DRAFT MINUTES OF THE 29TH CSC MEETING HELD ON 5TH AUGUST 2021.

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AGENDA ITEM I:-

RECTIFICATION OF MINUTES OF THE 28TH CSC MEETING HELD ON 29TH JUNE 2021.

Sr. No	*Agenda Items/ Contents OF 28th CSC meeting:*
1	***ITEM I:*** *CONFIRMATION OF THE MINUTES OF THE 27TH CLINICAL STUDIES COMMITTEE MEETING.* ***ITEM II:*** *PAK VENT TRIAL COMPLETION REPORT.* ***ITEM III:*** *BIO EQUIVALENCE STUDY OF EMPA-Q 25MG TABLET BY M/S OLIVE WORLDWIDE (SMC-PVT.) LTD.* ***ITEM IV:*** *BIO EQUIVALENCE STUDY OF QAZZO 20MG TABLET BY M/S OLIVE WORLDWIDE (SMC-PVT.) LTD.* ***ITEM V:*** *BIO EQUIVALENCE STUDY OF RIVA Q 20MG TABLET BY M/S OLIVE WORLDWIDE (SMC-PVT.) LTD.* ***ITEM VI:****BIO EQUIVALENCE STUDY OF ZUNE 40MG TABLET BY M/S OLIVE WORLDWIDE (SMC-PVT.) LTD.* ***ITEM VII:****APPLICATION FOR APPROVAL OF CLINICAL TRIAL TITLED, "A MULTICENTER, RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED STUDY TO ASSESS SAFETY AND EFFICACY OF SIR1-365 IN PATIENTS WITH SEVERE COVID-19)", PROTOCOL NO. SIR365-US-101. F. No.03-72/2021-DD (PS)*

The 29th Meeting of the CSC was held on 5th August 2021 2021 through Zoom under the chairmanship of Dr. Abdur Rashid, Director Pharmacy Services Division / Chairman (CSC) in Committee Room-II, 4th Floor, Drug Regulatory Authority of Pakistan, Islamabad.

2. The meeting was attended by the following members: -

Sr. No.	**Name**	**Designation**
01	Dr. Abdur Rashid.	Chairman CSC / Director, Division of Pharmacy Services-DRAP.
02	Ahmad Din Ansari.	Secretary CSC / Additional Director, Division of Pharmacy Services-DRAP.

3. Following members attended the meeting online through Zoom:

01	Dr. Faiza Bashir.	Chairman, Pakistan Health Research Council or his nominee, Islamabad.
02	Prof. Dr. Javed Akram.	Professor of Medicine, Physician, Vice Chancellor, University of Health Sciences, Lahore.
03	Prof. Brig. (R), Muzammil Hassan Najmi.	Professor of Pharmacology, Foundation University, Islamabad.
04	Dr. Farhana Badar.	Biostatistician & Epidemiologist, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore.
05	Prof. Dr. Rizwana Chaudhri	Principal Scientist Shifa Tameer e Millat University, Islamabad. Co-opted Member.
06	Dr. Naseem Salahuddin.	Director Infectious Diseases Indus Hospital, Karachi Co-opted Member.
07	Dr. Aamir Jaffary	Sindh Institute of Urology & Transplantation (SIUT), Karachi Co-opted Member.
	Prof: Dr. Mushtaq Ahmed	Professor of Cardiology, Bach Khan Medical College, Mardan, KPK Co-opted Member.
08	Dr. Beena Ali	Head of Medical Affairs, M/s CCL Pharmaceuticals, Lahore. Co-opted Member.
09	Mr. Nadeem Alamgir	Representative of Pharma Bureau Observer.

4. Meeting started with the recitation of Holy Verses of the Quran by Ahmad Din Ansari, Secretary CSC. The Secretary CSC welcomed all the members & informed the background of the meeting and presented the agenda. Mr. Muhammad Adnan Faisal Saim, Deputy Director (Pharmacy Services Division), Mr. Muhammad Ansar, Assistant Director and Mr. Ahsan AD were also present in the meeting.

AGENDA ITEM I:

CONFIRMATION OF THE MINUTES OF THE 27TH CLINICAL STUDIES COMMITTEE MEETING.

1. Confirmation of Minutes of 27th CSC meeting held on 24th June 2021. Since, the occurrence of Covid-19 pandemic majority of the meeting are being conducted online through zoom.

2. The members of CSC were requested to confirm the minutes electronically through email. Confirmatory email will be made part of the minutes to satisfy legal provision.

Submitted for consideration of CSC.

Decision:

All the Members of the CSC unanimously confirmed the Minutes of 27th CSC meeting held on 24th June 2021.

Decision of 29th CSC meeting.

The decision of 28th meeting was upheld and all the Members of the CSC unanimously confirmed the Minutes of 27th CSC meeting held on 24th June 2021.

AGENDA ITEM II:

PAK VENT TRIAL COMPLETION REPORT.

1. The CSC in its 25th meeting held on 28th April 2021, unanimously approved to conduct Clinical Validation of Pakvent-I manufactured by Project Management Organization at CMH Rawalpindi as per submitted protocol.

2. Mr. Humayun, Assistant Manager, NESCOM, Islamabad, has submitted handwritten letter addressed to Director MDMC, DRAP, wherein he has enclosed the clinical trial report duly signed by Maj. Gen. Rao Ali Shan. The Director MDMC has forwarded the same to Director Pharmacy Services.

3. Following is the Pak Vent Trial Completion Report.

Subj: Pak Vent Trial Completion Report

1. *The report includes a brief background about indigenously designed ventilator in Pakistan along with its testing criteria, methodology and crux of extreme hard work by Doctors and Engineers to bring it at par with internationally manufactured ventilators.*
2. ***Background.***
   a. *Pak Vent (designed by NESCOM) version 1.0 was delivered to CMH Rwp to conduct human trials in late November 2000 under patronage of Maj Gen Rao Ali Shan Khan, Advisor in Anesthesiology Pakistan Army & Col Ahmed Mujadid Khan Burki, Cl. Anaes and Cl Intensivist. 1st trial was given to an entitled patient intra-operatively on 26th Nov, 2020 using controlled volume mode (V-CMV) with TIVA (total intravenous anesthesia).*

It was a successful trial as patient remained ventilated and oxygenated throughout the procedure. DRAP (Drug Regulatory Authority of Pakistan was approached tor its validation who after two visits to CMNH Rwp approved it as testing site for its use.

3. ***Methodology**:*
   a. *A series of test trials have been conducted since then till date comprising of 50 trials being documented on Clinical Validation Performa provided by NBC (National Biomedical Committee). The total human ventilatory support time by Pak vent is measured to be 395 hours till now. Pak Vent has 3 types of modes i.e., Pressure, Volume & Non-invasive. All the aforementioned modes have been tested successfully in the presence of engineers and calibration errors; technology errors have been fived with no harm to the patients.*
4. *Research aspects were also kept in mind and international protocol for the approval of new technology was followed throughout the testing phases. Data has been recorded after prior approval of patients/ next of kin of patient. Consent was given by patient himself in OT settings and by next of kin in ICU setting for use of this prototype ventilator. Consent form was read aloud and displayed to patients & next of kin before start of procedure. Only those who consented for its use, were considered. Data collected on Performa is kept confidential till date.*
5. *Data was collected by only designated personals by principal investigator and record is kept in a bolted safe. Statistician has been taken on board for analyzing data and provision of results. During testing of Pak Vent version 1 a stand by internationally manufactured ventilator was also kept spare in order to provide safe ventilation to any unforeseen event.*
6. *The inclusion criteria constitute as follows:*
   a. *Age 18 and above*
   b. *Both Genders i.e., Male & Female*
   c. *Hemodynamically stable patients with no pre-morbid in Operation theatre*
   d. *Moderate and critically ill patients in ICU*
7. *The exclusion criteria constitute as follows:*
   a. *Age < 18*
   b. *Decline of informed consent:*
   c. *Pre-Cardiac Arrest State Patients*
8. *The exclusion criteria aim to minimize bias.*
9. ***Conclusion:***
   a. *Apropos above it is suggested that Pak Vent can be now safely registered with DRAP, hence your kind approval in this regard is highly treasured.*

10. Maj Gen Rao Shan Ali Khan has submitted another letter on 28th June 2021 wherein he has stated that with ref to above letter, it is to clarify that PAKVENT-1(developed by National Engineering and Scientific Commission-NESCOM) underwent engineering design validation and testing at Pakistan Innovation and Testing Centre (PITC)-Pakistan Engineering Council (PEC). After successful culmination of engineering trials at PEC, clinical trials of PAKVENT-1 were conducted at Combined Military Hospital (CMH), Rawalpindi in late November 2020 under supervision of Maj Gen Rao Ali Shan Khan, Consultant Anesthesiologist, Advisor in Anesthesiology Pakistan Army & Col Ahmed Mujadid Khan Burki, Consultant Anesthesiologist and Consultant Intensivist. All the modes were thoroughly tested as per National Bio-ethics Committee (NBC) approved clinical validation protocol. The ref report was submitted to DRAP after completion of clinical trials at CMH.

Submitted for evaluation, consideration and perusal of CSC.

Decision:

The Clinical Studies Committee after detailed deliberation recommended to refer the Clinical Validation Report of Pakvent-I, submitted by Maj Gen Rao Ali Shan Khan, Consultant Anesthesiologist, Advisor in Anesthesiology Pakistan Army, Combined Military Hospital (CMH), to Medical Devices Board (MDB) through Division of Medical Devices and Medicated Cosmetics.

Decision of 29th CSC meeting.

The decision of 28th CSC meeting was upheld which is reproduced as under:-

The Clinical Studies Committee after detailed deliberation recommended to refer the Clinical Validation Report of Pakvent-I, submitted by Maj Gen Rao Ali Shan Khan, Consultant Anesthesiologist, Advisor in Anesthesiology Pakistan Army, Combined Military Hospital (CMH), to Medical Devices Board (MDB) through Division of Medical Devices and Medicated Cosmetics.

AGENDA ITEM III:

BIO EQUIVALENCE STUDY OF EMPA-Q 25MG TABLET BY M/S OLIVE WORLDWIDE (SMC-PVT.) LTD.

The case is the application from Mr. Mohsin Ali Jawa, CEO, M/s Olive Worldwide wherein, he had applied for approval of study titled "A balanced, open labeled, randomized, analyst blind, single center, to treatment, to period, to sequence, crossover design single dose oral bioequivalence study of Empa- Q tablet (each tablet contains Empagliflozin 25 mg) of Boehringer Ingelheim (USA) in 24+2 (Standby) normal, health, adult, male, human subject under fasting conditions".

2. The short summary of the proposed study is as under;

i. **Study title:** A balanced, open labeled, randomized, analyst blind, single center, to treatment, to period, to sequence, crossover design single dose oral bioequivalence study of Empa- Q tablet (each tablet contains Empa gliflozin 25 mg) of Boehringer Ingelheim (USA) in 24+2 (Standby) normal, health, adult, male, human subject under fasting conditions.

ii. **Investigational Product:** Empa-Q (Empagliflozin) 25mg tablet Manufactured by Wilshire Laboratories, Lahore.

iii. **Reference Product:** Jardiance (Empagliflozin) 25mg tablet Manufactured by Boehringer Ingelheim (USA).

iv. **Sponsor:** M/s Olive Bio Center.

v. **CRO and BA/BE Study Site:** Olive Worldwide (SMC-PVT) Ltd.

vi. **Principal Investigator:** Dr. Maryam Behram

vii. **Medical/ clinical investigator:** Dr. Mujahida Salamat

viii. **Funding Source**: M/s Olive Bio Center.

ix. **Cost of the Project**: Not Mentioned

x. **Subjects enrolment**: 24 healthy, male Subjects will be enrolled in the study.

3. The details of the submitted documents are as under;

S.No.	Document	Remarks
1	Application on prescribed form-IIA	Application on Form – IIA is provided.
2	Prescribed processing fee	Processing fee of Rs.200000/- deposited vide challan number 2027341, dated 24th March 2021.
3	Name of Investigational Product (including all available names; trade, generic or INN name, chemical code, etc.,)	Attached
4	Dosage Form of Investigational Product	Attached
5	Formulation of Investigational Product	Attached
6	Pharmacodynamics and Pharmacokinetics of Investigational Product	Attached
7	Purpose of study defining the indication along with the anticipated cost of the project and sources of fund	Primary objective of the study to compare a single dose oral Bioavailability profile of Empa-Q tablet (Empagliflozin) 25mg of Wilshire Laboratories private limited vs Jardiance tablets of M/s Boehringer Ingelheim

		(USA) 24-year healthy adult male human subject under fasting conditions. M/s Olive Biocentre is funding source.
8	Proposed center for the study	M/s Olive Worldwide BABE Study center.
9	Investigational design and study plan	Attached
10	Pre-clinical or clinical data or safety studies	Attached
11	Final protocol	Attached.
12	Detail of the investigator (Principal investigator, analysts, and others along with CV)	CVs of the following are attached: Dr. Maryam Behram (PI) Dr. Mujahida Salamat (Medical/ Clinical Investigator Miss Sumbal Afroz (QA manager) Dr Urwa Asif (Bio Analytical Manager)
13	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Attached
14	Approval of National Bio-ethics Committee (NBC)	Not provided.
15	Site approval by the Ethics committee	M/s Olive World Wide (SMC-PVT) Ltd.
16	Informed consent (English and Urdu)	Attached.
17	Summary of the protocol or synopsis (Investigational Product)	Attached.
18	Adverse Event Reporting Form	Attached.
19	Name of the monitor or clinical research associate	N/A
20	Evidence of registration in the country of origin (GMP certificate along with CoPP or Free sale certificate)	Evidence of registration in the country of origin (GMP certificate along with CoPP or Free sale certificate) of Jardiance Tablet required.
21	Copy of registration letter if registered in Pakistan	Copy of registration letter for Empa-Q Tablets along with GMP of Wilshire Laboratories is attached.
22	Proposed label of investigational product	Not provided & Investigational Product is registered in Pakistan.
23	Quantity of investigational product to be used in the study along with justification (Note: All the quantities of the each of investigational product should be procured from one single source)	As per the randomization schedule, single dose of either one tablet of test; Empa-Q Tablet (Each Tablet contains Empagliflozin 25mg) (T) or one Tablet of Reference: Jardiance Tablet (Each Tablet contains empagliflozin 25 mg) (R) will be administered orally in sitting posture with dosing fluid in each period depending on the randomization schedule. Two sets of subjects will be made for dosing i.e. subject no. 01 to 12 and subject no. 13 to 24.
24	Undertaking on affidavit.	Not Attached.

04. After initial scrutiny following shortcomings observed:

i. Applicant is using Olive Biocentre, DRAP approved Bioequivalence Studies Centre, while this name is not approved by DRAP.
ii. Approval from National Bio-ethics Committee (NBC) is not provided.
iii. Copy of registration letter of the reference drug is not provided.
iv. Proposed label for reference product is not provided.
v. As per Form II-A Olive Bio Centre will provide the Funds for study while as per other documents Dr. Muhammad Zakir, Wilshire Laboratories is sponsor.
vi. Anticipated cost of project not provided.
vii. As per IRB approval Ms. Yamema Younatan is physician while her qualification is Pharm-D, M-Phil (Pharmacy).
viii. Documentation of funding and source of funding of IRB is required.
ix. Qualification of Dr. Urvah Asif is B.Sc. honors, M. Sc. Chemistry.
x. In all attached CVs work place has not been mentioned under heading of work experience.
xi. Analytical/ bioanalytical method along with validation record is required.
xii. Undertaking on stamp paper required.
xiii. Soft copy of the application along with relevant documents is required.

05. The Shortcomings were communicated to applicant vide this office letter No. 14-08/2021 DD (PS) dated 07th May 2021. Applicant submitted their reply along with revised documents. Following is the reply of the applicant in Form.

Shortcomings Communicated	**Reply Extracted from revised submitted documents**
Applicant is using Olive Biocentre, DRAP approved Bioequivalence Studies Centre, while this name is not approved by DRAP.	The name Olive BioCenter is being used as a short form of the name Olive Worldwide (SMC-Pvt) Ltd. Nonetheless, the full name Olive Worldwide (SMC-Pvt) Ltd has been used in the revised documents.
Approval from National Bio-ethics Committee (NBC) is not provided.	Attached.
Copy of registration letter of the reference drug is not provided.	Attached.
Proposed label for reference product is not provided.	Not attached.
As per Form II-A Olive Bio Centre will provide the Funds for study while as per other documents Dr. Muhammad Zakir, Wilshire Laboratories is sponsor.	Olive Worldwide (SMC-Pvt) Ltd will provide for all the facilities required for the study. This includes residence of volunteers, Olive Worldwide (SMC-Pvt) Ltd staff salary, processing, storage and transportation of samples, bioanalytical and data analysis and protocol and report writing services. Dr. Muhammad Zakir of the Wilshire labs will pay the charges for conduction of the study at point of completion.

Anticipated cost of project not provided.	The estimated cost of the project is USD 25000.
As per IRB approval Ms. Yamema Younatan is physician while her qualification is Pharm-D, M-Phil (Pharmacy).	The typographic error has been rectified in revised documents.
Documentation of funding and source of funding of IRB is required.	IRB members do not receive any monetary benefit.
Qualification of Dr. Urvah Asif is B.Sc. honors, M. Sc. Chemistry.	The typographic error has been rectified in revised documents.
In all attached CVs work place has not been mentioned under heading of work experience.	The error has been rectified. Respective workplace has been mentioned in revised documents.
Analytical/ bioanalytical method along with validation record is required.	Proposed analytical/bioanalytical method has been provided in the revised documents. The validation record can only be validated once we gain permission to enroll volunteers since a volunteer's plasma sample (containing Empagliflozin) is required for method validation. Link for method is followings. https://ijpsr.com/bft-article/new-validated-rp-hplc-method-for-the-estimation-of-empagliflozin-in-human-plasma/?view=fulltext
Undertaking on stamp paper required.	Provided.
Soft copy of the application along with relevant documents is required.	Not provided.

6. The applicant has already circulated to Clinical Study Committee group.

Submitted for evaluation, consideration and perusal of CSC.

Decision:

The CSC after detailed deliberation decided to approve the BA/BE Study titled "A balanced, open labeled, randomized, analyst blind, single center, two-period, two sequence, crossover design single dose oral bioequivalence study of Empa-Q Tablet (each tablet contains Empagliflozin 25 mg) of Wilshire Laboratories (Pvt.) Ltd. With Jardiance Tablet (each tablet contains empagliflozin 25mg) of Boehringer Ingelheim (USA) in 24+2 (Standby) normal, healthy, adult, male, human subject under fasting conditions" at DRAP approved BA/BE Center, M/s Olive Worldwide (SMC-PVT.) Ltd, Lahore.

Decision of 29th CSC meeting.

The CSC was appraised about the difference in name of DRAP approved BA/BE centre i.e M/s Olive Worldwide (SMC-PVT.) Ltd, Lahore and name mentioned on NBC approval letter i.e. M/s Olive BioCentre. The CSC after detailed deliberation decided to approve the BA/BE Study titled "A balanced, open labeled, randomized, analyst blind, single center, two-period, two sequence, crossover design single dose oral bioequivalence study of Empa-Q Tablet (each tablet contains Empagliflozin 25 mg) of Wilshire Laboratories (Pvt.) Ltd. With Jardiance Tablet (each tablet contains empagliflozin 25mg) of Boehringer Ingelheim (USA) in 24+2 (Standby) normal, healthy, adult, male, human subject under fasting conditions" at DRAP approved BA/BE Center namely M/s Olive Worldwide (SMC-PVT.) Ltd, Lahore subject to submission of NBC approval mentioning the correct name of BA/BE centre & documents regarding the mode of acquiring/ import of reference drug i.e. Jardiance Tablet 25mg from M/s Boehringer Ingelheim, USA as per study protocol.

AGENDA ITEM IV:

BIO EQUIVALENCE STUDY OF QAZZO 20MG TABLET BY M/S OLIVE WORLDWIDE (SMC-PVT.) LTD.

The case is an application from Mr. Mohsin Ali Jawa, CEO, M/s Olive Worldwide wherein, he had applied for approval of study titled "A balanced, open labeled, randomized, analyst blind, single center, two treatment, two period, two sequence, crossover design single dose oral bioequivalence study of Qazzo Tablet (Each Tablet contains rosuvastatin calcium 20mg) of Wilshire Laboratories (Pvt) Ltd. with Crestor Tablet (each tablet contains Rosuvastatin Calcium 20mg) of AstraZeneca (Canada) in 24 normal, healthy, adult, male, human subject under fasting conditions.

2. The short summary of the proposed study is as under;

i. **Study title:** A balanced, open labeled, randomized, analyst blind, single center, two treatment, two period, two sequence, crossover design single dose oral bioequivalence study of Qazzo Tablet (Each Tablet contains rosuvastatin calcium 20mg) of Wilshire Laboratories (Pvt) Ltd. with Crestor Tablet (each tablet contains Rosuvastatin Calcium 20mg) of AstraZeneca (Canada) in 24 normal, healthy, adult, male, human subject under fasting conditions.

ii. **Investigational Product:** Qazzo (Rosuvastatin Calcium) 20mg Tablet Manufactured by Wilshire Laboratories, Lahore.

iii. **Reference Product:** Crestor (Rosuvastatin Calcium) 20mg Tablet Manufactured by AstraZeneca (Canada).

iv. **Sponsor:** M/s Olive Bio Center.

v. **CRO and BA/BE Study Site:** Olive BioCenter.

vi. **Principal Investigator:** Dr. Maryam Behram

vii. **Medical/ Clinical investigator:** Dr. Mujahida Salamat

viii. **Funding Source**: M/s Olive Bio Center.

ix. **Cost of the Project**: Not Mentioned

x. **Subjects enrolment**: 24 healthy, male Subjects will be enrolled in the study.

3. The details of the submitted documents are as under;

S.No.	Document	Remarks
1	Application on prescribed form-IIA	Attached.
2	Prescribed processing fee	Processing fee of Rs.200030/- deposited vide challan number 2027339, dated 24th March 2021.
3	Name of Investigational Product (including all available names; trade, generic or INN name, chemical code, etc.,)	Attached
4	Dosage Form of Investigational Product	Tablet
5	Formulation of Investigational Product	Each film coated tablet contains Rosuvastatin (as calcium) 20mg.
6	Pharmacodynamics and Pharmacokinetics of Investigational Product	Attached
7	Purpose of study defining the indication along with the anticipated cost of the project and sources of fund	Primary objective of the study to compare a single dose oral Bioavailability profile of Qazzo tablet (Rosuvastatin as calcium) 20mg of Wilshire Laboratories private limited vs Crestor Tablets of M/s Crestor Tablet of AstraZeneca (Canada) in 24 healthy, adult, male, human subject under fasting conditions. Anticipated cost not provided. M/s Olive Biocentre is funding source.
8	Proposed center for the study	M/s Olive BioCenter.
9	Investigational design and study plan	Attached
10	Pre-clinical or clinical data or safety studies	Attached
11	Final protocol	Attached.
12	Detail of the investigator (Principal investigator, analysts, and others along with CV)	CVs of the following are attached: Dr. Maryam Behram (PI) Dr. Mujahida Salamat (Medical/ Clinical Investigator Miss Sumbal Afroz (QA manager) Dr Urwa Asif (Bio Analytical Manager)

13	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Attached
14	Approval of National Bio-ethics Committee (NBC)	Not provided.
15	Site approval by the Ethics committee	M/s Olive BioCenter
16	Informed consent (English and Urdu)	Consent form is about empagliflozin.
17	Summary of the protocol or synopsis (Investigational Product)	Attached.
18	Adverse Event Reporting Form	Attached.
19	Name of the monitor or clinical research associate	Dr. Muhammad Zohaib
20	Evidence of registration in the country of origin (GMP certificate along with CoPP or Free sale certificate)	Evidence of registration in the country of origin (GMP certificate along with CoPP or Free sale certificate) of Crestor Tablet required.
21	Copy of registration letter if registered in Pakistan	Copy of registration letter for Qazzo Tablets along with COPP and GMP of Wilshire Laboratories is attached.
22	Proposed label of investigational product	Not provided & Investigational Product is registered in Pakistan.
23	Quantity of investigational product to be used in the study along with justification (Note: All the quantities of the each of investigational product should be procured from one single source)	24 subjects will be enrolled in crossover study. Each will receive one dose. So quantity of investigational product to be used in study is 24 tablets
24	Undertaking on affidavit.	Not Attached.

04. After initial scrutiny following shortcomings observed:

i. Applicant is using Olive Biocentre, DRAP approved Bioequivalence Studies Centre, while this name is not approved by DRAP.
ii. Approval from National Bio-ethics Committee (NBC) is not provided.
iii. Copy of registration letter of the reference drug is not provided.
iv. Proposed label for reference product is not provided.
v. As per Form II-A Olive Bio Centre will provide the Funds for study while as per other documents Dr. Muhammad Zakir, Wilshire Laboratories is sponsor.
vi. Anticipated cost of project not provided.
vii. As per IRB approval Ms. Yamema Younatan is physician while her qualification is Pharm-D, M-Phil (Pharmacy).
viii. Documentation of funding and source of funding of IRB is required.
ix. Qualification of Dr. Urvah Asif is B.Sc. honors, M. Sc. Chemistry.
x. In all attached CVs work place has not been mentioned under heading of work experience.
xi. Analytical/ bioanalytical method along with validation record is required.
xii. Undertaking on stamp paper required.

xiii. Soft copy of the application along with relevant documents is required.

05. The shortcomings were communicated vide this office letter No. 14-11/2021 DD (PS) dated 24th May 2021. Following is the reply of the applicant.

Shortcomings Communicated	**Reply of the Firm**
Applicant is using Olive Biocentre, DRAP approved Bioequivalence Studies Centre, while this name is not approved by DRAP.	The name Olive BioCenter was being used as a short form of the name Olive Worldwide (SMC-Pvt) Ltd, and the DRAP approved name, Olive Worldwide (SMC-Pvt) Ltd has been used in all the revised documents.
Approval from National Bio-ethics Committee (NBC) is not provided.	Attached.
Copy of registration letter of the reference drug is not provided.	NDA approval attached
Proposed label for reference product is not provided.	Proposed label of investigational product is attached but label of reference product not attached.
As per Form II-A Olive Bio Centre will provide the Funds for study while as per other documents Dr. Muhammad Zakir, Wilshire Laboratories is sponsor.	Olive Worldwide (SMC-Pvt) Ltd will provide for all the facilities required for the study. This includes residence of volunteers, Olive Worldwide (SMC-Pvt) Ltd staff salary, processing, storage and transportation of samples, bioanalytical and data analysis and protocol and report writing services. Dr. Muhammad Zakir of the Wilshire labs will pay the charges for conduction of the study at point of completion.
Anticipated cost of project not provided.	The estimated cost of the project is USD 25000.
As per IRB approval Ms. Yamema Younatan is physician while her qualification is Pharm-D, M-Phil (Pharmacy).	The typographic error has been rectified in revised documents.
Documentation of funding and source of funding of IRB is required.	IRB members do not receive any monetary benefit.
Qualification of Dr. Urvah Asif is B.Sc. honors, M. Sc. Chemistry.	The typographic error has been rectified in revised documents.
In all attached CVs work place has not been mentioned under heading of work experience	The error has been rectified. Respective workplace has been mentioned in revised documents.
Analytical/ bioanalytical method along with validation record is required.	Proposed analytical/bioanalytical method has been provided in the revised documents. The method can only be validated once we gain permission to enroll volunteers since a volunteer's plasma sample (containing Rosuvastatin) is required for method validation.

Undertaking on stamp paper required.	The required document has been provided in the revised version.
Soft copy of the application along with relevant documents is required.	Soft copy of application has been provided.

6. The soft copy of application has been shared with CSC members in Clinical Study Committee group for evaluation and consideration of the members.

submitted to the quires of this office. Soft copy of application has been sent to CSC members and co-opted members and case has been included as agenda item in 28th CSC meeting, as discussed.

Submitted for consideration of CSC.

Decision:

The CSC after detailed deliberation decided to approve the BA/BE Study titled "A balanced, open labeled, randomized, analyst blind, single center, two treatment, two-period, two sequence, crossover design single dose oral bioequivalence study of Qazzo Tablet (each tablet contains Rosuvastatin Calcium 20 mg) of Wilshire Laboratories (Pvt.) Ltd. With Crestor Tablet (each tablet contains Rosuvastatin Calcium 20mg) of AstraZeneca (Canada) in 24 normal, healthy, adult, male, human subject under fasting conditions" at DRAP approved BA/BE Center, M/s Olive Worldwide (SMC-PVT.) Ltd, Lahore.

Decision of 29th CSC meeting.

The CSC was appraised about the difference in name of DRAP approved BA/BE centre i.e M/s Olive Worldwide (SMC-PVT.) Ltd, Lahore and name mentioned on NBC approval letter i.e. M/s Olive BioCentre. The CSC after detailed deliberation decided to approve the BA/BE Study titled "A balanced, open labeled, randomized, analyst blind, single center, two treatment, two-period, two sequence, crossover design single dose oral bioequivalence study of Qazzo Tablet (each tablet contains Rosuvastatin Calcium 20 mg) of Wilshire Laboratories (Pvt.) Ltd. With Crestor Tablet (each tablet contains Rosuvastatin Calcium 20mg) of AstraZeneca (Canada) in 24 normal, healthy, adult, male, human subject under fasting conditions" at DRAP approved BA/BE Center namely M/s Olive Worldwide (SMC-PVT.) Ltd, Lahore subject to submission of NBC approval mentioning the correct name of BA/BE centre & documents regarding the mode of acquiring/ import of reference drug i.e. Crestor Tablet 20mg from M/s AstraZeneca, Canada as per study prorocol.

AGENDA ITEM V:

BIO EQUIVALENCE STUDY OF RIVA Q 20MG TABLET BY M/S OLIVE WORLDWIDE (SMC-PVT.) LTD.

The Case is an the application from Mr. Mohsin Ali Jawa, CEO, M/s Olive Worldwide wherein, he had applied for approval of study titled "A balanced, open labeled, randomized, analyst blind, single center, two treatment, two period, two sequence, crossover design single dose oral bioequivalence study of Riva Q Tablet (Each Tablet contains Rivaroxaban 20mg) of Wilshire Laboratories (Pvt) Ltd. with Xarelto Tablet (each tablet contains Rivaroxaban 20mg) of Bayer (Canada) in 28 normal, healthy, adult, male, human subject under fasting conditions.

2. The short summary of the proposed study is as under;

i. **Study title:** A balanced, open labeled, randomized, analyst blind, single center, two treatment, two period, two sequence, crossover design single dose oral bioequivalence study of Riva Q Tablet (Each Tablet contains Rivaroxaban 20mg) of Wilshire Laboratories (Pvt) Ltd. with Xarelto Tablet (each tablet contains Rivaroxaban 20mg) of Bayer (Canada) in 28 normal, healthy, adult, male, human subject under fasting conditions.
ii. **Investigational Product:** Riva Q Tablet (Each Tablet contains Rivaroxaban 20mg) Manufactured by Wilshire Laboratories, Lahore.
iii. **Reference Product:** Xarelto Tablet (each tablet contains Rivaroxaban 20mg) Manufactured by Bayer (Canada).
iv. **Sponsor:** M/s Olive Bio Center.
v. **CRO and BA/BE Study Site:** Olive BioCenter.
vi. **Principal Investigator:** Dr. Maryam Behram
vii. **Medical/ Clinical investigator:** Dr. Mujahida Salamat
viii. **Funding Source**: M/s Olive Bio Center.
ix. **Cost of the Project**: Not Mentioned
x. **Subjects enrolment**: 28 healthy, male Subjects will be enrolled in the study.

3. The details of the submitted documents are as under;

S.No.	Document	Remarks
1	Application on prescribed form-IIA	Attached.
2	Prescribed processing fee	Processing fee of Rs.200030/- deposited vide challan number 2027340, dated 24th March 2021.
3	Name of Investigational Product (including all available names; trade, generic or INN name, chemical code, etc.,)	Attached

4	Dosage Form of Investigational Product	Tablet
5	Formulation of Investigational Product	Each tablet contains Rivaroxaban 20mg.
6	Pharmacodynamics and Pharmacokinetics of Investigational Product	Attached
7	Purpose of study defining the indication along with the anticipated cost of the project and sources of fund	The Primary objective of the study was to compare a single dose oral Bioavailability profile of Riva Q tablet (Rivaroxaban 20mg of Wilshire Laboratories private limited vs Xarelto tablets M/s Bayer (Canada) in 28 healthy, adult, male, human subject under fasting conditions. **(Typographical Error)** **Anticipated cost not provided**. M/s Olive Biocentre is funding source.
8	Proposed center for the study	M/s Olive BioCenter.
9	Investigational design and study plan	Attached
10	Pre-clinical or clinical data or safety studies	Attached
11	Final protocol	Attached.
12	Detail of the investigator (Principal investigator, analysts, and others along with CV)	CVs of the following are attached: Dr. Maryam Behram (PI) Dr. Mujahida Salamat (Medical/ Clinical Investigator Miss Sumbal Afroz (QA Manager) Dr Urwa Asif (Bio Analytical Manager)
13	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Attached
14	Approval of National Bio-ethics Committee (NBC)	Not provided.
15	Site approval by the Ethics committee	M/s Olive BioCenter
16	Informed consent (English and Urdu)	Attached.
17	Summary of the protocol or synopsis (Investigational Product)	Attached.
18	Adverse Event Reporting Form	Attached.
19	Name of the monitor or clinical research associate	Dr. Muhammad Zohaib
20	Evidence of registration in the country of origin (GMP certificate along with CoPP or Free sale certificate)	**Evidence of registration in the country of origin (GMP certificate along with CoPP or Free sale certificate) of Xarelto Tablet required.**

21	Copy of registration letter if registered in Pakistan	Copy of registration letter for Riva Q Tablets **for export purposes** is attached.
22	Proposed label of investigational product	Not provided & Investigational Product is registered in Pakistan for export purposes.
23	Quantity of investigational product to be used in the study along with justification (Note: All the quantities of the each of investigational product should be procured from one single source)	**24 subjects will be enrolled in crossover study. Each will receive one dose. So quantity of investigational product to be used in study is 24 tablets**
24	Undertaking on affidavit.	Not Attached.

04. After initial scrutiny following shortcomings observed:

i. The BA/BE center is Olive Biocentre, that is not approved by DRAP.
ii. Approval from National Bio-ethics Committee (NBC) is not provided.
iii. Copy of registration letter of the reference drug is not provided.
iv. Proposed label for reference product is not provided.
v. As per Form II-A Olive Bio Centre will provide the Funds for study while as per other documents Dr. Muhammad Zakir, Wilshire Laboratories is sponsor.
vi. Anticipated cost of project not provided.
vii. As per IRB approval Ms. Yamema Younatan is physician while her qualification is Pharm-D, M-Phil (Pharmacy).
viii. Documentation of funding and source of funding of IRB is required.
ix. Qualification of Dr. Urvah Asif is B.Sc. honors, M. Sc. Chemistry.
x. In all attached CVs work place has not been mentioned under heading of work experience.
xi. Evidence of registration in the country of origin (GMP certificate along with CoPP or Free sale certificate) of Xarelto Tablet required.
xii. As per title of the study subjects are 28 while as per quantity of drug to be used subjects are 24.
xiii. Analytical/ bioanalytical method along with validation record is required.
xiv. Undertaking on stamp paper required.
xv. Many typographical errors that need to be reviewed.
xvi. Soft copy of the application along with relevant documents is required.

05. In the view of above, shortcomings were communicated to the applicant vide this office No F. No. 14-10/2021 DD (PS) dated 24th May 2021.

06. The reply from Mohsin Ali Jawa, CEO, M/s Olive Worldwide (SMC-Pvt.) Ltd has been evaluated as followings

Shortcomings Communicated	**Reply of the Firm**
The BA/BE center is Olive Biocentre, that is not approved by DRAP.	The name Olive BioCenter was being used as a short form of the name Olive Worldwide (SMC-Pvt) Ltd, and the DRAP approved name, Olive Worldwide

	(SMC-Pvt) Ltd has been used in all the revised documents.
Approval from National Bio-ethics Committee (NBC) is not provided.	Attached.
Copy of registration letter of the reference drug is not provided.	Attached.
Proposed label for reference product is not provided.	Not attached.
As per Form II-A Olive Bio Centre will provide the Funds for study while as per other documents Dr. Muhammad Zakir, Wilshire Laboratories is sponsor.	Olive Worldwide (SMC-Pvt) Ltd will provide for all the facilities required for the study. This includes residence of volunteers, Olive Worldwide (SMC-Pvt) Ltd staff salary, processing, storage and transportation of samples, bioanalytical and data analysis and protocol and report writing services. Dr. Muhammad Zakir of the Wilshire labs will pay the charges for conduction of the study at point of completion.
Anticipated cost of project not provided.	The estimated cost of the project is USD 25000.
As per IRB approval Ms. Yamema Younatan is physician while her qualification is Pharm-D, M-Phil (Pharmacy).	The typographic error has been rectified in revised documents.
Documentation of funding and source of funding of IRB is required.	IRB members do not receive any monetary benefit.
Qualification of Dr. Urvah Asif is B.Sc. honors, M. Sc. Chemistry.	The typographic error has been rectified in revised documents.
In all attached CVs work place has not been mentioned under heading of work experience.	The error has been rectified. Respective workplace has been mentioned in revised documents.
Evidence of registration in the country of origin (GMP certificate along with CoPP or Free sale certificate) of Xarelto Tablet required.	Copy of SmPC of reference product and NDA approval attached.
As per title of the study subjects are 28 while as per quantity of drug to be used subjects are 24.	The mistake has been rectified in the revised documents.
Analytical/ bioanalytical method along with validation record is required.	Proposed analytical/bioanalytical method has been provided in the revised documents. The method can only be validated once we gain permission to enroll volunteers since a volunteer's plasma sample (containing Rivaroxaban) is required for method validation.
Undertaking on stamp paper required.	The required document has been provided in the revised version.

Soft copy of the application along with relevant documents is required.	Soft copy of application has been provided.

7. The soft copy of application has been already shared in Clinical Study Committee group for evaluation, consideration and perusal of CSC members and Co-Opted members.

Submitted for evaluation and consideration of CSC.

Decision:

The CSC after detailed deliberation decided to approve the BA/BE Study titled "A balanced, open label, randomized, analyst-blind, single center, two-treatment, two-period, two-sequence, crossover design single dose oral bioequivalence study of Riva Q Tablet (Each Tablet contains Rivaroxaban 20 mg) of Wilshire Laboratories (Pvt) Ltd. with Xarelto Tablet (Each Tablet contains Rivaroxaban 20 mg) of Bayer (Canada) in 28 normal, healthy, adult, male, human subjects under fasting conditions" at DRAP approved BA/BE Center, M/s Olive Worldwide (SMC-PVT.) Ltd, Lahore.

Decision of 29th CSC meeting.

The CSC was appraised about the difference in name of DRAP approved BA/BE centre i.e M/s Olive Worldwide (SMC-PVT.) Ltd, Lahore and name mentioned on NBC approval letter i.e. M/s Olive BioCentre. The CSC after detailed deliberation decided to approve the BA/BE Study titled "A balanced, open label, randomized, analyst-blind, single center, two-treatment, two-period, two-sequence, crossover design single dose oral bioequivalence study of Riva Q Tablet (Each Tablet contains Rivaroxaban 20 mg) of Wilshire Laboratories (Pvt) Ltd. with Xarelto Tablet (Each Tablet contains Rivaroxaban 20 mg) of Bayer (Canada) in 28 normal, healthy, adult, male, human subjects under fasting conditions" at DRAP approved BA/BE Center namely M/s Olive Worldwide (SMC-PVT.) Ltd, Lahore subject to submission of NBC approval mentioning the correct name of BA/BE centre & documents regarding the mode of acquiring/ import of reference drug i.e. Xarelto Tablet 20 mg from m/s Bayer, Canada as per study protocol .

AGENDA ITEM VI:

BIO EQUIVALENCE STUDY OF ZUNE 40MG TABLET BY M/S OLIVE WORLDWIDE (SMC-PVT.) LTD.

The Case is an application from Mr. Mohsin Ali Jawa, CEO, M/s Olive Worldwide wherein, he had applied for approval of study titled "A balanced, open labeled, randomized, analyst blind, single center, two treatment, two period, two sequence, crossover design single dose oral bioequivalence study of Zune Tablet (Each Tablet contains Esomeprazole Magnesium 40mg) of Wilshire Laboratories (Pvt) Ltd. with Nexium Tablet (each tablet contains Esomeprazole Magnesium 40mg) of AstraZeneca (Canada) in 24 normal, healthy, adult, male, human subject under fasting conditions.

2. The short summary of the proposed study is as under;

i. **Study title:** A balanced, open labeled, randomized, analyst blind, single center, two treatment, two period, two sequence, crossover design single dose oral bioequivalence study of Zune Tablet (Each Tablet contains Esomeprazole Magnesium 40mg) of Wilshire Laboratories (Pvt) Ltd. with Nexium Tablet (each tablet contains Esomeprazole Magnesium 40mg) of AstraZeneca (Canada) in 24 normal, healthy, adult, male, human subject under fasting conditions.

ii. **Investigational Product:** Zune Tablet (Each Tablet contains Esomeprazole Magnesium 40mg) Manufactured by Wilshire Laboratories, Lahore.

iii. **Reference Product:** Nexium Tablet (each tablet contains Esomeprazole Magnesium 40mg) Manufactured by AstraZeneca (Canada).

iv. **Sponsor:** M/s Olive Bio Center.

v. **CRO and BA/BE Study Site:** Olive BioCenter.

vi. **Principal Investigator:** Dr. Maryam Behram

vii. **Medical/ Clinical investigator:** Dr. Mujahida Salamat

viii. **Funding Source**: M/s Olive Bio Center.

ix. **Cost of the Project**: Not Mentioned

x. **Subjects enrolment**: 24 healthy, male Subjects will be enrolled in the study.

3. The details of the submitted documents are as under;

S.No.	Document	Remarks
1	Application on prescribed form-IIA	Attached.
2	Prescribed processing fee	Processing fee of Rs.200030/- deposited vide challan number 2027338, dated 24th March 2021.
3	Name of Investigational Product (including all available names; trade, generic or INN name, chemical code, etc.,)	Attached
4	Dosage Form of Investigational Product	Tablet
5	Formulation of Investigational Product	Each tablet contains Esomeprazole Magnesium equivalent to Esomeprazole 40mg.
6	Pharmacodynamics and Pharmacokinetics of Investigational Product	Attached

7	Purpose of study defining the indication along with the anticipated cost of the project and sources of fund	The Primary objective of the study was to compare a single oral dose oral Bioavailability profile of Zune tablet (Esomeprazole Magnesium 40mg) of Wilshire Laboratories private limited vs Nexium tablets of M/s AstraZeneca (Canada) in 24 healthy, adult, male, human subject under fasting conditions. **Anticipated cost not provided**. M/s Olive Biocentre is funding source.
8	Proposed center for the study	M/s Olive BioCenter.
9	Investigational design and study plan	Attached
10	Pre-clinical or clinical data or safety studies	Attached
11	Final protocol	Attached.
12	Detail of the investigator (Principal investigator, analysts, and others along with CV)	CVs of the following are attached: Dr. Maryam Behram (PI) Dr. Mujahida Salamat (Medical/ Clinical Investigator Miss Sumbal Afroz (QA Manager) Dr Urwa Asif (Bio Analytical Manager)
13	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Attached
14	Approval of National Bio-ethics Committee (NBC)	Not provided.
15	Site approval by the Ethics committee	M/s Olive BioCenter
16	Informed consent (English and Urdu)	Attached.
17	Summary of the protocol or synopsis (Investigational Product)	Attached.
18	Adverse Event Reporting Form	Attached.
19	Name of the monitor or clinical research associate	Dr. Muhammad Zohaib
20	Evidence of registration in the country of origin (GMP certificate along with CoPP or Free sale certificate)	**Evidence of registration in the country of origin (GMP certificate along with CoPP or Free sale certificate) of Nexium Tablet required.**
21	Copy of registration letter if registered in Pakistan	Copy of registration letter for Zune Tablets is attached.
22	Proposed label of investigational product	Not provided & Investigational Product is registered in Pakistan.
23	Quantity of investigational product to be used in the study along with justification (Note: All the quantities of the each of investigational product	**24 subjects will be enrolled in crossover study. Each will receive one dose. So quantity of investigational product to be used in study is 24 tablets**

	should be procured from one single source)	
24	Undertaking on affidavit.	Not Attached.

04. After initial scrutiny following shortcomings observed:

i. The BA/BE center i.e. Olive Biocentre, is not approved by DRAP.
ii. Approval from National Bio-ethics Committee (NBC) is not provided.
iii. Proposed label for reference product is not provided.
iv. As per Form II-A Olive Bio Centre will provide the Funds for study while as per other documents Dr. Muhammad Zakir, Wilshire Laboratories is sponsor.
v. Anticipated cost of project not provided.
vi. As per IRB approval Ms. Yamema Younatan is physician while her qualification is Pharm-D, M-Phil (Pharmacy).
vii. Documentation of funding and source of funding of IRB is required.
viii. Qualification of Dr. Urvah Asif is B.Sc. honors, M. Sc. Chemistry.
ix. In all attached CVs work place has not been mentioned under heading of work experience.
x. Evidence of registration in the country of origin (GMP certificate along with CoPP or Free sale certificate) of Nexium Tablet required.
xi. Analytical/ bioanalytical method along with validation record is required.
xii. Undertaking on stamp paper required.
xiii. Soft copy of the application along with relevant documents is required.

05. The shortcomings were communicated to the applicant vide this office letter No.F.14-09/2021 DD (PS) dated 24th May 2021.

06. The reply from Mr. Mohsin Ali Jawa, CEO, M/s Olive Worldwide (SMC-Pvt.) Ltd is as followings.

Shortcomings Communicated	**Reply submitted**
The BA/BE center i.e. Olive Biocentre, is not approved by DRAP.	The name Olive BioCenter was being used as a short form of the name Olive Worldwide (SMC-Pvt) Ltd, and the DRAP approved name, Olive Worldwide (SMC-Pvt) Ltd has been used in all the revised documents.
Approval from National Bio-ethics Committee (NBC) is not provided.	The approval letter has been attached with the revised document
Proposed label for reference product is not provided.	Proposed label of investigational product has been provided but proposed label of reference drug not attached.
As per Form II-A Olive Bio Centre will provide the Funds for study while as per other documents Dr. Muhammad Zakir, Wilshire Laboratories is sponsor.	Olive Worldwide (SMC-Pvt) Ltd will provide for all the facilities required for the study. This includes residence of volunteers, Olive Worldwide (SMC-Pvt) Ltd staff salary, processing, storage and transportation

	of samples, bioanalytical and data analysis and protocol and report writing services. Dr. Muhammad Zakir of the Wilshire labs will pay the charges for conduction of the study at point of completion
Anticipated cost of project not provided.	The estimated cost of the project is USD 25000.
As per IRB approval Ms. Yamema Younatan is physician while her qualification is Pharm-D, M-Phil (Pharmacy).	The typographic error has been rectified in revised documents.
Documentation of funding and source of funding of IRB is required.	IRB members do not receive any monetary benefit.
Qualification of Dr. Urvah Asif is B.Sc. honors, M. Sc. Chemistry.	The typographic error has been rectified in revised documents.
In all attached CVs work place has not been mentioned under heading of work experience.	The error has been rectified. Respective workplace has been mentioned in revised documents.
Evidence of registration in the country of origin (GMP certificate along with CoPP or Free sale certificate) of Nexium Tablet required.	SmPC of reference Product and NDA approval attached
Analytical/ bioanalytical method along with validation record is required.	Proposed analytical/bioanalytical method has been provided in the revised documents. The method can only be validated once we gain permission to enroll volunteers since a volunteer's plasma sample (containing Esomeprazole) is required for method validation.
Undertaking on stamp paper required.	The required document has been provided in the revised version.
Soft copy of the application along with relevant documents is required.	The requirement has been fulfilled for revised documents.

7. The soft copy of the application has already been shared with members and co-Opted members in Clinical Study Committee group for evaluation, consideration and perusal.

Submitted for consideration of CSC.

Decision:

The CSC after detailed deliberation decided to approve the BA/BE Study titled "A balanced, open label, randomized, analyst-blind, single center, two-treatment, two-period, two-sequence, crossover design single dose oral bioequivalence study of Zune Tablet (Each Tablet contains Esomeprazole Magnesium 40 mg) of Wilshire Laboratories (Pvt) Ltd. With Nexium Tablet (Each Tablet contains Esomeprazole Magnesium 40 mg) of AstraZeneca (Canada) in 24 normal,

healthy, adult, male, human subjects under fasting conditions." at DRAP approved BA/BE Center, M/s Olive Worldwide (SMC-PVT.) Ltd, Lahore.

Decision of 29th CSC meeting.

The CSC was appraised about the difference in name of DRAP approved BA/BE centre i.e M/s Olive Worldwide (SMC-PVT.) Ltd, Lahore and name mentioned on NBC approval letter i.e. M/s Olive BioCentre. The CSC after detailed deliberation decided to approve the BA/BE Study titled "A balanced, open label, randomized, analyst-blind, single center, two-treatment, two-period, two-sequence, crossover design single dose oral bioequivalence study of Zune Tablet (Each Tablet contains Esomeprazole Magnesium 40 mg) of Wilshire Laboratories (Pvt) Ltd. With Nexium Tablet (Each Tablet contains Esomeprazole Magnesium 40 mg) of AstraZeneca (Canada) in 24 normal, healthy, adult, male, human subjects under fasting conditions." at DRAP approved BA/BE Center namely M/s Olive Worldwide (SMC-PVT.) Ltd, Lahore subject to submission of NBC approval mentioning the correct name of BA/BE centre & documents regarding the mode of acquiring/ import of reference drug i.e. Nexium Tablet 40 mg from M/s AstraZeneca, Canada as per study protocol.

AGENDA ITEM - VII:

APPLICATION FOR APPROVAL OF CLINICAL TRIAL TITLED, "A MULTICENTER, RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED STUDY TO ASSESS SAFETY AND EFFICACY OF SIR1-365 IN PATIENTS WITH SEVERE COVID-19)", PROTOCOL NO. SIR365-US-101. F. No.03-72/2021-DD (PS)

Application is submitted by Dr. Iffat Khanum, Principal Investigator for SIR1-365 Phase I-B Trial in Pakistan, Department of Infectious Diseases, Aga Khan University Hospital, Karachi, dated 23rd June 2021, wherein request has been made for registration & approval of subject clinical trial. Application is submitted on prescribed Form-II with prescribed fee of Rs.200000/- paid vide challan number 50267226, dated 23rd June 2021.

2. Details of IMPs & purpose of the trial is as follows:

a. **Name of Investigational product, including all available names; trade, generic or INN name etc.:** SIR1-365 is a receptor-interacting protein kinase 1 (RIP1) inhibitor that is under development as a new investigational drug for the treatment of inflammatory diseases. SIR1-365 will be supplied as 10 mg, 25 mg, and 100 mg tablets.

b. **Purpose of trial defining the indication along with the anticipated cost of the project and sources of fund Primary objective:** The primary objective is to assess the overall safety and tolerability of SIRI-365 administered orally at 100 mg, TID for 14 days relative to the placebo group. Secondary Objectives: To assess the clinical efficacy of SIR1-365 in patients with severe COVID-19 To assess the effects of SIR1-365 on multiple inflammatory biomarker levels including C- reactive protein (CRP), ferritin, lymphocyte and neutrophil counts, cytokines, and chemokines To assess the effects of SIR1-365 on biomarkers indicative of target engagement in patients with severe COVID-19 To assess the effects of SIR1-365 on biomarkers indicative of kidney injury in patients with severe COVID-19.

c. **Source of funding:** Sironax USA, Inc, a Subsidiary of Sironax, Ltd (Sironax).

3. Application evaluated according to prerequisites of Form-II of the Bio-Study Rules 2017. The details of the submitted documents are as under;

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached.
2	Prescribed fee	Attached.
3	Investigator Brochure (s)	Attached. Version 4.0 (SIR1-365)
4	Final protocol	Protocol No.SIR365-US-101 Version 2.4 issued on 8th April 2021. Attached.
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries	USA, Mexico India & Pakistan.
7	Phase of trial.	Phase-IB.
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for import of trial material.	SIR1-365 (65 Bottles). Placebo (65 Bottles). Lab Kits=60 (Divided into two shipments)
9	Site of the trial	1. Aga Khan University Hospital Karachi. (CTS-0003) 2. Dow University of Health Sciences, Ojha Campus, Karachi. (CTS-0040) (Trial specific approved site) 3. Sindh Infectious Diseases Institute, Karachi. (CTS-0041) (Trial specific approved site)
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Only list of members of AKUH-IRB is attached. IRB approval along with list of IRB members is attached. Differentiation for Dow University Ojha Campus & Sindh Infectious Diseases Institute is not mentioned in the letter.

11	Approval of National Bio-ethics Committee (NBC)	Certificate Ref:No.4-87/NBC-COVID-85/21/1723, Dated 23rd June 2021 is attached.
12	CV's of the Investigators	CVs of following PIs are attached: i. Dr. Iffat Khanum. (PI) ii. Dr. Shobha Luxmi(Co-PI) iii. Dr. Muneeba Ahsan Sayeed. (Co-PI)
13	GMP certificate along with COPP & free sale certificate of the investigational product.	GMP Certificate of M/s Shanghai STA Pharmaceutical Product Co. Ltd, 31 Yiwei Road, building 15, Waigaoqiao Free Trade Zone, Shanghai, 200131, China is attached. COA for SIR1-365 is attached. FDA approval: IND-150853
14	Pre-clinical/clinical safety studies	Attached.
15	Summary of Protocol	Attached.
16	Summary of Investigator Brochure	Attached.
17	Adverse Event Reporting Form	Attached.
18	No of patients to be enrolled in each center.	60 Subjects globally. 20-40 Subjects anticipated to be enrolled in Pakistan
19	Name of Monitors & Clinical Research Associate	M/s Metrics Research (Pvt) Ltd, Karachi. Dr. Areeba Waqas (Site 401) Dr. Yasir Mahmood (Site 402a) Dr. Erum Choudry (Site 402b) Dr. Sayed Muhammad Sharib (Medical Monitor) Dr. Qurat Ul Ain (Clinical QA)
20	Evidence of registration in country of origin.	FDA approval: IND-150853
21	Copy of registration letter (if registered in Pakistan)	N/A.
22	Sample of label of the investigational product / drug.	Attached.
22	Duration of trial	06 Months
23	Undertaking on Stamp paper	Attached.

4. After initial scrutiny following observations were recorded:

i. FDA approval for investigational new drug certificate number IND150853 issued in the name of M/s Sironax Inc. USA (Sponsor/Responsible party of the trial), whereas GMP certificate of M/s Sironax Inc. USA is not provided.

ii. GMP Certificate of M/s Shanghai STA Pharmaceutical Product Co. Ltd, 31 Yiwei Road, building 15, Waigaoqiao Free Trade Zone, Shanghai, 200131, China is attached as a manufacturer of the IMPs (SIR1-365 Tablets), but any MoU/agreement between trial sponsor/IND certificate holder is not provided.

iii. As per provided data it is found that SIR1-365 supplied as 10 mg, 25 mg, and 100 mg tablets, so the following data is need to be provided:

a. Strength-wise import requirements of the IMPs.
b. Pack size of the bottle of IMPs need to be imported.

iv. IRB approval from Aga Khan University Hospital, Karachi is not provided.

v. IRB approval from Dow University of Health Sciences , Karachi is attached but in that approval letter name of the sites for which IRB approval letter issued need to be incorporated.

vi. Dow University of Health Sciences, Ojha Campus, Karachi. (CTS-0040) & Sindh Infectious Diseases Institute, Karachi. (CTS-0041) were approved for only clinical trial titled "*Immunoglobulin Therapy for passive Immunization of Critically Ill Covid-I9 Patients*". New applications for generalized clinical trial sites (for Phase-I, II, III & IV) are under process.

vii. As per U.S. National Trial Registry record the subject clinical trial is enlisted with identifier number NCT04622332 but list of participating countries / locations are not updated as only USA is mentioned in the registry.

5. Shortcomings recorded also communicated to the applicant vide letter number F.No.03-72/2021-DD (PS), dated 29th June 2021, response is yet awaited.

Technical documents (i.e. Non-Clinical & Clinical Data, Study Protocol & investigator's brochure along with summary etc.) were forwarded to all CSC experts through email for review & evaluation under sub-rule 4 of rule 7 of the Bio-Study Rules 2017, on 28th June 2021.

6.

Submitted for evaluation, consideration and perusal of CSC.

Decision:

The CSC after detailed deliberation decided to approve clinical trial titled, "A Multicenter, Randomized, Double-Blinded, Placebo-Controlled Study to Assess Safety and Efficacy of SIR1-365 In Patients with Severe COVID-19)" subject to submission of IRB approvals of the proposed site and any other shortcomings.

Decision of 29th CSC meeting.

The CSC after detailed deliberation decided to approve clinical trial titled, "A Multicenter, Randomized, Double-Blinded, Placebo-Controlled Study to Assess Safety and Efficacy of SIR1-365 in Patients with Severe COVID-19" and issue trial approval letter to conduct the trial at Aga Khan University Hospital Karachi. (CTS-0003) where as approval to conduct this trial at CTS i) Dow University of Health Sciences, Ojha Campus, Karachi and ii) Sindh Infectious Diseases Institute, Karachi will be decided in next CSC meeting after these sites are inspected and approved by CSC to conduct phase-I clinical trial.

AGENDA ITEM II:-

A RANDOMIZED DOUBLE-BLIND CONTROLLED CLINICAL TRIAL OF DWJ1248 IN PREVENTION OF COVID-19 INFECTION AFTER EXPOSURE OF SARS COV-2 F. No.03-73/2021 DD (PS).

The is an application from Prof. Dr. Javed Akram, CNIC No. 37405-4949969-7, of M/s Akram Medical Complex, Ayesha Siddiqa Road, Main Gulberg, Lahore, wherein the applicant has requested for approval or registration of clinical trial titled **A randomized, double-blind controlled clinical trial DWJ1248 in prevention of COVID-19 infection after the exposure of SAR COV-2.** The application is on Form-II of the Bio-Study Rules 2017. CRO in this trial is DRK.

2. It is submitted that application evaluated according pre- requisites as mentioned in Form-II of the Bio-Study Rules 2017, and following shortcoming observed:

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached
2	Prescribed processing fee	Fee of Rs.200,000/- online vide slip No.397656251781 dated 29.06.2021.
3	Investigator Brochure (s)	Attached
4	Final protocol	Attached.
5	Informed consent and participant information sheet (Urdu to English)	Attached.
6	List of participating countries	Pakistan, South Africa and south Korea
7	Phase of trial.	Phase III
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for import of trial material.	Camostat mesylate 200mg 300 box Placebo 300 box
9	Site of the trial	Akram Medical Complex, Lahore

		Avicenna Hospital, Lahore. National Hospital & Medical Center, Lahore Medicare Hospital Rawalpindi. **(NOT APPROVED BY DRAP)**
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	IRB approval of Avicenna Hospital is not attached.
11	Approval of National Bio-ethics Committee (NBC)	Attached. Ref:No.4-87/COVID-82/NBC/21/1743, Dated 24th June 2021.
12	CV's of the Investigators	CV of Prof. Javed Akram Prof. Dr Waheed Ahmed Dr. Nadia Majeed And Dr. Rizwana Chaudhary are attached.
13	GMP certificate along with COPP & free sale certificate of the investigational product.	GMP certificate of M/s Daewoong Pharmaceutical attached. **(**Camostat mesylate 200mg is not registered drug in South Korea as per information provided by DRK pharma Solution**)**
14	Pre-clinical/clinical safety studies	Attached.
15	Summary of Protocol	Attached.
16	Summary of Investigator Brochure	Attached.
17	Adverse Event Reporting Form	Attached.
18	No of patients to be enrolled in each center.	Total 1012 and 600 subjects will be enrolled in Pakistan.
19	Name of Monitors & Clinical Research Associate	DRK Pharma Solution, Lahore. Naveed Akbar, Project Lead, Hajira sajid CRA, Muhammad Sajid CRA, Usama Suleman CRA, Attiqa kayani CRA.
20	Evidence of registration in country of origin.	**Not attached**
21	Copy of registration letter (if registered in Pakistan)	Not registered in Pakistan
22	Sample of label of the investigational product / drug.	Attached

22	Duration of trial	12 Months
23	Undertaking on stamp paper.	Attached.

3. After evaluation, it was found that Medicare Hospital, Rawalpindi, is not approved as CTS, IRB approval from Avicenna Hospital not attached.

4. Soft copy of the application has been sent to CSC members through what's app for screening, assessment, review and evaluation.

SUBMITTED FOR CONSIDERATION OF CSC.

Decision of 29th CSC meeting.

The CSC after detailed deliberation decided to approve clinical trial titled, "A randomized double-blind controlled clinical trial ff DWJ1248 in prevention of Covid-19 infection after exposure of SARs COV-2" at following DRAP approved Clinical Trial Sites: -
Akram Medical Complex, Lahore.
Avicenna Hospital, Lahore.
National Hospital & Medical Center, Lahore.

AGENDA ITEM III:-

CHANGES IN PROROCOL AS VERSION 1.1 AND ICF AS VERSION 1.3 FOR CLINICAL TRIAL TITLED AS A PHASE III RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED CLINICAL TRIAL IN 18 YEARS OF AGE AND ABOVE TO DETERMINE THE SAFETY AND EFFICACY OF ZF2001, A RECOMBINANT NOVEL CORONA VACCINE (CHO CELL) FOR PREVENTION OF COVID-19.

The case is the letter from Prof. Javed Akram, PI, wherein he has requested for change in protocol (and related trial documents) received from sponsor of the trial. He has given the following background.

The recombinant novel coronavirus vaccine (CHO cell) jointly developed by Anhui Zhifei Longcom Biopharmaccutical Co., Ltd. and Institute of Microbiology, Chinese Academy of Sciences obtained the NMPA drug clinical trial approval on June 19, 2020, and the proposed indication is "prevention of 2019 coronavirus disease (COVID-19) caused by novel coronavirus infection". After obtaining the initial results of Phase Land Phase II clinical trials of this product, sponsor conducted technical communication of Phase Ill clinical trial protocol for people aged 18 and above with your center on November 4, 2020, It is planned to enroll 28,000 overseas subjects to evaluate the protective efficacy, immunogenicity and safety of COVID-19, and 1,000 domestic subjects to evaluate the safety and immunogenicity. At

present, the Phase III clinical trials are being carried out in China, Uzbekistan, Indonesia, Ecuador and Pakistan. As of February 15, 2021, 6830 subjects have been enrolled in Uzbekistan, and the third dose of vaccination has started; In the past two months, 81 suspected cases have been found, and no confirmed cases have been found Considering that since October 2020, the daily number of confirmed cases of COVID-19 in Uzbekistan has been continuously decreasing (statistics of WHO Global Health Observatory), daily number of newly added cases in recent 2 months is below 100, and most of them are mild or asymptomatic infected persons. According to the actual epidemiological situation in Uzbekistan, is difficult to catch effective cases if the original protocol is used for case monitoring. In order to improve the monitoring efficiency of COVID-19 cases in clinical trials, on the basis of referring to the latest technical guidelines, and drawing lessons from the clinical trial experience of products on the market at home and abroad, sponsor of the trial plans to apply for the adjustments to the diagnostic criteria of COVID-19 suspected cases and COVID-19 cases in the Phase III clinical trial protocol of recombinant novel coronavirus vaccine (CHO cells). The changes in the protocol have also been reflected by some changes in the other documents. Hopefully once the new version of the protocol is approved the changes in other documents shall also stand approved. The summary of the changes and the documents mentioned in Table 1 with reference to the previous and new document versions is given as attachment to the letter. In view of the fact that this product has started the third dose of vaccination and will enter the monitoring period of vaccine effectiveness and protection 14 days after the third dose, I am eager to get a reply from DRAP as soon as possible.

2. Major revisions of diagnostic criteria for suspected COVID-19 cases and COVID-19 cases in protocol is attached by the applicant and revised consent form in Urdu and English is attached.

3. Applicant is accompanying Fee of Rs.25,000/- along with NBC approval, IRB approvals amended protocol version 1.1, ICF version 1.3 (English/urdu), Cue card etc.

4. Soft copy of the application has been sent to the members CSC through what's app for screening, assessment, review and evaluation.

SUBMIITED FOR CONSIDERATION OF CSC

Decision of 29th CSC meeting.

The CSC after detailed deliberation decided to approve amended protocol i.e. Version 1.1 and amended ICF i.e. Version 1.3 for clinical trial titled "A phase III randomized, double blind, placebo controlled clinical trial in 18 years of age and above to determine the safety and efficacy of ZF2001, a recombinant novel corona vaccine (CHO cell) for prevention of covid-19".

AGENDA ITEM IV.

PROGRESS REPORT OF CLINICAL TRIAL TITLED AS A PHASE III RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED CLINICAL TRIAL IN 18 YEARS OF AGE AND ABOVE TO DETERMINE THE SAFETY AND EFFICACY OF ZF2001, A RECOMBINANT NOVEL CORONA VACCINE (CHO CELL) FOR PREVENTION OF COVID-19. (F.No.03-52/2021 DD (PS)).

The case is the progress reports submitted by DRK Pharma Solution regarding the recruitment status of the subjects. The study was approved on 19th March 2021 by CSC.

2. Following is the latest status of recruitment submitted on 7th July 2021.

Site Name	Screening	Screening Failure	Ist Dose	2nd Dose	3rd Dose
National Hospital & Medical Center, Lahore	2008	577	1000	429	325
Avicenna Medical College, Lahore	2380	913	101	625	407
UHS, Lahore	5281	1580	2512	1453	801
Central Park Medical college, Lahore	2395	752	1316	576	217
Aziz Fatima Hospital, FSD	1977	440	1015	667	448
Indus Hospital Karachi	1113	383	585	210	147
SZABMU, Islamabad	2086	572	1254	381	127
Al-Shifa Trust, Rawalpindi	3806	576	2654	1368	273

3. The AEs being reported for the vaccine and the placebo (solicited and unsolicited) are being collected and stored in the data base of the applicant. The actual report of these effecting the groups can be only assessed once the blind is opened. The interim analysis and final report for all AEs (in both groups) shall be provided when available.

SUBMITTED FOR CONSIDERATION OF CSC

Decision of 29th CSC meeting.

The CSC perused the progress report, submitted by M/s DRK Pharma solution (CRO), in above said trial.

AGENDA ITEM V:

PARTICIPATION CERTIFICATE FOR SUBJECTS INCLUDED IN CLINICAL TRIAL TITLED AS A PHASE III RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED CLINICAL TRIAL IN 18 YEARS OF AGE AND ABOVE TO DETERMINE THE SAFETY AND EFFICACY OF ZF2001, A RECOMBINANT NOVEL CORONA VACCINE (CHO CELL) FOR PREVENTION OF COVID-19. (F.No.03-52/2021 DD (PS)).

The case is the is request from Prof. Dr. Javed Akram, VC UHS, member CSC and PI of the trial titled as "A PHASE I RANDOMIZED, DOUBLE-BLIND, PARALLEL- CONTROLLED CLINICAL TRIAL IN 18 YEARS OF AGE AND ABOVE TO DETERMINE THE SAFETY AND EFFICACY OF ZF2001, A RECOMBINANT NOVEL CORONAVIRUS VACCINE (CHO CELLYEOR PREVENTION OF COVID-19" wherein he has stated that reference to your letter: F. No. 03-52/2021 DD (PS) Dated 16th February 2021, DRK Pharma Solution the licensed Clinical Research Organization having License No CRO-0001 dated 11th October 2019, had applied for approval for clinical trial to DRAP. This trial is being sponsored by Anhui Long com Biopharmaceutical Company China. We were given permission to conduct the trial vide letter No. 03-52/2021 DD (PS) Dated 15th February 2021. I am conducting this trial at my site as the lead investigator and covering the other 8 sites in Pakistan. Now that the government has started the vaccination drive. There is news that every citizen above the age of 18 has to get vaccinated. If the individual cannot provide a vaccine certificate being issued by the government some of the facilities shall be withdrawn. It is requested that since the undergoing trial was approved by the National Ethics Committee and subsequently fulfilling all the requirements by Clinical Study Committee of Pharmacy Division, DRAP. The subjects enrolled are finding it difficult to continue with the follow up in the trial. It is requested that the Government to please issue a certificate (excerpting them from forced vaccination till they complete the trial process) as these subjects are a part of an approved clinical trial. As per protocol 10.000 subjects are to be enrolled and 9000 + plus have been enrolled and vaccinated, some of these subjects (nearly 2000) have been given the 3rd dose. As half of these enrolled are given vaccine and half placebo with the commitment that after the interim analysis. The ones given placebo shall also the vaccinated. Hence covering the whole in trial population being vaccinated in the coming couple of months. Now under these circumstances those who have been given vaccine cannot get another vaccine (as this has not been proven safe) and if they are vaccinated they shall be considered a dropout from the current trial putting the whole trial data in jeopardy. This would be a setback to the scientific contribution from Pakistan. Hoping to get a positive response and further guidelines to follow in this case.

SUBMITTED FOR CONSIDERATION OF CSC.

Decision of 29th CSC meeting.

The CSC after detailed deliberation decided that as there is no legal provision in the Bio-Study Rules 2017 for issuance of such vaccination exemption certificates and it is also not the mandate/ prerogative of the CSC. So, The CSC decided to refer the same to the Authority for its consideration, deliberation and decision accordingly .

AGENDA ITEM VI

Subject: **APPLICATION FOR KAHANA NAU HOSPITAL TO ACT AS CLINICAL TRIAL SITE (F. No.15-32/2021 DD (PS)).**

The Case is an application on Form-I from. Usman Arif, Tehsil Headquarter (THQ) Hospital, Kahna Nau, Kasur Road, Lahore with covering letter from Institute of Social & Culture Studies, University of the Punjab, Lahore, stating details of ViDiSAM phase-II Trial Vitamin d Safety and Efficacy. The application is on Form-I of the Bio-Study Rules 2017 with fee of Rs.100,030/-.

2. It is submitted that application evaluated according pre- requisites as mentioned in Form-I of the Bio-Study Rules 2017, and as following are observations:

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached.
2	Prescribed processing fee	Fee challan of Rs.100,030/- attached submitted vide slip No. 2013471.
3	Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).	
4	Details of premises including layout plan of the site.	Lay out plan of proposed CTS attached.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached
6	Names and qualifications of the above sections along with their staff.	List of ViDiSAM trial team is attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Applicant has stated that Tehsil Headquarter (THQ), Kahna Nau is 100 bedded Hospital and offering and offering the following facilities. Accident & Emergency services, Daycare Services, Family Medicine, general surgery, Obstetrics & Gynecology, Pediatrics, Orthopedic surgery, Anesthesia, family medicine, Nutrition Clinic, T.B Clinic, Diabetic Clinic, pediatric Malnutrition Clinic, immunization Clinic, Family planning Clinic, Blood Bank, Laboratory, Radiology.
8	Undertaking on stamp paper	Attached.

3. Applicant has applied in Form-I for Clinical trial site for Phase-II, III & IV trials. In Phase 2 studies, researchers administer the drug to a group of patients with the disease or condition for which the drug is being developed. Typically involving a few hundred patients, these studies aren't large

enough to show whether the drug will be beneficial. Instead, Phase 2 studies provide researchers with additional safety data. Researchers use these data to refine research questions, develop research methods, and design new Phase 3 research protocols. Phase I & II mostly include Pharmacokinetics and pharmacodynamics studies. Phase I & II usually characterization of PK disposition of the parent drug and its metabolites in plasma, urine and serum is required.

4. As applicant has applied for clinical trial site for "Double Blind, Randomized, Placebo-controlled Trial of High dose Vitamin d Supplementation in the Treatment of complicated Severe Acute Malnutrition". We may consider the said clinical trial site particularly for said trial of high dose of Vitamin D.

5. After Evaluation of the it was found that name of hospital where clinical trial site exist is Tehsil Headquarters (THQ) Kahna Nau while the applicant is using the stamp of the Indus hospital Lahore, Kahna Nau campus. The applicant told that the THQ, Kahna Nau is working under supervision of the Indus hospital Lahore.

6. In the light of above discussion, the applicant may be asked to submit legal status of the applicant and MOU signed between THQ, Kahna Nau and Indus Hospital Network.

7. It is submitted that application has been made with covering letter of Institute of Social & Culture Studies, University of the Punjab, Quaid e Azam Campus, Lahore, who intend to conduct Clinical Trial, namely, ViDiSAM, wherein they have attached the application on Form-I from Dr. Usman Arif (Co-Investigator) of the said trial for issuance of license to act as clinical trial site at Tehsil Head Quarters (THQ), Hospital, Kahna Nau. The application has been evaluated as described at para 2/n. whereas, DRK pharma solution is CRO in ViDiSAM Trial. It is further submitted that following documents were asked from the applicant vide letter dated 24th May 2021;

i. Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).
ii. Names and qualifications of the above sections along with their staff.
iii. MOU/ agreement signed between Tehsil Headquarters, Kahna Nau and Indus Health Network.

8. The applicant has submitted the staff list and copy of agreement. It is submitted that all the documents as required in the light of Form-I of the Bio-Study rules 2017 are attached but it need further elaboration and clarification about the legal status of the applicant because as per submitted

agreement Government of the Punjab has signed agreement with Recep Tayyip Erdogan Hospital (RTEH) trust for management and operation of THQ Hospital Kahna Nau and then RTEP trust has made agreement with Indus Hospital. TORs of agreement between RTEH trust and Indus Hospital needs to be elaborated.

9. In the light of above, it is proposed that panel for inspection of proposed trial site i.e.THQ Hospital, Kahna Nau may be constituted to verify the facilities at the site. The panel may be requested to verify the legal status or TORs between RTEH Trust and Indus Hospital.

10. It is submitted that Director, Division of Pharmacy Services informed that he has scheduled inspection of Fatima Jinnah Medical University, Sir Ganga Ram Hospital, Lahore, on 07th June 2021 & directed to issue inspection letter with same panel, for subject clinical trial site as both trial site situated in the Lahore & for same clinical trial titled, "Double Blind, Randomized, Placebo-controlled Trial of High dose Vitamin D Supplementation in the Treatment of complicated Severe Acute Malnutrition".

11. The following panel was constituted.

a. Prof. Dr. Javed Akram, VC, UHS, UHS, Lahore.
b. Dr. Farhana Badar, Biostatistician, SKCH&RC, Lahore.
c. Dr. Abdur Rashid, Director Pharmacy Services Division, DRAP, Islamabad (coordinator).
d. Dr. Uzma Malik, Associate Professor, Mayo Hospital, Lahore.
e. Sheikh Abdul Rashid, FID, DRAP, Lahore.

12. The panel was requested that the applicant has applied for the Clinical Trial Site for Phase II, III & IV for study titled "Double Blind, Randomized, Placebo-controlled Trial of High dose Vitamin d Supplementation in the Treatment of complicated Severe Acute Malnutrition". The Panel is requested to verify the Facility as per requirements of Form-I of Bio-Study Rules 2017, Fitness of the Facility to carry out the said clinical trials of Phase-II, III & IV, required equipment/ machinery, SOPs and expertise to fulfil the criteria required to carry out the Clinical Trial. The panel shall also verify the Bioanalytical Lab. to conduct the pharmacokinetic studies for phase II trials. Panel also requested to verify the legal status of Recep Tayyip Erdogan Hospital (RTEH) trust for management and operation of THQ Hospital Kahna Nau & Indus Hospital.

13. The following members of the panel inspected the premises.

a. Prof. Dr. Javed Akram, VC, UHS, UHS, Lahore.
b. Dr. Farhana Badar, Biostatistician, SKCH&RC, Lahore.
c. Dr. Abdur Rashid, Director Pharmacy Services Division, DRAP, Islamabad (coordinator).
d. Sheikh Abdul Rashid, FID, DRAP, Lahore.

14. The inspection team has recommended the CTS for approval with following remarks.

"Based on the inspection, the technical people met and the documents reviewed and considering the findings of the inspection the panel verifies vide DRAP, Islamabad letter number

F.15-32/2021-DD (PS) dated 10.06.2021, that the applicant possesses the facility for conducting the clinical trials as applied."

15. The panel inspection report, however does not reflect any comment regarding the legal status of the applicant as requested in this division letter. Applicant has submitted incomplete/ partial agreement between TREHT and Indus Hospital and has hidden terms and conditions/ TORs of agreement. The legal status and act of applicant for hiding terms and condition of agreement in submitted documents needs clarification and same may be confirmed from panel members or the applicant.

SUBMITTED FOR CONSIDERATION OF CSC.

Decision of 29th CSC meeting.

The CSC after due deliberation, in the light of panel inspection report and the recommendation of panel of experts/ inspectors and as briefed by the chairman CSC/ panel member (coordinator) regarding the facility for conduct of trial at the site, unanimously decided to approve M/s Tehsil Headquarter (THQ) Hospital, Kahna Nau, Kasur Road, Lahore to act as clinical trial site (CTS) for phase III & IV clinical trials.

ADDITIONAL AGENDA

AGENDA ITEM I:-

Subject: **APPROVAL OF CLINICAL TRIAL SITE FROM RAWALPINDI INSTITUTE OF CARDIOLOGY. F. No.15-13/2021 DD (PS)**

Case is an application from Dr. Hamid Sharif Khan, Co-Investigator, IVUS_DAPT Trial has applied for license to act as Clinical Trial Site for Phase III clinical trials. The application is on Form-I of the Bio-Study Rules 2017 on stamp paper with fee of Rs.100,000/- submitted vide challan no. 1986104.

2. It is submitted that application evaluated according pre- requisites as mentioned in Form-I of the Bio-Study Rules 2017, and as following are observations:

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Form-I submitted on stamp paper.
2	Prescribed processing fee	Fee challan of Rs.100,000/- attached submitted vide slip No. 1986104.
3	Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and	Not Attached. RAWALPINDI INSTITUTE OF CARDIOLOGY IS A TERTIARY CARE GOVERNMENT INSTITUTE. ITS SERVICES ARE FREE OF

	names and addresses of its partners and in the case of company the name and address of the company and its directors).	COST, FUNDED BY GOVERNMENT OF THE PUNJAB, HEALTH DEPARTMENT.
4	Details of premises including layout plan of the site.	Layout plan not readable.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached.
6	Names and qualifications of the above sections along with their staff.	Prof. Dr. Azhar Mehmood Kiani Dr. Asim Javed. Dr. Hamid Sharif Khan.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Emergency: Capacity 28 bedded with 4 ventilators Timing 24/7 Operation Theater: Capacity 4 bedded Timing 27/7
8	Undertaking on stamp paper	Print of form 1 provided on stamp paper

3. Evaluation of the application is placed in tabulated form. If the seniors are satisfied provided documents, the case may be placed in the next forthcoming CSC meeting other we ask the firm if any further detail is required. Meanwhile firm may be asked to provided soft copy of the application so the same may be presented in CSC meeting. It is further added same application has been also submitted by on Form-I of the Bio-study Rules 2017 by Maj. General (R) Azhar Mehmood Kiani, Principal Investigator NUS-DAPT Trial.

4. Following panel was constituted by chairman CSC and panel conducted the inspection of M/s RIC, Rawalpindi on 03-08-2021.

i. Sh. Ansar Ahmed, Ex-Drug Controller, DRAP.
ii. Dr. Mujtaba Najabat Ali, NHT, NUST, Islamabad.
iii. Prof. Brig. (R) Muzammal Hassain Najmi, Professor of Pharmacology, Foundation University, Islamabad.
iv. Dr. Abdur Rashid, Director, Division of Pharmacy Services, DRAP, Islamabad (Coordinator)
v. Dr. Akhtar Ali Bandesha, Assistant Professor, Department of Cardiology, PIMS, Islamabad.

5. Remarks of the inspection team are followings;

"Keeping in view the cardiologic equipment, human resource, and technical expertise, training, documentation, waste management, it facilities with server, emergency- Cath lab, operation theatre, handling and resources, ambulatory services/ ambulance, pharmacy and other relevant facilities recommends Rawalpindi Institute of Cardiology, rawal Road Rwp recommends the Clinical trial site for phase III"

6. **SUBMITTED FOR CONSIDERATION OF CSC**.

Decision of 29th CSC meeting.

The CSC after due deliberation, in the light of panel inspection report and the recommendation of panel of experts/ inspectors, unanimously decided to approve M/s Rawalpindi Institute of Cardiology, Rawal Road, Rawalpindi to act as clinical trial site (CTS) for phase III clinical trials.

AGENDA ITEM II

TRA-1129940, LONGITUDINAL 2-YEAR BONE MARROW STUDY OF ELTROMBOPAG OLAMINE (SB-497115-GR) IN PREVIOUSLY TREATED ADULTS, WITH CHRONIC IMMUNE IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP).

Mr. Yasir Iqbal a subject of clinical trial titled ***"TRA-1129940, Longitudinal 2-Year Bone Marrow Study of Eltrombopag Olamine (SB-497115-GR) in Previously Treated Adults, with Chronic Immune Idiopathic Thrombocytopenic Purpura (ITP)"*** submitted the following complaint in the office of Director, Division of Pharmacy Services:

"*In his complaint he informed that on 13th March, 2010, he became ill and went to Hameed Latif Hospital for a check-up from Dr. Zeba Aziz. He was admitted in the hospital and stayed at the hospital for 10-12 days and was informed that he had Chronic Immune thrombocytopenia (ITP). Accordingly, his treatment was started and he had to visit the hospital 2-3 times a week. But, three months after the start of treatment, Dr Zeba Aziz informed him about a medicine namely Eltrombopag and said it was very successful in other countries. He said that he was made assured that he would be cured with the treatment of that medicine. It was also informed as that medicine was under clinical trial at that time in Pakistan, so it will be provided free of cost to him and the sponsored company would bear his expenses and if any mishap happened, the company would be responsible. He was also assured that the company is a multinational, namely GSK. He blamed Dr. Zeba Aziz, Dr. Muhammad Akram and Dr Abbas for their greediness for the fund of the trial because he was compelled to participate in the trial as he was their regular patient; therefore, he was given code number 000429 in the trial for patient identification. Accordingly, he informed that the treatment was started with 25mg of Eltrombopag. In the second week, the dose was increased to 50mg due to which he said that he felt pain and inflammation in his leg and went to the hospital for a check-up, where Dr. Zeba Aziz prescribed pain medication and increased the dose to 75mg. He said after taking 75mg Eltrombopag, his condition was worsened as he had severe pain and inflammation in leg along with vomiting. He called Dr Abbas and Dr. Zeba and was advised to visit the emergency of Hameed Latif hospital, where his ultrasound, CT scan were performed and was ultimately admitted in ICU. He said that his family was requested to pray for him, as Doctors informed his family that because of Eltrombopag he had developed Deep Vein Thrombosis (DVT) and also to pray that clotted blood should not block his trachea or heart as it would be fatal for him. He was admitted in his hospital and was shifted to warfarin to avoid clotting. He said that clots developed regularly so Dr. Zeba advised him to visit Dr. Ali in Shaukat Khanum Hospital, where after investigation he was asked to install inferior Venacava (IVC) filter, which he did. He said that not only he developed DVT in his leg but also has regular vomiting and cannot eat anything. He further added that his IVC filter is closed now and Doctors have informed him that there would be a big risk in its removal, might be a risk of his life.*

Concluding the statement, he said that because of commission/ funding, the Doctors of Hameed Latif had made him a guinea pig for the testing of Eltrombopag by not considering the harmful effects of the drug. He said his life has changed as he cannot lift any weight, neither can he go upstairs because of shortness of breath. He also added that he had a running business in Kuwait before the start of that drug, but, he spent his entire asset on his treatment. He requested for help. He also said that the trial of that company should never have been allowed at that time in Pakistan as in 2007 and 2008, GSK was fined for 300 Billion Dollars by US Court due to death of 14 children in a trial with a drug of that company. Further, in China, that company was also fined for 490 million pounds because of giving money to Doctors. Therefore, it would have been good, if that company had never been allowed for that trial in Pakistan. In the end, he said the doctors have ruined his life and future because he could not lift his children nor can he walk and earn for them. Therefore, he said that he needs justice to be done in the matter.

2. Among a list of documents, he provided, there was a certificate dated 9th January, 2013 of Dr. Muhammad Akram, Consultant Oncologist, Hameed Latif Hospital, which stated as under:

> *"Mr. Yasir Iqbal, 25 years/Male, resident of Gujranwala, diagnosed with chronic ITP in January, 2010. He then went to Hameed Latif Hospital for his treatment in June, 2010 and was started on to Eltrombopag in August 2010. After 1 month of initiation of Eltrombopag, he developed pain and swelling in left leg. Colour Doppler of the left leg showed extensive Deep Vein Thrombosis (DVT). He was started by Clexane and he responded well to the therapy and thrombosis was recanalized. But, after 3-4 months he again developed DVT leading to pulmonary embolism. When investigated he is also found to have positive for lupus antibody. To avoid this incidence of pulmonary embolism again, an inferior venacava filter was placed.*
>
> *Now he has been on steroid and immunomodulator drugs for the treatment of his chronic ITP and he is on regular follow up with us."*

3. Accordingly, Director, Division of Pharmacy Services, Chairman, Clinical Study Committee through letters communicated with the following:

a) Punjab Healthcare Commission for investigation and legal action;
b) Pakistan Medical and Dental Council (PMDC) for investigation and initiation of legal action against the concerned doctors;
c) Hameed Latif Hospital for investigation;
d) Provincial Pharmacovigilance Centre, the Punjab for investigation; and
e) GSK Pakistan for explaining their position and submission of the final report of the study.

4. No reply was received from PMDC and the Provincial Pharmacovigilance Centre of Punjab. However, the other three submitted as under:

I. The GSK Pakistan submitted that the subject matter with the complainant, Yasir Iqbal, is sub-judice in Consumer Court of Lahore and since the past few hearings the complainant hasn't been appearing before the concerned judge, despite several opportunities. Alongside, a civil suit was filed against the

complainant in Civil Court Lahore, where an injunction order is passed against the complainant and is in a field whereby, the complainant is restrained from maligning the company, making derogatory comments or filing any frivolous complaints during the pendency of his complaint before Consumer Court Lahore. It was said that the complainant has undoubtedly violated the Court Order and the company reserves the right to initiate contempt of court proceedings against him.

II. The Punjab Healthcare Commission replied that the incident took place in the year 2010. However, the Punjab Healthcare Commission Act, 2010 (PHC Act, 2010) was promulgated on 2nd of August, 2010 while Punjab Healthcare Commission was constituted in the year 2011 under the provision of Section 3 of the said Act; therefore, the PCH Act, 2010 does not have retrospective applicability as there is no section/clause in the said Act to that effect. Furthermore, it was said that as per sub-section (7) of Section 4 of the PHC Act, 2010, the commission inter-alia entertains complaints on reference by Superior Courts of the Country i.e. the Honourable Supreme Court of Pakistan and the Honourable Lahore High Court or Government/ Provincial Assembly of the Punjab. Therefore, because of the aforementioned sub-section (7) of Section 4 of the PHC Act, 2010, the Commission does not have the mandate to probe the instant complaint while remaining within the four corners of Law.

III. Hameed Latif Hospital, Lahore in its reply said that nevertheless, the matter is sub-judice, yet they consider it appropriate to reply to the DRAP and denied each and every averment, allegation, claim statement and demand made by the complainant.

a. It was said the Yasir Iqbal himself approached Dr. Zeba Aziz and her team in March, 2010 for his treatment of ITP. As per standard protocols of treatment of ITP, he was started with treatment of steroids as a first-line treatment for ITP, which did not show any results. Accordingly, he was started on Cyclosporine to increase "the platelet count" as per international acceptable recommendation. ITP did not respond positively to both of these drugs.

b. Professor Dr. Zeba Aziz accordingly recommended alternative treatments options such as Rituximab and/or Intravenous Immunoglobulin IVIG, however, Yasir Iqbal refused to receive this treatment on account of cost and expensiveness. Dr. Zeba Aziz also recommended "Splenectomy" a surgical procedure, that Mr. Yasir also refused to cite the lack of funds and requested to doctors of the hospital for financial assistance. Due to this continuous refusal of Mr. Yasir of the alternative standard expensive treatment available in Pakistan, the treatment of administering "Eltrombopag" for Chronic ITP was proposed by Dr. Zeba Aziz as free of cost under clinical trial. Therefore, Dr. Zeba proceeded with international protocols of treatment of ITP and only enrolled the subject in the study when Mr.

Yasir refused to went for other treatment options. He was informed about possible side effects in both verbal and written consent forms.

c. The treatment was started on 12th of August, 2010 with the standard dose of 50mg as per protocols and was he asked to visit on weekly basis for monitoring and progress. It was submitted by the hospital that Mr. Yasir was never given Eltrombopag 25mg which he falsely mentioned in his complaint showing his mala fide intentions. His platelets did not increase with 50mg of Eltrombopag, therefore, as per the protocol of the study, the dose was increased by 25 mg after two weeks to 75mg once daily on 6th September, 2010.

d. On 5th day of the new dose treatment, the subject informed the doctors on 11th September, 2010 that he had pain in his leg. The investigational drug was stopped immediately as Doppler ultrasound showed Deep Vein Thrombosis (DVT). He recovered from this acute condition in the next five days and all the cost was borne by the Sponsor i.e GSK for this treatment.

e. The twelve other subjects did suffer any side effects and their treatment was successful. He was provided with injection Clexane free of cost by the trial team for 6 months that resolved his DVT completely in February, 2011 as Doppler showed no evidence of any thrombus in his leg veins. He was advised to change his lifestyle like exercise and reduction of weight and control his blood pressure to minimize the reappearance of clots in his body. His last visit to Hospital was in July, 2013.

f. According to reviewed records he recovered completely from his SAE of "thromboembolic event", unfortunately, he developed DVT again after about 2 months, this time he was not on Eltrombopag for 6 months. The recurrent DVT was attributed by Doctors to his obesity, lazy lifestyle, smoking history and chronic ITP.

g. It was said that Yasir Iqbal went to the Court with the statement that the Eltrombopag was wrongly prescribed to him and has now changed his stance from wrong medicine to wrong dose prescription, although both of his stances are baseless. The matter is sub-judice in the court, yet out of respect for the DRAP, they have submitted the reply.

5. Meanwhile, the complainant approached the Lahore court and filed a writ petition under Article 199 of the Constitution of the Islamic Republic of Pakistan in case W.P. No. 45033 of 2021 titled "Yasir Iqbal Versus Government of Pakistan", where he prayed that Respondent No. 2 i.e. Drug Regulatory Authority of Pakistan may kindly be directed to make arrangements for the petitioner to get treatment in a foreign country and to bear all the expenses of the treatment of the

petitioner in foreign country expeditiously accordance with the law, to meet the end of justice. The Honourable court on 09th of July, 2021 ordered as under:

*"**Through instant petition, petition is seeking direction for decision on his pending application for making arrangements for petitioner to get treatment in foreign country and also compensate him for his treatment. Add that petitioner would be satisfied if a direction is issued to respondent No. 2 to decide the petitioner pending application strictly in accordance with law, after hearing petitioner and all concerned, through a well-reasoned speaking order, preferably within a period of fifteen days from the date of receipt of certified copy of this order."***

6. In compliance with the decision of Honourable court the case is submitted before CSC to decide the case of making arrangements for petitioner to get treatment in foreign country and also compensate him for his treatment in light of National and International Law.

SUBMITTED FOR CONSIDERATION OF CSC

Decision of 29th CSC meeting.

CSC after detailed deliberation decided to defer the matter and to call the applicant/ complainant, Dr. Zeba Aziz of M/s Hameed Latif Hospital, Lahore and representative of GSK, Pakistan for personal hearing to have their point of view on the issue in forthcoming CSC meeting to proceed further.

AGENDA ITEM III (The case was included in agenda with special permission of Chairman CSC)

Subject: **APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE FROM DEPARTMENT SOCIAL & PREVENTIVE PEDIATRICS, FJMU & SIR GANGA RAM HOSPITAL, LAHORE F. NO.15-19/2021 DD (PS).**

The case is an application from Dr. Rameeza Kaleem, CNIC No. 35202-2918812 M/s Fatima Jinnah Medical University/ Sir Ganga Ram Hospital Lahore wherein She has requested for Clinical Trial Site situated at Department Social & Preventive Pediatrics, FJMU & Sir Ganga Ram Hospital, Lahore. The application is on Form-I of the Bio-Study Rules 2017 with fee of Rs.100,000/- .

2. It is submitted that application evaluated according pre- requisites as mentioned in Form-I of the Bio-Study Rules 2017, and as following are observations:

S. No.	Required Documents / Information	Page No.	Remarks

1	Application on prescribed Form-I of The Bio-Study Rules 2017.	07	Attached. CNIC No. not correct.
2	Prescribed processing fee	03-04	Fee challan of Rs.100,000/- attached submitted vide slip No. 2013295.
3	Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).	05	Not attached. it is submitted that Sir Ganga Ram Hospital (SGRH) is a 908 bedded hospital in Lahore, Pakistan. Sir Ganga Ram Hospital is now an affiliated hospital to the Fatima Jinnah Medical University (FJMU). The department of Social & Preventive pediatrics was established in 1992 at SGRH. It is one of the Tew departments of its kind providing preventive, promotive, and rehabilitative services to children and their families. It provides not only indour and outdoor services hut also outreach services to families of the community attached to the department. It also provides specialized nutrition rehabilitative services to malnourished children. Departmental researches provide a valuable body of evidence-based information and informative ideas for decision-making. It is hereby requested to kindly register the Department of Social é Preventive Pediatrics, Gange Ram Hospital Lahore as a clinical trial site as it fulfills all the pre-requisites required by GCP guidelines.
4	Details of premises including layout plan of the site.	11	Lay out plan of Department of Social and Preventive Pediatrics FJMU & Sir Ganga Ram Hospital, Lahore is attached.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	08	Nutrition ward/ Stabilization Center is 6 bedded having baby electronics weighing scales, stadiometer, infantometer, nebulizer, glucometer, refrigerator. Nutrition Clinic having stadiometer, infantometer, weighing scale, vaccination center-ice linedrefrigrator-2 Outdoor Clinic; Stethoscope, torch, thermometer.
6	Names and qualifications of the above sections along with their staff.	12	Attached
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	10	Details of Allied Facilities including Emergency Services and ambulatory service. Sir Ganga Ram Hospital is now an affiliated hospital to the Fatima Jinnah Medical College. It is now being extended over another 22 kanals land and will provide an additional 400 beds. The name of this new hospital (extension) is Fatima Jinnah Hospital. Although it is an all female medical college, the faculty consists of highly qualified male as well as female teachers. The college has

			well-equipped laboratories, airconditioned dissection hall, lecture theatres with audio-visual aids for teaching purposes, pathology museum, clinical academic rooms, a well-equipped library and an auditorium for seminars and international conferences. A purpose-built accident and emergency department has been added. The hostel for students is within walking distance from the college. It consists of six blocks. Two new blocks are being built to accommodate more students. At the moment there are around one thousand students living in the hostel.
8	Undertaking on stamp paper	11	Attached.

3. Evaluation of the application is given above in tabulated form. If the competent authority is satisfied with provided documents, the case may be placed in the next forthcoming CSC meeting otherwise we may ask the firm if any further detail is required. Meanwhile firm may be asked to provided soft copy of the application so the same may be presented in CSC meeting.

5. The Chairman CSC asked that what tests are conducted during clinical trial and replied that reply of the question is related to the Director (PS) and Additional Director (PS) being Chairman CSC and Secretary CSC and having vote as expert for the Clinical Studies Committee (CSC).

6. As per experts usually during Phase 1 studies, researchers test a new drug in normal volunteers (healthy people). In most cases, 20 to 80 healthy volunteers or people with the disease/condition participate in Phase 1. Phase 1 studies are closely monitored and gather information about how a drug interacts with the human body. Researchers adjust dosing schemes based on animal data to find out how much of a drug the body can tolerate and what its acute side effects are. As a Phase 1 trial continues, researchers answer research questions related to how it works in the body, the side effects associated with increased dosage, and early information about how effective it is to determine how best to administer the drug to limit risks and maximize possible benefits. This is important to the design of Phase 2 studies.

7. In Phase 2 studies, researchers administer the drug to a group of patients with the disease or condition for which the drug is being developed. Typically involving a few hundred patients, these studies aren't large enough to show whether the drug will be beneficial. Instead, Phase 2 studies provide researchers with additional safety data. Researchers use these data to refine research questions, develop research methods, and design new Phase 3 research protocols.

8. Reference pre-para, it is submitted that testing required for Phase II, III & IV varies for different studies. As per my understanding Phase I & II mostly include Pharmacokinetics and pharmacodynamics studies. Phase I & II usually characterization of PK disposition of the parent drug and its metabolites in plasma, urine and serum is required. In phase III usually, clinical findings are required and rarely evaluation of drug-drug interaction potential with agents commonly prescribed for such patients, drug-drug interaction potential with agents having narrow safety window is required. Phase IV is mostly observational/ post-marketing studies.

9. The following panel was constituted by the chairman CSC

a. Prof. Dr. Javed Akram, VC, UHS, Lahore.
b. Dr. Farhana Badar, Biostatician, SKCH&RC, Lahore.
c. Dr. Abdur Rashid, Director Pharmacy Services Division, DRAP, Islamabad (coordinator).
d. Dr. Uzma Malik, Associate Professor, Mayo Hospital, Lahore.
e. Sheikh Abdul Rashid, FID, DRAP, Lahore.

10. The following panel conducted the inspection of proposed CTS.

a. Prof. Dr. Javed Akram, VC, UHS, Lahore.
b. Dr. Farhana Badar, Biostatician, SKCH&RC, Lahore.
c. Dr. Abdur Rashid, Director Pharmacy Services Division, DRAP, Islamabad (coordinator).
d. Prof. Dr. Nadeem Irfan Bukhari, University College of Pharmacy, Punjab university, Lahore.
e. Sheikh Abdul Rashid, FID, DRAP, Lahore.

11. The remarks of the panel were following;

"Based on inspection, technical people met, and documents reviewed and considering the findings of the inspection, the panel verifies vide DRAP, Islamabad letter No.F.15-19/2021 DD (PS) dated 07.05.2021, that the applicant possesses the facility for conducting the clinical trials as applied"

SUBMITTED FOR CONSIDERATION OF CSC

Decision of 29th CSC meeting.

The CSC after due deliberation, in the light of panel inspection report and the recommendation of panel of experts/ inspectors and as briefed by the chairman CSC/ panel member (coordinator) regarding the facility for conduct of trial at the site, unanimously decided to approve the Department of Social & Preventive Pediatrics situated at M/s Sir Ganga Ram Hospital, Lahore to act as clinical trial site (CTS) for phase III & IV clinical trials.