poisoning, or for the use in suspected ethylene glycol or methanol ingestion, either alone or in combination with haemodialysis. The drug is already approved in USA,UK, Canada and Israel Fomepizole was deliberated by the NDAC (Antimicrobial, Antiparasitic & Antifungal, Antiviral) in its meeting held on 28.09.2012. The NDAC noted that Methanol and glycol poisoning are unexpected and unpredicted events often not at sites of immediate vicinity of hospitals. Therefore a time bound and protocol based clinical trial may not be feasible. The drug is already approved in USA, UK etc. Therefore committee recommended for approval of the drug based on the published data submitted by the firm subject to the condition that all efforts will be made to get the information of drug use pattern and PMS data. This data should be presented before the committee after 1 year. After deliberation, the Committee opined that Fomepizole is indicated for the treatment of ethylene glycol or methanol poisoning, for the use in suspected ethylene glycol or methanol ingestion, either alone or in combination with hemodialysis. Therefore, a time bound protocol based clinical trial may not be feasible. Hence the Committee recommended for the approval of the drug subject to condition as recommended by the NDAC.
6.	Fingolimod	**Applicant: M/s Sun Pharma, M/s MSN Labs** This Directorate has received an application for grant of permission for the grant of permission to manufacture and market Fingolimod Hydrochloride 0.5mg Capsule indicated for the treatment of patients with relapsing forms of Multiple Sclerosis (MS) to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability. The drug is approved in USA, UK, European Union, Australia & Switzerland. The Proposal of the firm was placed before the NDAC (Neurology & Psychiatry) committee in its

		meeting held on 17.12.2011. The NDAC recommended for approval for manufacture and marketing the drug in the country subject to condition that the single dose BE study is carried out and product is proven to be bioequivalent with the innovator product and after approval of the drug, the phase IV clinical trial should be conducted on 100 subjects within a period of 2 years. The protocol for the phase IV study should be submitted within1 month of approval of the drug to DCGI for approval. The recruitment shall be initiated within one month of approval of protocol and the status should be submitted to the office of DCGI on monthly basis. Recruitment of the subjects should be at least at the rate of 25% of the total subjects quarterly. The interim analysis of the data shall be carried out every six month after 1st recruitment of the patient and submitted to the office of DCG(I). After deliberation, the Committee opined that the proposal doesn't meet the criteria for waiver of local clinical trial. Therefore, the committee recommended that local clinical trial in Indian patient is required to be conducted with the drug before considering its approval for marketing in the country.
7.	Pasireotide	**Applicant** : **M/s Novartis Healthcare Pvt. Ltd.** This Directorate has received an application for grant of permission to import & market Pasireotide solution for injection 0.3mg/1ml, 06.mg/1ml and 0.9mg/1ml indicated for the treatment of Cushing's disease. The drug is reported to be approved by European Union on 23.02.2012 and orphan drug designation is given in US and Europe. The Proposal of the firm was placed before the NDAC (Metabolism and Endocrinology) committee in its meeting held on 23.03.2013. The NDAC opined that Cushing's disease is a very rare disease and life threatening disease for which there is no medical therapy. The NDAC recommended for approval of the drug without local clinical trial subject to condition that Phase IV clinic al trial on atleast 50 patients with one

		year duration of treatment should be conducted. After getting protocol etc. approved from DCG(I). The marketing permission should be reviewed after one year. After deliberation, the Committee opined that the drug is indicated for the treatment of cushing's disease for which there is no medical therapy. Therefore, the Committee recommended that clinical trial waiver may be granted for giving permission to manufacture & market the drug subject to condition that PMS study should be conducted as per recommendation of NDAC.
8.	FDC of Episil	**Applicant: M/s. Biocon Limited** This Directorate has received an application for grant of permission to import and market Fixed Dose Combination of episil™ which is a multidose spray device containing six ingredients i.e. Glycerol dioleate, Soy phosphatidylcholine (lecithin), Ethanol, Propylene glycol, Polysorbate 80mg and peppermint oil oromucosal liquid for the treatment of oral mucositis. It is approved in USA, Sweden and Israel. The proposal was deliberated by NDAC (Oncology and Hematology) in its meeting held on 08.12.2012 and the NDAC opined that 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 NDAC 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 at least 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 NDAC for review.

		The firm again made presentation of data/ information to support their claims that the product is medical device before the NDAC in its meeting held on 26.08.2013. The firm also presented safety and efficacy data. The NDAC opined that the product is a new drug not a medical device in Indian scenario. As regards to waiver of clinical trial the NDAC recommended that the firm may wait till the recommended of Prof. Ranjit Roy Chaudhary committee in this regards is considered by the government. Alternatively firm may conduct clinical trial after getting protocol etc. approved from CDSCO After deliberation, the Committee opined that the proposal doesn't meet the criteria for waiver of local clinical trial. Therefore, the Committee recommended that local clinical trial in Indian patient is required to be conducted with the drug before considering its approval for marketing in the country.
9.	Azacitidine	**Applicant: M/s Intas & M/s Natco Pharma Limited** This Directorate has received an application for grant of permission to manufacture & market Azacitidine 100 mg/vial indicated for the treatment of adult patients who are not eligible for haematopoietic stem cell transplantation (HSCT) with: • Intermediate-2(INT-2) and high-risk myelodysplastic syndromes (MDS) according to the International Prognostic Scoring System (IPSS), • Chronic myelomonocyticleukaemia (CMML) with 10-29 % marrow blasts without myeloproliferative disorder, • Acute myeloid leukaemia (AML) with 20-30 % blasts and multi-lineage dysplasia, according to World Health Organisation (WHO) classification. It is reported that the drug is approved by US- FDA since 19.05.2004, EMEA December 2008 Israel, UK since 2001, Philippines, Hong Kong, Japan, Turkey, Thailand, Argentina & South Korea. The Proposal of the firm was placed before the NDAC (Oncolgy & Haematology) committee in its meeting held on 18.10.2013. The NDAC 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 disease. • 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 only. The result 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. NDAC Committee recommended for giving waiver of clinical trial and recommended for giving permission to manufacture and market the drug in the country to the firm. After deliberation, the Committee opined that the drug is indicated for the treatment of all sub types of myelodys plastic syndrome which is rare disease and there is no medical therapy. Therefore, the Committee recommended that clinical trial waiver may be granted for giving permission to manufacture & market the drug as per recommendation of NDAC.
10.	Rigorafinib	**Applicant**: **M/s Bayer Pharma** This Directorate has received an application for grant of permission to import & market Regorafenib film coated Tablet 40mg indicated for the treatment of patients with metastatic colorectal cancer (CRC) who have been previously treated

		with, or are not considered candidates for, fluoropyrimidine –based chemotherapy, an anti-VEGF Therapy and if KRAS wildtype, an anti-EGFR therapy It is reported that Regorafenib is approved by USFDA on 27.09.2012. The proposal was deliberated in NDAC (Oncology and Haematology) in its meeting held on 26.08.2013. The NDAC (Oncolgy & Haematolgoy) opined that the proposed drug is for treatment of Colorectal Cancer which is unmet need. The firm presented the phase-III clinical trial data in which Indian population was not enrolled. The firm requested the grant of clinical trial waiver. The NDAC recommended for grant of permission for import and marketing of Regorafenib 40mgTablet for subject to the condition to conduct of phase IV clinical trial and submit the protocol before the NDAC. However Prof. Dr. Ranjit Roy Chaudhary committee recommendation should be referred for grant of clinical trial waiver. After deliberation, the Committee opined that the drug is indicated for the treatment of patients with metastatic colorectal cancer (CRC) who have been previously treated with, or are not considered candidates for, fluoropyrimidine -based chemotherapy, an anti-VEGF Therapy and if KRAS wildtype, an anti-EGFR therapy, for which currently there is no medical therapy available. Therefore the Committee recommended for giving permission to import& market the drug subject to condition that phase-IV clinical trial should be conducted after getting protocol etc. approved from DCGI.