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

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The 28th Meeting of the CSC was held on 29th June 2021 through Zoom under the chairmanship of Dr. Abdur Rashid, Director Pharmacy Services Division / Chairman (CSC). At the 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.
03	Muhammad Adnan Faisal Saim	Deputy 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. Nadeem Irfan Bukhari.	Professor of Bio-Pharmaceutics & Pharmacokinetics, University of Punjab, Lahore.
04	Prof. Dr. Rizwana Chaudhri	HOD Gynecologist Holy Family Hospital, Rawalpindi Co-opted Member.
07	Dr. Ahson Siddiqui	MBBS, DTCP, MCPS, MPH (London) as Chest Specialist, Karachi. Co-opted Member.
08	Dr. Beena Ali	Head of Medical Affairs, M/s CCL Pharmaceuticals, Lahore. Co-opted Member.
09	Raeef Ahmed	Representative of Pharma Bureau Observer.

4. Meeting started with the recitation of holy verses of the Quran by Ahmad Din Ansari, Secretary CSC. Secretary, CSC welcomed all the members & informed the background of the meeting. Then, Secretary CSC left the remaining meeting. In absence of Mr. Ahmad Din Ansari (Secretary CSC), Mr. Muhammad Adnan Faisal Saim, Deputy Director (Pharmacy Services Division), presented the agenda as secretary in the light of provision given in Bio-Study Rules 2017.

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 are 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.

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.

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	CVs of the following are attached:

	investigator, analysts, and others along with CV)	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.

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.

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)	Attached

	approval of sites with complete composition of committee i.e. names and designation of members.	
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.

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	Each tablet contains Esomeprazole

	Product	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 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 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.

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.