Minutes of the 25th meeting of the APEX Committee held on 03.11.2015 under the Chairmanship of Secretary, Health and Family Welfare for supervising clinical trials on New Chemical Entities in the light of the directions of the Hon'ble Supreme Court of India dated 03.01.2013.

Present:

1. Shri B. P. Sharma,
   Secretary, Department of Health and Family Welfare
   and Chairman, Apex Committee

2. Dr Soumya Swaminathan,
   Secretary, Department of Health Research and
   DG , ICMR.

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

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

Special Invitee:

1 Shri K. B. Aggrawal
Additional Secretary (Food and Drugs)
Department of Health and Family Welfare, New Delhi

2 Dr G N Singh ,
Drugs Controller General(I)

3 Dr. V.G. Somani,
Joint Drugs Controller (I), FDA Bhawan, New Delhi

Initiating the discussion, the Chairman, Apex Committee welcomed the members of the Committee and special invitees to the meeting. Thereafter, the Committee deliberated upon each of the agenda items and recommended as following:

Item No. 1. Proposals of Clinical Trials related to New Chemical Entities (NCEs) recommended by Technical Committee.

(1) A Phase II Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of FG-3019 in Patients with Idiopathic Pulmonary Fibrosis. Protocol No: FGCL-3019-067

The Apex Committee after detailed deliberations, concurred with the recommendations of Technical Committee as detailed in agenda notes annexed at **Annexure-I.** Further, the Apex Committee directed that the Technical Committee be asked to workout feasibility of providing Post Trial Access to the patient included in the placebo group. The Apex Committee also opined that other drugs of the manufacturer viz., Nintedanib which is being considered for clinical trial waiver as part of other proposal for this indication (IPF) in this meeting, could also be made available to the participants in the Placebo Group.

(2) A randomized, double-blind, placebo-controlled Phase I clinical study to evaluate the safety, tolerability and pharmacokinetics of ZYDPLA1, a novel DPP- IV inhibitor, following oral administration in healthy volunteers. Protocol No: ZYDPLA1 1001

The Apex Committee, after detailed deliberations, concurred with the recommendations of Technical Committee for approval of clinical trial protocol for conduct of the study, as detailed in agenda notes annexed at **Annexure-I.**

(3) A safety, pharmacokinetics and pharmacodynamics study of CPL-2009-0031 in healthy volunteers and patients with Type 2 Diabetes mellitus (T2D M)"manufactured indigenously by Cadila Pharmaceuticals Limited. Protocol No: CRSC12015

The Apex Committee after detailed deliberations, concurred with the recommendations of Technical Committee for approval of clinical trial protocol for conduct of phase-I study, as detailed in agenda notes annexed at **Annexure-I.**

(4) A multi-center, randomized, double-blind, placebo controlled study to investigate the efficacy and safety of 52 weeks treatment with QGE031 s.c. in asthma patients not adequately controlled by medium- or high-dose ICS plus LABA with or without OCS". Protocol No: CQGE031B2204

The Apex Committee after detailed deliberations, concurred with the recommendations of Technical Committee for approval of clinical trial protocol for conduct of the study, as detailed in agenda notes annexed at **Annexure-I.** However, the Committee decided that the condition of specific inclusion of trial sites from Eastern part of the country need not be visited upon.

Annexed

(5) A randomized, double-blind, placebo-controlled Phase I clinical study to evaluate the safety, tolerability and pharmacokinetics of ZYAN1, a novel PHD-2 Inhibitor, following oral administration in healthy volunteers. Protocol No: ZYAN11001.

The Apex Committee after detailed deliberations, concurred with the recommendations of Technical Committee for approval of clinical trial protocol for conduct of the study, as detailed in agenda notes annexed at **Annexure-I**.

Item No. 2. Waiver of Clinical Trial in Indian population for approval of New Drugs and Devices falling under the category of Drugs, which have already been approved outside India.

(1) Nintedanib Capsules 100 mg and 150 mg of M/s. Boehringer Ingelheim India Pvt. Ltd.

The Apex Committee after detailed deliberations concurred with the recommendations of Technical Committee for approval of waiver of local clinical trial, as detailed in agenda notes annexed at **Annexure-II**.

(2) Dabrafenib Mesylate capsule 50/75mg of M/s. Glaxo Smith Kline Pharmaceuticals Limited.

The Apex Committee after detailed deliberations concurred with the recommendations of Technical Committee for approval of waiver of local clinical trial, as detailed in agenda notes annexed at **Annexure-II**.

(3) "Celox Gauze and Celox Z Fold Gauze of M/s. Emergo India Consulting Pvt. Ltd.

The Apex Committee after detailed deliberations concurred with the recommendations of Technical Committee for approval of waiver of local clinical trial, as detailed in agenda notes annexed at **Annexure-II**.

(4) Sofosbuvir (400 mg) + Ledipasvir (90 mg) of M/s Mylan Pharmaceutical (Import), M/s Mylan Labs, M/s Hetero Labs Limited & M/s.Natco Pharma Ltd.

The Apex Committee after detailed deliberations concurred with the recommendations of Technical Committee for approval of waiver of local clinical trial, as detailed in agenda notes annexed at **Annexure-II**.

(5) Daclatasvir 30 mg and 60 mg Tablet of M/s Hetero Labs Limited & M/s Natco Pharma Ltd.

The Apex Committee after detailed deliberations concurred with the recommendations of Technical Committee for approval of waiver of local clinical trial, as detailed in agenda notes annexed at **Annexure-II**.

(6) Siltuximab of M/s Johnson & Johnson Private Limited.

The Apex Committee after detailed deliberations concurred with the recommendations of Technical Committee for approval of waiver of local clinical trial, as detailed in agenda notes annexed at **Annexure-II**.

(7) Inactivated Polio Vaccine of M/s Serum Institute India.

The Apex Committee after detailed deliberations concurred with the recommendations of Technical Committee for approval of waiver of local clinical trial, as detailed in agenda notes annexed at **Annexure-II**.

Other Item (1)

The Apex Committee directed that a suitable criteria should be evolved as a guidance for taking decisions in matters relating to waiver of clinical trials including the level at which such decisions should be taken. The Committee was of the view that all such proposals need not be brought before the Apex Committee.

Other Item (2)

Joint Secretary (R) informed that in a meeting held under the chairmanship of Principal Secretary to PM on 02.11.2015, it was decided that the MoHFW will bring out a document to provide clarity in matters relating to clinical trials which have already been discussed with industry, academia and other stakeholders within a period of 30 days. In this connection, it was noted that the matter had been discussed in two meetings held under the chairmanship of Secretary, HFW and minutes of those meetings are under finalisation. Secretary, DHR agreed to convene a meeting at her level to discuss other residual issues.

The meeting ended with vote of thanks to and from the Chairman.

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AGENDA NOTES

25th Meeting of Apex Committee

Agenda

1. Proposals of Clinical Trials related to New Chemical Entities (NCEs) recommended by Technical Committee.
2. Waiver of Clinical Trial in Indian population for approval of New Drugs and Devices falling under the category of Drugs, which have already been approved outside India.

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Item No: 01

Proposals of Clinical Trials related to NCEs recommended by Technical Committee.

The Technical Committee evaluated the 05 cases (02 cases of 28th Technical Committee and 03 cases of 29th Technical Committee meeting) related to clinical trial of NCEs considering all aspects of safety, efficacy especially in terms of the three parameters viz. risk versus benefit to the patients, innovation vis-a-vis existing therapeutic option and unmet medical need in the country. After detailed deliberation, the Committee recommended all 05 cases of NCEs. The recommendations of the Technical Committee in respect of these 05 cases related to clinical trial of NCEs which were recommended by the Technical Committee are enclosed as **Annexure-I.**

The details of these 05 proposals and recommendations of the Technical Committee and SEC are as given below for consideration of Apex Committee:

28th Technical Committee meeting:

1) Proposal No: 01

Phase II study of the drug FG-3019 is a Global Clinical trial which will be carried out in USA, and Canada besides India vide Protocol No: FGCL-3019-067, details of which are as following:

Protocol title of the Clinical trial:	A Phase II Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of FG-3019 in Patients with Idiopathic Pulmonary Fibrosis
Name of the Drug:	FG-3019
Name of the Applicant	Excel Life Sciences Pvt. Ltd. D-62, 1st floor, Sector2, Noida-201301 Uttar Pradesh, India
Name of the Sponsor:	FibroGen, Inc. 409 Illinois Street San Francisco, California 94158 USA
Name of the Manufacturer:	Boehringer Ingelheim Pharma GmbH & Co. KG Birkendorfer Str. 65 88397 Biberach/Riss Germany.
Type of Clinical Trial:	Global
Phase of the study:	Phase II

Consideration by Subject Expert Committee:

The proposal was deliberated upon by the SEC in its meeting held on 30.06.2015. After detailed deliberation the committee recommended the conduct of the study subject to the conditions that the failure and intolerance to perfinedone (only approved drug for IPF) should be carefully assessed by the investigator before including them into the trial. The reasons for the failure shall be explicitly documented in source document. Recommendations of the SEC are at **Annexure –I**.

Consideration by Technical Committee

After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation. Recommendations of the Technical Committee are at **Annexure –I**

Proposal No: 02

Phase I study of the drug ZYDPLA1 to be carried out in India only vide Protocol No: ZYDPLA1 1001, details of which are as following:

Protocol title of the Clinical trial:	A randomized, double-blind, placebo-controlled Phase I clinical study to evaluate the safety, tolerability and pharmacokinetics of ZYDPLA1, a novel DPP- IV inhibitor, following oral administration in healthy volunteers.
Name of the Drug:	ZYDPLA1
Name of the Applicant	Zydus Research Centre,Cadila Healthcare Limited, Survey No. 396/403, Opp. Sarvottam Hotel, Nr. Nova Petrochemicals, Sarkhej-Bavla N.H. No. 8A, Moraiya, Ahmedabad-382213 Gujarat, India,
Name of the Sponsor:	Same as above
Name of the Manufacturer:	Cadila Healthcare Limited, Survey No. 417, 419 & 420, Sarkhej Bavla, N. H. No. 8A, Moraiya, Tal. Sanand, Ahmedabad - 382 210. India.
Type of Clinical Trial:	India specific
Phase of the study:	Phase-I

Consideration by IND Committee:

The proposal was deliberated upon by the IND in its meeting held on 06.02.2015. The Committee noted from the firm's presentation that the proposed study is a multicentric trial in USA and India and pK study in USA commenced with the approval of the FDA and is currently under progress. After detailed deliberation the Committee recommended the proposed study subject to following conditions:-

- Cardiac monitoring should be monitored by Cardiologist.
- Upper limit of Haemoglobin should be less than 15 g/dL.
- Complete chemical structure should be submitted to CDSCO.
- DSMB should be constituted to monitor the study.

Accordingly, revised protocol etc. should be revised and submitted to DCGI. Recommendations of the IND are at **Annexure –I**.

Consideration by Technical Committee

After detailed deliberation, the Committee recommended to conduct the study as per the IND recommendation. Recommendations of the Technical Committee are at **Annexure –I**

The Committee may deliberate the proposals and give its recommendations.

29th Technical Committee meeting:

Proposal No: 03

Phase I/II study of the drug CPL-2009-0031 Film coated tablets (35mg, 70mg & 140mg) will be carried out in India vide Protocol No: CRSC12015, details of which are as following:

Protocol title of the Clinical trial:	A safety, pharmacokinetics and pharmacodynamics study of CPL-2009-0031 in healthy volunteers and patients with Type 2 Diabetes mellitus (T2D M)"manufactured indigenously by Cadila Pharmaceuticals Limited.
Name of the Drug:	CPL-2009-0031 Film coated tablets (35mg, 70mg & 140mg)
Name of the	Cadila Pharmaceuticals Limited, 1389-Trasad Road, Dholka – 387810, Dist – Ahmedabad, Gujarat.

Applicant	
Name of the Sponsor:	Same as above
Name of the Manufacturer:	Same as above
Type of Clinical Trial:	India specific
Phase of the study:	Phase- I/II

Consideration by IND Committee:

Recommendation of the IND meeting on 06.08.2015:

The proposal was deliberated upon by the IND Committee in its meeting held on 06.08.2015. After detailed deliberation the Committee recommended to conduct Phase-I clinical trial in healthy volunteers as per stage-I of the protocol, based on the 28 days repeat dose toxicity study report and comparative pK study conducted with the Investigational product vs Sitagliptin in rats. Further toxicity studies of duration as prescribed in Schedule-Y need to be carried out as the molecule will go in further clinical developmental stages. Recommendations of the IND Committee are at **Annexure –I.**

Consideration by Technical Committee

After detailed deliberation, the Committee recommended the conduct of the study as per the IND Committee recommendation. Recommendations of the Technical Committee are at **Annexure –I**

Proposal No: 04

Phase IIb study of the drug QGE031 is a Global Clinical trial which will be carried out in USA, and Canada besides India vide Protocol No: CQGE031B2204, details of which are as following:

Protocol title of the Clinical trial:	A multi-center, randomized, double-blind, placebo controlled study to investigate the efficacy and safety of 52 weeks treatment with QGE031 s.c. in asthma patients not adequately controlled by medium- or high-dose ICS plus LABA with or without OCS".
Name of the Drug:	QGE031
Name of the Applicant	Novartis Healthcare Private Limited, Sandoz House, Shivsagar Estate, Dr. Annie Besant Road, Worli Mumbai - 400 018

Name of the Sponsor:	Same as above
Name of the Manufacturer:	Novartis Pharma AG, Schaffhauserstrasse 101, CH-4332 Stein, Switzerland
Type of Clinical Trial:	Global Clinical Trial
Phase of the study:	IIb

Consideration by SEC Committee:

Recommendation of the SEC :

The proposal was deliberated upon SEC. After detailed deliberation the committee recommended the conduct of the study subject to the following conditions.

1. Patient with tropical pulmonary eosinophilia should be excluded.

2. Adrenaline should be provided for the management of hypersensitivity at the trial site.

3. Trial site should be selected from Eastern part of the country.

Recommendations of the SEC are at **Annexure –I**.

Consideration by Technical Committee

After detailed deliberation, the Committee recommended the conduct of the study as per the SEC recommendation. Recommendations of the Technical Committee are at **Annexure –I**

Proposal No: 05

Phase I study of the drug ZYAN1 to be carried out in India only vide Protocol No: ZYAN11001, details of which are as following:

Protocol title of the Clinical trial:	A randomized, double-blind, placebo-controlled Phase I clinical study to evaluate the safety, tolerability and pharmacokinetics of ZYAN1, a novel PHD-2 Inhibitor, following oral administration in healthy volunteers.
Name of the Drug:	ZYAN1
Name of the Applicant	Zydus Research Centre, Cadila Healthcare Limited, Survey No. 396/403, Opp. Sarvottam Hotel, Nr. Nova Petrochemicals, Sarkhej-Bavla N.H. No. 8A,Moraiya, Ahmedabad-382213 Gujarat, India

Name of the Sponsor:	Same as above
Name of the Manufacturer:	Cadila Healthcare Limited Survey No. 417, 419 & 420,Sarkhej Bavla, N. H. No. 8A, Moraiya, Tal. Sanand, Ahmedabad - 382 210. India.
Type of Clinical Trial:	India specific
Phase of the study:	Phase-I

Consideration by IND Committee:

The proposal was deliberated upon by the IND in its meeting held on 06.02.2015. The Committee noted from the firm's presentation that the proposed study is multicentric in Australia and India and the firm has received permission from the regulatory authorities of Australia to conduct the study. After detailed deliberation the Committee recommended the proposed study subject to the following conditions:-

- Study should be conducted under the full time monitoring of a Cardiologist.
- Upper limit of Haemoglobin should be less than 15 g/dL.
- Complete chemical structure should be submitted to CDSCO.
- DSMB should be constituted to monitor the study.

Accordingly, revised protocol etc. should be revised and submitted to DCGI. Recommendations of the IND are at **Annexure –I.**

Based on the IND Committee recommendation, the firm submitted the revised clinical trial protocol and the proposal was deliberated in the Technical Committee in its meeting held on 21.08.2015.

Consideration by Technical Committee on 21.08.2015

After detailed deliberation, the Committee sought the clarification and presentation on following observation.

1. Animal details indicating the pharmacology and mechanism of action of the NCE are not explained clearly. The details of proof of pharmacological action in the given therapeutic indication, which justify further trials in human, are not given.
2. The hypoxia related disorder which is mentioned as one of the proposed indication is too general and needs to be specified.

Recommendations of the Technical Committee are at **Annexure –I.**

Based on the recommendation of the Committee, the firm was asked to present the proposal before the Committee.

Recommendation of the Technical Committee on 12.10.2015: Accordingly the firm gave presentation before the Committee. After deliberation, the Committee recommended the conduct of the study.

Item No: 02

Waiver of Clinical Trial in Indian population for approval of New Drugs and Devices falling under the category of Drugs, which have already been approved outside India.

07 proposals (04 from New Drugs Division, 02 from Biological and 01 from Medical Device) were placed before the Technical Committee for consideration of permission for manufacture/ import for marketing in the country without local clinical trial. Out of these 06 proposals, 02 proposals (S. No 04 and 05 of **Annexure-II**) have not been recommended by the SEC. However various representations have been received through e-mail from the stakeholders and associations to reconsider the proposal for approval of the drug for import/manufacturing and marketing with waiver of local clinical trial.

The details of recommendations of the Technical Committee along with recommendation of the SEC are annexed at **Annexure-II.**

The Committee may deliberate the proposals.

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Annexure-I

List of 02 cases of clinical trial of NCEs along with their evaluations and recommendations of the Technical Committee in its 28th Meeting.

Proposal No	Details of the proposal	Assessment of the Proposal *vis –a vis* specified Parameters	Recommendation 1. Subject Expert Committee 2. Technical Committee
1.	**Name of the Drug:** FG-3019 **Protocol No** : FGCL-3019-067 **Phase of the Study:** Phase II **Name of the Applicant** : Excel Life Sciences Pvt. Ltd. D-62, 1st floor, Sector2, Noida-201301 Uttar Pradesh, India **Name of the Sponsor:** FibroGen, Inc. 409 Illinois Street San Francisco, California 94158 USA **Name of the Manufacturer:** Boehringer Ingelheim Pharma GmbH & Co. KG Birkendorfer Str. 65 88397 Biberach/Riss Germany. **Title:** A Phase 2 Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of FG-3019 in Patients with Idiopathic Pulmonary Fibrosis	**Assessment of Risk vs. Benefit to the patients**: The safety profile of the test drug from various preclinical pharmacokinetic, repeat dose toxicity, phase I and ongoing phase II clinical study justify the conduct of the study. **Innovation *vis-à-vis* Existing Therapeutic Option**: The purpose of the study is to evaluate safety and efficacy of FG-2019 in patients with idiopathic pulmonary fibrosis. **Unmet Medical Need in the country**: The test drug may provide an additional treatment option in patients with idiopathic pulmonary fibrosis.	**1. SEC Recommendation on 30-06-15:** After detailed deliberation the committee recommended the conduct of the study subject to the conditions that the failure and intolerance to perfinedone (only approved drug for IPF) should be carefully assessed by the investigator before including them in to the trial. The reasons for the failure shall be explicitly documented in source document. **2.Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended to conduct the study as per the SEC recommendation.
2.	**Name of the Drug:** ZYDPLA1 **Protocol no:** ZYDPLA1 1001 Phase of the Study: Phase I Name of the	**Risk versus benefit to the patients** As this is a first in human trial, safety and tolerability yet to be defined, though considered safe on basis of pre-clinical results. Subjects taking part in this phase I study might not have any direct benefit from this study other than the benefit of	**1.Recommendation of the IND Committee** : The Committee noted from the firm's presentation that the proposed study is a multicentric trial in USA and India and pK study in USA commenced with the approval of the FDA and is currently under progress. After detailed deliberation the

	Applicant: Zydus Research Centre, Cadila Healthcare Limited, Survey No. 396/403, Opp. Sarvottam Hotel, Nr. Nova Petrochemicals, Sarkhej-Bavla N.H. No. 8A, Moraiya, Ahmedabad-382213 Gujarat, India, **Name of the Sponsor:** Same as above. **Name of the manufacturer:** Cadila Healthcare Limited Survey No. 417, 419 & 420, Sarkhej Bavla, N. H. No. 8A, Moraiya, Tal. Sanand, Ahmedabad - 382 210. India. **Title:** A randomized, double-blind, placebo-controlled Phase I clinical study to evaluate the safety, tolerability and pharmacokinetics of ZYDPLA1, a novel DPP-IV inhibitor, following oral administration in healthy volunteers	free medical checkup but they will contribute to the medical science by helping us generate the safety and tolerability data on this new chemical entity which will be helpful for many other people in future. **Innovation *vis-a-vis* existing therapeutic option** Oral route of administration with dosing frequency once a week only **Unmet medical need in the country:** Better compliance for diabetic patients as the dosing frequency will be once a week	Committee recommended the proposed study subject to following conditions:- • Cardiac monitoring should be monitored by Cardiologist. • Upper limit of Haemoglobin should be less than 15 g/dL.. • Complete chemical structure should be submitted to CDSCO. • DSMB should be constituted to monitor the study. Accordingly, revised protocol etc. should be revised and submitted to DCGI **2. Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended to conduct the study as per the IND recommendation.

List of 03 cases of clinical trial of NCEs along with their evaluations and recommendations of the Technical Committee in its 29th Meeting.

Proposal No	Details of the proposal	Assessment of the Proposal *vis –a vis* specified Parameters	Recommendation 1. Subject Expert Committee /IND Committee 2. Technical Committee
3.	**Name of the Drug:** CPL-2009-0031 Film coated tablets (35mg, 70mg & 140mg) **Protocol No :** CRSC12015 **Phase of the Study:** Phase I/II **Name of the Applicant:** Cadila Pharmaceuticals Limited, 1389-Trasad Road, Dholka – 387810, Dist – Ahmedabad, Gujarat. **Name of the Sponsor:** Same as above **Name of the Manufacturer:** Same as above **Title:** A safety, pharmacokinetics and pharmacodynamics study of CPL-2009-0031 in healthy volunteers and patients with Type 2 Diabetes mellitus (T2DM)"manufactured indigenously by Cadila Pharmaceuticals Limited.	**Assessment of Risk vs. Benefit to the patients:** DPP-IV inhibitors have been suggested as drug candidates for the treatment of impaired glucose tolerance and T2DM. Sitagliptin, Saxagliptin and Vildagliptin which act by inhibiting DPP-IV, are currently used clinically for the treatment of T2DM with good safety and efficacy profile. The test drug used in the study is a pro drug of Sitagliptin. **Innovation *vis-à-vis* Existing Therapeutic Option:** The test drug is a prodrug of Sitagliptin which may have better safety profile than Sitagliptin. **Unmet Medical Need in the country:** Despite the availability of various antidiabetic treatments, the majority of the subjects fail to attain or maintain optimum glycemic control over time, increasing their risk for serious microvascular and macrovascular complications, majorly being cardiovascular outcomes.	1. **IND Recommendation on 06-08-15:** After detailed deliberation the Committee recommended to conduct Phase-I clinical trial in healthy volunteers as per stage-I of the protocol, based on the 28 days repeat dose toxicity study report and comparative pK study conducted with the Investigational product vs Sitagliptin in rats. Further toxicity studies of duration as prescribed in Schedule-Y need to be carried out as the molecule will go in further clinical developmental stages. **2.Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended the conduct of the study as per the SEC recommendation.
4.	**Name of the Drug:** QGE031 **Protocol No:** CQGE031B2204 **Phase:** IIb **Name of the Applicant:** Novartis Healthcare Private Limited, Sandoz	**Risk versus benefit to the patients:** The safety profile of the test drug from various pre clinical studies including repeat dose, reproductive and development toxicity, juvenile toxicity and clinical phase I, II studies justify the conduct of the study. Innovation vis a vis existing	1. **Recommendation of the SEC:** After detailed deliberation the committee recommended the conduct of the study subject to the following conditions. 1. Patient with tropical pulmonary eosinophilia should be excluded.

	House, Shivsagar Estate, Dr. Annie Besant Road, Worli Mumbai - 400 018. **Name of the Sponsor:** Same as above **Name of the Manufacturer:** Novartis Pharma AG, Schaffhauserstrasse 101, CH-4332 Stein, Switzerland **Title:** A multi-center, randomized, double-blind, placebo controlled study to investigate the efficacy and safety of 52 weeks treatment with QGE031 s.c. in asthma patients not adequately controlled by medium- or high-dose ICS plus LABA with or without OCS".	**therapeutic option-** The propose of the study is to investigate the efficacy and safety of 52 weeks treatment with subcutaneous QGE031 in asthma patients not adequately controlled with medium or high-dose inhaled corticosteroids and long acting β2-agonists with or without OCS. **Unmet need-** The test drug may be an alternative treatment option in asthma patients.	2. Adrenaline should be provided for the management of hypersensitivity at the trial site. 3. Trial site should be selected from Eastern part of the country. **2.Recommendation of the Technical Committee:** After detailed deliberation, the Committee recommended the conduct of the study as per the SEC recommendation.
5.	**Name of the Drug:** ZYAN1 **Protocol no:** ZYAN11001 **Phase of the Study:** Phase I **Name of the Applicant:** Zydus Research Centre, Cadila Healthcare Limited, Survey No. 396/403, Opp. Sarvottam Hotel, Nr. Nova Petrochemicals, Sarkhej-Bavla N.H. No. 8A, Moraiya, Ahmedabad-382213 Gujarat, India, **Name of the Sponsor:** Same as above. **Name of the manufacturer:** Cadila	**Risk versus benefit to the patients** As this is a first in human trial, safety and tolerability yet to be defined, though considered safe on basis of pre-clinical results. Subjects taking part in this phase I study might not have any direct benefit from this study other than the benefit of free medical checkup but they will contribute to the medical science by helping us generate the safety and tolerability data on this new chemical entity which will be helpful for many other people in future. **Innovation *vis-a-vis* existing therapeutic option:** Oral route of administration instead parentral route for the treatment of anemia of chronic diseases **Unmet medical need in the country:** Treatment of anemia of chronic diseases, and other hypoxia related disorders	**1. Recommendation of the IND Committee :** The Committee noted from the firm's presentation that the proposed study is multicentric in Australia and India and the firm has received permission from the regulatory authorities of Australia to conduct the study. After detailed deliberation the Committee recommended the proposed study subject to the following conditions:- ➢ Study should be conducted under the full time monitoring of a Cardiologist. ➢ Upper limit of Haemoglobin should be less than 15 g/dL. ➢ Complete chemical structure should be submitted to CDSCO. ➢ DSMB should be constituted to monitor the study. Accordingly, revised protocol etc. should be revised and submitted to DCGI.

	Healthcare Limited Survey No. 417, 419 & 420, Sarkhej Bavla, N. H. No. 8A, Moraiya, Tal. Sanand, Ahmedabad - 382 210. India. **Title:** A randomized, double-blind,placebo-controlled Phase I clinical study to evaluate the safety, tolerability and pharmacokinetics of ZYAN1, a novel PHD-2 Inhibitor, following oral administration in healthy volunteers.		**2. Recommendation of the Technical Committee 21.08.2015:** After detailed deliberation, the Committee sought the clarification and presentation on following observation. 1. Animal details indicating the pharmacology and mechanism of action of the NCE are not explained clearly. The details of proof of pharmacological action in the given therapeutic indication, which justify further trials in human, are not given. 2. The hypoxia related disorder which is mentioned as one of the proposed indication is too general and needs to be specified. Based on the recommendation of the Committee, the firm was asked to present the proposal before the Committee. **Recommendation of the Technical Committee 12.10.2015:** Accordingly the firm gave presentation before the Committee. After deliberation, the Committee recommended the conduct of the study.

Annexure-II

Recommendations of the 07 cases of Clinical trial waiver in Indian populations:

Sr. no.	Details of the proposals	Name of the Firm holding permission outside the country	Indication	1.Recommendation of the Technical Committee 2. Recommendation of the SEC
1.	Nintedanib Capsules 100 mg and 150 mg **Name of the Applicant:** M/s. Boehringer Ingelheim India Pvt. Ltd Approved in US on 15th Oct 2014 and EU on 15th January 2015	M/s. Boehringer Ingelheim India Pvt. Ltd	Indicated for the treatment of Idiopathic Pulmonary Fibrosis (IPF)	**1. Recommendations of the SEC:** The firm has made an application for grant of permission to import & market Nintedanib soft gelatin 100/150 mg capsules indicated for the treatment of Idiopathic Pulmonary Fibrosis (IPF) and to slow disease progression. The firm presented data on 20 Indian patients who participated in the Global clinical trial of the drug and submitted that safety and efficacy results of the Indian subset is comparable with the Global data & requested for waiver of local clinical trial as IPF is an orphan disease and also there is an unmet need of the drug for the disease. The Committee deliberated the proposal in detail and observed the following: 1. For IPF patients in India there is only limited treatment option. 2. This drug was approved as orphan drug by USFDA and also approved in EU in 2015. The Committee recommended for approval of Import and marketing of the drug with waiver of local clinical trial subject to the condition that- 1. Marketing approval initially shall be given only for two years. 2. The firm will conduct an active surveillance of all the patients who will be prescribed for a period of two years and protocol etc. should be submitted for evaluation. 3. The continued marketing of the drug beyond two years shall be

				based on the favorable risk benefit ratio on the data in the Indian population. **2. Recommendations of the Technical Committee:** The Committee deliberated the proposal and noted that the drug is already approved as orphan drug by USFDA and also approved in EU. Therefore, the Committee recommended for waiver of local clinical trial as per recommendation of the SEC. However, the Committee opined that it is required to clearly explain active surveillance and what is required to be submitted by the firm for doing active surveillance shall be clearly mentioned in the regulatory approval.
2.	Dabrafenib Mesylate capsule 50/75mg **Name of the Applicant:** M/s. Glaxo Smith Kline Pharmaceuticals Limited Approved by USFDA on 29th May, 2013, EU on 26th Aug 2013	M/s. Glaxo Smith Kline Pharmaceuticals Limited	Indicated for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600 mutation.	**1. Recommendations of the SEC** The firm made an application for grant of permission to import and market Dabrafenib mesylate capsules 50mg/ 75mg indicated for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600 mutation. The proposal was deliberated in the SEC meeting held on 28.01.2014 where the Committee had asked to obtain data of BRAF V600 mutation in Indian patients. The firm presented the presence of this mutation in 20 patients in the present SEC meeting. The Committee deliberated the proposal in detail and felt that : 1. There is no other option for these patients, who have a life-threatening disease. 2. The drug has been granted Orphan drug designation in the USA. Hence the drug may be granted permission for import and marketing without clinical trial subject to the condition that the firm shall submit safety data in first 20 patients post marketing to the Committee for continued marketing of the product. The firm shall also submit the detail BRAF V600 mutational data on the 20

				melanoma patients. **2. Recommendations of the Technical Committee:** The Committee deliberated the proposal and noted that the drug is already approved as orphan drug by USFDA and also approved in EU. Therefore, the Committee recommended for waiver of local clinical trial as per recommendation of the SEC.
3.	"Celox Gauze and Celox Z Fold Gauze" Name of the Applicant: M/s. Emergo India Consulting Pvt. Ltd Approved in USA, Canada, Serbia and Thailand, Brazil, China	**M/s. Med Trade Products Limited,** United Kingdom	Indicated to be used to achieve hemostasis in emergency situations for the temporary control of severe topical bleeding	**1. Recommendations of the SEC** The case has been reviewed by SEC –Oncology & Haematology in its meeting held on 21.07.2015. The committee has deliberated upon the proposal and recommended that the product may be granted marketing approval for the indication of temporary external use to control moderate to severe bleeding. The committee also felt that it would not be feasible or practical to conduct a trial on the product as it's use is in an emergency situation. The committee also noted that the product is approved in USA, Europe and Canada and that it is in global market for more than 5 years with no safety concerns. The firm is required to submit PSUR after 6-months which will be reviewed by the committee. **2. Recommendations of the Technical Committee:** After detailed deliberation, the Committee noted that the product is used in emergency situations. Further the product is marketed in USA, Europe, and Canada for more than 5 years with no safety concerns and as such there is no requirement of clinical trial for such product. Therefore, the Committee agreed with SEC recommendations.
4.	Sofosbuvir (400 mg) + Ledipasvir (90 mg) Name of the Applicant:	M/s Gilead Sciences, Inc	Indicated for the treatment of chronic hepatitis C (CHC) in adults (by M/s Mylan) Indicated for the	**1. Recommendations of the SEC** i) Recommendation for M/s Mylan: The firm presented the proposal for permission to manufacture

	M/s Mylan Pharmaceutical (Import) M/s Hetero Labs Limited M/s Natco Pharma Ltd		treatment of Chronic Hepatitis C virus (HCV) genotype 1 infection in adults (M/s Hetero & M/s Natco)	and market, with waiver of local clinical trial for a fixed-drug combination of Sofosbuvir and Ledipasvir, for "treatment of chronic hepatitis C (CHC) in adults". During the presentation, the company informed that the combination is already approved for the treatment of "chronic hepatitis C". A perusal of the documents provided indicates that the above fixed-drug combination is approved by US FDA and Health Canada for "treatment of chronic hepatitis C virus (CHC) genotype 1 infection in adults". Hence, the permission requested is for an indication that extends beyond the indication for which it is approved in other countries. Hence, the committee did not recommend marketing of the drug with waiver of local clinical trial. **ii) Recommendation for M/s Hetero:** The firm presented the proposal for permission to manufacture and market, with waiver of local clinical trial for a fixed-drug combination of Sofosbuvir and Ledipasvir, for "treatment of chronic hepatitis C (CHC) genotype 1 in adults". A perusal of the documents provided indicates that the above fixed-drug combination is approved by US FDA and Health Canada for "treatment of chronic hepatitis C virus (CHC) genotype 1 infection in adults". The permission requested is for an indication for which it is already approved in other countries. The currently available treatments for genotype 1 HCV infection (Interferon-ribavirin combination, or Sofosbuvir-Interferon-Ribavirin combination) are not effective in some such patients, and their use is not possible in some subgroups of patients, such as those with renal failure, prior organ transplantation,

				decompensated liver disease. In these patients, there is a need for this combination. Hence, the Committee felt that there may be a point in permitting marketing of the drug with waiver of local clinical trial subject to the following conditions: a) That a bioequivalence study will be carried out. b) The prescribing information, patient information sheet and all the material used for marketing will clearly indicate that the drug combination is not approved for treatment of infection with non-1 HCV genotypes. c) The firm will undertake a phase IV clinical trial, the protocol of which should be submitted. However, the Committee took cognizance of the order dated July 3, 2014, that "waiver of clinical trial in Indian population for approval of new drug, which have already been approved outside India, can presently be considered only in cases of national emergency, extreme urgency, and epidemic and for orphan drugs for rare diseases and drugs indicated for conditions/diseases for which there is no therapy'. The drug does not meet any of the situations listed above. Hence the Committee did not recommend waiver of the need for a local trial. **1. Recommendations of the Technical Committee:** The Committee deliberated the proposal in details and noted that there is no therapy for the treatment of genotype 1 HCV infection patients with renal failure, prior organ transplantation decompensated liver disease and cirrhotic condition where Interferon in combination with other HCV drugs is not useful. As the drug is already approved by USFDA, therefore, the Committee recommended that the application for new drug approval without local clinical trial can be considered

				provided that; the firm shall conduct BA/BE study in Indian population if the product is manufactured "as different" than the one approved in country of origin. Further, the product shall be approved for the indication for which it is approved in USA subject to condition of conduct of phase-IV study. It was also decided by the Committee to further get the matter examined by experts including , 1. One expert from Institute of Liver and Biliary Sciences (ILBS). 2. One expert from PGI, Chandigarh. 3. One expert from GB pant Hospital. Accordingly a meeting of experts to discuss the issue of waiver of local clinical trial on the new direct-acting antiviral drug for Hepatitis C treatment and to make new effective Hepatitis C regimen available in India was held on 28.10.2015 wherein the experts made following comments: I. Ledipasvir and Sofosbuvir is a combination of two antiviral drugs that prevent hepatitis C virus (HCV) from multiplying in the body and is indicated for treatment of chronic hepatitis C genotype 1 infection in adults. II. Ribavirin, the drug used in combination with Sofosbuvir has many side effects including haemolysis. Ribavirin is excreted through kidney and, therefore, the combination cannot be used in renal failure patients in particular. The currently available treatments for HCV infection (Interferon-Ribavirin combination, or Sofosbuvir-Interferon-Ribavirin combination) are not

				effective in certain sub group of patients with renal failure, Thalassemia, prior organ transplantation, and decompensated liver disease. As regard to clinical trial waiver, the experts desired to know the policy in this respect for approval of new drugs in the country. It was mentioned that as per the existing guidelines there are five criteria under which such waiver can be considered. These are national emergency, extreme urgency, epidemic, orphan drugs for rare diseases and condition/diseases for which there is no therapy. Experts after detailed deliberation opined that the FDC Sofosbuvir and Ledipasvir fall under the 5th criteria i.e. condition/diseases for which there is no therapy and recommended for waiver of local clinical trial for approval of the drug for "treatment of chronic hepatitis C virus (CHC) genotype 1 infection in adults". subject to same conditions as stipulated for approval of Sofosbuvir.
5.	Daclatasvir 30 mg and 60 mg Tablet **Name of the Applicant:** M/s Hetero Labs Limited M/s Natco Pharma Ltd	M/s BMS	Indicated in combination with other medicinal products for the treatment of chronic hepatitis C virus (HCV) infection in adults.	**1. Recommendations of the SEC** The firm presented the proposal for permission to manufacture and market Daclatasvir, with waiver of local clinical trial for "treatment of chronic hepatitis C (CHC) in adults, in combination with other medicinal products". The drug is already approved "in combination with other medicinal products for the treatment of chronic hepatitis C infection in adults". The available data show that the drug has activity against various genotypes of HCV, and is safe, except severe bradycardia when administered along with Amiodarone. The Committee felt that there may be a point in permitting marketing of the drug with

				waiver of local clinical trial subject to the following conditions: a. That a bioequivalence study will be carried out. b. The firm will undertake a phase IV clinical trial, the protocol of which should be submitted. However, the committee took cognizance of the order dated July 3, 2014, that "waiver of clinical trial in Indian population for approval of new drug, which have already been approved outside India, can presently be considered only in cases of national emergency, extreme urgency, and epidemic and for orphan drugs for rare diseases and drugs indicated for conditions/diseases for which there is no therapy'. The drug does not meet any of the situations listed above. Hence the Committee did not recommend waiver of the need for a local trial. **2. Recommendations of the Technical Committee:** The Committee deliberated the proposal in details and noted that the drug in combination with other medicinal product becomes imperative to expedite the treatment of all types of Hepatitis C. Hence, the Committee recommended that the application for approval of Daclatasvir without local clinical trial can be considered subject to the following condition: 1. The innovator has certified that there is technology transfer of the manufacturing process to the Indian manufacturer. 2. The firm shall conduct BA/BE study in Indian population. Accordingly the firm shall be asked to submit BA/BE protocol for approval. In the meantime the proposal may be got examined by an experts including , 1. One expert from Institute of Liver and Biliary Sciences (ILBS) 2. One expert from PGI, Chandigarh

				3. One expert from GB pant Hospital. Accordingly a meeting of experts to discuss the issue of waiver of local clinical trial on the new direct-acting antiviral drug for Hepatitis C treatment and to make new effective Hepatitis C regimen available in India on 28.10.2015 wherein the experts made following comments: I. Daclatasvir is indicated for the treatment of chronic hepatitis C in combination with other medicinal products. The drug has activity against various genotype of HCV. II. Ribavirin, the drug used in combination with Sofosbuvir has many side effects including haemolysis. Ribavirin is excreted through kidney and, therefore, the combination cannot be used in renal failure patients in particular. The currently available treatments for HCV infection (Interferon-Ribavirin combination, or Sofosbuvir-Interferon-Ribavirin combination) are not effective in certain sub group of patients with renal failure, Thalassemia, prior organ transplantation, and decompensated liver disease. As regard to clinical trial waiver, the experts desired to know the policy in this respect for approval of new drugs in the country. It was mentioned that as per the existing guidelines there are five criteria under which such waiver can be considered. These are national emergency, extreme urgency, epidemic, orphan drugs for rare diseases and condition/diseases for which there is no therapy. Experts after detailed deliberation opined that the drug Daclatasvir falls under the 5th criteria i.e. condition

				/diseases for which there is no therapy and recommended for waiver of local clinical trial for approval of the drug "in combination with other medicinal products for the treatment of chronic hepatitis C infection in adults" subject to same conditions as stipulated for approval of Sofosbuvir
6.	Siltuximab	M/s Johnson & Johnson Private Limited	Indicated for the treatment of patients with Multicentric Castleman's Disease (MCD) who are human immunodeficiency virus (HIV) negative and Human Herpesvirus-8 (HHV-8) negative.	**1. Recommendations of the SEC** After detailed deliberation the committee has recommended clinical trial waiver in respect of Siltuximab due to following reasons: 1. MCD is rare disease with no standard treatment at present, therefore it is a clear unmet need 2. It has orphan drugs status in USA and Europe. 3. It is approved in USA and Europe The drug has a favorable risk benefit profile. **2 Recommendations of the Technical Committee:** After detailed deliberation, the Committee recommended waiver of local clinical trial as per SEC recommendation 4.
7.	Inactivated Polio Vaccine	M/s Serum Institute India, Pune	Indicated for active immunization for the prevention of poliomyelitis caused by poliovirus Types 1, 2, and 3.	**1. Recommendations of the SEC** The committee deliberated the proposal in detail and noted that firm has requested for fast track approval of the vaccine without clinical trial in India since the vaccine is intended to be included in the National Immunization Programme and large quantity will be required. The firm is already importing the bulk from the same source and the formulation is exactly the same. Therefore, the Committee has recommended for Marketing Authorization (Form 45) of IPV in single dose and multi-dose (5 doses) presentations. 2. Recommendations of the Technical Committee:

				After detailed deliberation, the Committee recommended waiver of local clinical trial as per SEC recommendation.

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