MINUTES OF THE 12th MEETING OF THE APEX COMMITTEE HELD ON 07-03-2014 UNDER THE CHAIRMANSHIP OF SECRETARY, HEALTH AND FAMILY WELFARE FOR SUPERVISING CLINICAL TRIALS ON NEW CHEMICAL ENTITIES IN THE LIGHT OF DIRECTIONS OF THE HON'BLE SUPREME COURT OF INDIA DATED 03.01.2013

Present:

1. Shri Lov Verma, In Chair
   Secretary,
   Department of Health and Family Welfare.
2. Dr. V. M. Katoch
   Secretary, DHR & DG ICMR,
   New Delhi
3. Dr. Jagdish Prasad,
   Director General of Health Services,
   New Delhi
4. Dr. Arun K.Panda
   Joint Secretary,
   Ministry of Health & Family Welfare
5. Shri R.K. Jain,
   Addl. Secretary & DG (CGHS)
   Ministry of Health and Family Welfare
   (Special Invitee)
6. Dr. G.N. Singh
   DCG(I), FDA Bhavan, New Delhi
   (Special Invitee)

The Apex Committee was apprised that the 12th meeting of the Technical Committee was held on 28.02.2014 under the Chairmanship of DGHS and the committee deliberated various issues related to clinical trials. The minutes of the 12th meeting of the Technical Committee were circulated to the members.

The details of the deliberations made by the Committee are as under:

Evaluation of 47 cases of fresh proposals of clinical trials

The Committee observed that the Technical Committee in its 12th meeting have evaluated 47 cases of fresh proposals of clinical trials keeping in view the 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 I.**

The Committee deliberated on the details of the proposal and agreed to the recommendations of the Technical Committee which had cleared 28 out of 47 proposals. The minutes of the Technical Committee are annexed as Annexure II.

With regard to the recommendations of the Technical Committee on the following points :

1) Expansion of panel of Pharmacologists for NDACs ;

2) Review of the cases of the new drugs already approved and re-examined by NDAC in light of recommendations of 59th report of Parliamentary Standing Committee; and

3) Review of decision of limitation of 3 clinical trial per investigator,

The Committee noted the recommendations and decided that these issues be processed on file for seeking the approval of the Competent Authority. It was also decided that any policy matter/recommendations, outside the mandate of the Committee should be duly processed on file for obtaining the decision of the Competent Authority.

The meeting ended with a vote of thanks to the Chair.

Annexure- I

Sr. No.	Drug	Names of the Applicant	Division
1.	Liraglutide	Novo Nordisk	GCT
2.	Semaglutide	Novo Nordisk	GCT
3.	Glaritus®, Recombinant Insulin Glargine	Wockhardt	GCT
4.	Pasireotidediaspartate/	Novartis	GCT
5.	Lyophilized plasma – derived Factor VIII (EMOCLOT).	Max Neeman	GCT
6.	Obinutuzumab (GA101)	Roche	GCT
7.	Pertuzumab	Roche	GCT
8.	Trastuzumab	Roche	GCT
9.	Ranibizumab/ RFB002 (Lucentis)	Novartis	GCT
10.	Ranibizumab/ RFB002 (Lucentis)	Novartis	GCT
11.	Ranibizumab/ RFB002 (Lucentis)	Novartis	GCT
12.	Paclitaxel, Carboplatin,	Dr. Banavali	GCT
13.	Rituximab Injection	Roche	GCT
14.	QAW039	Novartis	GCT
15.	Pasireotide diaspartate	Novartis	GCT
16.	Liraglutide	Novo Nordisk	GCT
17.	Insulin degludec	Novo Nordisk	GCT
18.	Everolimus/RAD001	Novartis	GCT
19.	LIK066	Novartis	GCT
20.	Fibrinogen Concentrate (Human) (FCH)	Parexel	GCT
21.	Insulin Degludec	Novo Nordisk India Pvt Ltd	Biological (Recombinant)
22.	SII RMab – Human Rabies Monoclonal Antibody	Serum Institute of India	Biological (Recombinant)
23.	PEG-Interferon (PegInterferon alpha-2b)	Virchow Biotech Private Limited	Biological (Recombinant)
24.	Defuze (Enfuvertide)	Virchow Biotech Private Limited	Biological (Recombinant)
25.	Oral Rotavirus Vaccine 116E, Live Attenuated (Phase-III)	Bharat Biotec International Ltd,	Biological (Vaccine)
26.	Oral Rotavirus Vaccine 116E, Live Attenuated (Phase-IV)	Bharat Biotec International Ltd	Biological (Vaccine)

27.	Bivalent Oral Polio Vaccine (bOPV, Type 1 and 3)	Bharat Immunological and Biologicals Corporation Ltd, Bulandshahr	Biological (Vaccine)
28.	H1N1-09 Influenza Virus-Like Particle (VLP) Vaccine	Cadila Pharmaceuticals Limited	Biological (Vaccine)
29.	Myobacterium w (Mw)	Cadila Pharmaceuticals Limited	Biological (Vaccine)
30.	Allogenic Pancreatic Cancer Vaccine (DO-13)	Cadila pharmaceutical Ltd,	Biological (Vaccine)
31.	Trivalent Seasonal Influenza Virus-Like Particle (VLP) Vaccine	Cadila Pharmaceuticals Limited,	Biological (Vaccine)
32.	Rotavirus Vaccine (RIX-4414) Live Attenuated Oral Suspension.	GlaxoSmithKline Pharmaceuticals ltd.	Biological (Vaccine)
33.	DTwP-Hib-IPV vaccine (Easyfourpol™)	Panacea Biotec Ltd.	Biological (Vaccine)
34.	Fully liquid hexavalent DTwp-HepB-Hib-IPV Easysix™ vaccine.	Panacea Biotec Ltd.	Biological (Vaccine)
35.	Pneumococcal Polysaccharide Conjugate Vaccine Adsorbed (10-valent) -NUCOVAC®	Panacea Biotec Ltd.	Biological (Vaccine)
36.	Inactivated Hepatitis A vaccine	Prosper Channel Lifescience India Pvt. Ltd.,	Biological (Vaccine)
37.	Live Attenuated Pentavalent (G1-G2-G3-G4-G9) Human X Bovine Reassortant Rotavirus Vaccine (BRV-PV).	Serum Institute of India, Limited	Biological (Vaccine)
38.	R-STE-009 (Autologous Myoblast)	Reliance Life Sciences	Biological (Stem cell)
39.	R-STE-001 (Autologous cultured chrondrocytes)	Reliance Life Sciences	Biological (Stem cell)
40.	Autologous Adipose Derived Adult Stem cells.	Kasiak Research private ltd.	Biological (Stem cell)
41.	Autologous adipose derived adult stem cell	Kasiak Research private ltd.	Biological (Stem cell)
42.	Peri-Strips Dry® with Veritas® Collagen Matrix Staple Line Reinforcement Peri-Strips Dry® with Veritas® Collagen Matrix Circular Staple Line Reinforcement PSD Gel	Baxter India Pvt. Ltd,	Medical Device
43.	FDC of Tretinoin (as microsphere) Gel	Dr. Reddy's Laboratories Ltd.	FDC
44.	Tadalafil 10mg And Dapoxetine Hydrochloride 30mg	Hetero Labs Limited	FDC
45.	PNB-001 Capsules	PNB Vesper Life Science Pvt. Ltd., India	IND
46.	Centhaquin Injection	Pharmazz India Pvt. Ltd.	IND
47.	MiADMSA (Monoisoamyl 2,3-dimercaptosuccinic Acid)	DRDO, Gwalior	IND

ANNEXURE_II

MINUTES OF THE 12th MEETING OF TECHNICAL COMMITTEE HELD ON 28-02-2014 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, Director General of Health Services	Chairman
2.	Dr. Yash Paul, Prof and Head, Dept. of Cardiology, PGIMER Chandigarh	Member
3.	Dr. Raju titus Chacko, Prof. & Head, Dept. of Medical oncology, CMC, Vellore.	Member
4.	Dr. Kamlakar Tripathi Professor, Dept. of Medicine, Institute of Medical Sciences, BHU, Varanasi-221005	Member
5.	Dr. B.L. Sherwal, DDG(M) & Director-Prof., Dept. of Microbiology, LHMC & Associated Hospitals, New Delhi.	Member

From CDSCO:

1. Dr. G.N. Singh,
   Drugs Controller General (India)
2. Dr. V. G.Somani,
   Joint Drugs Controller (India)
3. Sh. A.K. Pradhan,
   Deputy Drugs Controller (India)
4. Mrs. A Vishala,
   Deputy Drugs Controller (India)
5. Sh. R. Chandrashekhar,
   Deputy Drugs Controller (India)

Dr. Jagdish Prasad, DGHS welcomed the members and briefed them about the outcome of the eleventh meeting of the Technical Committee which was held on 15.01.14 and 16.01.14. The minutes of the eleventh meeting approved by the Chairman were already circulated to the members.

Evaluation of 47 cases of fresh proposals of clinical trials

The details of 47 fresh proposals of clinical trials of new drugs (including INDs, Biological, FDCs and Medical device) and Global Clinical Trials were forwarded through e-mail to the members as per the format approved by the Committee in its fourth meeting. The list of these proposals is as under:

Sr. No.	Drug	Names of the Applicant	Division
1.	Liraglutide	Novo Nordisk	GCT
2.	Semaglutide	Novo Nordisk	GCT
3.	Glaritus®, Recombinant Insulin Glargine	Wockhardt	GCT
4.	Pasireotidediaspartate/	Novartis	GCT
5.	Lyophilized plasma – derived Factor VIII (EMOCLOT).	Max Neeman	GCT
6.	Obinutuzumab (GA101)	Roche	GCT
7.	Pertuzumab	Roche	GCT
8.	Trastuzumab	Roche	GCT
9.	Ranibizumab/ RFB002 (Lucentis)	Novartis	GCT
10.	Ranibizumab/ RFB002 (Lucentis)	Novartis	GCT
11.	Ranibizumab/ RFB002 (Lucentis)	Novartis	GCT
12.	Paclitaxel, Carboplatin,	Dr. Banavali	GCT
13.	Rituximab Injection	Roche	GCT
14.	QAW039	Novartis	GCT
15.	Pasireotide diaspartate	Novartis	GCT
16.	Liraglutide	Novo Nordisk	GCT
17.	Insulin degludec	Novo Nordisk	GCT
18.	Everolimus/RAD001	Novartis	GCT
19.	LIK066	Novartis	GCT
20.	Fibrinogen Concentrate (Human) (FCH)	Parexel	GCT
21.	Insulin Degludec	Novo Nordisk India Pvt Ltd	Biological (Recombinant)
22.	SII RMab – Human Rabies Monoclonal Antibody	Serum Institute of India	Biological (Recombinant)
23.	PEG-Interferon (PegInterferon	Virchow Biotech Private	Biological

	alpha-2b)	Limited	(Recombinant)
24.	Defuze (Enfuvertide)	Virchow Biotech Private Limited	Biological (Recombinant)
25.	Oral Rotavirus Vaccine 116E, Live Attenuated (Phase-III)	Bharat Biotec International Ltd,	Biological (Vaccine)
26.	Oral Rotavirus Vaccine 116E, Live Attenuated (Phase-IV)	Bharat Biotec International Ltd	Biological (Vaccine)
27.	Bivalent Oral Polio Vaccine (bOPV, Type 1 and 3)	Bharat Immunological and Biologicals Corporation Ltd, Bulandshahr	Biological (Vaccine)
28.	H1N1-09 Influenza Virus-Like Particle (VLP) Vaccine	Cadila Pharmaceuticals Limited	Biological (Vaccine)
29.	Myobacterium w (Mw)	Cadila Pharmaceuticals Limited	Biological (Vaccine)
30.	Allogenic Pancreatic Cancer Vaccine (DO-13)	Cadila pharmaceutical Ltd,	Biological (Vaccine)
31.	Trivalent Seasonal Influenza Virus-Like Particle (VLP) Vaccine	Cadila Pharmaceuticals Limited,	Biological (Vaccine)
32.	Rotavirus Vaccine (RIX-4414) Live Attenuated Oral Suspension.	GlaxoSmithKline Pharmaceuticals ltd.	Biological (Vaccine)
33.	DTwP-Hib-IPV vaccine (Easyfourpol™)	Panacea Biotec Ltd.	Biological (Vaccine)
34.	Fully liquid hexavalent DTwp-HepB-Hib-IPV Easysix™ vaccine.	Panacea Biotec Ltd.	Biological (Vaccine)
35.	Pneumococcal Polysaccharide Conjugate Vaccine Adsorbed (10-valent) -NUCOVAC®	Panacea Biotec Ltd.	Biological (Vaccine)
36.	Inactivated Hepatitis A vaccine	Prosper Channel Lifescience India Pvt. Ltd.,	Biological (Vaccine)
37.	Live Attenuated Pentavalent (G1-G2-G3-G4-G9) Human X Bovine Reassortant Rotavirus Vaccine (BRV-PV).	Serum Institute of India, Limited	Biological (Vaccine)
38.	R-STE-009 (Autologous Myoblast)	Reliance Life Sciences	Biological (Stem cell)
39.	R-STE-001 (Autologous cultured chrondrocytes)	Reliance Life Sciences	Biological (Stem cell)
40.	Autologous Adipose Derived Adult Stem cells.	Kasiak Research private ltd.	Biological (Stem cell)
41.	Autologous adipose derived adult stem cell	Kasiak Research private ltd.	Biological (Stem cell)
42.	Peri-Strips Dry® with Veritas® Collagen Matrix Staple Line Reinforcement Peri-Strips Dry® with Veritas® Collagen Matrix Circular Staple	Baxter India Pvt. Ltd,	Medical Device

	Line Reinforcement PSD Gel		
43.	FDC of Tretinoin (as microsphere) Gel	Dr. Reddy's Laboratories Ltd.	FDC
44.	Tadalafil 10mg And Dapoxetine Hydrochloride 30mg	Hetero Labs Limited	FDC
45.	PNB-001 Capsules	PNB Vesper Life Science Pvt. Ltd., India	IND
46.	Centhaquin Injection	Pharmazz India Pvt. Ltd.	IND
47.	MiADMSA (Monoisoamyl 2,3-dimercaptosuccinic Acid)	DRDO, Gwalior	IND

The Committee evaluated these proposals by 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 /MDAC /IND. The recommendations of the Committee in respect of these 47 proposals are as under:

- For proposal at Sr. No. 1 to 11, the Committee noted that there is no Pharmacologist present during NDAC deliberation, hence the written opinion of the Pharmacologist (from amongst the NDAC experts) shall be obtained.
- For proposal at Sr. No. 5 the Committee recommended that CDSCO shall obtain written opinion of Pharmacologist & Hematologist (from amongst the NDAC experts).
- For proposal at Sr. No. 9 to 11, the written opinion of pharmacologist and endocrinologist (from amongst the NDAC experts) shall be obtained.
- For proposal at Sr. No. 18, the Firm should submit undertaking to provide post trial access, free of cost for those subjects who benefit clinically.
- For proposal at Sr. No. 19, the Committee recommended that the NDAC may re-deliberate the matter in view of the large number of exclusion criteria including the feasibility for enrolling subjects for this trial.
- For proposal at Sr. No. 20, the Committee noted that it is a case where the clinical trial permission was already granted and therefore, needs no further deliberation. The Committee recommended that the current status of the trial shall be obtained.
- For proposal at Sr. No. 21, the Committee noted that the firm proposes to conduct the study on 1000 patients. Therefore, the Committee recommended that the firm should submit their plan to enroll so many patients in nine centers within one year.
- For proposal at Sr. No. 29 and 30, the Committee observed that the trial is proposed to be conducted in cancer patients. Therefore, the Committee recommended that these proposals should again be referred to their respective NDACs Committees for consultation of oncologists as they are for oncology indication.
- For Proposals at Sr. No. 38 and 39, the Committee recommended that the firm should submit the details of specialty of the investigators involved in the study and also should ensure that there is equal geographic distribution of the centers. For proposal at Sr. No. 38 which is for urinary incontinence it is recommended that the investigators should be included from urology and Gynecology.

- For remaining 28 cases mentioned at Sr. No. 12, 13, 14, 15, 16, 17, 22, 23, 24, 25, 26, 27, 28, 31, 32, 33, 34, 35, 36, 37, 40, 41, 42, 43, 44, 45, 46 and 47 the Committee recommended for giving permission to conduct the trials.

Proper representation of experts including Pharmacologist during NDAC deliberation

The attention of the Committee was drawn to its earlier meetings wherein it has observed that NDACs have made recommendations for the conduct of clinical trial etc. in several cases wherein there was no proper representation of the concerned specialist including Pharmacologist. In some of the NDAC's the experts members have retired, some of the members are no more associated with the organization and some of them have refused due to their busy schedule. The present practice is that the Pharmacologist specified for particular NDACs are only called to offer expert opinion.

The Committee after deliberation recommended that whenever a Pharmacologist in the panel is absent, the minutes of the NDACs alongwith the presentation of the firms and/or supportive literature may be referred to the Pharmacologist approved in the panel of NDAC for his/her expert opinion.

It was also opined by DCG(I) and agreed by the members of the Committee that Coordinator of Adverse Drug Reactions (ADRs) monitoring centers who happens to be the Senior Pharmacologist of the Medical Colleges may also be taken as expert for NDAC from the 150 ADR monitoring centers on the board of Pharmacovigilance Programme of India (PvPI), Ghaziabad. This would be treated as panel of expert of Pharmacologists from which office of DCG(I) would call experts as per need of the proposal so that in each and every proposal one or more Pharmacologist is present.

Action taken by CDSCO on the recommendation of Parliamentary Standing Committee

The Committee was further apprised 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. The report has made various recommendations and observations on approval of certain new drugs. As per action taken report, it was decided that the drug would be referred to NDACs for examination and review related to continue marketing of these drugs and updating of their product monographs in light of recent knowledge & regulatory changes overseas.

Accordingly, some of the proposals have already been referred and deliberated in the NDAC meetings. In certain cases, the NDACs have recommended for continued marketing of the drugs and in some cases the NDACs have requested to furnish additional safety data in order to take further action.

The Committee after deliberation recommended that such proposals should be referred to the Committee for their review.

Representation to reconsider the condition to limit of more than three clinical trial per Investigator

The Committee was apprised that as per actions taken on the recommendations of Prof. Ranjit Roy Chaudhury Expert Committee to formulate policy and guidelines for approval of new drugs, clinical trials and banning of drugs, it was made mandatory that the sponsor shall ensure that the number of clinical trials an investigator can undertake should be commensurate with the nature of the trial, facility available with the investigator etc. However, under no circumstances the number of trials should be more than three at a time.

The Committee was further informed that various representations have been received from stake holders to reconsider the decision to limit the number of clinical trials supervised by an investigator. It was stated that the time required to spend on a clinical trial vary from study to study and from stage to stage in a given study. For example OPD based study require less time when compared to inpatients studies or study in critically ill patients. Also attention required is much more during the enrollment stage of the study when the patients are getting recruited (will again vary depending on slow or rapidly recruiting trial), stabilizes during the treatment period and is minimal when the patient is in long term follow-up /post treatment /completion. Putting a number cap abruptly will also result in de-growth of current good sites/ investigators and well developed research set ups/ departments as they cannot participate in multiple studies even though they have capabilities, staff and infrastructure to do so.

The Chairman informed that the said issue should be decided after wider consultations including the stake holders. Further action will be taken accordingly.

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