1. RECOMMENDATIONS OF THE NDAC (ANTIMICROBIAL, ANTIPARASITIC, ANTIFUNGAL AND ANTIVIRAL) HELD ON 11.02.2012:-

The NDAC (Antimicrobial, Antiparasitic, Antifungal and Antiviral) deliberated the proposals on 11.02.2012 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
1	**Ulinastatin**		The committee noted that sepsis is a serious/life threatening disease where mortality rate is very high. The firm also clarified on various points raised by the experts. After deliberation committee recommended for approval of the drug subject to the following conditions:- i.) The drug should be supplied to hospital only and the label/package insert should mention "For hospital use only". ii.) The drug should be used in hospitalized patients (Intensive Care Unit /High Dependency Unit). iii.) Post marketing (Phase IV) comparative trial should be conducted on at least 200 patients within 2 years of approval. iv.) Protocol for the said phase IV study should be submitted within 3 months of approval v.) Package insert to be circulated should be got evaluated by the committee before the product is launched for marketing in the country.
2	**Nimorazole**		Committee recommended that double-blind, double dummy phase III clinical trial in Indian subjects should be conducted. Accordingly protocol, names of sites, investigators etc should be submitted for evaluation by the committee. Clinical trial sites should be geographically distributed in the country and at least 50% of the sites should be in multispeciality hospitals.
3	**Sulindac**		The committee recommended that the proposed clinical trial should be double blind, double dummy study in patients with osteoarthritis. Accordingly revised protocol should be submitted to DCG(I) for approval. Clinical trial sites should be geographically distributed in the country and at least 50% of the sites should be in multispeciality hospitals. The clinical trial

			data generated should be placed before the committee for further action. As regards to the other indication proposed for the drug, the committee opined that based on data of clinical trial generated in osteoarthritis, approval of the drug for other indications also can be considered subject to PMS study. Above decision will apply for all the applicants seeking approval for this drug.
4	**Octenidine**		Committee recommended that detailed post marketing data generated in those countries where the drug is marketed should be submitted to the office of DCGI which shall be evaluated by the committee by circulation for taking further decision in the proposal.
5	**Rilpivirine**		The drug is indicated for HIV which is a serious and life threatening disease. Committee recommended for approval of the drug subject to post marketing trial (phase IV trial). However before approval the firm should conduct single dose bioequivalence study and the data should be submitted to the office of DCG(I).
6	**Boceprevir**		Committee recommended for approval of the study subject to the following conditions:- i.) Subjects aged ≥ 18 yrs and ≤ 65 yrs should be enrolled in the study. ii.) Pregnant and lactating women should be excluded from the study.
7	**Conjugated Estrogen Injection**		Committee recommended for approval of the study subject to condition that the study should be titled as a pilot study. It should be randomized study and all subjects should receive standard care of therapy. One group should receive conjugated estrogen and other group shall receive placebo. The subjects should be given single dose of estrogen or placebo.
8	**Meropenem 1000mg/500mg +Tazobatum 125mg/62.5mg Injection**		Committee recommended that protocol should be revised as follows:-. Phase III clinical trial should be conducted on 300 patients in which subjects should be randomized in a 1:1:1 ratio to receive any one of the following.

			i.) Meropenem + Tazobactum in the ratio of 8:1 ii.) Meropenem + Tazobactum in the ratio of 4:1 iii.) Meropenem The study should be conducted at 4 sites geographically distributed in the country and there should be clinician involved in the study at each site. Complete undertakings of the Investigators as per Appendix VII of Schedule Y should be submitted alongwith the revised protocol to the office of DCG(I) for approval. The clinical trial data so generated should be placed before the committee for evaluation and further action.
9	**Clobetasol Propionate+ Ofloxacin+ Ornidazole+ Terbinafine (0.05%+0.75%+2.0 %+1.0% w/w)**		Firm has withdrawn their proposal. Committee did not recommend the FDC as the same was found to be irrational and committee stated that a physician should be able to diagnose a bacterial, protozoal, fungal, or allergic/autoimmune disorder and then treat them accordingly. Preparing & using this cream means, treating the disease without diagnosis and there may be drug-drug interaction also. Further there is no rationale in combining all these four drugs.
10	**Chromium Picolinate 250mcg +Folic Acid 1mg +Inositol 100mg +Lycopene 3mg +Nicotinamide 100mg +Selenium 100mcg +Vitamin B6 3mg +Vitamin B12 15mcg +Zinc Sulphate 61.08mg Tablet**		Committee recommended for approval as vitamin/mineral supplementation in vitamin/mineral deficiency.
11	**Sulphadoxine-Pyrimethamine**		Committee agreed for the proposed study design subject to the following conditions:- i.) Subjects aged ≥ 18 yrs and ≤ 45 yrs should be enrolled in the study. ii.) Subjects with haemoglobin level < 7 should be excluded. iii.) Subjects with parasitemia positive should be excluded. However the committee recommended that before giving approval of the study by DCG(I), the applicant

			should submit the details to DCG(I) of sites where the study will be conducted alongwith names of Investigator, his/her C.V. alongwith Undertaking by the Investigators for each site. After submission of above documents, DCG(I) may give permission for conducting the proposed clinical trial.
12	**CXA 201**		Committee recommended for approval subject to condition that subjects aged ≥ 18 yrs and ≤ 65 yrs should be enrolled in the study. However before formal approval, the firm should submit clinical study report of Phase II study and copy of approval of the study from other countries to the office of DCG(I).
13	**Tafenoquine**		Committee agreed in principle for the combined Phase 2b and Phase 3 study. However the firm should be allowed at present to conduct the phase 2b part of the protocol subject to the following conditions:- i) 15% of the subjects in India should undergo ophthalmologic assessment. ii) Subjects aged ≥ 16 yrs and ≤ 65 yrs should be enrolled in the study. After completion of the Phase 2b part of the protocol, the firm will submit completely analyzed data of phase 2b which will be examined by the committee to consider the phase 3 part of the study
14	**Reduced dose Efavirenz (EFV)**		Committee recommended for approval subject to the following conditions:- i.) Subjects aged ≥ 18 yrs and ≤ 65 yrs should be enrolled in the study. ii.) COA of the Investigational Product should be submitted to the office of DCG(I).
15			Committee recommended for approval subject to the following conditions:- i.) Subjects aged ≥ 18 yrs and ≤ 65 yrs should be enrolled in the study. ii.) COA of the Investigational Product should be submitted to the office of DCG(I). iii.) Blood culture should be mandatory to have data on NDM and MTB complex.

16	**Rifapentine/ Isoniazid**		Proposed study is to compare 4 weeks daily rifapentine/isoniazid regimen to a standard 9 months daily isoniazid for prevention of TB in HIV infected patients without active TB. Committee desires sound justification for the proposed regimen of Rifapentine/isoniazid in view of recently published articles in NEJM showing efficacy of weekly rifapentine/INH 900mg doses equivalent to 9 months efficacy of daily dose of INH. Compliance issue and post trial cost implementation should also be submitted.

2. RECOMMENDATIONS OF THE NDAC (ANTIMICROBIAL, ANTIPARASITIC, ANTIFUNGAL AND ANTIVIRAL) HELD ON 14.04.2012:-

The NDAC (Antimicrobial, Antiparasitic, Antifungal and Antiviral) deliberated the proposals on 14.04.2012 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
1	**Ambisome, Miltefosine, Paromomycin**		Committee recommended for giving permission to conduct the study subject to the following conditions:- i) Pediatric patients should be enrolled only in district hospitals under direct supervision of pediatricians who will be the investigators for the sites. The Undertaking from the pediatricians (Investigators) should be submitted to DCG(I) as per appendix VII of Schedule Y before initiation of the study. ii) In case of pediatric patients, informed consent should be taken from their parents. In case parents are not available, informed consent should be obtained from legally acceptable representative of the subject. iii) The pediatric patients should be followed up on long term basis as part of pharmacovigilance. iv) Undertaking by the Investigators from all the PHCs and the district hospitals should be submitted to DCG(I) before initiation of the study.
2	**Etravirine 100mg Tablets**		Committee recommended for giving permission to market the drug subject to the following conditions:- i) It should be used only in situations where other treatments have failed or cannot be used because of side effects. For such situations, there is an unmet need of anti HIV drugs and local clinical trial is waived off. ii) The formulation should be tested at IPC before launching the product in the market.

			The other applicants for manufacturing permission should conduct single dose Bioequivalence study in Indian subjects and the data should be submitted to DCG(I) for his consideration and approval.
3	**Sorivudine 3% cream**		The firm clarified that the proposed study is planned to be conducted for development of the drug for India. The study is a comparative study of Sorivudine cream versus Acyclovir cream in herpes zoster patients. The committee opined that acyclovir cream is not standard care for herpes zoster. Therefore committee did not recommend for the proposed study. In case the firm proposes to conduct clinical trials comparing with standard care of therapy for herpes zoster, revised protocols etc. should be placed before the committee for consideration.
4	**Cefozopran Hydrochloride Injection**		The drug is available only in Japan and the clinical data submitted is not adequate. Committee recommended that the firm should submit reports of Phase II clinical trials generated with the drug in proposed indication and same should be placed before the committee for further consideration of their proposed phase III clinical trial.
5	**Antiretroviral drugs**		During presentation the firm clarified that they will conduct the study in India on 75 subjects out of 600 subjects globally. The committee recommended for giving permission to conduct the study subject to the following conditions:- i) The applicant should submit an undertaking before initiation of the study that number of subjects from India in the study will be 75. ii) Another undertaking stating that the patients who benefit from the study will be given the medications under post trial access programme should be submitted by the applicant. iii) COA of the Investigational Drugs should be submitted to DCG(I) before initiation of the study. iv) Upper age limit of subjects to be included in the study should be 65.

6	**Antiretroviral drugs**		The committee recommended for giving permission to conduct the study subject to the following conditions:- i) COA of the Investigational Drugs should be submitted to DCG(I) before initiation of the study. ii) The applicant should submit an undertaking stating that the patients who benefit from the study will be given the medications under post trial access programme. iii) Upper age limit of subjects to be included in the study should be 65.
7	**Antiretroviral drugs**		Committee did not recommend the protocol due to the following points:- i) Regimen used is not the one used under national programme. ii) With clear national and global guidelines to promote breast feeding in HIV positive infants, it is not appropriate to recommend the trial of this nature. iii) Those who are on ART for at least > 4 weeks prior to delivery will be eligible for the study and HAART regimen will be changed for participating in the study. In one study arm HAART will be discontinued after delivery. This leads to serious ethical concern because the women had been started on ART for her own health and changing regimen for research purpose may not be appropriate. If the applicant submits revised protocol addressing the above issues, the same may be placed before the committee for further consideration.
8	**CXA201**		The committee recommended that the applicant should submit Phase II clinical study report of CXA 201 and details of sites, Investigators, their CVs, Ethics Committees, its members alongwith SOPs for various activities and the same should be placed before the committee for further consideration.

9	**Etravirine**		The firm has withdrawn their proposal.
10	**Stavudine**		The committee recommended for giving permission to conduct the study subject to the condition that upper age limit of patients to be included in the study should be 65 years.
11	**A-623 (Blisibimod)**		The committee recommended for giving permission to conduct the study subject to the condition that the treatment period in the extension study is initially limited for a period of 1 year. Within the 1 year period, the firm shall submit data of the core Phase II study for consideration of the extension study for further period. Before grant of formal approval, the firm should submit an undertaking to DCG(I) in this regard.
12	**Sifalimumab**		The committee recommended for giving permission to conduct the study subject to the condition that the upper age limit of patients should be 65 years**.**

3. RECOMMENDATIONS OF THE NDAC (ANTIMICROBIAL, ANTIPARASITIC, ANTIFUNGAL AND ANTIVIRAL) HELD ON 25.05.2012:-

The NDAC (Antimicrobial, Antiparasitic, Antifungal and Antiviral) deliberated the proposals on 25.05.2012 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
1	**Artesunate 100mg + Lumefantrine 480mg Tablets**		Committee recommended that firm should conduct pharmacokinetic study with the combination after which a Phase III study should be conducted in statistically significant number of subjects in clinical trial sites geographically distributed across the country out of which at least 50% sites should be selected from government hospitals. Protocol for PK study should be submitted to DCG(I) for approval, however, complete protocol for Phase III study should be placed before the committee for approval.
2	**Artemether 60mg + Lumefantrine 360mg tablet**		Committee observed that the combination is already approved in various strengths for the same indication. Patient compliance will be better with the new strength of the FDC. Therefore, the committee recommended for the grant of permission to market the product.
3	**Artesunate 25mg/50mg/100mg + Piperaquine Phosphate 105mg/210mg/420mg tablets**		Committee recommended that Pharmacokinetic study, Phase II (Dose finding) study and Phase III study is required to be conducted with the combination in a Phasewise manner. Accordingly, initially protocols etc. for PK study and Phase II (Dose finding) study should be placed before the committee for approval.
4	**Cefuroxime 250/500mg + Ofloxacin 100mg/200mg Tablets**		FDC of Cefuroxime 250/500mg +Ofloxacin 100mg/200mg Tablets is not approved anywhere in the world. There is no literature supporting the use of combination of Cefuroxime 250/500mg + Ofloxacin 100mg/200mg Tablets in uncomplicated UTI and typhoid fever.

			The use of such FDC may also lead to development of resistance, therefore the committee did not recommend the grant of permission for the product.
5	**Nadifloxacin 1% + Adapalene 0.1% w/w Gel**		The clinical trial data submitted by the firm is not adequate. The FDC is not approved anywhere in the world. Committee recommended that firm should conduct a three arm study comparing combination of Nadifloxacin + Adapalene Vs. Nadifloxacin Vs. Adapalene on statistically significant number of subjects in sites geographically distributed across the country out of which at least 50% sites should be selected from government hospitals. Complete protocol for the three arm study should be placed before the committee for approval.
6	**Ferrous Ascorbate 33 mg + Folic Acid 5mg + Vitamin B12 15mcg Capsules**		Committee recommended that firm should conduct clinical trial on atleast 300 subjects in clinical trial sites geographically distributed across the country out of which at least 50% sites should be selected from government hospitals. Complete protocol for the study should be placed before the committee for approval.
7	**Cephalexin ER 375/750mg + Clavulanate Potassium 125mg Tablet**		FDC is not approved in any country and futher the clinical trial data generated by the firm is not adequate to support the efficacy of the formulation. Therefore, the committee did not recommend for the FDC.
8	**Imipenem 1g + Cilastatin 1g powder for injection**		Committee observed that same drug product is available in the country in lower strengths (Imipenem 250/500mg + Cilastatin 250/500mg) and in serious cases there is a requirement of higher dose of Imipenem 1gm + Cilastatin 1gm and recommended dose of Imipenem is 1 to 4gm per day. In addition to convenience in administration of the higher strength in such patients it will be economical also as stated by the representative of the firm. In view of above, committee recommended for the grant of permission to

			market the FDC of Imipenem 1gm + Cilastatin 1gm Powder for Injection in adults.
9	**Smofkabiven Emulsion for infusion**		Committee recommended that Phase III clinical trial with the product is required to be carried out in the country at clinical trial sites geographically distributed across the country. The firm should therefore submit complete protocol for Phase III trial to the committee for approval.
10	**Smofkabiven Peripheral Emulsion for infusion**		Committee recommended that Phase III clinical trial with the product is required to be carried out in the country at clinical trial sites geographically distributed across the country. The firm should therefore submit complete protocol for Phase III trial to the committee for approval.
11	**Smofkabiven electrolyte free emulsion for infusion**		Committee recommended that Phase III clinical trial with the product is required to be carried out in the country at clinical trial sites geographically distributed across the country. The firm should therefore submit complete protocol for Phase III trial to the committee for approval.
12	**Ferrous Bisglycinate chelate 60mg + Zinc 15mg + Folic Acid 1mg + Cyanocobalamin 5mcg tablets**		In the clinical trial, there was no difference observed in terms of efficacy in 60 and 120mg groups of elemental iron from ferrous bisglycinate. The FDC is not approved in any other country. The committee opined that data on this FDC is not adequate. Hence the committee did not recommend for the grant of permission for the FDC.
13	**Fish Oil (Docosahexaenoic Acid) 500mg/250mg(200mg/100 mg) + Folic Acid 5mg soft gelatin capsules**		The firm has applied for DHA and Folate supplementation. There is no information on DHA deficiency and the management by exogenous DHA. The data submitted is also not adequate in support of use of the product in vitamin and mineral deficiency.

			In view of above the committee did not recommend for the product.
14	**Ferrous Fumarate 150mg + L-Histidine HCl 4 mg + L-Lysine HCl 25mg + Glycine 10mg + Pyridoxine 1.5mg + Folic Acid 0.5mg + Cyanocobalamin 2.5mcg Capsules**		The committee observed that the data submitted in support of the use of the product for anaemia due to nutritional deficiencies, iron deficiency secondary to peptic ulcer, pregnancy & lactation, anaemia due to heavy bleeding during menstruation, prophylaxis in iron deficiency status is not adequate. In view of above, the committee did not recommend for the grant of permission for the product.
15	**FDC of Amino acids, minerals and vitamins**		The committee observed that the data submitted in support of the use of the product an adjunct to anti-diabetic drugs and antihypertensives. Physical and mental stress. Post operative recovery, nutritional supplement during pregnancy and lactation is not adequate. In view of above, the committee did not recommend for the grant of permission for the product.
16	**Zoonocide-surface protectant and disinfectant**		Committee recommended that firm should conduct a disinfection test in Indian conditions on Gram +ve(S.aureus), Gram-ve (E.Coli) and Fungi – Candida as per WHO guidelines and submit the report which should be placed before the committee for consideration.
17	**Germ Free 24 -surface protectant & disinfectant**		Committee recommended that firm should conduct a clinical trial with the product in Indian subjects on Gram +ve(S.aureus), Gram-ve (E.Coli) and Fungi – Candida as per WHO guidelines. Protocol for the study should be submitted to the DCG(I) for his approval. The results of the study should be placed before the committee for approval.
18	**Conivaptan Hydrochloride 20mg/4ml injections**		Committee observed that the drug is indicated for euvolemic hyponatremia in hospitalized patients which is life threatening condition. The committee recommended for the grant of

			permission for the drug subject to condition that firm should conduct Phase IV study with the product in atleast 300 subjects at study centres geographically distributed across the country and protocol should be submitted to the office of DCG(I) before approval of the drug.
19	**Cefditoren Pivoxil Dry Powder for Suspension 100mg/5ml**		Committee recommended for the grant of permission to conduct the proposed Bioequivalence study.

4. RECOMMENDATIONS OF THE NDAC (ANTIMICROBIAL, ANTIPARASITIC, ANTIFUNGAL AND ANTIVIRAL) HELD ON 28.09.2012:-

The NDAC (Antimicrobial, Antiparasitic, Antifungal and Antiviral) deliberated the proposals on 28.09.2012 and recommended the following:-

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
1	**Cefozopran Hydrochloride Injection**		Committee recommended for giving permission to both the protocols – i) Community Acquired Pneumonia (CAP) and ii) Complicated Urinary Tract Infections and Pyelonephritis subject to the following conditions:- In case of CAP trial, following two reasons for hospitalization mentioned in the inclusion criteria should be deleted: a) Inability to take therapy. b) Clinical judgment of Investigators The reason for hospitalization should include two or more criteria specified. In case of Complicated Urinary Tract Infections and Pyelonephritis trial, intravenous treatment in both the arms should continue for 7 days. After that it should be switched over to oral therapy.
2	**Liposomal Amphotericin B**		Committee recommended for giving permission to conduct the study subject to the following conditions:- i) Intercurrent illness should be defined. ii) The study may be conducted only at the District Hospital Level. After completion of 300 patients' data with safety, operational feasibility and efficacy, the data should be submitted for evaluation of the committee for consideration of proposal of conducting the study at PHC level. iii) Test dose is mentioned as 1mg at one place and 5mg at another place. It should be specified as 1mg. iv) Rescue treatment should be given to those who do not respond and those who

			deteriorate. v) Undertaking by the Investigator as per Appendix VII of Schedule Y from each District Hospital should be submitted.
3	**Fomepizole Injection**		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.
4	**Monofer solution for injection**		During the presentation the firm requested for waiver of local clinical trial and sought marketing approval of the drug for iron deficiency anemia when oral therapy is not feasible. The firm is conducting clinical trials in Indian patients as part of Global clinical trial. Committee recommended that the firm should submit formal request for approval of the drug for specific indication alongwith the report of clinical trial conducted in Indian patients as part of global clinical trial for examination of the committee.
5	**Raltegravir 400mg tablets**		In order to prevent the development of resistance, the drug should be used only in cases of failure of retroviral therapy. Therefore committee did not recommend for approval of the drug for the proposed additional indication.
6	**Azithromycin IP tablet 250/500mg**		Committee recommended for giving permission for marketing the drug in uncomplicated multidrug resistant enteric fever only subject to condition that package insert should mention the class effect of macrolide antibiotic about risk of cardiac deaths.
7	**Amphotericin B injection emulsion 5mg/ml**		Committee recommended for a clinical trial to be conducted with Amphotericin B injection emulsion comparing with the conventional Amphotericin injection. Accordingly protocol etc. should be submitted to DCG(I) for approval.

8	**Cefixime tablet 200mg, Dispersible tab 100mg, Oral suspension IP 50mg/5ml**		Committee recommended for approval of the additional indication – Treatment of enteric (typhoid) fever.
9	**Doripenem 1g injection**		Doripenem 1g strength formulation is not approved in any country. Although 1g dose may be required in certain patients, approval of 1g formulation as additional strength may lead to use of the strength in patients who may not need 1g dose. Therefore, committee did not recommend for giving permission to the proposed strength.
10	**Linezolid SR tab 1200mg**		Committee recommended for giving permission to conduct the proposed bioequivalence study and clinical trial.
11	**Gentian Violet**		The present study will use Gentian violet at much lower concentrations of 0.00165% where there is no staining of the oral mucosal surfaces and no evidence of mucosal surface irritation or ulceration. Therefore, committee recommended for giving permission to conduct the proposed study.
12	**Boceprevir**		Committee recommended for giving permission to conduct the proposed study subject to the following conditions:- **i)** Upper age limit of subjects to be included in the study should be 65 years. **ii)** The firm should provide post trial access of the therapy for the subjects responded in the clinical trial.
13	**Low anticoagulant heparin (sevuparin/DF02)**		Malaria is a disease which has special relevance to Indian health scenario. Committee recommended for giving permission to conduct the proposed study subject to the condition that initially the study should be conducted on 20 patients and the interim results should be reviewed by NDAC for consideration of further continuation of the study.
14	**MEDI-546**		Committee recommended for giving permission to conduct the proposed study

15	**Epratuzumab**		Committee recommended that the firm should submit the inclusion and exclusion criteria for the study and also interim results of the core studies from which the patients will be rolled over for examination of the committee.
16	**CXA-201**		Committee recommended for giving permission to conduct the proposed study subject to submission of details of trial sites from across the country which should be tertiary care hospitals having not less than 150 beds and medical colleges. Details of such sites should be submitted to DCG(I) for his consideration and approval of the study.
17	**Rifapentine/ Isoniazid**		Data submitted is not adequate to address the following issues:- **i)** The possibility of increased serious adverse effects of daily dose of Rifapentine vs. once weekly use. **ii)** PK study has shown that peak conc of rifapentine is associated with better efficacy than increased AUC in daily dose schedule. This also raises doubt about the efficacy of daily dose. Hence Committee did not recommend for giving permission to conduct the proposed study.
18	**Chromium Picolinate + Folic acid + Inositol +Lycopene + Nicotinamide + Selenium + Vitamin B6 + Vitamin B 12 + Zinc Sulphate tablets**		The firm has proposed to market the product as vitamin-mineral supplementation. The lycopene and inositol in this product has no relevance for this condition. Hence committee did not recommend for approval of the FDC.
19	**Zoonocide (Surface Shield)**		Based on the satisfactory report submitted by the firm on disinfection test to complete bactericidal efficacy (S. aureus and E. coli) and fungicidal efficacy (Candida) test, committee recommended for approval of the product.

5. RECOMMENDATIONS OF THE NDAC (ANTIMICROBIAL, ANTIPARASITIC, ANTIFUNGAL AND ANTIVIRAL) HELD ON 16.03.2013:

The NDAC (Antimicrobial, Antiparasitic, Antifungal & Antiviral) deliberated the proposals on 16.03.2013 and recommended the following:

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
Special agenda 1 to 10			
1 to 10	1. **Posaconazole Oral suspension 40mg/ml** 2. **Maraviroc Tablet 150mg/300mg** 3. **Raltegravir (as potassium) film coated 100mg** 4. **PentosanPolysulfate sodium capsules 100mg** 5. **Anidulafungin injection 50mg/100mg per vial** 6. **Darunavir Tablet 300mg** 7. **Colistimethate** 8. **Lomefloxacin** 9. **Pefloxacin** 10. **Sparfloxacin**		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, 8 drugs are in the category of (Antimicrobial, Antiparasitic, Antifungal & Antiviral) which are given below:- 1. Posaconazole Oral suspension 40mg/ml

			2. Maraviroc Tablet 150mg/300mg 3. Raltegravir (as potassium) film coated 100mg 4. PentosanPolysulfate sodium capsules 100mg 5. Anidulafungin injection 50mg/100mg per vial 6. Darunavir Tablet 300mg 7. Colistimethate 8. Lomefloxacin 9. Pefloxacin 10. Sparfloxacin The NDAC (Antimicrobial, Antiparasitic, Antifungal & Antiviral) 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 these 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 Pharmacovigilance Programme of India (PvPI) and iii) the firm concerned.

			The Dossier shall be circulated to all the experts of the NDAC (Antimicrobial, Antiparasitic, Antifungal & Antiviral) for their further review. If needed manufacturer may be requested to make their Presentation before the NDAC on safety and efficacy of the drugs. The NDAC further recommended the following :- CDSCO may collect the following information on all the 10 drugs i) The date of approval of each drug. ii) The date of manufacturing and marketing of each drug by the manufacturer. iii) The mandatory PSUR reports submitted by these companies. iv) Pharmacovigilance data if any from PVPI on these drugs. v) Marketing status of these drugs. vi) Global Marketing status of these drugs. vii) Clause,condition and opinion under which permission was granted for these drugs. In respect of the three drugs viz. lomfloxacin, Pefloxacin, and sparfloxacin the committee recommended that the following additional information should be obtained and submitted to the committee for examination in the next meeting. 1. Name of countries where currently these drugs are marketing. 2. Name of the countries if any where these drugs have been withdrawn/prohibited due to safety, lack of efficacy or other reasons. 3. Is there any company marketing these drugs in the country. As soon as the above information is

			available, a meeting may be called. In the meeting, the recommendations of the other 2 committees may be placed which would be discussed. Specific opinion from NACO on antiretroviral drugs (Maraviroc, Raltegravir and Darunavir) should also be taken.
11	**Etimicin Sulfate Injection**		The committee recommended for the submission of detailed phase III clinical trial reported to be conducted in Indian subjects and rational of taking only 50 subjects of each indication i.e. RTI, UTI, Skin &post surgical bacterial infection. Committee further stated that in LRTI aminoglycoside is not standard treatment and rational of taking amikacin for this indication as comparator needed to be justified and similarly in case of skin &post surgical bacterial infection . PSUR data from China should be provided to the committee for review.
12	**Ampucare**		Committee noted that proposal seems to be confusing as documents given to DCG(I) is for 1. Manufacturing and marketing of AmPucare 50mg topical formulation for all types of indication of non Healing wounds i.e.Diabetic foot ulcer, Bed sores, Venous Ulcer, Arterial Ulcers, Varicose Veins, Skin infections, War wounds, Chromic Diabetic Wounds, Burns. 2. The firm has proposed to conduct mutlicentric, randomized, double blind, phase III clinical trial to evaluate efficacy of AmPucare in diabetic foot ulcer only. 3. Composition and Standardization of preparation and Toxicity data of formulation is not provided. The committee recommendedtofurnish complete documents as per Appendix I of

			Schedule-Y alongwith the proposed clinical trial protocol etc. for further review by the committee.
13	**Arbekacin Injection**		The committee opined that the proposal of the firm to conduct clinical trial in its present form cannot be consider for approval and recommended that the protocol should be revised as under - 1. The primary objective of the study should be for assessment of safety and efficacy of the drug in patients with MRSA positive Speticima and pneumonia where vencomycin is indicated 2.The age limitof subjects should be 18-65 years. 3. Renal functions of the subjects should be monitored at the baseline and day 3 and day 7. 4. The trial sites should be multispecialty hospital and have competence and facility for testing of MRSA. The revised clinical trial protocolalongwith the sites etc.should be submitted to the committee for examination.
14	**Safe Touch 24**		The committee reviewed the report of the clinical trial and recommended for approval of the product.
15	**Balofloxacin Tablets 200mg**		The committee recommended for giving permission to conduct the proposed bioequivalence study. However for the marketing approval of the proposed strength, the firm is required to conduct phase III clinical trial comparing 200 mg BD versus 100mg BD in 200 subjects. The sites should be multispecialty hospitals/institute, geographically distributed across the country. Accordingly clinical trial protocol etc should be submitted to the DCG (I) for

			approval.
16	**Amoxycillin Trihydrate extended release tablet 775 mg**		The committee recommended for giving permission to conduct the proposed bioequivalence study. However for the marketing approval of the proposed formulation, the firm is required to conduct phase III clinical trial comparing ER formulation with the conventional formulation in 200 subjects.Accordingly clinical trial protocol etc.should be submitted to the DCG (I) for approval.
17	**Cefuroxime Sodium + Sulbactam Sodium**		The committee recommended that a clinical trial of Cefuroxime Sodium + Sulbactam Sodium versus Cefuroxime in four indications vizspecticimia, meningitis, bone & joint infections, surgical prophylaxis on a total of 200 subjects (50 for each indication) should be conducted after getting protocol etc. approved from DCG (I). The results of the study should be submitted to the committee for consideration of the proposal to market the FDC for the proposed additionalindications i.e. UTI, Skin and Skin Sturcute infection, speticimia, meningitis, bone and joint infection, obstretic and gynocological infections, ear nose and throat infections as well as surgical prophylaxis except Gonorihea.
18	**Diltiazem + Lignocaine**		The committee recommended for the conduct of the proposed clinical trial as per the protocol submitted subject to condition that the sites should be multispecialty hospitals/institute, geographically distributed across the country. The details of the proposed sites, ICD, undertaking by the investigator, sponsor etc. as per the new notification should be submitted to the DCG(I) for approval of the clinical trial.
19			The committee recommended that a

	Olimel with (electrolytes),N4E,N7E,N9E with Lipid Emulsion (Olive oil and soyabean oil), Amino Acid, Glucose(E denotes Olimel with electrolytes)		phase III clinical trial should be conducted on 200 subjects after getting protocol etc. approved from the DCG (I). The sites for the study should be multispecialty hospitals/institutes, geographically distributed across the country. The report of the study should be submitted to the committee for examination.
20	**Balofloxacin 100mg + Ornidazole 500mg tablet**		The committee opined that there is no rational in combining Balofloxacin with Ornidazole and hence not recommended for approval.
21	**Piperaquine + Dihydroartemisinin**		The committee recommended for proposed amendments in the clinical trial protocol. However, for waiver to any study specific procedure/parameter in the study protocol shall be approved by the competent authority i.e. the DCG(I) is required to be obtained.
22	**Adenosylcobalamin+ Ferrous Ascorbate + Folic Acid IP + Zinc Sulphate**		The Committee noted that the combination may not necessarily require high amount of Adenosylcobalamin unless there is specific case of deficiency of both iron and vitamin B12. Therefore committee did not recommend the proposal for iron deficiency anaemia. However if the proposed formulation is intended for nutritional deficiency anaemia, a clinical trial on minimum 200 subjects is required to be conducted after getting protocol etc approved from the DCG(I).
23	**Ceftriaxone + Sulbactam + EDTA**		Committee noted that the firm has asked for the grant of permission to conduct clinical trial to compare the efficacy and safety of Ceftriaxone + Sulbactam + EDTA with Meropenem in infections caused by β-lactamase producing gram – ve bacteria for export to EU and USA.As the said formulation has already been approved by DCG(I) for the same

			indication therefore the committee recommended that proposed clinical trial data can be generated for export purpose subject to approval by the DCG (I).
24	**Vaginal Probiotics**		Committee noted that VSL#3 formulation is approved by office of DCG(I)however Florisia vaginal tablet is not approved by this office. 1. The comparison of probiotic by oral and vaginal route has no rational. 2. Two branded probiotics preparation are not 100% matching in composition namely VSL#3 & Florisia. Therefore they cannot be considered equivalent & comparison would be difficult. 3. Rational of Probiotic formulation with 8 different bacterial strains in VSL#3 & 3 bacterial stain in Florisia need to be specifically mentioned. 4. It is difficult to ascertain which microbial strain is beneficial for urovaginal route. As far as project is concerned rational of each constituents of the formulation to be used for the study should be stated and accordingly the formulation be suggested. It is advised by the committee to conduct proof of concept study initially through vaginal route for UTI.

6. RECOMMENDATIONS OF THE NDAC (ANTIMICROBIAL, ANTIPARASITIC, ANTIFUNGAL AND ANTIVIRAL) HELD ON 12.04.2013:

The NDAC (Antimicrobial, Antiparasitic, Antifungal & Antiviral) deliberated the proposals on 12.04.2013 and recommended the following:

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
1	**Curcumin**		The committee opined that there is no human data in support of antimalarial efficacy of either curcumin or Biocurcumax. In the proposed design there is no comparison with standard of care. Hence, Committee recommended for a proof-of-concept study with different doses of Curcumin/Biocurcumax. Accordingly revised protocols etc. should be submitted to the committee for examination
2	**Levamisole**		Committee recommended for giving permission for the trial, subject to the condition that the study should be double blind and the parameters relapse rate and time to relapse should be assessed. Accordingly, revised protocol should be submitted to DCG(I) for his approval.
3	**Calcitriol + FishOil + Eicosapentaenoic Acid + Docosahexaenoic Acid + Methylcobalamin + Folic Acid Boron + Calcium Carbonate**		The Committee opined that there are no supportive data and rationale for the use of various ingredients of the proposed FDC in osteoporosis. Hence, the Committee did not recommend for the approval of the product.
4	**Ceftazidime Avibactum**		The proposal is for one study under two identical protocols viz D4280C00002 & D4280C00004. Committee recommended for giving approval for the protocol viz D4280C00002 subject to the following conditions:

			(i) Upper age limit should be 65 years. **(ii)** Sites should be multispecialty hospitals, having emergency facilities and Institutional Ethics Committee. For other protocol, proper justification for conducting the same study under said protocol should be submitted for examination to the committee.
5	**Delamanid**		The committee recommended for giving approval for the trial. However, the final decision may be taken in consultation with Central TB Division of DGHS.
6	**ART-123**		Committee recommended for giving permission to conduct the clinical trial subject to condition that upper age limit of the subjects should be 65 years.
7	**PF-04236921**		The firm has withdrawn the clinical trial proposal.
8	**Belimumab (HGS1006)**		The committee recommended for giving permission to conduct the clinical trial.
9	**LY2127399**		The committee recommended for giving permission to conduct the Phase 3b extension study subject to the condition that the trial sites should be multispecialty hospitals with emergency facilities.
10	**Superoxidized Solution**		It is wrongly included in the agenda, hence no action required.
11	**OctenidineHCl**		Committee recommended that the firm should determine the MIC for S. aureus (MRSA) and C.albican. The firm should also conduct a clinical trial as per WHO guidelines. The protocol etc. should be submitted to the committee alongwith the MIC data as above for examination.

12	**Cephalexin + Clavulanate Potassium**		Committee recommended that a comparative double blind trial of Cephalexin+ Clavulanate Potassium vs Cephalexin should be conducted to show the superiority of the FDC. Protocol etc. should be submitted to the committee for examination.
13	**Protocol amendment Rifamycin**		The committee recommended for addition of subjects in the ongoing clinical trial to make the total sample size to 1032 patients only at those sites which have institutional ethics committee.

7. RECOMMENDATIONS OF THE NDAC (ANTIMICROBIAL, ANTIPARASITIC, ANTIFUNGAL AND ANTIVIRAL) HELD ON 23.05.2013:

The NDAC (Antimicrobial, Antiparasitic, Antifungal & Antiviral) deliberated the proposals on 23.05.2013 and recommended the following:

AGENDA NO.	NAME OF DRUG		RECOMMENDATIONS
1	**Biapenem for Injection 300 mg/ vial**		Committee recommended for giving permission to conduct the study subject to the following conditions:- **i)** Community acquired pneumonia patients should not be included in the study. **ii)** There should be stratified random sampling. **iii)** For sample size calculation, statistically the non –inferiority margin should be 5%. **iv)** Sites should be medical colleges/multispecialty hospitals with emergency facilities. **v)** The criteria for all the three complicated infections should be defined in the protocol. The above information should be submitted to DCGI before giving final approval.
2	**Primaquine**		Committee recommended for giving permission to conduct the study subject to the following conditions:- **i)** Subjects aged 18 to 65 years should be enrolled in the study. **ii)** In subjects in whom relapse occurs in 28 days, chloroquine level should be estimated at Day 6 with the preserved samples. Based on the results, the study in children can be planned for further consideration.

3	**Ebastine oral suspension**		Committee recommended that a Phase III clinical trial in children is required to be conducted. Accordingly, protocol etc. for the study should be submitted to the committee for evaluation.
4	**Nevirapine 400 mg ER Tablets**		Committee recommended for giving permission to conduct the proposed bioequivalence study. Based on the results of the bioequivalence study, the matter will be taken up for further consideration.
5	**Artesunate + Piperaquine Phosphate** **Re-examination**		Committee recommended for giving permission to conduct the proposed PK study and Phase II study. However committee opined that the firm should also conduct a PK study under fed condition. Result of the PK study should be submitted and got evaluated by CDSCO before initiating the Phase II study.
6	**Nadifloxacin + Adaplene** **Re-examination**		The firm did not turn up for presentation, therefore the committee deferred the proposal.
7	**ASP Glosair 400 Cartridge(Hydrogen Peroxide) Solution**		Committee recommended that antimicrobial efficacy study against S. aureus, E. coli and C. albicans is required to be conducted. Accordingly, protocol etc. for the study should be submitted to the committee for evaluation.
8	**One tab of tenofovirdisoproxilfumerate + emtricitabine IP + two tab of Nevirapine IP**		Committee recommended for giving permission to conduct the proposed bioequivalence study. Based on the results of the bioequivalence study, the matter will be taken up for further consideration.
9	**Azithromycin + Ofloxacin**		Committee opined that there is no rationality of the combination. Therefore the committee did not recommend for the proposal.
10	**Dried Ferrous Sulphate IP Eq to elemental Iron 100/20mg +**		Committee recommended for giving permission to market the combination subject to condition that the firm should

	Folic Acid 0.5/0.1mg		conduct post marketing surveillance study within one year of approval after getting protocol approved from CDSCO.
11	**Folic Acid 5mg+ Metylcobalamine2mg + Pyridoxine Hydrochloride35mg**		Committee opined that there does not seem to be sufficient justification of combining the three vitamins in the amount mentioned. Firm may make presentation with their justification before the committee.
12	**Monofer solution for Injection** **Re-examination**		The committee reviewed the data of safety and efficacy of the drug including the Indian data conducted as a part of global clinical trial and recommended for marketing approval of the product.
13	**Doripenem 1 gm Powder for Injection** **Re-examination**		The committee opined that a clinical trial should be conducted to prove the safety, efficacy and advantages of Doripenem 1 gm Powder for Injection. Accordingly protocol etc. should be submitted to the committee for evaluation.

8. RECOMMENDATIONS OF THE NDAC (ANTIMICROBIAL, ANTIPARASITIC, ANTIFUNGAL AND ANTIVIRAL) HELD ON 23.08.2013:

The NDAC (Antimicrobial, Antiparasitic, Antifungal & Antiviral) deliberated the proposals on 23.08.2013 and recommended the following:-

AGENDA NO.	DRUG NAME		RECOMMENDATIONS
1	**Raltegravir, Etravirine, Emtricitabine/ Tenofovir DF, Darunavir, Ritonavir**		The committee discussed the proposal and recommended for approval of the study subject to the approval of HMSC and opinion of NACO to be obtained.
2	**Raltegravir, Etravirine, Emtricitabine/Tenofovir DF, Darnavir, Ritonavir**		The committee discussed the proposal and recommended for approval of the study subject to the approval of HMSC and opinion of NACO to be obtained.
3	**Ceftazidime, Avibactum**		The committee discussed the proposal and recommended for approval of the study.
4	**Ceftazidime, Avibactum**		The committee discussed the proposal and did not recommend for approval of the study as the sensitivity to ceftazidime-avibactum not available before randomisation and there are chances that the patients with serious infection are randomised to the treatment of ceftazidime-avibactum.
5	**Defuze**		The committee after the discussion opined that the product Enfuvirtide is completely a novel product and not a generic version of internationally approved product FUZEON and it should be referred to IND committee.
6	**Nadifloxacin + Adaplene**		The committee opined that the study design is not appropriate and needs to be redesigned to a double blind with a sound basis for sample size calculation.
7	**Azithromycin +**		Firm did not turn up for presentation. However committee opined that both drugs cefixime as

	Cefixime		well as Azithromycin are not used together in clinical practice. Further there are chances of misuse with the proposed FDC. The proposed FDC is not approved anywhere in the world and there is no published data on the FDC. Hence the committee did not recommend.
8	**1 tablet of Tenofovir Disoproxil Fumarate + Emtricitabine IP + 2 tablet of Nevirapine IP**		FDC of Tenofovir Disoproxil Fumarte + Emtricitabine is already approved. Nevirapine is also approved. Firm has proposed for manufacturing and marketing of these two already approved formulations. BE study data presented by the firm was found to be satisfactory. Committee opined that an opinion of NACO shall also be taken before considering for approval of the said combipack for manufacturing and marketing in the country.
9	**Calcium citrate maleate eq. to Calcium 250mg + Vitamin D3 IP 400IU (Powder form) film coated tablet**		Firm did not turn up for presentation. However committee opined that firm should make a detailed presentation before the committee.
10	**Artesunate for Injection 30mg/120mg**		The proposal is for change in pack size without any change in respect of strength and dosages. The committee recommended for the giving permission to manufacture and market the drug in the country.
11	**Artesunate Injection with Phosphate Buffer 60mg/6 ml**		The firm presented the report of clinical trial of Artesunate Injection with Phosphate Buffer in comparison to already approved formulation before the committee. The committee recommended the grant of permission to manufacture and market the product in the country.
12	**Nandrolone Decanoate Injection 25/50/100 mg**		The committee observed that HIV is lifelong disease and drug to be used for long duration. Data presented by firm on Nandrolone decanoate is only for short term use. There is no sufficient safety and drug interaction data with ART or HARRT therapy. The committee opined that based on available data Nandrolone decanoate can't be approved for

			HIV associated wasting, however opinion from NACO may be taken.
13	**Tioconazole 100 mg vaginal tablets**		The committee recommended for grant of permission to conduct of clinical trial with the condition that candida species identification by culture should be done in each individual and the addition of two more clinical trial sites including one in north India.
14	**Dibasic Sodium Phosphate + Monobasic Sodium Phosphate + Sodium Chloride + Calcium Chloride Solution**		The committee opined that firm should conduct a phase-III clinical trials on Indian patients. Firm should submit protocol etc., for examination by the committee.
15	**Arbekacin Sulphate 200mg/4ml**		The committee recommended the grant of permission for conduct of clinical trial with the condition that ethics committee of trial site should be registered with office of DCG (I).
16 to 18	**Sparfloxacin, Pefloxacin, Lomefloxacin**		The committee members informed that they themselves are not using these drugs and opined that there is no sufficient data available on the use of these drugs in India. However committee desired that information as to whether any manufacturers is presently manufacturing and marketing these drugs in the country should be obtained from State Drugs Controllers and same along with available data may be examined by the committee in next meeting.

9. RECOMMENDATIONS OF THE NDAC (ANTIMICROBIAL, ANTIPARASITIC, ANTIFUNGAL AND ANTIVIRAL) HELD ON 22.11.2013:

The NDAC (Antimicrobial, Antiparasitic, Antifungal and Antiviral) deliberated the proposals on 22.11.2013 and recommended the following:-

AGENDA NO.	DRUG NAME		RECOMMENDATIONS
1.	**Etimicin Sulphate injection**		Earlier the proposal was examined by the NDAC (Antimicrobial, Antiparasitic Antifungal and Antiviral) in its meeting held on 16.03.2013 and the Committee after deliberation recommended for the submission of detailed Phase III clinical trial reported to be conducted in Indian subjects and rational of taking only 50 subjects of each indication i.e. RTI, UTI, Skin & post surgical bacterial infection. Committee further stated that in LRTI aminoglycoside is not standard treatment and rational of taking amikacin for this indication as comparator needed to be justified and similarly in case of skin & post-surgical bacterial infection. PSUR data from China should be provided to the committee for review." The firm should present the safety data separately for each indication in 50 patients along with microbiological culture data to review in the committee.
2.	**Ulinastatin Injection**		The firm has granted the permission to manufacture and market Ulinistatin on 03.04.2012 with the condition to conduct Phase IV trial. In order to comply the said condition of Phase IV trial the firm has submitted the Phase IV protocol. However the firm was asked to revise and submit the revised protocol for further necessary action. In the mean time, the firm initiated the phase IV study to comply the above

			requirement. The committee opined that the office of DCG (I) may take necessary action.
3.	**Amphoterecin B Enteric-coated25mg tablets**		The firm presented the comparative data of Amphoterecin intravenous preparations which cannot be 100% extrapolated to oral. Further no evidence of orally administered formulation in animal model Leishmaniasis. Committee opined to produce the relevant data head to head comparison with the intended oral and available intravenous formulation of Amphotericin B. This is to ensure avoidance of the possibility of development of resistance to this precious antileishmaniasis and antifungal drug.
4.	**Glucose+SMO Flipid (Soya Bean+Triglycerides Medium chain+Olive Oil refined+Fish Oil rich in Omega 3-acid)+Amino Acid Solution (13%+20%) Injection**		Committee recommended for conducting the phase III trial with the condition that trial shall be conducted in 50% government hospitals and the study report shall be placed before committee for their consideration.
5.	**Amino Acid Solution with electrolytes+Glucose+Lipid Emulsion Injection**		Committee recommended for conducting the phase III trial with the condition that trial shall be conducted in 50% government hospitals and the study report shall be placed before committee for their consideration.
6.	**Darunavir 600mg + Ritonavir 100mg tablets**		Firm presented that Darunavir is co-administered with Ritonavir. The firm was told that this is not a BE study. They should conduct a study in appropriate number of subject (after getting the protocol approved) to demonstrate that there is no PK interaction when both the components are given separately and given as FDC (having products from the same manufacturer).Firm should submit this Pharmacokinetic study report before the committee and issue of CT waiver will be

			considered later on for granting approval of manufacturing and marketing permission.
7.	**Lactobacilllus acidophilus & Bifidobacteriumanimalis 1.0 billion cfu + Saccharomyces boulardii 5.0 billion cfu capsule**		Firm has proposed the FDC for the treatment of antibiotic associated diarrhoea, in acute infections diarrhoea and alleviating symptoms of IBS. The committee opined that the FDC can be considered only for antibiotic associated diarrhoea. However, a clinical trial is required to be conducted in the country with proposed FDC vis-a-vis FDC+antibiotic. Accordingly, the firm shall submit the protocol before the committee for further consideration.
8.	**Amoxicillin Trihydrate IP 654.1 eq. to 562.5 mgof Amoxicillin + Amoxycillin Sodium IP 480.8 eq. to 437.5mg of Amoxycilin + Potassium Clavulanate IP 76.2 eq. to 62.5mg of Clavulanic SR tablet**		The proposed formulation of Amoxicillin + Clavulanic acid 1g + 62.5g is intended to be used as two tablets twice daily that means daily dose of Amoxicillin will be 4 gms. Committee opined that 4g of Amoxicillin is very high in Indian context and unless safety profile of this drug is established in the Indian patient, the proposal cannot be considered.
9.	**Meropenem 1gm + Tazobactam 125mg/250mg injection**		The firm presented the study report with three arm treatment study. The study data presented does not inspire the confidence in the study. Hence the raw data (Case record forms for two centres specifically CHC Hospital, Gazipur, UP & MVJ Medical College & Research Hospital, Bangalore) should be submitted along with detailed microbiological culture data to the committee for review.
10.	**Dried Ferrous Sulphate IP 150mg Eq. to elemental Iron 45mg +Folic Acid IP 0.4mg**		It was observed by the committee that the various strengths have been applied by the firm for the FDC of ferrous sulphate and folic acid as enteric coated on the requirements of NHRM. The committee opined that expert opinion of

	Enteric coated tablet and Dried Ferrous Sulphate 150mg Eq. to elemental Iron 45mg (as **Enteric coated granules) +Folic Acid IP 0.5mg Hard gelatin capsule**		three haematologists (Dr. Subhash Verma, PGIMER, Chandigarh, Dr. Bikas Mehdi, PGIMER, Chandigarh, Dr. P.S. Gahlot, Rohtak Medical College) shall be taken before considering for approval of manufacturing and marketing of the FDC in various strengths. Meanwhile firm should also submit phase IV trial protocol which was recommended by the committee previously.
11.	**Clinical trial with Moxifloxacin+Clofazimine+Ethambutol+Pyrazinamide+Isoniazid+Protthionamide+ Kanamycin**		All the drugs are individually approved in India for various indications. Out of globally 400 patients, from India 100 Patients will be recruited in this trial. The STREAM study/proposed study has commenced in Ethiopia, Vietnam and south Africa since July 2013. Only MDR resistant subjects showing Quinolone sensitive Mycobacterium tuberculosis infection will be enrolled as per the proposed protocol. The committee opined that there is no safety data with moxifloxacin at the dosage 800mg over a period of 9 month. Further hepatotoxicity, hypothyroidism with the other drugs in the proposed regimen is also a concern . The applicant should submit data available on the SAE, & AE's with the proposed regimen for further deliberation by the members.

10. RECOMMENDATIONS OF THE NDAC (ANTIMICROBIAL, ANTIPARASITIC, ANTIFUNGAL AND ANTIVIRAL) HELD ON 28.02.2014:

The 10th NDAC (Antimicrobial, Antiparasitic, Antifungal & Antiviral) meeting deliberated the proposals on 28.02.2014 and recommended the following:-

AGENDA NO.	DRUG NAME		RECOMMENDATIONS
1.	**Octenidine Dihydrochloride 0.3% and 0.1%**		After deliberation the Committee recommended that proposed study should be conducted in Government Hospitals and the Principal Investigators should be Microbiologist.
2.	**Bedaquiline tablets (100mg)**		The firm presented preclinical and clinical data on the safety and efficacy of the drug and requested for the waiver of requirement of phase-III clinical trial in India. The firm has conducted Phase IIb study only. The committee noted that as part of global clinical trial only 5 patients were enrolled from India. The number of subject from India was not considered adequate to address the safety concern. The committee therefore does not recommend for the waiver of clinical trial.
3.	**Raltegravir Potassium** **(PSC)**		The Firm presented the safety data of the drug. The Committee after deliberation noted the recommendation of the parliament standing committee (PSC) to evaluate the drug in the present scenario. Drug is registered in 114 countries. It is already approved by USFDA in 2007. It was informed that trial was conducted on 66 Indian patients as a part of global clinical trial before obtaining approval of the DCG(I). The committee observed that the drug has been used in large number of patients with a reasonable safety profile in the Indian patients. It was also noted that in India Raltegravir is only recommended by NACO as third line drug. Therefore marketing of the drug may be permitted as per the NACO recommended indication only i.e as a third line treatment drug.

4.	**Colistimethate** **(PSC)**		The Committee was informed that the Parliamentary Standing Committee (PSC) of the Ministry of Health & Family Welfare had presented its 59th report to the Parliament on the functioning of CDSCO. This Directorate had approved the Colistimethate, to be indicated for the treatment of serious infection caused by gram negative bacteria, including LRTI, UTI, where commonly used antibacterial agent are ineffective because of bacterial resistant. The firm presented the safety data and published reports of clinical trials on the drug. The committee noted that the drug is being marketed in UK and USA. The drug has also being used in Japan and Europe since 1950. The firm reported that they have conducted PK study of colistin in critically ill patients (N=15) with multi drug-resistant gram- negative bacilli infection. The total patient exposure for reporting period of colistimethate sodium is 2,93,009 DDDs from 2008. Further the firm informed that a PMS study is ongoing on 100 patients. There have been no major safety concerns and changes in safety profile since marketing in India. The Committee after deliberation recommended for continued marketing of the drug and directed the firm to submit the PMS report as soon as it is completed.
5.	**Anidulfungin** **(PSC)**		The committee was informed that the Parliamentary Standing Committee (PSC) of the Ministry of Health & Family Welfare had presented its 59th report to the Parliament on the functioning of CDSCO. This Directorate had approved the Anidulafungin 50mg/100mg (Injection) on 26th Feb. 2009, to be indicated for treatment of invasive candidiasis including candidemia and esophageal, candidiasis in adult patients. The firm presented the safety data and

			published reports of clinical trials on the drug. After deliberation, the committee recommended the continuous marketing of the drug however, the firm is asked to extend the PSUR for another two years.
6.	**Etimicin Sulfate Injection**		The firm presented detailed phase-III clinical trial report of Etimicin inj. The Committee noted that Amikacin is not used as monotherapy but as an add-on therapy except in UTI. Hence Amikacin as comparator to the investigational drug is not appropriate. There were several queries in the data. The explanations provided by the firm were not convincing, e.g. the efficacy of Amikacin in UTI was much below the expected level. Whereas none of the subjects on Amikacin showed nephrotoxicity and ototoxicity. This is particularly surprising as many of the subjects were above the 50 years of age. In patients of respiratory tract infections, the choice of Amikacin is not a standard practice. After deliberation, the Committee recommended that the firm should conduct another phase-III clinical trial with proper design and in statistically significant number of subjects and the sites should be geographically distributed across the country. Accordingly clinical trial protocol etc. is required to be submitted before the Committee for further review.
7.	**Cidofovir Dihydrate Injection 75mg/ml**		The committee deliberated on the request of the firm to give waiver of CT of cedofovir. It was noted this is not an unmet need as other alternatives anti-viral drugs are available. The cidofovir offers advantage of administration however, the data on safety profile in Indian subjects is not available particularly with reference to nephrotoxicity. The committee therefore, did not recommended for waiver of Phase III clinical trial.
8.	**Cefditoren Pivoxil Dry powder for suspension 100 mg/5 ml**		The firm had presented the BE study report to the committee, which was found to be satisfactory and the committee recommended

			for the manufacturing and marketing Cefditoren Pivoxil Dry powder for suspension 100 mg/5ml in the country.
9.	**Nitrofurantoin dispersible tablets 50 mg**		The firm presented the BE study protocol before the committee, which was found to be satisfactory and the committee recommended for conducting of BE study before granting permission for manufacturing and marketing by the DCGI.
10.	**Micafugin 100 mg for injection**		The Committee opined that the usual adult dose of the drug is 100mg. Hence, the 100 mg pack is appropriate in place of 2 vials of 50mg (already marketed in India) for adult patient. Also the proposed strength is approved in USA, Canada, and Australia. In the view of the above the committee recommends marketing of the proposed higher strength, the indication being as approved earlier.
11.	**Nadifloxacin+Adaplene**		The protocol presented by the firm was found satisfactory. The power of the study is 80% with 10 % dropout. The committee recommended for conducting clinical trial with the condition that at least one site of north east region shall also be included.
12.	**Ofloxacin 200mg+Ornidazole 500mg injection**		The committee noted the recommendation of the Parliament standing committee (PSC) and evaluated this drug in present scenario. The firm presented the data of Phase III trial data. The committee noted that parenteral use of anti bacterial in acute Diarrhea is not recommended routinely.There is no specific advantage of giving flouriquinolone and Imidazole in parenteral form as both can be given individually, if indicated. The FDC will not be rational. Hence the committee did not recommend the FDC for continued marketing in India for the present approved indication of diarrhea.
13.	**Ferrous Sulphate eq. to Elemental Iron+ Folic Acid IP**		The committee noted the FDC of Ferrous Sulphate 335mg/67 mg+ Folic Acid 0.5/0.1 mg enteric coated tablets was approved with a condition that Phase IV trial shall be conducted within one year. Now, the applicant has

			requested for manufacturing and marketing of various additional strength of the said FDC. The Phase IV clinical trial report earlier directed to be conducted is still awaited. The committee opined that there is no evidence of superiority of enteric coated tablet. On the contrary there is evidence that such a formulation may be less effective. The committee was also informed that some manufacturers in the country are already manufacturing proposed strengths for NRHM programme. The committee opined that opinion of NRHM may be sought before considering further.
14.	**Eravacycline**		M/s PSI CRO has applied for the grant of permission to conduct a phase III clinical trial to assess the efficacy and safety of Eravacycline compared with Ertapenem in complicated intra-abdominal infections". After the detailed deliberation, the NDAC recommended for the conduct of the trial subject to the condition that the sites should be geographically distributed including north eastern and north western region of the India. Accordingly the applicant shall submit the list of sites for approval prior to grant of clinical trial permission.
15.	**Isoniazid Tablets**		M/s BJ Medical College, Pune **(**Dr. Ramesh A Bhosale**)** requested for permission to conduct a phase IV clinical trial with Isoniazid tablets as preventive therapy among HIV-infected women in high TB prevalence settings. There is a concern about treatment of latent TB infection in India as there is an increased load of active TB cases in India. Furthermore, patients with active TB may be mistakenly treated as LTBI and this will further amplify the problem of drug resistance. The NDAC after deliberation has not recommended for the conduct of the proposed clinical trial.

16.	**Raltegravir+Etravirine+ Emtricitabine**		**M/s. B J Medical College** has requested for permission to conduct an institutional open-label **Phase IV**, prospective interventional, strategy study in resource limited settings (RLS) for HIV infected participants with triple class experience or resistance to NRTIs, NNRTIs and PIs and who are failing their current regimen. After deliberation, the NDAC recommended for conduct of the study with the condition that the prior approval of NACO and HMSC are submitted by the applicant to CDSCO.
17.	**Tenofovir Disoproxil Fumarate + Emtricitabine tablet IP 300mg/200mg and Two tablet of Nevirapine IP 200mg**		NACO agreed to the recommendations made by the NDAC during its meeting held on 23.8.2013 and it was recommended that permission may be granted for manufacture and market of proposed co-pack in the country.
18.	**Raltegravir+Etravirine+ Emtricitabine**		**M/s. YRG Care** has requested for permission to conduct an institutional open-label **Phase IV**, prospective interventional, strategy study in resource limited settings (RLS) for HIV infected participants with triple class experience or resistance to NRTIs, NNRTIs and PIs and who are failing their current regimen. After deliberation, the NDAC recommended for conduct of the study with the condition that the prior approval of NACO and HMSC are submitted by the applicant to CDSCO.

11. RECOMMENDATIONS OF THE NDAC (ANTIMICROBIAL, ANTIPARASITIC, ANTIFUNGAL AND ANTIVIRAL) HELD ON 18.06.2014:

The 11th NDAC meeting (**Antimicrobial, Antiparasitic, Antifungal & Antiviral**) deliberated the proposals on 18-06-2014 (Wednesday) and recommended the following:-

AGENDA NO.	DRUG NAME		RECOMMENDATIONS
1	**Darunavir 300mg Tablet**		The firm did not turn up for their presentation. Hence the proposal was deferred.
2	**Fungisome iv infusion 1mg per 10,25 and 50mL**		The firm has applied for conducting Phase III clinical trial to evaluate new therapy with the reduced doses of Fungisome and subsequent treatment with Miltefosine. Fungisome and Miltefosine are already approved in the country for the indication. The firm has presented Phase-II CT data approved by DCGI earlier. The Committee deliberated the proposal and after careful evaluation of the protocol recommended for the grant of permission for conducting clinical trial as per proposed protocol.
3	**Ulinastatin 50000/100000 IU injection**		The firm has presented the proposal to conduct Phase IV clinical trial. The drug is already approved for the indication. The firm is conducting the trial in compliance to the condition imposed by the DCGI at the time of manufacturing and marketing permission. The Committee deliberated the matter in detail and after careful scrutiny noted that additional data are required to be generated on the efficacy and safety of the drug in Indian population and recommended for conduct of double-blind CT in statistically significant sample size in multispecialty hospitals with emergency facilities distributed throughout the country.
4	**Garenoxacin mesylate 200 mg tablets (additional**		The NDAC examined the proposal and observed that the firm was unable to submit any published trial report of the drug for the claimed indication. Further, the product is not

	indication)		approved internationally for the proposed indication and therefore the committee did not recommend the proposal.
5	**Ofloxacin 200mg per 50mL in 5% w/v dextrose solution** **(Intravenous infusion)**		The NDAC examined the matter and opined that : 1. the proposed formulation is to be administered over a period of 60 minutes whereas the approved formulation i.e. 200mg/100ml is administered over a period of 30 minutes only. 2. The product was approved at US in 1992. The firm did not present the current status of the proposed product in US market. The committee recommended that initially the firm shall submit details w.r.t. above points before further consideration by the committee.
6	**Nevirapine 400mg Extended Release tablets**		The matter was earlier discussed in NDAC meeting (23-05-2013) and the committee recommended for conduct of BE study. Accordingly the firm conducted the BE study of Nevirapine 400mg Extended Release tablets with Nevirapine 400mg Extended Release tablets (Viramune XR 400mg, Boehringer Inc USA) in 42 subjects and submitted data. The NDAC (Anti-microbial) examined the BE study data and recommended approval for Nevirapine 400mg Extended Release tablets.
7	**Terbinafine Gel 1%w/w gel**		Proposal was deferred as the firm did not turn up for presentation. Hence the proposal was deferred
8	**Primaquine Phosphate - SR tablets 15mg/30mg**		This application is for permission to manufacturer & market **Primaquine phosphate Sustained release tablets (15mg/30mg)** for radical cure to prevent relapse of P.vivax malaria and also for prevention of transmission of falciparum malaria particularly in areas where there is potential for relapse of malaria. The committee noted that the firm conducted double blind, double dummy, randomized comparative

			multicenter Phase- 3 study in three arms of Primaquine phosphate **(15mg),** Primaquine phosphate **(SR 15mg)** and Primaquine phosphate **(SR 30mg)** on a 288 subjects at 06 sites and also bioequivalence study of Primaquine phosphate 30mg SR tablets compared with primaquine 15mg tablets in 12+2 subject. The NDAC (anti-microbial) Committee has examined trial data & BE data and recommended that the data did not reveal superiority of the test SR formulation i.e. 15 mg or 30 mg over the conventional dosage formulation for prevention of P.vivax. The committee also opined that the method of estimation of G6PD level and use of biomarker for differentiating relapse or recrudescence shall also be submitted for further consideration.
9	**Amphotericine - B emulsion (15mg / kg and 20mg/kg)**		Firm presented the protocol. The committee recommended that the trial may be permitted with the following conditions :- a. Proposed arm of Amphotericin emulsion i.e. 15 mg/kg shall be deleted as the results have shown that it is less efficacious. b. that the firm shall present data initially on 4 patients before the committee duly reviewed by the DSMB for further consideration and approval for conducting trial on rest of the proposed patients. c. Committee also opined that the study shall be reworded as clinical study in place of Field study. In terms of Risk/ Benefit, the committee opined that the proposed formulation outweighs the risk. Regarding unmet need and Innovation vis a vis current therapy, the committee opined that the proposed formulation will be useful in Kala-azar patients.
10	**Piperaquine Tetraphosphate as Piperaquine Tetraphosphate +**		The committee noted that firm has conducted clinical trial on 150 subjects on the proposed higher strength as a part of Global Clinical Trial in India.

	Dihydroartemisinin		FDC of Piperaquine Tetraphosphate as Piperquine Tetraphosphate Tetrahydrate (QP) 320mg + Dihydroartemisinin (DHA) (40mg) is approved in Belgium, France, Spain, Germany, Italy and U.K. etc. The committee recommends approval for the proposed higher strength of FDC in adults only. The committee recommended for conduct of Phase-3 Clinical trial in children before consideration for approving the lower strength. Accordingly, the protocol shall be submitted for further deliberation before the committee.
11	**Tolperisone HCl+Paracetamol IP**		The proposal was deferred as the firm did not turn up for presentation. Hence the proposal was deferred
12	**Meropenem + Tazobactam Injection.**		The proposed FDC of **Meropenem (1gm) + Tazobactam (125mg/250mg) injection** was deliberated in the NDAC (Antimicrobial, Antiparasitic & Antifungal, and Antiviral) meeting (22.11.2013) and the committee opined that the study report with three arm did not inspire the confidence in the study. Hence, the raw data (Case record forms for two centres i.e. CHC Hospital, (Gazipur, UP) & MVJ Medical College & Research Hospital, Bangalore should be submitted along with detailed microbiological culture data to the committee for review. The firm presented the data before the committee. The committee observed that out of the total 8 sites approved, three sites showed no enrollment of patients and the firm did not present any documentary evidence. Out of 5 sites, one site has enrolled 16 patients whereas one of other sites has enrolled 109 patients and therefore there is a high skewed pattern of patient enrollment. The committee also noted that the data presented are not convincing and appear to be tempered. The committee recommended for conducting

			a fresh trial and accordingly protocol shall be submitted.
13	**Cephalexin + Clavulanate Potassium**		As per the recommendations of the NDAC previously, firm presented the protocol before the committee for conducting the clinical trial. The committee recommended for conducting the proposed trial. In terms of Risk/ Benefit, the committee opined that the FDC will have superiority over Cephalexin alone. Regarding unmet need and Innovation vis a vis current therapy, the committee opined that the proposed FDC will be useful in the said resistant patients. The committee also recommended to include at least one site from North-East region of India.
14	**Protocol Number: 341-12-003 (Version 1.0)**		The application is for permission to conduct a non-interventional, observational, prospective study to characterize the management & outcome of ***Clostridium difficile*** **infection** in Asia Pacific Countries in terms of patient demographics, medical history, prior and concomitant medications, including antimicrobial agents, clinical laboratory data, and disease characteristics. Also, to describe the diagnosis, management and treatment regimen(s) of patients with CDI, clinical outcomes of CDI patients, including recurrence of CDI and to obtain stool samples from the patients with CDI for further analysis. The study will be conducted in 13 countries (Singapore, Hong Kong, Philippines, Thailand, Vietnam, Indonesia, Australia, China, Japan, Malaysia, Korea, Taiwan and India), all in Asian pacific region. Globally, 1,300 subjects and 100 subjects from India with a confirmed diagnosis of CDI in terms of diarrheal symptoms and positive stool test result for CDT or toxigenic C. difficile, or colonoscopic findings of PMC will be enrolled. This will be 8 months duration trial at 06 centers in India. The NDAC has examined the matter and opined that the proposal does not come under the regulatory purview.

15	**Protocol No: P N: 3-001** **ART-123**		On 01 Oct 2012, the applicant firm was permitted to conduct randomized, Double-Blind, Placebo-Controlled, Phase- 3 Study to assess the Safety and Efficacy of **ART-123** (**Recombinant Human Soluble Thrombomodulin**, supplied as 6.0 mg in glass ampoules for dilution upto 1.0 ml with normal saline) in Subjects with **Severe Sepsis and Coagulopathy**. The drug is given by IV- bolus or rapid IV infusion, in the range of 0.06 – 6.0 mg/kg/day over a period of 15 minutes. The Drug is approved in **JAPAN** Since **May 12, 2008**. So far a total of 93,000 patients have been exposed to this drug in Japan. The trial is being conducted in **US, Canada, France, Belgium, Netherlands, Spain, UK and Czech Republic** with estimated enrollment of Globally 800 patients (globally) and 120 subjects in India. The basic trial protocol was assessed for risk / benefit ratios, criteria of innovation / standard care of therapies and the unmet medical need. All amendments in the present protocol have been evaluated by the NDAC in comparison to the previous one in terms of the said criteria and recommends approval for these amendments. The NDAC has examined the matter and observed that there may be two possible adverse Drug Reactions i.e. Bleeding, Immunogenicity and anaphylactic reaction as it is protein drug. The committee has requested for detailed justification for each amendment in Tabular format, detailed Post-Market Surveillance Data from Japan and also the casualty assessment by the DSMB in terms of deaths occurred within 4hrs, 8 hrs., 24 hrs. and all-cause mortality
16	**Protocol No: D4280C0006** **Ceftazidime Avibactam**		The applicant firm has withdrawn the proposal.

17	**Puristeril 340 & Citrosteril**		Firm presented the proposal. The committee opined that the microbiological data using the dialysate fluid be generated and submitted for review.