MINUTES OF THE 19TH CSC MEETING HELD ON 12TH FEBRUARY 2021.

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The 19th Meeting of the CSC was held on 12th February 2021 through Zoom under the chairmanship of Dr. Abdur Rashid, Director Pharmacy Services Division / Chairman (CSC). At the Committee Room, 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	Abdul Sattar Sohrani.	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. Nadeem Irfan Bukhari.	Professor of Bio-Pharmaceutics & Pharmacokinetics, University of Punjab, Lahore.
03	Prof. Dr. Javed Akram.	Professor of Medicine, Physician, Vice Chancellor, University of Health Sciences, Lahore.
04	Dr. Farhana Badar.	Biostatistician & Epidemiologist, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore.

4. Meeting started with the recitation of holy verses of the Quran by Abdul Sattar Sohrani, Secretary CSC. Chairman, CSC welcomed all the members & appreciated active participation of members online through Zoom.

AGENDA ITEM - I: CONFIRMATION OF THE MINUTES OF THE 18TH CLINICAL STUDIES COMMITTEE MEETING.

1.1 Confirmation of Minutes of 18th CSC meeting, held on 26th December 2020. Since the occurrences of COVID pandemic majority of the meetings are being conducted online through Zoom.

1.2 It becomes difficult to sign the minutes by every member, which is a legal requirement. To overcome this legality, it is suggested that the minutes of the CSC meeting will be sent through email to every participating member for confirmation.

1.3 The members are requested to confirm the minutes electronically. Confirmatory email will be made part of the minutes to satisfy legal provision.

1.4. Submitted for consideration of CSC.

1.5 ***Decision of 19th CSC meeting:***

Minutes of the 18th meeting of CSC were confirmed by the committee. The committee also approved the procedure for confirmation of minutes of the meeting through email, correspondence emails will be the part of the minutes.

AGENDA ITEM - II: COMPLIANCE REPORT IN PURSUANCE OF SUPREME COURT'S ORDER DATED 15-01-2019 IN C.P. NO.73 OF 2018 (REGARDING MECHANISM TO COMMERCIALIZE RESEARCH BREAKTHROUGH).

2.1. Honorable Supreme Court of Pakistan, while disposing the case under Constitution Petition No.73 of 2018 regarding the "Mechanism to Commercialize Research Breakthrough" order on 15th January 2019, Honourable Supreme Court of Pakistan approved the recommendation of Committee constituted by the then Honourable Chief Justice of Pakistan and made them part of Order for implementation.

2.2. The following recommendation of committee was accepted in orders passed by Honourable Supreme Court on 15th of January, 2018, while deciding a case in constitution petition No.73 of 2018 regarding mechanism to commercial research breakthrough in Pakistan:

I. *"Clause 7 regarding the constitution of Clinical Studies Committee under the Rule.13 of the Bio-Study Rule, 2017, should be amended to include the following as well: -*
   a. *Vice Chancellor, University of Health Sciences or their nominee.*
   b. *Vice Chancellor, University of the Punjab or their nominee.*
   c. *Head of CEMB/CAMB Lahore.*

II. *Clause 8 to be amended as follows: -*
   a. *Stem Cells as a separate category of therapeutic goods should be included in the rules.*
   b. *Clinical Studies Committee to be notified by DRAP within one week.*
   c. *Stem Cells/Cells Research and Laboratory Guidelines should be developed by the CSC Committee within a period of three months.*
   d. *The CSC to co-opt Prof. Dr. Sheikh Riaz-ud-Din as it Member to avail benefit of his expertise immediately after notification of CSC.*

2.3. Clinical Studies Committee deliberated the matter in its 1st meeting, held on 7th February, 2019 and refer the matter to its sub-committee, which finalize the draft stem cells guidelines.

2.4. Draft *National Biosafety Regulations for Research Development & Production of Human Stem Cells* were developed & submitted by Dr. Asma Ali Khan, Assistant Professor, CEMB. These guidelines were also discussed in the meeting at Law & Justice Commission of Pakistan, held on 6th July 2020.

2.5. Draft guidelines were uploaded on official website of DRAP after approval from CEO-DRAP, on 14th December 2020 for comments from stakeholders & the general public within 15 days. Stipulated time for comments completed on 31st December 2020.

2.6. Draft guidelines shared with CSC members through email on 13th January 2021 for deliberations & comments. Draft guidelines are placed before CSC & if approved then forwarded to the Authority for final approval & notification. **(Annex-I)**

2.7. Submitted for consideration of CSC.

2.8 *Decision of 19th CSC meeting:*

CSC unanimously approved the guidelines titled "National Biosafety Regulations for Research Development & Production of Human Stem Cells" for onward submission to the Authority for further perusal.

AGENDA ITEM - III: TENURE OF CO-OPTED MEMBERS IN CLINICAL STUDIES COMMITTEE.

3.1. Bio-Study Rules, 2017 were notified with the approval of Federal Government in exercise of powers conferred by section 23 of drug regulatory Authority of Pakistan Act 2012 vide S.R.O.697 (l)12018.

3.2. Hon'able Supreme Court of Pakistan passed orders on 15th January, 2019, while deciding a case in constitutional petition No.73/2018 regarding mechanism to commercialize research breakthrough in Pakistan

I. "Clause 7 regarding the constitution of Clinical Studies Committee under the Rule 13 of the Bio-Study Rule, 2017, should be amended to include following as well:

i. Vice Chancellor, University of Health Sciences or their nominee.
ii. Vice Chancellor, University of the Punjab or their nominee.
iii. Head of CEMB/CAMB Lahore.

II. In 66th meeting of Authority held on 19th June 2019, Division of Pharmacy Services was directed to immediately process the amendments under section 23 of the DRAP Act 2012, for approval from the Federal Government.

3.3. The matter placed before CSC in its 6th meeting, CSC decided as follows:

Decision of 6th CSC meeting (held on20th January 2020):

All proposed names already approved by the CEO-DRAP are approved by CSC as Co-Opted members.

3.4. Accordingly, file was moved to M/o N.H.S. R&C after approval from CEO-DRAP by Deputy Director (Legal Affairs) for vetting of the Law and Justice Division. After discussion of the Secretary with SAPM, following panel of experts was referred to CEO, DRAP for placing before the DRAP Authority for consideration, recommendation and thereafter to resubmit the draft notification to M/o Law & Justice for vetting:-

i. Dr. Naseem Salahuddin, Director Infectious Diseases Indus Hospital, Karachi, Sindh;
ii. Dr. Aamir Jaffary, Sindh Institute of Urology & Transplantation (SIUT), Karachi, Sindh

iii. Dr. Rizwana Chaudhry, HOD Gynecologist Holy Family Hospital, Rawalpindi, The Punjab; and

iv. Prof: Dr. Mushtaq Ahmed, Professor of Cardiology, Bacha Khan Medical College Mardan, Khyber Pakhtunkhwa.

3.5. The CSC with prior approval of CEO, DRAP coopted above panel of experts referred by M/o N.H.S. R&C. Later on, same was discussed in 75th meeting of the Authority held on 30th January 2020:

The Authority noted that:

1, Under the Bio-Study Rules, 2017 there is no provision of nomination of any member by name, however under rule 13 (1)(j) CSC has the power to nominate any person as a coopted member.

2. Previously, the notification of amendments in the Bio-Study Rules, 2017 was approved in the 66th meeting of the Authority in light of the directions of Hon'able Supreme Court in CP No. 73 of 2018.

Therefore, the Authority decided:

1. *To recommend the Clinical Studies Committee to include following as co-opted members for a period of 6 months only under Rule 13(1)(j) of the Bio-Study Rules, 2017 in light of proposal of IUI/o NHS, R & C.*

   i. Dr. Salahuddin, Director Infectious Diseases Indus Hospital, Karachi,
   ii. Dr. Aamir Jaffary, Sindh Institute of Urology & Transplantation (SIUT), Karachi, Sindh;
   iii. Dr. Rizwana Chaudhry, Gynecologist Holy Family Hospital, Rawalpindi, The Punjab;
   iv. Prof: Dr. Mushtaq Ahmed, Professor of Cardiology, Bacha Khan Medical College Mardan, Khyber Pakhtunkhwa.

2. *To request Wo NHS, R & C to process the notification of amendments in the Bio-Study Rules, 2017, as approved by Authority in its 66th meeting to avoid the delay and non-compliance of Court orders.*

3.6. **Decision of 11th CSC meeting (held on 20th May 2020):**

The CSC after discussion decided that at the moment Co-opted members should not be changed as there is a pandemic.

Even after completion of the 6 months CSC may again Co-opt for further six month to utilize their experties.

3.7 It is submitted that as decided by CSC in its 11th meeting the tenure of the co-opted members was completed on 20th January 2021, nominated members along with additional two members as suggested by Chairman CSC mentioned below for nomination as co-opted members of the CSC:

i. Dr. Salahuddin, Director Infectious Diseases Indus Hospital, Karachi,
ii. Dr. Aamir Jaffary, Sindh Institute of Urology & Transplantation (SIUT), Karachi, Sindh;
iii. Dr. Rizwana Chaudhry, Gynecologist Holy Family Hospital, Rawalpindi, The Punjab;
iv. Prof: Dr. Mushtaq Ahmed, Professor of Cardiology, Bacha Khan Medical College Mardan, Khyber Pakhtunkhwa.
v. Dr. Ahsan Siddiqui, MBBS, DTCP, MCPS, MPH (London) as Chest Specialist, Karachi.
vi. Dr. Beena Ali, Regulatory Affairs & AEFI, Lahore.

3.8 Submitted for consideration of CSC.

3.9 *Decision of 19th CSC meeting:*

CSC unanimously co-opted following experts for a period of one year:

i. *Dr. Naseem Salahuddin, Director Infectious Diseases Indus Hospital, Karachi,*
ii. *Dr. Aamir Jaffary, Sindh Institute of Urology & Transplantation (SIUT), Karachi, Sindh;*
iii. *Dr. Rizwana Chaudhry, Gynecologist Holy Family Hospital, Rawalpindi, The Punjab;*
iv. *Prof: Dr. Mushtaq Ahmed, Professor of Cardiology, Bacha Khan Medical College Mardan, Khyber Pakhtunkhwa.*
v. *Dr. Ahsan Siddiqui, MBBS, DTCP, MCPS, MPH (London) as Chest Specialist, Karachi.*
vi. *Dr. Beena Ali, Regulatory Affairs & AEFI, Lahore.*

AGENDA ITEM - IV:

REGISTRATION OF PHASE-I & PHASE-II

4.1 Phase-I & Phase-II clinical studies required pharmacokinetic studies in addition to clinical parameters. The licensed clinical trial site/facilities are not equipped with basic instruments/facilities to conduct bioanalytical analysis.

4.2 It is therefore submitted that, the applicants desirous of phase-I/II clinical trial should also submit application for licence to conduct bioanalytical analysis.

4.3 It is disparity that generic products are being registered for bioequivalence on the facilities having clinical / bioanalytical facilities both, whereas investigational products are being registered without supportive bioanalytical facilities.

4.4 Submitted for consideration of CSC.

4.5 *Decision of 19th CSC meeting:*

CSC after detailed deliberation deferred the agenda at the moment & constituted a sub-committee comprising of following experts:

i. *Prof. Dr. Javed Akram, V.C. U.H.S. Lahore.*
ii. *Dr. Abdur Rashid, Chairman CSC/Director Pharmacy Services-DRAP.*
iii. *Brig. (Retd) Muzammil Hassan Najmi*
iv. *Prof. Nadeem Irfan, Professor of Bio-Pharmaceutics & Pharmacokinetics, University of Punjab, Lahore.*
v. *Farhana Badar, Biostatistician & Epidemiologist, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore.*

2. One day training at U.H.S. Lahore will be organized in the month of March 2021 for the sub-committee. After the training the sub-committee will formulate a proforma for inspection.

3. This sub-somite will conduct inspections of BA/BE Studies Center, the quorum of the panel will be four members.

AGENDA ITEM - V:

DELIBRATION ON "RANDOMIZED, DOUBLE BLINDED, PARALLEL, PLACEBO CONTROLLED, PHASE-I CLINICAL TRIAL TO EVALUATE THE SAFETY & IMMUNOGENICITY OF INACTIVATED SARS-COV-2 VACCINE IN HEALTHY POPULATION AGED 18 & ABOVE"

5.1. The subject matter was discussed in the 18th CSC meeting held on 26th December 2020 for deliberation on Sinopharm vaccine status & the CSC decided as follows:

Decision of 18th CSC meeting:

The CSC after detailed deliberation and owing to situation of COVID-19 pandemic in Pakistan in order to protect the patients, decided as follows:

The CSC decided that PI of the Phase-I clinical trial of Sinopharm Vaccine may be asked for withdrawal of the trial voluntarily as after completion of the Phase-III clinical trial and use on large scale in Chinese Armed Forces and grant of emergency use authorization in U.A.E. there is no need to continue Phase-I clinical trial of the same vaccine in Pakistan.

5.2. Accordingly, CSC decision was communicated to Principal Investigator of subject trial for compliance. Principal Investigator of subject trial submitted reply as follows:

Kindly refer to your letter of 29th December 2020 on the above subject. As mentioned during the NCOC meeting held on 23rd December 2020 as well, for us need of Pakistani people comes first. The objective of conducting this clinical trial was also to build national capacity in Vaccine development. In the light of your letter, we will approach Sinopharm to see what can be done to facilitate prompt a import of Vaccine for the healthcare workers.

5.3. Submitted for consideration of CSC.

5.6 Chairman CSC informed the committee regarding background & informed regarding completion of the recruitment & the trial.

Decision of 19th CSC meeting:

CSC appreciated the efforts of DRAP & ICCBS for the phase-I trial & vaccine availability in the Pakistan.

AGENDA ITEM - VI:

CONVALESCENT PLASMA TREATMENT IN COVID-19 PATIENTS: NON-RANDOMISED OPEN LABEL CLINICAL TRIAL AT A TERTIARY CARE CENTER IN PAKISTAN. F.No.03-28/2020 DD (PS).

6.1. Application from Dr. Natasha Ali (Co-Principal Investigators), Associate Professor Hematology, Department of Pathology & Laboratory Medicine/Oncology, Aga Khan University, dated 22nd April 2020, forwarded by Dr. Masud Ur Rehman, Secretary CSC / Additional Director, Division Pharmacy Services through email, wherein request has been made for registration &

approval of subject clinical study, which will be carried out at Section of Hematology & Transfusion Medicine, Department of Pathology and Laboratory Medicine, Aga Khan University Hospital, Karachi. Application is not on prescribed Form-I & II of the Bio-Study Rules 2017 and prescribed fee for approval & registration of Clinical Trial Site & Clinical Studies is not provided.

6.2. The study carried out under the supervision of Dr. Muhammad Hasan (PI).

6.3. The primary objective of the study "To investigate the efficacy and safety of transfusing convalescent plasma collected from patients who have recovered from COVID-19 disease to patients admitted at Aga Khan University Hospital for the management of active COVID-19 disease".

6.4. Due to COVID-19 pandemic application was placed in the 10th CSC meeting, held on 28th April 2020. CSC approved the study subject to fulfilment of all prerequisites.

6.5. Shortcomings communicated on 27th July, 2020, 26th August 2020, 16th October 2020 & a final reminder issued on 27th October 2020. Applicant also contacted telephonically and informed regarding shortcoming, but response is yet awaited and following shortcomings still need to be fulfilled:

i) Prescribed processing fee of Rs.200000/- as per S.R.O.1047(I) /2019, dated 12th September 2019 is not deposited yet.
ii) Investigator Brochure is not provided.
iii) Provided study protocol is not as per ICH-GCP Guidelines.
iv) Phase of trial is not described.
v) Summary of Protocol & Investigator's brochure is not provided.
vi) Sample of label for the investigational product / drug is not attached.

6.6. Application placed before CSC in its 17th meeting & CSC decided as follows:

Decision of 17th CSC meeting:

CSC after detailed deliberation decided to defer the study entitled as Convalescent Plasma Treatment in Covid-19 Patients: Non-Randomised Open Label Clinical Trial at A Tertiary Care Center In Pakistan till report is submitted by Dr. Tahir Shamsi of his approved study of convalescent plasma and for fulfillment of following shortcomings

i) Prescribed processing fee of Rs.200000/- as per S.R.O.1047(I) /2019, dated 12th September 2019 is not deposited yet.
ii) Investigator Brochure is not provided.
iii) Provided study protocol is not as per ICH-GCP Guidelines.
iv) Phase of trial is not described.
v) Summary of Protocol & Investigator's brochure is not provided.
vi) Sample of label for the investigational product / drug is not attached.

6.7 Submitted for consideration of CSC.

6.8. ***Decision of 19th CSC meeting:***

CSC after detailed deliberation rejected the application.

AGENDA ITEM - VII:

REQUEST FOR APPROVAL AND REGISTRATION OF BIOEQUIVALENCE STUDY OF AZITMA® (AZITHROMYCIN DIHYDRATE) 500MG TABLET OF M/S SAMI PHARMACEUTICALS (PVT) LTD WITH ZITHROMAX® (AZITHROMYCIN DIHYDRATE) 500MG TABLET OF M/S PFIZER PAKISTAN. F. No. 14-06/2020 DD (PS).

7.1. Application submitted by Dr. Raza Shah, General Manager, Center for Bioequivalence Study and Clinical Research (CBSCR), University of Karachi, for approval of subject Bioequivalence Study, under the Bio-study rules, 2017.

7.2. The summary of the proposed study is as under;

i. **Study title:** A Single Center, Open Label, Randomized, Single Dose, two way Cross-over Study to compare the bioavailability of Azitma® (Azithromycin dihydrate) 500mg tablet with Zithromax® (Azithromycin dihydrate) 500mg tablet, in healthy Pakistani subjects.
ii. **Investigational Product:** Azitma® (Azithromycin dihydrate) 500mg tablet of M/s Sami Pharmaceuticals (Pvt) Ltd., F-95, S.I.T.E. Karachi.
iii. **Reference Product:** Zithromax® (Azithromycin dihydrate) 500mg tablet of M/s Pfizer Pakistan.
iv. **Sponsor:** M/s Sami Pharmaceuticals (Pvt) Ltd., F-95, S.I.T.E. Karachi.
v. **CRO and BA/BE Study Site:** Center for Bioequivalence Studies and Clinical Research (CBSCR), ICCBS, University of Karachi, Karachi.
vi. **Principal Investigator:** Dr. Muhammad Raza Shah
vii. **Co-Principal Investigator:** Dr. Naghma Hashmi
viii. **Funding Source**: The sponsor
ix. **Cost of the Project**: Tentative cost of study is Rs.38,00,000.
x. **Subjects enrolment**: 38 Subjects will be enrolled in the study.

7.3. 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.300000/- deposited vide challan number 2050042, dated 09th December 2020.
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	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so its nor applicable.
6	Pharmacodynamics and Pharmacokinetics of Investigational Product	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so its nor applicable.
7	Purpose of study defining the indication along with the anticipated cost of the project and sources of fund	A Single Center, Open Label, Randomized, Single Dose, two way Cross-over Study to compare the bioavailability of Azitma® (Azithromycin dihydrate) 500mg tablet with Zithromax® (Azithromycin dihydrate) 500mg tablet, in healthy Pakistani subjects. Tentative cost of study is Rs.38,00,000 & will be provided by M/s Sami Pharmaceuticals (Pvt) Ltd., Karachi.
8	Proposed center for study	Center for Bioequivalence Studies & Clinical Research, ICCBS, University of Karachi, Karachi. DRAP approved BA/BE Studies Center.
9	Investigational design and study plan	A single center, open label, randomized, single dose, two period, two way cross-over study. Subjects will receive one single dose per treatment period, separated by a washout period of fourteen (14) days. Blood samples will be taken up to 120 hours post-dose.
10	Pre-clinical or clinical data or safety studies	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so it's not applicable.
11	Final protocol	Attached.
12	Detail of the investigator (Principal investigator, analysts and others along with CV)	CVs of following are attached: Prof. Dr. Raza Shah (PI) Dr. Naghma Hashmi (Co-PI) Dr. Naveed Yunus (Co-PI)
13	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Attached. IRB approval, Ref.# ICCBS/CBSCR/IEC/LET-033/2020, dated 09th November 2020, issued by Independent Ethics Committee of the ICCBS, University of Karachi is attached.
14	Approval of National Bio-ethics Committee (NBC)	NBC-PHRC approval certificate Ref:No.4-87/NBC-557/20/ 816, dated 15th December 2020

		is attached.
15	Site approval by the Ethics committee	Center for Bioequivalence Studies & Clinical Research, ICCBS, University of Karachi, Karachi is approved as a BA/BE Studies Center from DRAP.
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 country of origin (GMP certificate along with CoPP or Free sale certificate)	N/A
21	Copy of registration letter if registered in Pakistan	Attached only for Azitma® (Azithromycin dihydrate) 500mg tablet of M/s Sami Pharmaceuticals (Pvt) Ltd., Karachi. Not provided for Zithromax® (Azithromycin dihydrate) 500mg tablet of M/s Pfizer Pakistan.
22	Proposed label of investigational product	Commercial label of reference product is attached & claimed that as both investigational drug & reference drugs are registered in Pakistan so it is not applicable.
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)	A. FOR REFERENCE PRODUCT i. Sample Size=38 ii. Investigational drug for clinical phase= 38 Tablets iii. For Retention/Archiving= 5 times of study drug= 38×5 = 190 Tablets. iv. Total no. of Tablets = For clinical phase +Retention /Archiving 38+190 = 228 Tablets. B. FOR TEST PRODUCT i. Sample Size=38 ii. Investigational drug for clinical phase= 38 Tablets iii. For Retention/Archiving= 5 times of study drug= 38×5 = 190 Tablets. iv. Total no. of Tablets = For clinical phase +Retention /Archiving 38+190 = 228 Tablets.
24	Undertaking on affidavit.	Attached.

7.4. For technical evaluation, technical documents (i.e. Study Protocol & investigator's brochure) forwarded to experts through email on 13th January 2021, for review & evaluation under sub-rule 4 of rule 7 of the Bio-Study Rules 2017.

7.7. Submitted for consideration of CSC.

7.8. Prof. Dr. Raza Shah joined the meeting & briefed the CSC regarding their application.

7.9 *Decision of 19th CSC meeting:*

The CSC after detailed deliberation decided to approve the BA/BE Study titled "Bioequivalence Study of Azitma® (Azithromycin Dihydrate) 500mg Tablet of M/s Sami Pharmaceuticals (Pvt) Ltd with Zithromax® (Azithromycin Dihydrate) 500mg Tablet of M/s Pfizer". However, applicant will provide details of reference product (i.e. CoPP & GMP certificate) & other evident documents for import of reference product, as per the Bio-Study Rules 2017 and reference standard may be any stringent regulatory authority / innovator product.

AGENDA ITEM - VIII:

REQUEST FOR APPROVAL AND REGISTRATION OF BIOEQUIVALENCE STUDY OF DELANZO™DR 60MG (DEXLANSOPRAOLE) CAPSULE OF M/S SAMI PHARMACEUTICALS (PVT) LTD WITH DEXILANT® 60MG (DEXLANSOPRAOLE) CAPSULE. F. No. 14-02/2020 DD (PS)

8.1. Application submitted by Dr. Raza Shah, General Manager, Center for Bioequivalence Study and Clinical Research (CBSCR), University of Karachi, for approval of subject Bioequivalence Study, under the Bio-Study Rules, 2017.

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

i. **Study title:** A Single Center, Open Label, Randomized, Single Dose, two way Cross-over Study to compare the rate & extent of absorption of Delanzo™DR 60mg (Dexlansopraole) Capsule of M/s Sami Pharmaceuticals (Pvt) Ltd with Dexilant® 60mg (Dexlansopraole) Capsule, in healthy Pakistani subjects.
ii. **Investigational Product:** Delanzo™DR 60mg (Dexlansopraole) Capsule of M/s Sami Pharmaceuticals (Pvt) Ltd., F-95, S.I.T.E. Karachi.
iii. **Reference Product:** Dexilant® 60mg (Dexlansopraole) Capsule.
iv. **Sponsor:** M/s Sami Pharmaceuticals (Pvt) Ltd., F-95, S.I.T.E. Karachi.
v. **CRO and BA/BE Study Site:** Center for Bioequivalence Studies and Clinical Research (CBSCR), ICCBS, University of Karachi, Karachi.
vi. **Principal Investigator:** Dr. Muhammad Raza Shah
vii. **Co-Principal Investigator:** Dr. Naghma Hashmi
viii. **Funding Source**: The sponsor
ix. **Cost of the Project**: Tentative cost of study is Rs.60,00,000.
x. **Subjects enrolment**: 60 Subjects will be enrolled in the study.

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

S.No.	Documents	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 2050045, dated 09th December 2020.
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	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so it is not applicable.
6	Pharmacodynamics and Pharmacokinetics of Investigational Product	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so it is not applicable.
7	Purpose of study defining the indication along with the anticipated cost of the project and sources of fund	A Single Center, Open Label, Randomized, Single Dose, two way Cross-over Study **to compare the rate & extent of absorption** of Delanzo™DR 60mg (Dexlansopraole) Capsule of M/s Sami Pharmaceuticals (Pvt) Ltd with Dexilant® 60mg (Dexlansopraole) Capsule, in healthy Pakistani subjects. The tentative cost of the study is Rs.60,00,000 & will be provided by M/s Sami Pharmaceuticals (Pvt) Ltd., Karachi.
8	Proposed center for the study	Center for Bioequivalence Studies & Clinical Research, ICCBS, University of Karachi, Karachi. DRAP approved BA/BE Studies Center.
9	Investigational design and study plan	A single-center, open-label, randomized, single-dose, two-period, two-way cross-over study. Subjects will receive one single dose per treatment period, separated by a washout period of seven (07) days. Blood samples will be taken up to 24 hours post-dose.
10	Pre-clinical or clinical data or safety studies	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so it's not applicable.
11	Final protocol	Attached.
12	Detail of the investigator	CVs of the following are attached:

	(Principal investigator, analysts, and others along with CV)	Prof. Dr. Raza Shah (PI) Dr. Naghma Hashmi (Co-PI) Dr. Naveed Yunus (Co-PI)
13	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	IRB approval, Ref.# ICCBS/CBSCR/IEC/LET-031/2020, dated 09th November 2020, issued by Independent Ethics Committee of the ICCBS, University of Karachi is attached.
14	Approval of National Bio-ethics Committee (NBC)	NBC-PHRC approval certificate Ref:No.4-87/NBC-550/20/ 815, dated 15th December 2020 is attached.
15	Site approval by the Ethics committee	Center for Bioequivalence Studies & Clinical Research, ICCBS, University of Karachi, Karachi is approved as a BA/BE Studies Center from DRAP.
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)	N/A
21	Copy of registration letter if registered in Pakistan	Copy of registration letter for Delanzo™DR 60mg (Dexlansopraole) Capsule of M/s Sami Pharmaceuticals (Pvt) Ltd, is attached. Whereas registration letter for Dexilant® 60mg (Dexlansopraole) Capsule is not provided.
22	Proposed label of investigational product	Commercial label of reference product is attached & claimed that as both investigational drug & reference drugs are registered in Pakistan so it is not applicable.
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)	C. FOR REFERENCE PRODUCT v. Sample Size=60 vi. Investigational drug for clinical phase= 60 Capsule. ii. For Retention/Archiving= 5 times of study drug= 60×5 = 300 viii. Total no. of capsules = For clinical phase +Retention /Archiving 60+300 = 360 Capsules D. FOR TEST PRODUCT i. Sample Size=60 ii. Investigational drug for clinical phase= 60 Capsule. iii. For Retention/Archiving= 5 times of study drug= 60×5 = 300 iv. Total no. of capsules = For clinical phase +Retention /Archiving 60+300 = 360 Capsules

24	Undertaking on affidavit.	Attached.

8.4. For technical evaluation, technical documents (i.e. Study Protocol & investigator's brochure) forwarded to experts through email on 13th January 2021, for review & evaluation under sub-rule 4 of rule 7 of the Bio-Study Rules 2017.

8.5. Submitted for consideration of CSC.

8.6. Prof. Dr. Raza Shah joined the meeting & briefed the CSC regarding their application.

8.7. *Decision of 19th CSC meeting:*

The CSC after detailed deliberation decided to approve the BA/BE Study titled "Bioequivalence Study of Delanzo™ DR 60mg (Dexlansopraole) Capsule of M/s Sami Pharmaceuticals (Pvt) Ltd with Dexilant® 60mg (Dexlansopraole) Capsule". However, applicant will provide details of reference product (i.e. CoPP & GMP certificate) & other evident documents for import of reference product, as per the Bio-Study Rules 2017 and reference standard may be any stringent regulatory authority / innovator product.

AGENDA ITEM - IX:

REQUEST FOR APPROVAL AND REGISTRATION OF BIOEQUIVALENCE STUDY OF MOFEST® (MOXIFLOXACIN) 400MG TABLET OF M/S SAMI PHARMACEUTICALS (PVT) LTD WITH AVELOX® (MOXIFLOXACIN) 500MG TABLET OF M/S BAYER PAKISTAN. F. No. 14-04/2020 DD (PS).

9.1. Application submitted by Dr. Raza Shah, General Manager, Center for Bioequivalence Study and Clinical Research (CBSCR), University of Karachi, for approval of subject Bioequivalence Study, under the Bio-study rules, 2017.

9.2. The summary of the proposed study is as under;

i. **Study title:** A Single-Center, Open-Label, Randomized, Single-Dose, two-way Cross-over Study to compare the rate & extent of absorption of Mofest® (Moxifloxacin) 400mg Tablet of M/s Sami Pharmaceuticals (Pvt) Ltd with Avelox® (Moxifloxacin) 500mg Tablet of M/s Bayer Pakistan, in healthy Pakistani subjects.
ii. **Investigational Product:** Mofest® (Moxifloxacin) 400mg Tablet of M/s Sami Pharmaceuticals (Pvt) Ltd., F-95, S.I.T.E. Karachi.
iii. **Reference Product:** Avelox® (Moxifloxacin) 500mg Tablet of M/s Bayer Pakistan.
iv. **Sponsor:** M/s Sami Pharmaceuticals (Pvt) Ltd., F-95, S.I.T.E. Karachi.
v. **CRO and BA/BE Study Site:** Center for Bioequivalence Studies and Clinical Research (CBSCR), ICCBS, University of Karachi, Karachi.
vi. **Principal Investigator:** Dr. Muhammad Raza Shah
vii. **Co-Principal Investigator:** Dr. Naghma Hashmi
viii. **Funding Source**: The sponsor
ix. **Cost of the Project**: Tentative cost of the study is Rs.38,00,000.

x. **Subjects enrolment**: 38 Subjects will be enrolled in the study.

9.3. 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 2050041, dated 09th December 2020.
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	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so it is not applicable.
6	Pharmacodynamics and Pharmacokinetics of Investigational Product	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so it is not applicable.
7	Purpose of study defining the indication along with the anticipated cost of the project and sources of fund	A Single-Center, Open-Label, Randomized, Single-Dose, two-way Cross-over Study to compare the rate & extent of absorption of Mofest® (Moxifloxacin) 400mg Tablet of M/s Sami Pharmaceuticals (Pvt) Ltd with Avelox® (Moxifloxacin) 500mg Tablet of M/s Bayer Pakistan, in healthy Pakistani subjects. The tentative cost of the study is Rs.38,00,000 & will be provided by M/s Sami Pharmaceuticals (Pvt) Ltd., Karachi.
8	Proposed center for the study	Center for Bioequivalence Studies & Clinical Research, ICCBS, University of Karachi, Karachi. DRAP approved BA/BE Studies Center.
9	Investigational design and study plan	A single-center, open-label, randomized, single-dose, two-period, two-way cross-over study. Subjects will receive one single dose per treatment period, separated by a washout period of seven (07) days. Blood samples will be taken up to 72 hours post-dose.

10	Pre-clinical or clinical data or safety studies	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so it's not applicable.
11	Final protocol	Attached.
12	Detail of the investigator (Principal investigator, analysts, and others along with CV)	CVs of the following are attached: Prof. Dr. Raza Shah (PI) Dr. Naghma Hashmi (Co-PI) Dr. Naveed Yunus (Co-PI)
13	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	IRB approval, Ref.# ICCBS/CBSCR/IEC/LET-034/2020, dated 09th November 2020, issued by Independent Ethics Committee of the ICCBS, University of Karachi is attached.
14	Approval of National Bio-ethics Committee (NBC)	NBC-PHRC approval certificate Ref:No.4-87/NBC-556/20/875, dated 16th December 2020 is attached.
15	Site approval by the Ethics committee	Center for Bioequivalence Studies & Clinical Research, ICCBS, University of Karachi, Karachi is approved as a BA/BE Studies Center from DRAP.
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)	N/A
21	Copy of registration letter if registered in Pakistan	Copy of registration letter for Mofest® (Moxifloxacin) 400mg Tablet of M/s Sami Pharmaceuticals (Pvt) Ltd, Karachi is attached whereas, registration letter of Avelox® (Moxifloxacin) 500mg Tablet of M/s Bayer Pakistan is not provided.
22	The proposed label of investigational product	Commercial label of reference product is attached & claimed that as both investigational drug & reference drugs are registered in Pakistan so it is not applicable.
23	Quantity of investigational product to be used in the study along with justification (Note:	E. FOR REFERENCE PRODUCT ix. Sample Size=38 x. Investigational drug for clinical phase= 38 Tablets xi. For Retention/Archiving= 5 times of study drug= 38×5 =

	All the quantities of the each of investigational product should be procured from one single source)	190 xii. Total no. of tablets = For clinical phase +Retention /Archiving 38+190 = 228 Tablets. F. FOR TEST PRODUCT i. Sample Size=38 ii. Investigational drug for clinical phase= 38 Tablets iii. For Retention/Archiving= 5 times of study drug= 38×5 = 190 iv. Total no. of tablets = For clinical phase +Retention /Archiving 38+190 = 228 Tablets. i.
24	Undertaking on affidavit	Attached.

9.4. For technical evaluation, technical documents (i.e. Study Protocol & investigator's brochure etc.) forwarded to experts through email on 13th January 2021, for review & evaluation under sub-rule 4 of rule 7 of the Bio-Study Rules 2017.

9.5. Submitted for consideration of CSC.

9.6. Prof. Dr. Raza Shah joined the meeting & briefed the CSC regarding their application.

9.7. *Decision of 19th CSC meeting:*

*The CSC after detailed deliberation decided to approve the BA/BE Study titled "*Bioequivalence Study of Mofest® (Moxifloxacin) 400mg Tablet of M/s Sami Pharmaceuticals (Pvt) Ltd with Avelox® (Moxifloxacin) 500mg Tablet Of M/s Bayer*". However, applicant will provide details of reference product (i.e. CoPP & GMP certificate) & other evident documents for import of reference product, as per the Bio-Study Rules 2017 and reference standard may be any stringent regulatory authority / innovator product.*

AGENDA ITEM - X:

REQUEST FOR APPROVAL AND REGISTRATION OF BIOEQUIVALENCE STUDY OF OCVIR™ 400/100MG (SOFOSBUVIR/VELPATASVIR) TABLET OF M/S SAMI PHARMACEUTICALS (PVT) LTD WITH EPCLUSA® 400/100MG (SOFOSBUVIR/VELPATASVIR) TABLET OF M/S GILEAD SCIENCES LTD. F. No. 14-03/2020 DD (PS)

10.1. Application from Dr. Raza Shah, General Manager, Center for Bioequivalence Study and Clinical Research (CBSCR), University of Karachi, for approval of subject Bioequivalence Study, under the Bio-study rules, 2017.

10.2. The summary of the proposed study is as under;

i. **Study title:** A Single Center, Open Label, Randomized, Single Dose, two way Cross-over Study to compare the bioavailability of Ocvir™ 400/100mg (Sofosbuvir/Velpatasvir) tablet of M/s Sami Pharmaceuticals (Pvt) Ltd with Epclusa® 400/100mg (Sofosbuvir/Velpatasvir) tablet of M/s Gilead Sciences Ltd, in healthy Pakistani subjects.

ii. **Investigational Product:** Ocvir™ 400/100mg (Sofosbuvir/Velpatasvir) tablet of M/s Sami Pharmaceuticals (Pvt) Ltd., F-95, S.I.T.E. Karachi.
iii. **Reference Product:** Epclusa® 400/100mg (Sofosbuvir/Velpatasvir) tablet of M/s Gilead Sciences Ltd.
iv. **Sponsor:** M/s Sami Pharmaceuticals (Pvt) Ltd., F-95, S.I.T.E. Karachi.
v. **CRO and BA/BE Study Site:** Center for Bioequivalence Studies and Clinical Research (CBSCR), ICCBS, University of Karachi, Karachi.
vi. **Principal Investigator:** Dr. Muhammad Raza Shah
vii. **Co-Principal Investigator:** Dr. Naghma Hashmi
viii. **Funding Source**: The sponsor
ix. **Cost of the Project**: Tentative cost of study is Rs.64,00,000.
x. **Subjects enrolment**: 64 Subjects will be enrolled in the study.

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

S.No.	Documents	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 2050039, dated 09th December 2020.
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	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so it is not applicable.
7	Purpose of study defining the indication along with the anticipated cost of the project and sources of fund	A Single Center, Open Label, Randomized, Single Dose, two way Cross-over Study to compare the bioavailability of Ocvir™ 400/100mg (Sofosbuvir/Velpatasvir) tablet of M/s Sami Pharmaceuticals (Pvt) Ltd with Epclusa® 400/100mg (Sofosbuvir/Velpatasvir) tablet of M/s Gilead Sciences Ltd, in healthy Pakistani subjects. The tentative cost of the study is Rs.64,00,000 & will be provided by M/s Sami Pharmaceuticals (Pvt) Ltd., Karachi.
8	Proposed center for the study	Center for Bioequivalence Studies & Clinical

		Research, ICCBS, University of Karachi, Karachi. DRAP approved BA/BE Studies Center.
9	Investigational design and study plan	A single-center, open-label, randomized, single-dose, two-period, two-way cross-over study. One single dose per treatment period, separated by a washout period of seven (07) days will be received by the subjects. Blood samples will be taken up to 72 hours post-dose.
10	Pre-clinical or clinical data or safety studies	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so it is not applicable.
11	Final protocol	Attached.
12	Detail of the investigator (Principal investigator, analysts, and others along with CV)	CVs of the following are attached: Prof. Dr. Raza Shah (PI) Dr. Naghma Hashmi (Co-PI) Dr. Naveed Yunus (Co-PI)
13	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	IRB approval, Ref.# ICCBS/CBSCR/IEC/LET-035/2020, dated 09th November 2020, issued by Independent Ethics Committee of the ICCBS, University of Karachi is attached.
14	Approval of National Bio-ethics Committee (NBC)	NBC-PHRC approval certificate Ref:No.4-87/NBC-495/20/610, dated 29th October 2020 is attached.
15	Site approval by the Ethics committee	Center for Bioequivalence Studies & Clinical Research, ICCBS, University of Karachi, Karachi is approved as a BA/BE Studies Center from DRAP.
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)	N/A
21	Copy of registration letter if registered in Pakistan	Copy of registration letter for Ocvir™ 400/100mg (Sofosbuvir/Velpatasvir) tablet of M/s Sami Pharmaceuticals (Pvt) Ltd is attached. Whereas registration letter for Epclusa® 400/100mg (Sofosbuvir/Velpatasvir) tablet of M/s Gilead Sciences Ltd., is not provided.

22	Proposed label of investigational product	Commercial label of reference product is attached & claimed that as both investigational drug & reference drugs are registered in Pakistan so it is not applicable.
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)	G. FOR REFERENCE PRODUCT i. Sample Size=64 ii. Investigational drug for clinical phase= 64 Tablets iii. For Retention/Archiving= 5 times of study drug= 64×5 = 320 iv. Total no. of tablets= For clinical phase +Retention /Archiving 64+320 = 384 Tablets II. FOR TEST PRODUCT i. Sample Size=64 ii. Investigational drug for clinical phase= 64 Tablets iii. For Retention/Archiving= 5 times of study drug= 64×5 = 320 iv. Total no. of tablets= For clinical phase +Retention /Archiving 64+320 = 384 Tablets
24	Undertaking on affidavit.	Attached.

10.4. For technical evaluation, technical documents (i.e. Study Protocol & investigator's brochure etc.) forwarded to experts through email on 13th January 2021, for review & evaluation under sub-rule 4 of rule 7 of the Bio-Study Rules 2017.

10.5. Submitted for consideration of CSC.

10.6. Prof. Dr. Raza Shah joined the meeting & briefed the CSC regarding their application.

10.7. ***Decision of 19th CSC meeting:***

The CSC after detailed deliberation decided to approve the BA/BE Study titled "Bioequivalence Study of Ocvir™ 400/100mg (Sofosbuvir/Velpatasvir) Tablet of M/s Sami Pharmaceuticals (Pvt) Ltd with Epclusa® 400/100mg (Sofosbuvir/Velpatasvir) Tablet Of M/s Gilead Sciences Ltd". However, applicant will provide details of reference product (i.e. CoPP & GMP certificate) & other evident documents for import of reference product, as per the Bio-Study Rules 2017 and reference standard may be any stringent regulatory authority / innovator product.

AGENDA ITEM - XI:

REQUEST FOR APPROVAL AND REGISTRATION OF BIOEQUIVALENCE STUDY OF NOVIDATE® (CIPROFLOXACIN) 250MG/5ML SUSPENSION OF M/S SAMI PHARMACEUTICALS (PVT) LTD WITH CIPROXIN® 250MG/5ML SUSPENSION OF BAYER PAKISTAN. F. No. 14-05/2020 DD (PS).

11.1 Application submitted by Dr. Raza Shah, General Manager, Center for Bioequivalence Study and Clinical Research (CBSCR), University of Karachi, for approval of subject Bioequivalence Study, under the Bio-study rules, 2017.

11.2. The summary of the proposed study is as under;

i. **Study title:** A Single-Center, Open-Label, Randomized, Single-Dose, two-way Cross-over Study to compare the rate & extent of absorption of Novidate® (Ciprofloxacin) 250mg/5ml Suspension with Ciproxin® (Ciprofloxacin) 250mg/5ml Suspension, in healthy Pakistani subjects.
ii. **Investigational Product:** Novidate® (Ciprofloxacin) 250mg/5ml Suspension of M/s Sami Pharmaceuticals (Pvt) Ltd., F-95, S.I.T.E. Karachi.
iii. **Reference Product:** Ciproxin® (Ciprofloxacin) 250mg/5ml Suspension, of M/s Bayer Pakistan, Limited
iv. **Sponsor:** M/s Sami Pharmaceuticals (Pvt) Ltd., F-95, S.I.T.E. Karachi.
v. **CRO and BA/BE Study Site:** Center for Bioequivalence Studies and Clinical Research (CBSCR), ICCBS, University of Karachi, Karachi.
vi. **Principal Investigator:** Dr. Muhammad Raza Shah
vii. **Co-Principal Investigator:** Dr. Naghma Hashmi
viii. **Funding Source**: The sponsor
ix. **Cost of the Project**: Tentative cost of the study is Rs.24,00,000.
x. **Subjects enrolment**: 24 Subjects will be enrolled in the study.

11.3. 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 2050043, dated 09th December 2020.
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	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so it is not applicable.
6	Pharmacodynamics and Pharmacokinetics of Investigational Product	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so it is not applicable.
7	Purpose of study defining the indication along with the anticipated cost of the project and sources of fund	A Single-Center, Open-Label, Randomized, Single-Dose, two-way Cross-over Study to compare the rate & extent of absorption of Novidate® (Ciprofloxacin) 250mg/5ml Suspension with Ciproxin® (Ciprofloxacin) 250mg/5ml Suspension, in healthy Pakistani subjects. The tentative cost of the study is Rs.24,00,000 &

		will be provided by M/s Sami Pharmaceuticals (Pvt) Ltd., Karachi.
8	Proposed center for the study	Center for Bioequivalence Studies & Clinical Research, ICCBS, University of Karachi, Karachi. DRAP approved BA/BE Studies Center.
9	Investigational design and study plan	A single-center, open-label, randomized, single-dose, two-period, two-way cross-over study. Subjects will receive one single dose per treatment period, separated by a washout period of seven (07) days. Blood samples will be taken up to 24 hours post-dose.
10	Pre-clinical or clinical data or safety studies	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so it's not applicable.
11	Final protocol	Attached.
12	Detail of the investigator (Principal investigator, analysts, and others along with CV)	CVs of the following are attached: Prof. Dr. Raza Shah (PI) Dr. Naghma Hashmi (Co-PI) Dr. Naveed Yunus (Co-PI)
13	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	IRB approval, Ref.# ICCBS/CBSCR/IEC/LET-035/2020, dated 09th November 2020, issued by Independent Ethics Committee of the ICCBS, University of Karachi is attached.
14	Approval of National Bio-ethics Committee (NBC)	Not provided.
15	Site approval by the Ethics committee	Center for Bioequivalence Studies & Clinical Research, ICCBS, University of Karachi, Karachi is approved as a BA/BE Studies Center from DRAP.
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)	N/A
21	Copy of registration letter if registered in Pakistan	Print of online provisional list with registration number 047142 for Novidate® (Ciprofloxacin) 250mg/5ml Suspension of M/s Sami

		Pharmaceuticals (Pvt) Ltd., F-95, S.I.T.E. Karachi, is attached but the copy of registration letter is not provided.
22	Proposed label of investigational product	Not provided & claimed that as both investigational drug & reference drugs are registered in Pakistan so its nor applicable.
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)	H. FOR REFERENCE PRODUCT v. Sample Size=24 vi. Investigational drug for clinical phase= 3 Dry suspension Bottles vii. For Retention/Archiving= 5 times of study drug= 3×5 = 15 viii. Total no. of suspension Bottles= For clinical phase +Retention /Archiving 3+15 = 18 Bottles I. FOR TEST PRODUCT ii. Sample Size=24 ii. Investigational drug for clinical phase= 3 Dry suspension Bottles For Retention/Archiving= 5 times of study drug= 3×5 = 15 Bottles Total no. of suspension Bottles = For clinical phase +Retention /Archiving 3+15 = 18 Bottles
24	Undertaking on affidavit.	Attached.

11.4. After initial scrutiny following shortcomings observed:

i. Copy of registration letter of the reference & investigational products are not provided.
ii. Proposed label of the investigational & reference product is not provided.

11.5. Above-mentioned shortcomings communicated to the applicant, dated 12th January 2021.

11.6. In response to this division's letter, applicant informed that mentioned IMP is applied for registration in DRAP, & **withhold** this project until grant of registration letter by DRAP.

11.7. Submitted for consideration of CSC.

11.8. Prof. Dr. Raza Shah joined the meeting & briefed the CSC regarding their application.

11.9. *Decision of 19th CSC meeting:*

The CSC after detailed deliberation & as per request of applicant the application decided for six (06) months, until application completed as per the Bio-Study Rules 2017 as soon as possible.

AGENDA ITEM - XII:

REQUEST FOR APPROVAL OF FAZAIA RUTH PFAU MEDICAL COLLEGE, KARACHI TO ACT AS CLINICAL TRIAL SITE. F. No.15-04/2021 DD

12.1. Application submitted by Brig. Dr. Muhammad Abid (Retd) of Fazaia Ruth Pfau Medical College, Karachi, dated 21st January 2021.Site is situated at PAF base Faisal , Main Shahra-e-Faisal, Karachi. Wherein the request has been made to license their hospital with DRAP to act as

Clinical Trial Site. Application is on prescribed form along with prescribed fee of Rs.100000/- paid vide challan number 2064576, dated 5th January 2021.

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

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached.
2	Fee	Rs.100000/- paid vide challan number 2064576, dated 5th January 2021.
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).	Any legal evidence/ documents are not attached. It is submitted that the site is working under Pakistan Air Force.
4	Details of premises including layout plan of the site.	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.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Attached.

12.3. As power conferred by CSC to Chairman CSC for constitution of inspection panel, Chairman CSC constituted panel for inspection. Following members of panel inspected the clinical trial site:

i.	**Dr. Abdur Rashid** (Coordinator) Chairman CSC/Director, Division of Pharmacy Services-DRAP.
ii.	**Dr. Najam Us Saquib** Additional Director-DRAP, Karachi.
iii.	**Dr. Naseem Salahuddin** Director Infectious Diseases Indus Hospital, Karachi.

12.4. After inspection, panel submitted report with following remarks:

Keeping in view facility provided by Pakistan Air Force. Equipment, documentations, generators, pharmacy, safety system, emergency handling, IT exclusively in PAF,

archive room, access limited, human resource, trainings, recommends Fazaia Ruth Pfau Medical College, PAF Faisal Hospital, Main Shahra-e-Faisal Karachi as Clinical Trial Site

12.5. Concluding status / remarks of inspection panel:

Recommended for approval.

12.6. Submitted for consideration of CSC.

12.7 ***Decision of 19th CSC meeting:***

The CSC after detailed deliberation and as per inspection panel recommendations decided to approve M/s Fazaia Ruth Pfau Medical College, PAF Faisal Hospital, Main Shahra-e-Faisal Karachi as Clinical Trial Site.

AGENDA ITEM - XIII:

REQUEST FOR APPROVAL TO IMPORT STUDY MEDICINES FOR RESEARCH PROJECT TITLED AS "AZITHROMYCIN & CEFEXIME TREATMENT OF TYPHOID IN SOUTH ASIA TRIAL (ACT-SOUTH ASIA TRIAL). F.NO.03-51/2020 DD (PS).

13.1. Application submitted by Prof. Dr. Farah Naz Qamar, Associate Professor, Department of Pediatrics & Child Health, Aga Khan University Hospital, Karachi, dated 24th December 2020, on prescribed Form-II along with a fee of Rs.200000/- deposited vide challan no.1908194, dated 08th December 2020. Wherein request has been made for registration & approval of subject clinical trial, which will be carried out at following clinical trial sites:

i. Aga Khan University Hospital Main Campus, Stadium Road, Karachi
ii. Aga Khan University Hospital for Women, Karim Abad, Karachi.
iii. National Institute of Child Health (NICH), Karachi.

13.2. The details regarding sponsor & responsible party is as under:

i. **Sponsor:** Oxford University Clinical Research Unit, Vietnam.
ii. **Collaborators:**
    a. University of Oxford.
    b. Medical Research Council.
    c. Department for International Development, United Kingdom.
    d. Wellcome Trust.
iii. Information provided by (Responsible Party):

Oxford University Clinical Research Unit, Vietnam.

13.3. The trial comprises of following objectives;

i. Primary Outcome Measures :
ii.

Treatment Failure [Time Frame: Within 28 days of treatment initiation]

A composite outcome of treatment failure by the 28th day after the initiation of treatment will be defined by either of the following events: 1.Clinical failure: persistence of fever on day 7 (168 h) post treatment initiation OR The need for rescue treatment as judged by the Trial Clinician OR The development of any complication (e.g., clinically significant bleeding, fall in the Glasgow Coma Scale score, perforation of the gastrointestinal tract) OR Syndromic enteric fever relapse within 28 days of initiation of treatment. 2.Microbiological failure: a positive blood-culture for S. Typhi or S. Para typhi on day 7 of treatment regardless of the presence of fever (microbiological failure) OR blood culture-confirmed typhoid fever relapse within 28 days of initiation of treatment.

iii. Secondary Outcome Measures :

a. Fever clearance time (FCT) in patients in each treatment arm [Time Frame: at least 2 days]. The FCT will be the time from the first dose of a study drug until a temperature of < 37.5°C (axillary); < 38.0°C (oral) has been achieved.
b. Time from onset of treatment to treatment failure [Time Frame: Within 28 days of treatment initiation]. The time to treatment failure will be the time from the first dose of a study drug until an event occurs defined as a treatment failure.
c. Time from symptom onset to treatment failure [Time Frame: Within 28 days of treatment initiation]. The time to treatment failure will be the time from the day of the first symptom until an event occurs defined as a treatment failure.
d. Adverse event [Time Frame: Within 90 days]. Adverse events will be graded (grade 3/4 adverse events, serious adverse events, adverse events of any grade leading to modification of study drug dose or interruption/early discontinuation);
e. Faecal carriage of S.Typhi or S.Paratyphi [Time Frame: One- and three-month follow-up]. Positive culture of faeces sample for S.Typhi or S.Paratyphi.
f. cost effectiveness of treatment [Time Frame: Initiation of treatment and one-month follow-up visit]. The incremental cost-effectiveness ratio (ICER) will comprise of the total costs per case, real outpatient and in-patient costs, total direct and indirect costs for the family and healthcare system and health outcomes converted to Disability Adjusted Life Years (DALYs). The cost per DALY averted will be compared against multipliers of the gross domestic product/capita in each of the four countries to establish the cost-effectiveness of the combination regimen.

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached.
2	Prescribed processing fee	Rs.200000/- deposited vide challan no.1908194, dated 08th December 2020.
3	Investigator Brochure (s)	Attached but not as per ICH-GCP guidelines.
4	Final protocol	Attached. Version 1.3
5	Informed consent and	Attached

	participant information sheet (Urdu to English)	
6	List of participating countries	Bangladesh, India, Nepal & Pakistan
7	Phase of trial.	Phase – IV
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.	i. Azithromycin 250mg (285 Strips) ii. Azithromycin 500mg (140 Strips) iii. Azithromycin Suspension 30ml & 50ml. (300 Bottles) iv. Cefixime (360 Strips)
9	Site of the trial	1. Aga Khan University Hospital Main Campus, Stadium Road, Karachi 2. Aga Khan University Hospital for Women, Karim Abad, Karachi. 3. National Institute of Child Health (NICH), Karachi. Clinical Trial Sites at serial number 2 & 3 are not approved from DRAP.
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Attached.
11	Approval of National Bio-ethics Committee (NBC)	Attached. Ref:No.4-87/NBC-492/20/505, dated 19th October 2020.
12	CV's of the Investigators	CVs of following (P.Is) are attached: i. Prof. Dr. Farah Naz Qamar, AKUH, Karachi. ii. Dr. Sonia Qureshi, AKUH, Karachi.
13	GMP certificate along with COPP & free sale certificate of the investigational product.	Attached.
14	Pre-clinical/clinical safety studies	Articles Attached.
15	Summary of Protocol	Attached.
16	Summary of Investigator Brochure	Not provided & claimed that as all drugs used in the trial are already registered & widely used worldwide so not applicable.
17	Adverse Event Reporting Form	Attached.
18	No of patients to be enrolled in each center.	375
19	Name of Monitors & Clinical	CV of Naveed Ahmed is attached.

	Research Associate	
20	Evidence of registration in country of origin.	Relevant documents are not provided, whereas Patient Information Leaflets (PIL) of following are attached; i. Azithro-100/Azithro-200 (Azithromycin) Oral Suspension. ii. Azithro-250/Azithro-500 (Azithromycin) Tablets iii. Fixim-200/Fixim-400 (Cefixime) Tablets. iv. Fixim DT-100 (Cefixime) Dispersible Tablets. All above drugs manufactured by M/s National Healthcare (Pvt) Ltd, Nepal.
21	Copy of registration letter (if registered in Pakistan)	Zetro™ & Cefiget™ leaflets(PIL) are attached, which are not related with IMP used in the trial.
22	Sample of label of the investigational product / drug.	Attached.
22	Duration of trial	36 Months
23	Undertaking on Stamp paper	Attached.

13.5. After initial scrutiny following shortcomings observed:

i. Following applied clinical trial sites are not approved yet:
   a. Aga Khan University Hospital for Women, Karim Abad, Karachi.
   b. National Institute of Child Health (NICH), Karachi.
ii. Evidence of registration in country of origin is not provided.(CoPP/Free sale certificate)
iii. Irrelevant documents attached as evidence of registration in Pakistan.

13.6. Applicant informed regarding shortcomings vide letter even number dated 13th January 2021 but yet response is awaited.

13.7. For technical evaluation, technical documents (i.e. Study Protocol & investigator's brochure etc.) forwarded to experts through email on 15th January 2021, for review & evaluation under sub-rule 4 of rule 7 of the Bio-Study Rules 2017.

13.8. Submitted for consideration of CSC.

13.9 Decision of 19th CSC meeting:

The CSC after detailed deliberation decided to approve the clinical trial titled, "Azithromycin & Cefixime Treatment of Typhoid in South Asia Trial (Act-South Asia Trial)", subject to provision of IMPs evidence of registration in country of origin (i.e. CoPP & GMP certificate). After fulfilment of prerequisites trial may be conducted at DRAP-approved site(s) only, as per the Bio-Study Rules 2017 as soon as possible.

2. Applications for following clinical Trial Site(s) will be provided on separate applications & will be inspected for decision:

i. Aga Khan University Hospital for Women, Karim Abad, Karachi.

ii. National Institute of Child Health (NICH), Karachi.

AGENDA ITEM - XIV:

REQUEST FOR REGISTRATION OF CLINICAL TRIAL TITLED "A RANDOMIZED, DOUBLE-BLIND, POSITIVE CONTROLLED STUDY TO EVALUATE EFFICACY & SAFETY OF FUKE QIANJIN CAPSULE IN PATIENTS WITH PELVIC INFLAMMATORY DISEASES.". F.NO.03-53/2021 DD (PS).

14.1. Application Prof. Dr. M. Raza Shah, General Manager, Center for Bioequivalence Studies and Clinical Research (CBSCR), The University of Karachi, Karachi, dated 05th January 2021, on prescribed Form-II along with a fee of Rs.200000/- deposited vide challan no.0814000, dated 31st December 2020. Wherein request has been made for registration & approval of subject clinical trial.

14.2. The details regarding sponsor & responsible party is as under:

i. **Primary objective: Primary objective:** Randomized, double-blind and positive-controlled clinical trial to assess the efficacy and safety of Fuke Qianjin Capsule compared to Doxycycline Hyclate Tablet in patients with mild to medium PID and its sequalae.
ii. **Sponsor:** M/s Zhuzhou Qianjin Pharmaceutical Co., Ltd, China.
iii. **Name of Finished Product/Investigational Product/Trade Name:** Fuke Qianjin Capsule.
iv. **Name of Active Ingredient(s):** Fuke Qianjin capsule consists of radix moghaniae, radix rosae laevigatae, herba Andrographis, caulis mahoniae, zanthoxylum dissitum hemsl, radix angeliae sinensis, caulis spatholobi, radix codonopsis.
v. **Purpose of Trial:** Randomized, double-blind & positive-controlled clinical trial to assess the efficacy and safety of Fuke Qianjin Capsule compared to Doxycycline Hyclate Tablet in patients with mild to medium Pelvic Inflammatory Diseases (PID) & its sequelae.
vi. **Cost of Project:** The total expected budget for this research project is around 50,000 US dollars (including tax).
vii. **Source of Fund:** This clinical trial is funded by Zhuzhou Qianjin Pharmaceutical Co., LTD. China.
viii. **Medication:**

a. **Test group:** metronidazole tablets doxycycline hyclate tablets simulant are consecutively taken for 14 days, while Fuke Qianjin capsule is consecutively taken for 28 days.
b. **Control group:** metronidazole tablets + doxycycline hyclate tablets. are consecutively taken for 14 days, while Fuke Qianjin capsule simulation is consecutively taken for 28 days. Fuke Qianjin Capsules and their simulants are taken as 2 capsules at a time, 3 times a day, orally after breakfast, lunch, and dinner, respectively; Metronidazole Tablets are taken as 2 tablets (0.2 g/tablet) at a time, twice a day, at the same time as breakfast and dinner,

respectively; Doxycycline Hyclate Tablet and their simulants are taken as 1 tablet (0.1 g/tablet, Doxycycline Hyclate Tablet calculated as C22H24N2O8) at a time, twice a day, at the same time as breakfast and dinner, respectively. During the observation period, sexual life should be prohibited, or barrier contraceptive tools should be used, and spicy raw, cold, and greasy foods should be avoided.

ix. Name & quantity of Investigational Medicinal Products utilized in the trial:

S.No.	Description	Metronidazole Tablets	Fuke Qianjin Capsules	Doxycycline Hyclate Tablets
01	No. of dose per day (1-14 days)	2+2=4 Tablets	2+2+2=6 Capsules	1+1=2 Tablets
02	No. of dose per day (15-28 days)	-	2+2+2=6 Capsules	-
03	Total Dose (1-14 days)	4*14 = 56	6*14=84 Capsules	2*14=28 Tablets
04	Total Dose (15-28 days)	-	6*14=84 Capsules	-
05	No. of dose per patient for 28 days	56 Tablets	168 Capsules	28 Tablets
06	Total no. of tablets for 198 patients	56*198 = 11088 Tablets	168*198=33264 Capsules	28*198=5544 Tablets
07	Retention Samples for archiving (3 times of trial requirement)	11088*3=33264 Tablets	33264*3=99792 Capsule	5544*3=16632 Tablets
08	Total no. of tablets for 198 patients + Retention Samples for archiving	11088+33264= 44352 Tablets	33264+99792=133056 Capsules	5544+16632=22176 Tablets

14.3. Application scrutinized/evaluated according to pre-requisites as mentioned in 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 processing fee	Rs.200000/- deposited vide challan no.0814000, dated 31st December 2020.
3	Investigator Brochure (s)	Attached but not as per ICH-GCP guidelines.
4	Final protocol	Attached. Version 2.0
5	Informed consent and participant information sheet (Urdu to English)	Attached.

6	List of participating countries	China & Pakistan.
7	Phase of trial.	Phase – II
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.	v. Fuke Qianjin Capsules (133056 Capsules) vi. Metronidazole Tablets (44352 Tablets) vii. Doxycycline Hyclate Tablets (22176 Tablets)
9	Site of the trial	4. Jinnah Post Graduate Medical Center, Rafiqui Sarwar Shaheed Road, Karachi Cantonment, Karachi City, Sindh 75510. 5. Other Collaborative Hospitals. Above mentioned clinical trial site (JPMC) is not approved for the subject clinical trial, only gynae section of JPMC is approved by DRAP. Whereas Other Collaborative Hospitals are not described.
10	Institutional Review Board (IRB) approval of sites with the complete composition of committee i.e. names and designation of members.	IRB approval along with composition attached.
11	Approval of National Bio-ethics Committee (NBC)	Attached. Ref: No.4-87/NBC-565/20/1097, dated 04th January 2021.
12	CV's of the Investigators	CVs of the following (P.Is) is attached: iii. Prof. Dr. Raza Shah.
13	GMP certificate along with COPP & free sale certificate of the investigational product.	Attached only for Fuke Qianjin Capsules manufactured by M/s ZhuZhou QianJin Pharmaceutical Co., Ltd. No details provided regarding GMP/CoPP for the following IMPs: i. Metronidazole Tablets (44352 Tablets) ii. Doxycycline Hyclate Tablets (22176 Tablets)
14	Pre-clinical/clinical safety studies	Articles Attached.
15	Summary of Protocol	Attached.
16	Summary of Investigator Brochure	Not provided.
17	Adverse Event Reporting Form	Attached.
18	No. of patients to be enrolled in each center.	In total, **198** cases/subjects with active Pelvic Inflammatory Disease (PID) will be enrolled & randomized equally into two groups.

19	Name of Monitors & Clinical Research Associate	CV of Muhammad Iqbal Afridi, JPMC, Karachi. Jahanara Ainuddin, Dow University of Health Sciences, Department of Gynae & Obstetrics, Karachi. Dr. Khadija Bano, Chairperson Faculty of Obstetrics & Gynecology, Jinnah Sindh Medical University, Karachi. is attached.
20	Evidence of registration in the country of origin.	i. Fuke Qianjin Capsules (133056 Capsules) manufactured by M/s ZhuZhou QianJin Pharmaceutical Co., Ltd. ii. Metronidazole Tablets (44352 Tablets) iii. Doxycycline Hyclate Tablets (22176 Tablets) * No details provided regarding GMP/CoPP for IMPs mentioned at serial number ii & iii.
21	Copy of registration letter (if registered in Pakistan)	Not applicable
22	Sample of the label for the investigational product/drug.	Attached.
22	Duration of trial	12 Months
23	Undertaking on Stamp paper	Attached.

14.4. After initial scrutiny following shortcomings observed:

i. Evidence of registration in the country of the following IMPs is in Chinese language hence can't verified.:
   a. Metronidazole Tablets
   b. Doxycycline Hyclate Tablets

ii. GMP certificate along with COPP & free sale certificate of the manufacturer of the following investigational product is in Chinese language hence can't verified.:
   a. Metronidazole Tablets
   b. Doxycycline Hyclate Tablets

14.5. Applicant informed regarding shortcomings vide letter even number dated 18th January 2021 but yet response is awaited.

14.6. For technical evaluation, technical documents (i.e. Study Protocol & investigator's brochure etc.) forwarded to experts through email on 15th January 2021, for review & evaluation under sub-rule 4 of rule 7 of the Bio-Study Rules 2017.

14.7. Submitted for consideration of CSC.

14.8 ***Decision of 19th CSC meeting:***

The CSC after detailed deliberation decided to approve the clinical trial titled, "Randomized, Double-Blind, Positive Controlled Study to Evaluate Efficacy & Safety of Fuke Qianjin Capsule in Patients with Pelvic Inflammatory Diseases.". However, applicant will provide translated documents (i.e. CoPP & GMP certificate) for investigational medicinal products (IMPs). Further TCM (Fuke Qianjin) should be assayed & certificate of analysis (COA) along with report will be submitted to the committee, as per the Bio-Study Rules as soon as possible.

AGENDA ITEM - XV:

REGULATORY APPROVAL FOR JIANGSU PACIFIC MEINOUKE BIOPHARMACEUTICALS (PMBP) PROTOCOL-MPZ-II-02, FOR "A MULTICENTER, SEAMLESS, RANDOMIZED, THIRD-PARTY-BLIND CLINICAL TRIAL TO EVALUATE THE SAFETY & EFFICACY OF MEPLAZUMAB (INJECTION) IN ADDITION TO STANDARD CARE FOR THE TREATMENT OF COVID-19 IN HOSPITALIZED ADULTS" F.NO.03-54/2021 DD (PS).

15.1 Application submitted by Dr. Nosheen Nasir, Assistant Professor, Department of Medicine-MC, Aga Khan University Hospital, Karachi, dated 14th January 2021, on prescribed Form-II along with a fee of Rs.200000/- deposited vide challan no.0831706, dated 12th January 2021. Wherein request has been made for registration & approval of subject clinical trial, which will be carried out at Aga Khan University Hospital Main Campus, Stadium Road, Karachi.

15.2. The details regarding trial, sponsor & responsible party is as under:

i. **Sponsor:** Jiangsu Pacific Meinuoke Biopharmaceutical Co. Ltd., China.

ii. Contact information: Address no.128 Hehai West Road, Xinbei District (National High-Tech Industrial Development Zone), Changzhou City, Jiangsu province, China, Zip Code: 213022, Tel: 13401159747.

iii. Primary Objective of the study:

To evaluate the safety, tolerability, pharmacokinetic characteristics and occupancy characteristics of peripheral blood cell receptors of Meplazumab for injection in healthy people and provide reference for the drug's clinical phase II study dose.

iv. Number of subjects to be recruited:

a. For Pakistan:
100 patients in stage 1
50 patients in stage 2

b. Treatment arms are globally randomized, with ratio of 0.25 (low dose), 0.25 (medium dose), 0.25 (high dose), 0.25 (control).
Dose depends on patient weight so it will be difficult to calculate how many vials will be required in each arm. Roughly, for an average 75 weight:

c. After stage 1, Interim Analysis will be done to select the most effective and safe dose for stage 2. Currently, one can estimate as per the high dose arm, the required vials per subject, would be 5 vials per subject. So total vials 1170 are planned to be shipped and after 15% addition, it will be a total of 1346 vials.

Low dose			**Medium dose**			**High dose**			**Control**		
Dose (mg/kg)	Vials/Subject	Roundup vials	Dose (mg/kg)	Vials/Subject	Roundup vials	Dose (mg/kg)	Vials/Subject	Roundup vials	Dose (mg/kg)	Vials/Subject	Roundup vials
0.12	**0.9**	**1**	**0.4**	**3**	**3**	**0.6**	**4.5**	**5**	**0**	**0**	**0**
This is stage 1, assuming subject average body weight is 75kg.											

d. Dose depends on patient weight so it will be difficult to calculate how many vials will be required in each arm. Roughly, for an average 75 weight:

e. After stage 1, Interim Analysis will be done to select the most effective and safe dose for stage 2. Currently, one can estimate as per the high dose arm, the required vials per subject, would be 5 vials per subject. So total vials 1170 are planned to be shipped and after 15% addition, it will be a total of 1346 vials.

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached.
2	Prescribed processing fee	Rs.200000/- deposited vide challan no.0831706, dated 12th January 2021
3	Investigator Brochure (s)	Attached.
4	Final protocol	Attached. Version 1.0/20200820 Protocol no. MPZ-I-01 Protocol no. MPZ-I-02
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries	USA, Brazil, & Pakistan
7	Phase of trial.	Phase – II/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.	Approximately 1170 vials will be required for the trial and after 15% addition, it will be a total of **1346 vials.**
9	Site of the trial	Aga Khan University Hospital Main Campus,

		Stadium Road, Karachi.
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Attached.
11	Approval of National Bio-ethics Committee (NBC)	Attached. Ref:No.4-87/COVID-58/NBC-21/1140, dated 12th January 2021.
12	CV's of the Investigators	CVs of following (P.Is) are attached: iv. Dr. Nosheen Nasir, Assistant Professor, Department of Medicine-MC, Aga Khan University Hospital, Karachi. v. Sayed Faisal Mahmood, AKUH, Karachi.
13	GMP certificate along with COPP & free sale certificate of the investigational product.	Not provided.
14	Pre-clinical/clinical safety studies	Any published data is not shared. Matter discussed in following sections of Investigator's Brochure: IB section 1.3 for Non-Clinical data IB section 1.4. for Clinical data IB section 6.13 for safety data of Meplazumab.
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.	For Pakistan: 100 subjects for Phase-I 50 subjects for Phase-II
19	Name of Monitors & Clinical Research Associate	M/s IQVIA Solutions Pakistan (Pvt) Ltd., Karachi CVs of following CRA are attached: Sadia Altaf. Bharti Kachela. Both are employees of M/s IQVIA Pakistan.
20	Evidence of registration in country of origin.	Not provided.

21	Copy of registration letter (if registered in Pakistan)	Not provided.
22	Sample of label of the investigational product / drug.	Attached.
22	Duration of trial	Study duration for each subject will be 84±7 days from randomization in each stage.
23	Undertaking on Stamp paper	Not provided.

15.4. Technical documents (i.e. Study Protocol & investigator's brochure etc.) were forwarded to all CSC experts for review & evaluation under sub-rule 4 of rule 7 of the Bio-Study Rules 2017, please.

15.5. Submitted for consideration of CSC.

15.6. ***Decision of 19th CSC meeting:***

The CSC after detailed deliberation decided to approve the clinical trial titled, "A Multicenter, Seamless, Randomized, Third-Party-Blind Clinical Trial to Evaluate The Safety & Efficacy of Meplazumab (Injection) In Addition To Standard Care For The Treatment of Covid-19 In Hospitalized Adults", subject to conditions that pharmacokinetic/pharmacodynamic studies of the trial will be conducted at DRAP-approved BA/BE Studies centers, as per the Bio-Study Rules.

AGENDA ITEM - XVI:

REQUEST FOR REGISTRATION OF CLINICAL STUDY TITLED "ANTI-CORONAVIRUS THERAPIES TO PREVENT PROGRESSION OF COVID-19. F. No.03-57/2021-DD (PS).

16.1 Application submitted by Dr. Khawar Kazmi, Visiting Faculty Department of Medicine, Professor & Consultant Cardiologist, Aga Khan University Hospital, Karachi, dated 02nd February 2021, on prescribed Form-II along with a fee of Rs.200000/- deposited vide challan no.0831707, dated 01st February 2021. Wherein request has been made for registration & approval of subject clinical trial, which will be carried out at following clinical trial sites:

S.No.	Clinical Trial Site	Site P.I.	Expected enrollment
01	Aga Khan University Hospital, Karachi. (National Coordinating & Participating Site)	National Coordinator: Dr. Khawar Kazmi. Site P.I. Dr. Zainab Samad.	Inpatient: 50 Outpatient: 150
02	Tabba Heart Institute, Karachi.	Dr. Bashir Hanif, Medical Director & Head of Cardiology.	Inpatient: 50 Outpatient: 100

03	Jinnah Post Graduate Medical Center / Jinnah Sindh Medical University, Karachi.	Dr. Zeeshan Ali, Associate Professor of Medicine.	Inpatient: 50

16.2. The study is also enlisted at U.S. National Trial Registry under identification number: NCT04324463. The summary regarding sponsor, responsible party & trial is as under:

i. **Sponsor:** Hamilton Health Sciences through its Population Health Research Institute, Canada.

ii. **Collaborators:**
   a. Bayer

iii. **Information provided by (Responsible Party):**
   Population Health Research Institute, Canada.

iv. **Name of Investigational product , including all available names ; trade , generic or INN name etc.**
   a. Anti - inflammatory : colchicine vs. control . (both inpatient and outpatient)
   b. Antithrombotic : acetylsalicylic acid (ASA) vs. control (outpatient only.
   c. Antithrombotic : combination of ASA and rivaroxaban vs. control . (Inpatient only)
   d. Interferon-Beta, subcutaneous injection

v. **Purpose of trial defining the indication along with the anticipated cost of the project and sources of fund**:
   a. The aim of the study is to evaluate anti - inflammatory and anti-thrombotic therapy to determine whether they prevent clinical progression of COVID-19 in outpatients and inpatients . Disease progression and mortality appear to be related to an intense inflammatory response and secondary thrombosis in the pulmonary , cardiac and cerebral vasculature . We will likely need combinations of several widely available and affordable interventions that target different pathways (e.g. inflammation, thrombosis) to substantially reduce the risk of COVID - 19 disease progression . We need to test these treatments as soon as possible after diagnosis.
   b. Source of funding : Hamilton Health Sciences through its Population Health Research Institute (PHRI), Canada.

16.3. The trial comprises of following primary objectives;

i. Outpatient trial - Colchicine vs. control and Aspirin vs. control [Time Frame: 45 days post randomization] composite of hospitalization or death.
ii. Inpatient trial - Interferon-β vs. control and Colchicine vs. control [Time Frame: 45 days post randomization] invasive mechanical ventilation or death.
iii. Inpatient trial - Aspirin and rivaroxaban vs. control [Time Frame: 45 days post randomization] invasive mechanical ventilation or death

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached.

2	Prescribed processing fee	Rs.200000/- deposited vide challan no.0831707, dated 01st February 2021.
3	Investigator Brochure (s)	Attached, version 28.0 Package Leaflets of Drugs
4	Final protocol	Attached. Version 15.0
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries	Argentina, Brazil, Canada, Chile, Columbia, Ecuador, Egypt, India, Philippines, Russia, Saudi Arabia, United Arab Emirates, United States of America & Pakistan
7	Phase of trial.	It is claimed that the study is combination of Phase – II & III design
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.	viii. Aspirin 75mg Tablets (7280 Tablets) ix. Colchicine 0.5 mg Tablets (10740 Tablets) x. Xarelto (Rivaroxaban) 2.5 mg Tablets (5488 Tablets). xi. Interferon-ß (No Details Provided).
9	Site of the trial	6. Aga Khan University Hospital, Karachi 7. Tabba Heart Institute, Karachi. 8. Jinnah Postgraduate Medical Center, Karachi. *All clinical trial sites are not approved from DRAP for subject Clinical Trial.
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Attached.
11	Approval of National Bio-ethics Committee (NBC)	Attached. Ref:No.4-87/COVID-56/NBC/20/1148, dated 13th January 2021.
12	CV's of the Investigators	CVs of following (P.Is & Co-PIs) are attached: vi. Dr. Sayed Khawar Abbas Kazmi, AKUH, Karachi. vii. Dr. Zainab Samad, AKUH, Karachi. viii. Dr. Bashir Hanif, Tabba Heart Institute, Karachi. ix. Dr. Zeeshan Ali, JPMC, Karachi.
13	GMP certificate along with COPP & free sale certificate of the	1. GMP certificates of followings are attached: a. M/s Tiofarma B.V., Benjamin Franklinstraat, Netherlands.

	investigational product.	b. M/s Bayer AG, Leverkusen, Germany. c. M/s Almac Clinical Services Limited, Northern Ireland, UK. 2. COPP are attached for following IMPs: a. Xarelto (Rivaroxaban) 2.5 mg Tablets. Mfg. by Bayer AG, Leverkusen, Germany * COPP for following IMPs are not provided: a. Colchicine 0.5mg Tablets. b. Aspirin 75mg Tablets. c. Interferon-ß SQ Injections.
14	Pre-clinical/clinical safety studies	EMA assessment report for Xarelto (Rivaroxaban) is 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.	Attached.
19	Name of Monitors & Clinical Research Associate	Monitoring plan is attached.
20	Evidence of registration in country of origin.	COPP is attached only for Xarelto (Rivaroxaban) 2.5 mg Tablets. Mfg. by Bayer AG, Leverkusen, Germany. No relevant documents provided for following IMPs: a. Colchicine 0.5mg Tablets. b. Aspirin 75mg Tablets. c. Interferon-ß SQ Injections.
21	Copy of registration letter (if registered in Pakistan)	Copy of registration letter for Xarelto (Rivaroxaban) 2.5 mg Tablets. Mfg. by Bayer AG, Leverkusen, Germany is attached.
22	Sample of label of the investigational product / drug.	Attached for following IMPs: a. Colchicine 0.5mg Tablets. b. Rivaroxaban 2.5mg Tablets. c. Aspirin (ASA) 75mg Tablets. d. Interferon-ß SQ Injections.
22	Duration of trial	12 Months
23	Undertaking on Stamp paper	Attached.

16.5 After initial scrutiny following shortcomings observed:

i. Evidence of registration in country of origin (CoPP/Free sale certificate) is not provided for following products:
   a. Colchicine 0.5mg Tablets.
   b. Aspirin 75mg Tablets.
   c. Interferon-ß
ii. No details for quantity of drug / trial material to be imported is provided for interferon-ß SQ Injections.

16.6 In the view of above, it is proposed that the above-mentioned shortcomings may communicate to the applicant, DFA attached.

16.7 Technical documents (i.e. Study Protocol & investigator's brochure etc.) were forwarded to all CSC experts for review & evaluation under sub-rule 4 of rule 7 of the Bio-Study Rules 2017, on 1st February 2021.

16.8 Submitted for consideration of CSC.

16.9. ***Decision of 19th CSC meeting:***

The CSC after detailed deliberation deferred till fulfilment of all prerequisites & clinical trial site(s) approval.

AGENDA ITEM - XVII:

REQUEST FOR APPROVAL OF M/S TABBA HEART INSTITUTE, KARACHI TO ACT AS CLINICAL TRIAL SITE TO CONDUCT CLINICAL STUDY TITLED "ANTI-CORONAVIRUS THERAPIES TO PREVENT PROGRESSION OF COVID-19. F. No.15-10/2021-DD (PS).

17.1 Application submitted by Dr. Bashir Hanif (CNIC-42101-1855677-5), Executive Director, Medical Director of M/s Tabbaa Heart Institute, Karachi, dated 02nd February 2021, the site is situated at ST-01, Block-2, Federal "B" area, Karachi. Wherein the request has been made to license the subject site with DRAP to act as Clinical Trial Site. Application is on prescribed form-I along with a prescribed fee of Rs.100000/- paid vide challan number 2060446 (unverified), dated 25th January 2021.

17.2. After initial scrutiny summary of the application & attached documents is as follows:

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached.
2	Prescribed processing fee	Rs.100000/- paid vide challan number 2060446 (Not verified from B&A Division of DRAP), dated 25th January 2021.
3	Particulars regarding the legal status of the applicant i.e. in the case of proprietorship the names	Expired registration certificate is attached. The legal status of the

	of proprietors and their addresses, in the case of a 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).	firm/company needs to be provided.
4	Details of premises including layout plan of the site.	Layout plan of the premises is needed to be provided.
5	Details of the section-wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	List of some equipment is attached but section-wise details of equipment need to be provided.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling, etc.	Attached.
8	Undertaking on stamp paper	Not provided.

17.3. Following shortcomings observed after initial scrutiny:

a. Particulars regarding the legal status of the applicant/firm need to be provided.
b. The layout plan of the premises is not provided.
c. Section-wise equipment list not provided.
d. Undertaking on stamp paper not provided.
e. The deposited fee challan is not verified by the Budget & Accounts Division of DRAP.

17.4. Submitted for consideration of CSC.

17.5 ***Decision of 19th CSC meeting:***

The CSC after detailed deliberation decided to authorize the Chairman CSC for the constitution of inspection panel for the inspection of M/s Tabba Heart Institute, Karachi. The case will be again placed before the CSC for further deliberations and decisions after submission of inspection report. Meanwhile applicant is directed to fulfill all prerequisite as per the Bio-Study Rules.

AGENDA ITEM – XVIII

REQUEST FOR APPROVAL OF M/S JINNAH POSTGRADUATE MEDICAL CENTER, KARACHI TO ACT AS CLINICAL TRIAL SITE TO CONDUCT CLINICAL STUDY TITLED "ANTI-CORONAVIRUS THERAPIES TO PREVENT PROGRESSION OF COVID-19. F. No.15-11/2021-DD (PS).

18.1 Application submitted by Dr. Zeeshan Ali (CNIC-41302-2164032-9), Associate Professor, Medicine Ward-07, Jinnah Post Graduate Medical Center, Karachi, dated 01st February 2021. Wherein the request has been made to license the **COVID Isolation Unit Ward-23**, Jinnah Post Graduate Medical Center, Karachi to act as Clinical Trial Site. Application is on prescribed form-I along with a prescribed fee of Rs.100000/- paid vide challan number 2060448, dated 25th January 2021.

18.2. After initial scrutiny summary of the application & attached documents is as follows:

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached.
2	Prescribed processing fee	Rs.100000/- paid vide challan number 2060448, dated 25th January 2021.
3	Particulars regarding the legal status of the applicant i.e. in the case of proprietorship the names of proprietors and their addresses, in the case of a 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).	The applied site is a public sector tertiary care hospital.
4	Details of premises including layout plan of the site.	The layout plan of the premises is not provided.
5	Details of the section-wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	The list of equipment in ward-23 is attached.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling, etc.	Attached.
8	Undertaking on stamp paper	Not provided.

18.3. Following shortcomings observed after initial scrutiny:

a. The layout plan of the premises is not provided.
b. Undertaking on stamp paper not provided.

18.4. Above mentioned shortcomings were communicated to applicant on 9th February 2021, response is awaited.

18.5 Submitted for perusal, discussion and decision of CSC.

18.6 *Decision of 19th CSC meeting:*

The CSC after detailed deliberation decided to authorize the Chairman CSC for the constitution of inspection panel for the inspection of M/s Jinnah Postgraduate Medical Center, Karachi. The case will be again placed before the CSC for further deliberations and decisions after submission of inspection report. Meanwhile applicant is directed to fulfill all prerequisite as per the Bio-Study Rules.

AGENDA ITEM - XIX:

PRELIMINARY CLINICAL TRIAL REPORT OF CLINICAL STUDY TITLED "IMMUNOGLOBULIN THERAPY FOR PASSIVE IMMUNIZATION OF CRITICALLY ILL COVID-19 PATIENTS" F. No.03-29/2020 DD (PS)

19.1 Preliminary trial report forwarded by from Prof. M. Saeed Quraishy, Vice Chancellor, Dow University of Health Services, Karachi, vide letter reference number: DUHS/VC/2021/01-13, dated 15th January 2021.

19.2. Another report forwarded from Dow University of Health Services, Karachi, dated 09th February 2021. Wherein F.R. is a preliminary report for a Clinical trial titled *"Anti-COVID-19 IVIG therapy for Passive Immunization of critically ill COVID-I9 patient"*

19.3 Both reports were shared with CSC members for review & evaluation under sub-rule 4 of rule 7 of the Bio-Study Rules 2017, on 10th February 2021. Report is attached **Annex II & III**

19.4 Submitted for consideration of CSC.

19.5 Chairman CSC briefed the committee regarding trial summary & its results. Executive summary of the trial is as follows:

EXTXCUTIVE SUMMARY

This is the detailed clinical study report of phase-I clinical trial titled "Clinical trial investigation: Anti-COVID-19 IVIG therapy for Passive Immunization of critically ill COVID-19 patients" (CT-0022) conducted at Dow University of Health Sciences post approval from Drug Regulatory Authority Pakistan in May 2020. The clinical trial was approved for 50 participants with l0 control (receiving Standard of Care treatment) and 40 tests (receiving Standard of Care + C-IVIG dose) where test population was further subdivided into four dosage arms (0.15,0.2,0.25 and 0.3 g/kg). The prime objective of the trial was to determine the safest and the most efficacious dosage of the C-IVIG treatment while initiating the trial with the lowest dosage arm and escalating sequentially provided safety is demonstrated.

Drug related safety was monitored in all patients during C-IVIG infusion (except in comparator group), during hospital stay and on 28-day after enrollment in study. No drug related Adverse

Events were reported during infusion and during hospital day as monitored regular through vital measurement, physical observation and laboratory tests related to renal and liver function.

Mortality prevention was the primary outcome of efficacy measured by 28-day mortality in intervention (C-IVIG dosages) and comparator (control) arm. Intervention arm III (0.25glkg) was found most effective in preventing mortality (13.5 times more survival benefit as compared to comparator arm) followed by intervention arm I (0.l5glkg) which provided 6 times more survival benefit compared to comparator arm. All dosage arms were found to provide better survivability percentage in comparison to control group. All intervention arms showed reduction of duration for supplemental oxygen need and improvement in lung functionality demonstrated by increased Horowitz index when compared with comparator ann. Although not statistically significant, all other efficacy related laboratory markers including CRP, LDH, Ferritin, platelets, WBC and ALC showed improvement on outcome day in intervention arms compared with comparator arm. Radiological findings in intervention arms also improved from enrollment day to outcome day to day-28 of enrollment.

Therefore, keeping the safety profile and efficacy data of the dmg as observed in phase-I trial, a multicenter Phase-II/Phase-III trial should be conducted to support the present healthcare repertoire with a potential treatment in this time of pandemic.

19.6 Decision of 19th CSC meeting:

The CSC appreciated the efforts & CSC will support the research in the Pakistan & when applicant forward Phase-II/III trial application will be placed before the committee. Chairman CSC also suggested that CSC should issue an appreciation letter to the applicant.

AGENDA ITEM - XX:

SIX MONTHLY PROGRESS REPORT OF D-LIVR STUDY

20.1 Six monthly progress report of D-LIVR study " A PHASE 3, MATRIX DESIGN, PARTIALLY DOUBLE-BLIND, RANDOMIZED STUDY OF THE EFFICACY AND SAFETY OF 50 MG LONAFARNIB/ 100 MG RITONAVIR BID WITH AND WITHOUT 180 MCG PEG IFN-ALFA-2A FOR 48 WEEKS COMPARED WITH PEG IFN-ALFA-2A MONOTHERAPY AND PLACEBO TREATMENT IN PATIENTS CHRONICALLY INFECTED WITH HEPATITIS DELTA VIRUS BEING MAINTAINED ON ANTI-HBV NUCLEOS(T)IDE THERAPY (D-LIVR)", forwarded by Dr. Saeed Hamid, Director, Clinical Trial Unit, Aga Khan University Hospital, Karachi.

20.2 Summary of report is as follows:

Jun 2020 to Dec 2020				
Principal Investigator	Number of subjects	Screen failed	Patients Randomized	Serious Adverse

Name/ Site No	screened			events updates
Dr. Saeed Hamid/420	32	10	11	011-420-0016 Steven Johnson syndrome

20.3 Details of Serious Adverse Event is as follows:

Serious Adverse Event: Subject 011-420-0016 Subject 011-420-0016 is a 40 years of male enrolled in a study "A Phase 3, Matrix Design, Partially Double-Blind, Randomized Study of the Efficacy and Safety of 50 mg Lonafarnib/100 mg Ritonavir BID with and without 180 mcg PEG IFN-alfa-2a for 48 Weeks Compared with PEG IFN-alfa-2a Monotherapy and Placebo Treatment in Patients Chronically Infected with Hepatitis Delta Virus Being Maintained on Anti-HBV Nucleos(t)ide Therapy (D-LIVR)" Subject relevant medical history includes Chronic Hepatitis B since 2007 and Hepatitis D since 2016. Subject randomized to Lonafarnib/Ritonavir vs Placebo (Code not broken) and PEGINTERFERON ALFA-2A (PEGINTERFERON ALFA-2A) Solution group on 02 Nov 2020. On 23rd Dec 2020 patient develop maculopapular skin rashes on trunk front and back, fever, body ache, blisters on his abdomen, rashes around the orbit, oral mucosa and conjunctivitis. Patient reported his symptoms on 25th Dec and study medication (LNF, RTV/Placebo and PEG IFN alpha-21 injection) were immediately stopped. Anti HBV therapy was continued. On 26December patient had fever, blisters and rashes on abdomen and sloughing off skin and oral mucosa. Patient was advised to visit a local physician who prescribed Fexofenadine 120mg once a day, Famotidine 40mg once a day, Tab Betamethasone 0.5mg QD, tropical glucocorticoids for lips and eyes and acetaminophen 500mg TID for fever. Patient visited AKU CTU on 28th Dec 2020. He was well oriented in time, person and place. Patient was able to swallow liquids only due to ulcers in oral cavity.

- Fever started on 23rd December 2020 and resolved on 26th December 2020. it was unlikely related to LNF/RTV/Placebo. Possibly related to PEG IFN alpha-2a. Tab Panadol 500mg BID taken from 23d Dec 2020 to 26 Dec 2020.
- Maculopapular rashes which were diffuse not painful, no pruritis, (Grade 3) present on front and back of the trunk, abdomen and palms. Blisters on the lower abdomen. Rashes appeared on 24th December and are ongoing, no medication were taken. Possibly related to LNF/RTV and probably related to PEG IFN alpha 2a injection.
- Oral Ulcers (grade 4) appears on 24h Dec 2020 and ongoing associated with halitosis, dysphagia, greyish white coated tongue, greyish white membrane on buccal mucosa, crusting on lips, gray lesions on underside of tongue. Applied glucocorticoid gel on lips. Possibly related to LNF/RTV and probably related to PEG IFN alpha 2a.
- Bilateral conjunctivitis star burning and no discharge. Tropical glucocorticoid drops TID were taken. Possibly related to LNF/RTV and probably related to PEG IFN alpha 2a.
- Fatigue (grade 2) started from 23rd December 2020 and ongoing, no medication were taken. Unlikely related to LNF/RTV and Probably related to PEG IFN alpha 2a.
- Patient also took domperidone 10mg for nausea and vomiting from 14th Dec to 24th Dec 2020. Probably related to LNF/RTV and unlikely related to PEG IFN alpha 2a.

20.4 Routine labs were conducted, serum electrolytes, CRP, CBC and blood cultures were done from the AKU lab. ECG not done due to skin lesions. Dermatology consult was taken and diagnosed as Steven Johnson Syndrome and prescribed Tab Deltacortil 5mg BID for 15 days, Rigix 10mg QD for two weeks, Xerosto ointment for the lips BID, KMNO4 wash daily and Tab Betnesol gargles TID, DeKtarin oral gel twice a day, Nilstat oral drops thrice a day, Cap Diflucon150mg OD per week for two weeks and Magic wash. Follow up planned by telephone daily and will be seen physically after two weeks, or sooner if need be.

20.5 Submitted for consideration of CSC.

20.6. *Decision of 19th CSC meeting:*

The CSC after detailed deliberation decided to defer & further it is decided that the P.I. will asked to participate in next meeting of CSC & present the report before CSC.

AGENDA ITEM - XXI:

APPLICATION FOR APPROVAL OF LABORATORY ANIMAL SCIENCES & ADVANCE RESEARCH FACILITY AT DUHS FOR PRE-CLINICAL & TOXICOLOGICAL TRIAL OF DRUGS, DRUGS SUBSTANCE & NOVEL PHARMACEUTICAL & NUTRACEUTICAL MOLECULES. F. No.08-02/2021-DD (PS)

21.1 Application submitted by Dr. Talat Roome, Director, Laboratory Animal Sciences & Advanced Research Facility, forwarded by Prof. Mohammad Saeed Quraishy, Vice Chancellor, Dow University of Health Services, Karachi, vide letter reference number: DUHS/VC/2020/12-13, dated 30th December 2020. Wherein application has been made for approval of Pre-Clinical & Toxicological Trial of Drugs, Drugs Substance & Novel Pharmaceutical & Nutraceutical Molecules at Laboratory Animal Sciences & Advanced Research Facility at Dow University of Health Sciences, Karachi.

21.2 It is submitted that submitted application is not supported with any processing fee or prescribed application form.

21.3 Further, the application is not covered under the Bio-Study Rules. As per short title & commencement of the Bio-Study Rules the scope of the rules is as follows:

> "*They shall apply to all contract research organizations, laboratories for clinical research, bioavailability & bio-equivalence study centers or organizations operating in public or private sector, involved in clinical trials of therapeutic goods and bio-availability or bio-equivalence studies on human subjects".*

21.4 Information provided by applicant was also forwarded to CSC members for review through email on 11th February2021.

21.5 Submitted for consideration of CSC.

21.6. ***Decision of 19th CSC meeting:***

The CSC after detailed deliberation decided to authorize the Chairman CSC for the constitution of inspection panel for the inspection. The case will be again placed before the CSC for further deliberations and decisions after submission of inspection report.

ITEM XXII:

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.

This division received an application from Prof. Waheed Uz Zaman Tariq, CNIC No. 37405-4949969-7 from M/s Chughtais lab, 7 jail road, Main Gulberg, Lahore wherein the applicant has requested for approval or registration of 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.** The application is on Form-II of the Bio-Study Rules 2017.

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	Page No.	Remarks
1	Application on prescribed Form-II	01-02	Attached
2	Prescribed processing fee	03	Fee of Rs.200,000/- submitted vide Challan No. 2040471 dated 16.12.2020.
3	Investigator Brochure (s)	08-61	Attached
4	Final protocol	64-170	Attached.
5	Informed consent and participant information sheet (Urdu to English)	175-208	Attached.
6	List of participating countries	01	China, Pakistan, Ecuador, Uzbekistan and Indonesia.
7	Phase of trial.	01	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.	242	Injection Vials 11000 sets 25 ZF2001 Vaccine (Clinical Trial Protocol Number = LKM-2020-NCV-GJ01. (Version : December 1, 2020 V1.0])= 17250 Injection Vials 17250

			Placebo ZF2001 (Clinical Trial Protocol Number - LKM-2020-NCV GI01 (Version : December 1, 2020-V1.0] =17250 Injection Vials 17250 Subjects distribution material (thermometer/ruler/mask) =11000 sets PPE of investigators (Masks/protective clothing/face shield/disinfectant etc.)=200 sets Urine pregnancy test & urine cup=8000 Tourniquet=2000 Blood collection vessel holder =30 Sharps box (100/box)=30box Syringe 1.0 ml)= 32000 Timer =50 Medical cotton swab= 100800 Alcohol swab (100 swabs/box) =600 boxes Blood Lancet = 26000 Blood Taking pipe= 25000 Ep pipe Ep = 25000 Cryogenic Vials = 6000. Frozen storage box = 60 Pipette Nozzle 1000µl = 50000. Pipette Nozzle 200ul = 100000 Pipette Nozzle 10ul= 50000 Pipette 1000µl = 30 Pipette 200µl = 20 Pipette 10µl = 20 Oral swab collection kits =25000 Coronavirus Nucleic Acid testing kits = 18000 Nucleic Acid Extraction Kits (Purification Kits) =18000 Nucleic acid amplification tube = 18000 COVID-19 IgM/ IgG antibody testing kits (Magnetic beat Method) = 20000
9	Site of the trial	01	Agha Khan Hospital Karachi INDUS Hospital Karachi

			UHS, Lahore. Chughtais Lab Lahore. Central Park Teaching Hospital, Lahore. Avicenna Hospital, Lahore. Shaukat Khanum Hospital, Lahore Allama Iqbal Memorial & Teaching Hospital, Sialkot. Aziz Fatima Hospital Faisalabad
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	----	Not Attached
11	Approval of National Bio-ethics Committee (NBC)	06	Attached. Ref:No.4-87/COVID-57/NBC/21/1134, Dated 11th January 2021.
12	CV's of the Investigators	171 – 172	CV of Prof. Waheed Uz Zaman Tariq Attached. Site was details of PI required.
13	GMP certificate along with COPP & free sale certificate of the investigational product.	241	GMP certificate of M/s Anhui Zhifei Biopharmaceutical co ltd attached, COPP or Free Sale Certificate not attached. Newly developed product for Clinical trial phase III.
14	Pre-clinical/clinical safety studies	46-91	Given in investigator Brochure
15	Summary of Protocol	46-91	Attached.
16	Summary of Investigator Brochure	62-63	Attached.
17	Adverse Event Reporting Form	133	Attached.
18	No of patients to be enrolled in each center.	----	Total 10,000 subjects will be recruited in Pakistan as informed by the applicant.
19	Name of Monitors & Clinical Research Associate	01	DRK Pharma Solution, Lahore. Faheem Shahzad, Talha Javed, Dr. Adeel Khan, Dr. Abdul Qaseem Khan, Laraib Khatoon, Amna Saeed Bhatti, mahir Ahmed

			Khan.
20	Evidence of registration in country of origin.	-----	Not attached
21	Copy of registration letter (if registered in Pakistan)	------	N/A
22	Sample of label of the investigational product / drug.	---	Not provided.
22	Duration of trial	20	Three months.
23	Undertaking on stamp paper.	04	Attached.

3. After evaluation following shortcomings were communicated vide this division letter dated 13th January 2021:

i) Data of Phase I & II Trial may provided.
ii) IRB approval from each trial site is required along with composition of committee i.e. names and designation of members.
iii) Separate application for each clinical trial site is required on Form 1 of Bio-Study Rules 2017.
iv) Justification for Quantity of drug / trial material to be imported is required.
v) COPP, Free sale Certificate and evidence of registration in the country of origin (if applicable) required.
vi) Detailed CV of principal investigator for each trial site is required.
vii) Soft Copy of Final Protocol, Investigator Brochure, Pre-clinical data & Safety studies and Phase I & II trial data required for onward submission to Expert is required.

4. After receiving reply of the Firm following was the evaluation.

Queries asked	**Reply of the Firm**
Data of Phase I & II trial may be provided	Attached.
IRB approval from each trial site is required along with composition of committee i.e. names and designation of members.	Following IRB Approvals attached; 1. Chughtai lab, Lahore 2. Central Park Hospital, Lahore. 3. Aziz Fatima Hospital, Faisalabad. 4. Avicenna Hospital Lahore. 4. UHS, Lahore. 5. National Hospital and Medical Center.
Separate application for each clinical trial site is required on Form 1 of Bio-Study Rules 2017.	Applications for approximately 04 sites has been submitted and evaluated.
Justification for Quantity of drug / trial material to be imported is required.	The justification of importing the amount of vaccine/ placebo mentioned is to cover the 10000 subjects (three doses) and for any loss due to

	damage to vial during cold chain transportation and storage and also breakage (page246/corr.). Further, representative of DRK verbally told that they will import vaccine/ placebo as per approval by CSC other medicines mentioned in the list will be purchased locally.
COPP, Free sale Certificate and evidence of registration in the country of origin (if applicable) required.	The product has not been yet registered in any country and hence phase III trial.
Detailed CV of principal investigator for each trial site is required.	CVs of Prof. Waheed Uz zaman Tariq (Chughtai lab) Dr. Aun Raza (SKMH&RC) Dr. Muhammad Ahmed (Central parks Medical College and Hospital) Dr. Waheed Ahmed (Avicenna Medical College and Hospital) Dr. Awais Aslam (Aziz Fatima Hospital) Prof. Muhammad Ishaque (National Hospital and Medical Center) Prof. Javaid Akram (UHS) Are attached.
Soft Copy of Final Protocol, Investigator Brochure, Pre-clinical data & Safety studies and Phase I & II trial data required for onward submission to Expert is required.	Has been provided on USB

9. It was requested that file may be forwarded for nomination of Expert for evaluation of Study material under rule 7(4) of Bio-Study Rules 2017. The Higher Authorities directed to include in the agenda and same with the relevant experts of CSC.

10. Submitted for consideration of CSC.

11. ***Decision of 19th CSC meeting:***

The CSC after detailed deliberation decided to approve the clinical trial titled "A Phase III Randomized, Double Blind, Placebo Controlled Clinical Trial in 18 Years of Age & Above to Determine the Safety and Efficacy of ZF2001, A Recombinant Novel Corona Vaccine (Cho Cell) for Prevention of COVID-19", to be conducted at Aga Khan University Hospital, Karachi, National Hospital & Medical Center, Lahore & University of Health Sciences Lahore, as these are already approved sites. Further it is also decided by CSC the quantity already mentioned in the application for import of the investigational medicinal products (IMPs) & other related materials used in the trial allowed to import at once.

2. Trial progress reports will be submitted after every two weeks & if there is any SAEs or AEFIs then will be reported within 24 hours.

ITEM XXIII:

APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE FROM ABDUL WAHEED TRUST HOSPITALS/ INSTITUTIONS AS CLINICAL TRIAL SITE.

This is an application from Abdul Waheed Sheikh CNIC No.35201-1304557-7 of M/s Abdul Waheed Trust, Avicenna Medical college & Hospital phase IX, DHA, Bedian road, Lahore wherein he has applied for Clinical trial site situated at Avicenna Medical college & Hospital Bedian road Lahore for Phase II, III & IV Clinical Trials. Application is on Form -I of the Bio-Study Rules 2017 with prescribed 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.	06-07	Attached
2	Prescribed processing fee	04-05	Fee challan of Rs.100,000/- attached submitted vide slip No. 2047926 dated 20th January 2021.
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).	45-113	Attached
4	Details of premises including layout plan of the site.	114-139	Attached
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	---	Not Attached
6	Names and qualifications of the above sections along with their staff.	09	Training list of participants is attached, whereas required list of section wise staff with their qualification is not provided.

7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	10-27	Attached
8	Undertaking on stamp paper	06	Attached.

3. After evaluation, it was noticed that application is from Abdul Waheed Sheikh, chairman Abdul Waheed Trust. Under the Umbrella of Abdul waheed Trust, Avicenna Medical college, Avicenna Hospital, Avicenna dental College and hospital, Gulfreen Nursing College and Institute of Allied Health sciences are working. Applicant has attached the documents of all above mentioned site,

4. Applicant may be asked to specific clinical trial site along with documents of that particular site. The same was discussed with representative of applicant and he informed that Avicenna Hospital is the Clinical trial site and later on submitted documents.

5. Submitted documents were evaluated according to 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.	140	Attached. Applicant has mentioned Avicenna Hospital as Clinical Trial Site. Form -1 is without signature.
2	Prescribed processing fee	04-05	Fee challan of Rs.100,000/- attached submitted vide slip No. 2013368 dated 25th January 2021.
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).	164-183	Attached.
4	Details of premises including layout plan of the site.	154-155 186-187	Layout plan of Dental College is attached.
5	Details of the section wise equipment and machinery	180-192	Attached

	required for the analytical or bio-analytical and clinical studies.		
6	Names and qualifications of the above sections along with their staff.	193-197	Attached
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	10, 199-218	This hospital claims following allied services: 1. Doctor Consultation & Personalized Care Plan. 2. Assisting with walking and transferring from bed to wheelchair. 3. Ambulatory Support. 4. Administration & Monitoring of Medication (Injection, IV Infusion etc.) 5. Wound Care & Dressing. 6. Vitals Monitoring. 7. Home Nursing Care. 8. Transportation to rehabilitation sessions, doctor appointments and personal events. 9. Quality Ambulance service to move patients. 10. High Quality Health Care services for our patients. 11. First Aid services for patients. 12. Hospital is equipped with high quality Intense Care Unit (ICU). 13. Hospital Also has Home Patients Service (Doctors can visit home). 14. Home Patients Physiotherapy services Attached

5. Applicant may be asked to submit signed Form-I and Details of premises including layout plan of the site instead of layout plan of dental college. It was decided that formalities may be fulfilled before issuing license.

6. Submitted for consideration of CSC.

7. ***Decision of 19th CSC meeting:***

The CSC after detailed deliberation decided to authorize the Chairman CSC for the constitution of inspection panel for the inspection of M/s Abdul Waheed Trust, Avicenna Medical

college & Hospital, Lahore. The case will be again placed before the CSC for further deliberations and decisions after submission of inspection report. Meanwhile applicant is directed to fulfill all prerequisite as per the Bio-Study Rules.

ITEM XXIV:

APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE FROM AZIZ FATIMA HOSPITAL FAISALABAD.

This is an application from Dr Awais Aslam, NIC No.33106-6290792-5 of M/s Aziz Fatima Hospital, Faisalabad has applied to act as Clinical Trial Site for phase-III clinical trials. Application is on Form-I of the Bio-Study Rules 2017 with prescribed fee of Rs.100,000/- deposited vide slip No. 2013369 dated 29th January 2021.

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.	05-06	Attached.
2	Prescribed processing fee	03	Fee challan of Rs.100,000/- attached submitted vide slip No. 2013369 dated 29th January 2021.
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).	---	Not Attached
4	Details of premises including layout plan of the site.	08	Firm has attached the readable layout plan of OPD 2nd Floor.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	17	Firm has attached that following material in phase III trial for covid-19 vaccine. Chairs 22 Tables 14 Bed 06 BP Apparatus 02 Oxygen cylinder 01

			Respirator 01 Ventilator 01 Refrigerator (2-8°C) 02 Partition curtains for 5 rooms Medicines Emergency kits and First Aid Stethoscopes 02 Inert facility 01 Telephone Set 02 Pulse Oximeter 02
6	Names and qualifications of the above sections along with their staff.	11	List of Trial staff is attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	13	Following specialized staff will be available at site during trial. Medical Consultant 02 Gynecologist Consultant 02 Pulmonologist consultant 01 Surgical consultant 01 2.Establishment of Emergency Room at the trial site with 24 hours availability of medical officer. 3. General Emergency ward of Aziz Fatima hospital. 4. For serious patients, 23 bedded ICU/ HDU of Aziz Fatima Hospital including all the required staff/ equipment and 07 ventilators. 5. for PCR positive cases, Covid-19 isolation ward already established at Aziz Fatima Trust hospital with 03 dedicated ventilators.
8	Undertaking on stamp paper	06	Attached.

3. After initial scrutiny following shortcomings observed:
   i. Particulars regarding the legal status is need to be provided.
   ii. Soft copy of the application is required for CSC.
4. Submitted for consideration of CSC.
5. ***Decision of 19th CSC meeting:***

The CSC after detailed deliberation decided to authorize the Chairman CSC for the constitution of inspection panel for the inspection of M/s Aziz Fatima Hospital, Faisalabad. The case will be again placed before the CSC for further deliberations and decisions after submission of inspection report. Meanwhile applicant is directed to fulfill all prerequisite as per the Bio-Study Rules.

ITEM XXV:

APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE FROM CENTRAL PARK TEACHING HOSPITAL LAHORE.

The case is an application from Dr. Muhammad Ahmed, NIC No.31304-4798820-7 of M/s Central Park Teaching Hospital, Lahore has applied to act as Clinical Trial Site for phase-II, III & IV clinical trials. Application is on Form-I of the Bio-Study Rules 2017 with prescribed fee of Rs.100,000/- deposited vide slip No. 2013370 dated 3rd February 2021.

2. The 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.	09-10	Attached.
2	Prescribed processing fee	03	Fee challan of Rs.100,000/- attached submitted vide slip No. 2013370 dated 3rd February 2021.
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).	---	Not Attached
4	Details of premises including layout plan of the site.	13	Layout Plan for 1st Floor attached (Not readable). Details are not provided.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	---	Not Attached
6	Names and qualifications of the above sections along with their staff.	15-18	Attached.
7	Details of the allied	12	The applicant has provided the following

	facilities associated with the trial center including ambulatory services, emergency handling etc.		names. 1. Ambulance 2. ICU 3. Emergency 4. Indoor 5. Cardiology 6. Pulmonology 7. Medicine Applicant has given the names of above facilities but details are not provided.
8	Undertaking on stamp paper	10	Attached.

3. After initial scrutiny following shortcomings observed:

iii. 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, is required.

iv. Details of premises including readable layout plan of the site is required.

v. Details of the section wise equipment and machinery required clinical studies is required.

vi. Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.

vii. Soft copy of the application is required for CSC.

4. Submitted for consideration of CSC.

5. Decision of 19th CSC meeting:

The CSC after detailed deliberation decided to authorize the Chairman CSC for the constitution of inspection panel for the inspection of M/s Central Park Teaching Hospital, Lahore. The case will be again placed before the CSC for further deliberations and decisions after submission of inspection report. Meanwhile applicant is directed to fulfill all prerequisite as per the Bio-Study Rules.

ITEM XXVI:

APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE FROM CHUGTAI LAB LAHORE.

The case is an application from Prof. Omar Rasheed Chughtai, NIC No.91509-0100470-1 of M/s Chughtai Lab Head Office, o7 Jail Road, Lahore has applied to act as Clinical Trial Site for phase-II, III & IV clinical trials. Application is on Form-I of the Bio-Study Rules 2017 with prescribed fee of Rs.100,000/- deposited vide slip No. 2043412 dated 27th January 2021.

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.	05-06	Application on Form-I of Bio-study Rules 2017. But application is signed by Prof. Waheed Uz Zaman Tariq instead of applicant i.e. Omar Rasheed Chughtai.
2	Prescribed processing fee	03	Fee challan of Rs.100,000/- attached submitted vide slip No. 2043412 dated 27th January 2021.
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).	---	Not Attached
4	Details of premises including layout plan of the site.	08	Firm has attached the layout plan of 2nd floor.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	---	Not Attached
6	Names and qualifications of the above sections along with their staff.	09	Section wise list of staff not provided. Firm has provided total staff list of Chughtai lab.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	10	The applicant has provided the following names. 8. Chughtai home Nursing care 9. Ambulance to move patients. 10. Sehat Services include injection, drips etc. 11. Sehat services at Chughtai Medical center. 12. First aid services. 13. ICU. 14. Doctors visit at home. 15. Physiotherapy at home. 16. First Aid at corporate Level.

			Details of ambulatory services, emergency handling etc. are required.
8	Undertaking on stamp paper	06	Attached but not signed by the applicant.

3. After initial scrutiny following shortcomings observed:

viii. Form-I along with undertaking duly signed by the applicant is required.

ix. Particulars regarding the legal status is need to be provided.

x. Details of premises required.

xi. Details of the section wise equipment and machinery need to be provided.

xii. Names and qualifications of the section wise staff need to be provided.

xiii. Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.

xiv. Soft copy of the application is required for CSC.

3. Later on, applicant submitted some documents. Following is the evaluation as per Form-I of the Bio-Study rules 2017.

S. No.	Required Documents / Information	Page No.	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	05-06 25	Application on Form-I of Bio-study applicant has submitted the undertaking with changed signatures.
2	Prescribed processing fee	03	Fee challan of Rs.100,000/- attached submitted vide slip No. 2043412 dated 27th January 2021.
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).	20-24A	Attached
4	Details of premises including layout plan of the site.	08	Firm has attached the layout plan of 2nd Floor.
	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	28	Applicant has provided the Chughtai lab head office equipment list.
	Names and qualifications of the above sections along with their staff.	09 29	Section wise list of staff not provided. Firm has provided total staff list of Chughtai lab. Applicant has further provided the list of personnel operating lab equipment's.
	Details of the allied facilities associated with the trial center including ambulatory	10 30-41	The applicant has provided the following names.

	services, emergency handling etc.		1. Chughtai home Nursing care 2. Ambulance to move patients. 3. Sehat Services include injection, drips etc. 4. Sehat services at Chughtai Medical center. 5. First aid services. 6. ICU. 7. Doctors visit at home. 8. Physiotherapy at home. 9. First Aid at corporate Level. Applicant has further attached the following documents • Home Care services agreement. • Term and Conditions for Vaccination • Term and conditions for Injection and Drips. • Intravenous line consent form • Patient information form • Patient care check list Details of ambulatory services, emergency handling etc. are required.
	Undertaking on stamp paper	06 25	Attached but not signed by the applicant. Applicant has submitted undertaking with changed signatures.

5. Submitted for consideration of CSC.

6. Decision of 19th CSC meeting:

The CSC after detailed deliberation decided to authorize the Chairman CSC for the constitution of inspection panel for the inspection of M/s Chughtai Lab, Lahore. Prof. Dr. Javed Akram & Dr. Farhana Badar will be the part of inspection panel, as they have already inspected the premises for Bioanalytical Laboratory. The case will be again placed before the CSC for further deliberations and decisions after submission of inspection report. Meanwhile applicant is directed to fulfill all prerequisite as per the Bio-Study Rules.

ITEM XXVII:

APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE FROM NATIONAL HOSPITAL AND MEDICAL CENTER LAHORE.

Application is from Prof. Dr. Muhammad Ishaq, NIC No.42201-1636805-3 of M/s National Hospital & Medical Center, Lahore. Wherein application is submitted for approval of Department of ENT, National Hospital & Medical Center, Lahore to act as Clinical Trial Site for phase-III

clinical trials. Application is on Form-I of the Bio-Study Rules 2017 with prescribed fee of Rs.100,000/- deposited vide slip No. 2013368 dated 25th January 2021.

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.	06-07	Attached
2	Prescribed processing fee	04-05	Fee challan of Rs.100,000/- attached submitted vide slip No. 2013368 dated 29th January 2021.
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).	---	Not Attached
4	Details of premises including layout plan of the site.	08	Only layout plan attached which is unreadable whereas details regarding premises is not provided.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	---	Not Attached
6	Names and qualifications of the above sections along with their staff.	09	Training list of participants is attached, whereas required list of section wise staff with their qualification is not provided.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	10	This hospital claims following allied services: 1. Doctor Consultation & Personalized Care Plan. 2. Assisting with walking and transferring from bed to wheelchair. 3. Ambulatory Support. 4. Administration & Monitoring of

			Medication (Injection, IV Infusion etc.) 5. Wound Care & Dressing. 6. Vitals Monitoring. 7. Home Nursing Care. 8. Transportation to rehabilitation sessions, doctor appointments and personal events. 9. Quality Ambulance service to move patients. 10. High Quality Health Care services for our patients. 11. First Aid services for patients. 12. Hospital is equipped with high quality Intense Care Unit (ICU). 13. Hospital Also has Home Patients Service (Doctors can visit home). 14. Home Patients Physiotherapy services Details of ambulatory services, emergency handling etc. are required.
8	Undertaking on stamp paper	07	Attached.

3. After initial scrutiny following shortcomings observed:

i. Particulars regarding the legal status is need to be provided.
ii. Details of premises including readable copy of layout plan of the site need to be provided.
iii. Details of the section wise equipment and machinery need to be provided.
iv. Names and qualifications of the section wise staff need to be provided.
v. Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.

4. Later on, applicant submitted some more documents and higher authorities also informed that the National Hospital and Medical center is already approved clinical trial site.

5. Submitted for consideration of CSC.

6. Decision of 19th CSC meeting:

The CSC after detailed deliberation decided to authorize the site to conduct 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". The site is already approved.

ITEM XXVIII:

APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE FOR "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." FROM UNIVERSITY OF HEALTH SCIENCES, LAHORE.

M/s University of Health Sciences, Lahore has submitted the documents. These documents include application on Form II of Bio-Study rules 2017 for approval or registration of clinical trial titles "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 coronavirus vaccine (CHO cell) for prevention of COVID-19."

19. Applicant has also attached undertaking on stamp paper along with Form-II, layout plan, IRB approval, copy of license to Act as clinical Trial site and a notification that states that following hospital and health facilities are nominated to handle any suspected adverse events experienced by volunteers participating in COVID-19 trials including ZF2001, at university of Health sciences, Lahore

1. Sheikh Zaid Hospital, Lahore.

2. Jinnah Hospital, Lahore.

3. Akram Medical Complex, Lahore.

20. Application for the study titles "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 coronavirus vaccine (CHO cell) for prevention of COVID-19." that has already been applied by Prof. Waheed Uz Zaman Tariq, CNIC No. 37405-4949969-7 from M/s Chughtais lab, 7 jail road, Main Gulberg, Lahore and University of Lahore is a Clinical Trial Site for this Study.

21. As per License issued to University of Health Sciences (UHS) the wording on License is that "M/s university of Health Sciences, Lahore is hereby licensed to act as Clinical trial Site for Phase III, Double Blind, placebo-controlled, randomized clinical trial of recombinant novel corona Virus vaccine (Adenovirus type 5 vector)". Now, Prof. Waheed Uz Zaman Tariq, has nominated UHS as clinical trial site for study 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 coronavirus vaccine (CHO cell) for prevention of COVID-19."

22. Guidance was sought that can UHS act as Clinical trial site based on previously issued license for this new study or a new application along with fee is required from UHS for this new study.

23. Replied by the higher Authorities that as licence has been issued on Form V and application of licence was filed on Form-I under rule 3, if particulars are different from the application from the license it needs correction by CSC.

23. Included in agenda for corrigendum after perusal of CSC.

24. Submitted for consideration of CSC.

25. *Decision of 19th CSC meeting:*

The CSC after detailed deliberation decided to authorize the site to conduct 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". The site is already approved.

ITEM XXIX:

CLINICAL TRIAL OF INDIGENIOUS VENTILATORS (PAKVENT-I VENTILATOR)

Application is from Muhammad, CNIC No. 36302-0466539-7 from M/s Project Management Organization wherein he has applied for clinical validation of Pakvent-1 Ventilator. The application is on Form-II of the Bio-Study Rules 2017 along with fee challan of Rs.200,000/.

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	Page No.	Remarks
1	Application on prescribed Form-II	04-05	Attached
2	Prescribed processing fee	02-03	Fee of Rs.200,000/- submitted vide Challan No. 2077447 dated 14.01.2021.
3	Investigator Brochure (s)	7-18	Attached but not as per ICH guidelines.
4	Final protocol	50-64	Clinical validation protocol for Pakistan manufactured ventilator system (PMVS) prepared by PEC is attached.
5	Informed consent and participant information sheet (Urdu to English)	72-77	Attached.
6	List of participating countries	04	Pakistan.
7	Phase of trial.	04	**Final Trial.** Phase of trial needs to properly described i.e. Phase I.II,III or IV.

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.	04	01 ventilator
9	Site of the trial	04	CMH Rawalpindi (Not approved as clinical trial site by DRAP)
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	----	Not Attached
11	Approval of National Bio-ethics Committee (NBC)	70	Attached. Ref:No.4-87/EMD-VENT-02/NBC/21/1123 dated January 08, 2021.
12	CV's of the Investigators	----	Not Attached
13	GMP certificate along with COPP & free sale certificate of the investigational product.	----	Not Attached
14	Pre-clinical/clinical, safety studies	19-49	No clinical and safety studies Attached
15	Summary of Protocol	----	Not Attached
16	Summary of Investigator Brochure	18	Attached but not as per ICH guidelines.
17	Adverse Event Reporting Form	109	Attached
18	No of patients to be enrolled in each center.	----	Not Attached
19	Name of Monitors & Clinical Research Associate	04	Capt. Raheel, Maj. Mudassar
20	Evidence of registration in country of origin.	-----	Not attached
21	Copy of registration letter (if registered in Pakistan)	----	Not Attached
22	Sample of label of the investigational product / drug.	----	Not Attached
22	Duration of trial	04	03 Months
23	Undertaking on stamp paper.	----	Not Attached

3. After evaluation, as per checklist provided in bio-Study Rules 2017, following shortcomings were observed.

i. Investigator Brochure (s) is not as per ICH guidelines.
ii. Clinical validation protocol for Pakistan manufactured ventilator system (PMVS) prepared by PEC is attached instead of final protocol.
iii. Written as **Final Trial.** Phase of trial needs to properly described i.e. Phase I, II, III or IV.
iv. Separate application on Form-I is required for approval of clinical trial site i.e. CMH Rawalpindi.
v. Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members, is not attached.
vi. GMP certificate along with COPP & free sale certificate of the investigational product is not attached.
vii. CV's of the Investigators not attached.
viii. Pre-clinical/clinical, safety studies are not attached.
ix. Summary of Protocol not attached.
x. Summary of Investigator Brochure is not as per ICH guidelines.
xi. No of patients to be enrolled in each center not described.
xii. Evidence of registration in country of origin not attached.
xiii. Copy of registration letter (if registered in Pakistan) not attached.
xiv. Sample of label of the investigational product / drug not attached.
xv. Undertaking on stamp paper not attached.

4. After scrutiny of the documents above mentioned shortcomings has been noted and requested due to limited knowledge of ventilators that file may be evaluated by person having some know how about ventilators or may be evaluated by seniors having grip on the ventilators.

5. Application has not been evaluated by any person having the knowledge on ventilators.

5. Further it is added that Expert group for Assessment/ evaluation of locally manufactured devices (Ventilators) was constituted by DRAP vide letter No. 16-5/2020 dated 3rd April & 4th April 2020. The third meeting of Expert Committee of Locally manufactured Ventilators. 3rd Meeting of expert committee on evaluation / Assessment of locally manufactured ventilators was held on 3rd July, 2020 and decided as follows: -

Decision:

In the end of meeting, Maj Gen Aslam Khan said that he won't agree with clinical testing of ventilators in the absence of simulator for ventilators. Since the ventilators have not gone through the routine procedures of simulation, animals testing, healthy volunteers and patients testing, therefore, testing through simulators for ventilators must be mandatory. In case the testing through simulators is not possible, then DRAP ethic committee approval should be solicited. Ethic committee should decide that due to COVID-19 these ventilators should not go through animal, healthy volunteers and patients testing. Dr. Abdur Rasheed briefed the participants that ethic committee is not in the mandate of DRAP, rather it is working as National Bio-Ethic Committee (NBC) in Pakistan Health and Research Council (PHRCH) under Ministry of National Health Services Regulation and Coordination. If the committee decided to go through the NBC then PEC should apply to NBC as an applicant for all the ventilators. After the approval of Expert Committee

on ventilators the PEC would individually apply to Clinical Study Committee as per the provision of Bio-Study Rules, 2017.

6. Further the DRAP vide letter No.F.6-5/2020-MD dated 13.04.2020 advised that "No ventilators shall be used on patients without prior approval of expert group on ventilators".

7. The decision of the Expert Group on ventilators was placed in CSC meeting held on 27.11.2020 and CSC decided as following;

Decision of 16th CSC meeting:

Dr. Muhammad Fakhruddin Aamir, Director (MDMC) /Chairman, Medical Device Board gave a detailed presentation for the mechanism to be adopted for the registration of locally manufactured medical devices/Ventilators. The committee after detailed deliberation and discussion made the following decisions;

- ***The Dr. Faiza Bashir (Member, CSC) informed the committee that NBC has asked different queries regarding electromedical devices development from PEC and their reply is still awaited. However, NBC is in the process of developing the SOP/guidelines for the clinical validation of locally manufactured electromedical devices (ventilators etc.) which will be finalized soon. The CSC advised Dr. Faiza Bashir, for sharing of guidelines after finalization, with the committee.***
- ***The applicants will apply to the Division of Pharmacy Services directly along with recommendations of Pakistan Engineering Council under Bio Study Rules, 2017.***

8. Accordingly, letters were written to Engr. Brig. Tariq Javaid (PEC), Dr. Faiza Bashir (NBC-PHRC) and three manufacturers.

9. In the light of above application is submitted for perusal of CSC.

10. Director MD&MC joined the meeting & briefed regarding applications received for ventilators and suggested that only manufacturer will authorize to apply for registration of ventilators. PEC has only role for technical aspects, it can't be an applicant for any application regarding ventilators.

11. ***Decision of 19th CSC meeting:***

The CSC after detailed deliberation decided to constituted a sub-committee which will be comprised of following experts:

i. *Biomedical engineers*
ii. *Anesthetist*
iii. *Pulmonologist*
iv. *Dr. Faiza Basheer*
v. *Prof. Dr. Javed Akram*
vi. *Dr. Abdur Rasheed*
vii. *Any other expert co-opted by the sub-committee.*

2. The Sub-committee will develop TORs & proforma for evaluation & inspection of ventilator trial applications.

3. CSC constituted following panel for inspection of ventilators trial application of Lahore region:

i. Prof. Dr. Javed Akram, V.C. UHS, Lahore. (Chairman)
ii. Dr. Farhana Badar
iii. Dr. Faheem Butt, Pulmonologist (from Shaukat Khanum Cancer Hospital & Research Center.
iv. Biomedical engineers (from Sheikh Zayed Hospital, Lahore.)
v. Prof. Dr. Sajjad Kazmi, Sheikh Zayed Hospital, Lahore.

4. CSC constituted following panel for inspection of ventilators trial application of Islamabad region:

i. Dr. Abdur Rashid, Chairman CSC-DRAP (Chairman)
ii. Maj. Gen. (Retd) Aslam
iii. Brig. (Retd) Muzammil Hassan Najmi
iv. Prof. Dr. Iqbal Memon, HOD Anesthesia, PIMS, Islamabad.
v. Dr. Afrasayab, Biomedical Engineer, NUST, Islamabad.
vi. Muhammad Mubashir Aslam, G.M. Plant, Innovative Health Technology, NUST, Islamabad.

5. Inspection panel may co-opt any relevant experts for the inspection. Further it is also decided that application for ventilators included in this meeting, inspection will be carried out without proforma.

6. Proforma will be developed by sub-committee later on.

ITEM XXX:

CLINICAL TRIAL OF INDIGENIOUS VENTILATORS (I-LIVE VENTILATOR)

This case an application from Dr. Jawad Hayder Meghji, CNIC No. 61101-19211575-1 from M/s Al-Technique Corporation of Pakistan Ltd., 4th Floor, Dhody Building, 52-E, Jinnah Avenue, P.O. Box 1878, Islamabad has applied for approval or registration of clinical trial, titled i-live Ventilator. The application is on Form-II of the Bio-Study Rules 2017 along with fee challan of Rs.200,000/.

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	Page No.	Remarks
1	Application on prescribed Form-II	03-04	Attached
2	Prescribed processing fee	03	Fee of Rs.200,000/- submitted

			vide Challan No. 2025535 dated 14.01.2021.
3	Investigator Brochure (s)	----	Not Attached
4	Final protocol	----	Not Attached
5	Informed consent and participant information sheet (Urdu to English)	05-07	Only consent form in English is attached.
6	List of participating countries	03	Pakistan.
7	Phase of trial.	03	Final Phase, 96 Hours
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.	03	01 ventilator
9	Site of the trial	03	Jinnah hospital Lahore
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	----	Not Attached
11	Approval of National Bio-ethics Committee (NBC)	----	Not Attached
12	CV's of the Investigators	----	Not Attached
13	GMP certificate along with COPP & free sale certificate of the investigational product.	----	Not Attached
14	Pre-clinical/clinical safety studies	----	Not Attached
15	Summary of Protocol	----	Not Attached
16	Summary of Investigator Brochure	----	Not Attached
17	Adverse Event Reporting Form	----	Not Attached
18	No of patients to be enrolled in each center.	----	Total 10,000 subjects will be recruited in Pakistan as informed by the applicant.
19	Name of Monitors & Clinical Research Associate	----	Not Attached
20	Evidence of registration in	-----	Not attached

	country of origin.		
21	Copy of registration letter (if registered in Pakistan)	----	Not Attached
22	Sample of label of the investigational product / drug.	----	Not Attached
22	Duration of trial	03	96 Hours
23	Undertaking on stamp paper.	----	Not Attached

3. After evaluation, it was observed that no document is attached as per checklist provided in bio-Study Rules 2017 except Fee, form II and patient consent in English.

4. It was communicated to Applicant vide this office letter dated 25.01.2021 submit all the documents as per checklist provided in Bio-study Rules 2017. Reply of the applicant is still awaited.

5. Submitted for consideration and perusal of CSC.

6. *Decision of 19th CSC meeting:*

The CSC after detailed deliberation decided to constituted a sub-committee which will be comprised of following experts:

viii. Biomedical engineers
ix. Anesthetist
x. Pulmonologist
xi. Dr. Faiza Basheer
xii. Prof. Dr. Javed Akram
xiii. Dr. Abdur Rasheed
xiv. Any other expert co-opted by the sub-committee.

2. The Sub-committee will develop TORs & proforma for evaluation & inspection of ventilator trial applications.

3. CSC constituted following panel for inspection of ventilators trial application of Lahore region:

vi. Prof. Dr. Javed Akram, V.C. UHS, Lahore. (Chairman)
vii. Dr. Farhana Badar
viii. Dr. Faheem Butt, Pulmonologist (from Shaukat Khanum Cancer Hospital & Research Center.
ix. Biomedical engineers (from Sheikh Zayed Hospital, Lahore.)
x. Prof. Dr. Sajjad Kazmi, Sheikh Zayed Hospital, Lahore.

4. CSC constituted following panel for inspection of ventilators trial application of Islamabad region:

vii. Dr. Abdur Rashid, Chairman CSC-DRAP (Chairman)
viii. Maj. Gen. (Retd) Aslam
ix. Brig. (Retd) Muzammil Hassan Najmi
x. Prof. Dr. Iqbal Memon, HOD Anesthesia, PIMS, Islamabad.

xi. Dr. Afrasayab, Biomedical Engineer, NUST, Islamabad.

xii. Muhammad Mubashir Aslam, G.M. Plant, Innovative Health Technology, NUST, Islamabad.

5. Inspection panel may co-opt any relevant experts for the inspection. Further it is also decided that application for ventilators included in this meeting, inspection will be carried out without proforma.

6. Proforma will be developed by sub-committee later on.

ITEM XXXI:

APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE FROM JINNAH HOSPITAL LAHORE.

It is an application from Dr. Jawad Hayder Meghii CNIC 61101-1921571-1 of M/s Al-Technique Corporation of Pakistan Ltd. 4th Floor, Dhodhy Building, 52-E, Jinnah Avenue, P.o. Box 1878, Islamabad. Ph:051-2604657, Fax:051-2829692. Has applied for the grant of license to the site for centers or clinical trial site or CRO or laboratory, situated at Jinnah 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.	01	Attached
2	Prescribed processing fee	02	Fee challan of Rs.100,000/- attached submitted vide slip No. 2025540 dated 14th January 2021.
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).	----	Not attached.
4	Details of premises including layout plan of	-----	Not Attached

	the site.		
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	-----	Not Attached
6	Names and qualifications of the above sections along with their staff.	------	Not Attached
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	-----	Not Attached
8	Undertaking on stamp paper	-----	Not Attached.

3. After evaluation, following shortcomings were found and communicated to applicant vide DRAP letter No. 22.01.2021.

i. Application should be from Principal investigator of Clinical Trial Site.
ii. 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) is required.
iii. Details of premises including layout plan of the site is required.
iv. Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies is required.
v. Names and qualifications of the above sections along with their staff is required.
vi. Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc. are required.
vii. Undertaking on stamp paper is required.
viii. Soft Copy of application required for onward submission to CSC.

4. Reply of the applicant is still awaited.

5. Submitted for consideration and perusal of CSC.

6. *Decision of 19th CSC meeting:*

The CSC after detailed deliberation decided to constituted a sub-committee which will be comprised of following experts:

i. Biomedical engineers
ii. Anesthetist
iii. Pulmonologist
iv. Dr. Faiza Basheer

v. *Prof. Dr. Javed Akram*
vi. *Dr. Abdur Rasheed*
vii. *Any other expert co-opted by the sub-committee.*

2. The Sub-committee will develop TORs & proforma for evaluation & inspection of ventilator trial applications.

3. CSC constituted following panel for inspection of ventilators trial application of Lahore region:

i. *Prof. Dr. Javed Akram, V.C. UHS, Lahore. (Chairman)*
ii. *Dr. Farhana Badar*
iii. *Dr. Faheem Butt, Pulmonologist (from Shaukat Khanum Cancer Hospital & Research Center.*
iv. *Biomedical engineers (from Sheikh Zayed Hospital, Lahore.)*
v. *Prof. Dr. Sajjad Kazmi, Sheikh Zayed Hospital, Lahore.*

4. CSC constituted following panel for inspection of ventilators trial application of Islamabad region:

i. *Dr. Abdur Rashid, Chairman CSC-DRAP (Chairman)*
ii. *Maj. Gen. (Retd) Aslam*
iii. *Brig. (Retd) Muzammil Hassan Najmi*
iv. *Prof. Dr. Iqbal Memon, HOD Anesthesia, PIMS, Islamabad.*
v. *Dr. Afrasayab, Biomedical Engineer, NUST, Islamabad.*
vi. *Muhammad Mubashir Aslam, G.M. Plant, Innovative Health Technology, NUST, Islamabad.*

5. Inspection panel may co-opt any relevant experts for the inspection. Further it is also decided that application for ventilators included in this meeting, inspection will be carried out without proforma.

6. Proforma will be developed by sub-committee later on.

ITEM XXXII:

RECOGNITION OF PAKISTAN INSTITUTE OF OPHTHAMOLOGY, AL SHIFA TRUST EYE HOSPITAL RAWALPINDI AS CLINICAL TRIAL SITE BY DRAP.

Brig (R) Rizwan Ullah Asghar (Executive Director) NIC number 31202-0257073-I of M/s ……Nil……..Business address and telephone number and fax number ……nil…….. has applied for renewal of license of clinical trial site. Applicant has applied for renewal of Clinical trial site while as per this office record, DRAP has not issued the license to this applicant. Rule 3 (2) of Bio-Study Rules 2017 states that (2) Every such application shall be accompanied with all the necessary records, information, documents, data and a non-refundable fee as specified under the Act. The fee shall be paid in the bank account of DRAP' Incomplete applications shall not be received. It was requested that application may not be entertained and applicant may be asked to submit new application for issuance of license for clinical trial along with all relevant documents.

2. Later on, applicant submitted application that was 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.	45	Attached
2	Prescribed processing fee	53-55	Fee challan of Rs.100,000/- & Rs.30/- attached submitted vide slip No. 2025528 & 2025529 respectively.
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).	-----	Not attached.
4	Details of premises including layout plan of the site.	11-33	Layout plan attached but not readable/ understandable. Details of premises not provided. May be verified by panel at the time of inspection.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	78-79	List of equipment is not as per minimum equipment list approved by CSC in its 2nd meeting.
6	Names and qualifications of the above sections along with their staff.	05-29	Section wise details regarding personal/ experts not provided whereas CVs of followings are attached. 1. Brig. (R) Rizwan Ullah Asghar 2. Dr. Wajid Ali Khan 3. Dr. Umme Sughra
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	89-95	Not attached.
8	Undertaking on stamp paper	60	Attached.

3. After evaluation it was found that applicant has attached extra documents. These documents are related to Alza Pharmaceuticals, Alshifa Eye Trust kohat, Muzafraabd and Sukkur etc. in the light of evaluation firm may be asked to provide following documents.

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. Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.

iii. Names and qualifications of the above sections along with their staff.

iv. Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.

v. Soft copy of application to be forwarded to CSC experts for consideration please.

4. The Director Pharmacy Services telephonically communicated Brig. (R) Rizwan on 20.01.2021 and asked him to provide the trust documents, soft copy etc. till tomorrow noon. The Chairman CSC further constituted the following panel.

Brig. (R) Muzammil Hussain Najmi
Dr. Rizwana Chaudhary
Dr. Farhana Badar
Mr. Adnan Faisal Saim
Dr. Abdur Rashid (coordinator)

5. Applicant did not submitted reply but Anyhow following members of panel conducted the inspection on 20.01.2021.

Dr. Abdur Rashid, Director Pharmacy Services, DRAP, Islamabad.
Prof. Brig. (R) Muzammil Hussain Najmi, Foundation University, Islamabad.
Adnan Faisal Saim, Deputy Director (PS), DRAP, Islamabad.

6. Remarks of inspection team are followings;

"Keeping in the view the facilities, Infrastructure, Equipment, IT system, Record and Documentation, Human resources, training and experience, panel unanimously recommended to Al-Shifa Trust eye Hospital Jhelum Road, Rawalpindi"

7. Panel has recommended for Approval the Al-Shifa Research Center, Al-Shifa Trust Eye Hospital, Jhelum Road, Rawalpindi.

8. Submitted for consideration of CSC.

9. *Decision of 19th CSC meeting:*

The CSC after detailed deliberation and as per inspection panel recommendations decided to approve M/s Al Shifa Trust Eye Hospital Rawalpindi, as Clinical Trial Site to conduct all clinical trials including trials related to eye.

ITEM XXXIII:

APPLICATION FOR APPROVAL OF CLINICAL TRIAL SITE BY MAROOF INTERNATIONAL HOSPITAL, ISLAMABAD.

Application is from Haroon Naseer CNIC 61101-7639943-3 of M/s Maroof International Hospital, 10th Avenue, F-10 Markaz, Islamabad has applied to act as Clinical trial Site for phase III & IV clinical trials. 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.	03, 83-84	Attached
2	Prescribed processing fee	81	Fee challan of Rs.100,000/- attached submitted vide slip No. 2059924 but not endorsed by budgets and accounts Division of DRAP.
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).	5-9	As per form issued by the Registrar of firm's address is House no. 139-A, street no3, Afzal town, Chaklal-3, Rawalpindi. Legal status of the applied clinical trial site is required.
4	Details of premises including layout plan of the site.	10-15	Attached. Readable copy of layout plan required.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	17	Applicant has stated that that we are applying for registration of a clinical trial site only for phase III & IV. Separate section wise equipment and machinery is required for the analytical or bio-analytical and clinical studies are needed for phase I & II trials. As we are not conducting such trials so this section is not applicable to our site.

6	Names and qualifications of the above sections along with their staff.	23-26	Attached
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	19-21	Clinical area, Emergency department, Radiology department, Laboratory, Nursing
8	Undertaking on stamp paper	84	Attached.

3. After evaluation and discussion with higher authorities following shortcomings were found
   i. Legal status of Applicant and Maroof international Hospital situated at 10th Avenue, F-10 Markaz, Islamabad is required.
   ii. Readable copy of layout plan is required.
   iii. Section wise details of equipment and machinery for clinical studies is required.
   iv. SOPs for emergency handling are required.

5. Shortcomings were telephonically communicated to Mujtaba Qadri of Maroof Hospital and following panel was constituted by the Chairman CSC;
   a. Dr. Abdur Rashid, Director Pharmacy Services Division, DRAP, Islamabad.
   b. Dr. Hafsa Karam Elahi, Additional Director (QA&LT), DRAP, Islamabad, (Co-opted member).
   c. Prof. Brig. (R) Muzammil Hassan Najmi, Professor of Pharmacology, Foundation University, Islamabad./ Prof. Munir Ahmed Malik, Shifa international Hospital, Islamabad.
   d. Prof. Dr. Rizwana Chaudhry, Shifa Tameer e Millat university, Rawalpindi.
   e. Miss Aqsa Hashmi, Assistant Director, Pharmacy Services Division, DRAP, Islamabad.

6. Haroon Naseer, CEO, Maroof International Hospital submitted reply. Application was from CEO, Maroof International Hospital without signature and seal of the firm.

7. Applicant has submitted Taxpayer Registration Certificate instead of 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). Applicant has provided the SOPs for emergency handling. Layout plan along with details id not attached with the submitted reply.

8. It was decided that legal status of the applicant will be verified at the time of inspection by the panel and its status will be determined after inspection to include proper particulars in the license.

9. The panel has conducted the inspection of the site and report has not been submitted yet. Submitted for perusal of CSC.

10. Following members of panel conducted the inspection on 04.02.2021.

   a. Dr. Abdur Rashid, Director Pharmacy Services Division, DRAP, Islamabad.
   b. Dr. Hafsa Karam Elahi, Additional Director (QA&LT), DRAP, Islamabad, (Co-opted member).

c. Prof. Brig. (R) Muzammil Hassan Najmi, Professor of Pharmacology, Foundation University, Islamabad./ Prof. Munir Ahmed Malik, Shifa international Hospital, Islamabad.
d. Prof. Dr. Rizwana Chaudhry, Shifa Tameer e Millat university, Rawalpindi.
e. Miss Aqsa Hashmi, Assistant Director, Pharmacy Services Division, DRAP, Islamabad.

11. Remarks of inspection team are followings;

"Keeping in the view the human resource, training, infrastructure, emergency facilities, other facilities, IT system, documentation and record & waste management, the panel recommends the clinical trial site of Maroof Research center, Maroof International hospital, F-10, Islamabad."

12. Panel has recommended for Approval the Maroof Research center, Maroof International hospital, F-10, Islamabad.

13. Submitted for consideration of CSC.

14. ***Decision of 19th CSC meeting:***

The CSC after detailed deliberation and as per inspection panel recommendations decided to approve M/s Maroof International Hospital, 10th Avenue, F-10 Markaz, Islamabad, as Clinical Trial Site.

AGENDA ITEM XXXIV:

INTERIM ANALYSIS REPORT OF CLINICAL TRIAL TITLED, "PHASE-III, DOUBLE BLIND, PLACEBO-CONTROLLED, RANDOMIZED CLINICAL TRIAL OF RECOMBINANT NOVEL CORONA VIRUS VACCINE (ADENOVIRUS TYPE 5 VECTOR)".

1. Principal Investigator: Maj. Gen. Prof. Dr. Aamer Ikram, Executive Director National Institute of Health, Islamabad.
2. Investigational products: Recombinant Novel corona virus vaccine (Adenovirus Type 5 Vector)
3. Purpose of the trial/study: To evaluate efficacy of Ad-5-nCoV in preventing virologically confirmed (PCR positive) COVID-19 disease occurring 14 days to 6 months after vaccination, regardless of severity. COVID-19 disease rates in Ad5-nCoV group will be compared with covID-19 rates in the control group".
4. Trial vaccine is co-developed by M/s CanSino Biologics Inc., China & Beijing Institute of Biotechnology, Academy of Military Medical Sciences, China & sponsored by M/s CanSino Biologics Inc. China.
5. Clinical Trial approved to be conducted on five following sites:
   i. Aga Khan University Hospital, Karachi.
   ii. The Indus Hospital, Karachi.
   iii. Shaukat Khanum Memorial Cancer & Research Hospital, Lahore.
   iv. Shifa International Hospital, Islamabad.

v. University of Health Sciences, Lahore.

6. Trial Subjects in Pakistan: Total 18000 Subjects.

7. Submitted for consideration of CSC.

8. Chairman CSC briefed regarding background of the subject agenda and the trial report was also shard with the CSC members with confidentiality.

8. Decision of the 19th CSC meeting:

Global Phase-III trial of recombinant Novel Coronavirus vaccine Adenovirus 5 (Ad-5-nCoV) in adults 18 years & above.

1. Interim statistical/analysis report_05Feb2021_Pakistan.docs(Confidential) forwarded by CanSino. As per report totally 17994 randomized subjects (9011 subjects in Ad-5-nCoV group & 8983 subjects in placebo group) received injection and has been observed for at least 28 days post injection. Among the subjects 101 subjects had biologically confirmed PCR positive COVID-19 & validated by the review committee and the disease occurred between 28-52 weeks after vaccination, 75 cases were from the placebo group & 26 cases from adeno-5-nCoV group.

2. The patients estimate of efficacy adeno-5-nCoV was 65.7% which was higher than the minimal requirements of 50% given in the WHO target product profile. Totally 20 subjects were reported, subjects had at least Serious Adverse Events (SAEs) (0.06%) was very low in both groups. In Pakistan 9 subjects had at least one SAEs, total 07 Subjects were died among them 05 deaths were from Adeno-5-nCoV group & 02 deaths were from placebo group, which needed investigation. It is pertinent to mention that SAEs reported in the Clinical Study Report were not intimated to Pakistan National Pharmacovigilance Center (PNPC) nor investigation reports were submitted to the Division of Pharmacy Services-DRAP.

3. As the Clinical Studies Committee members have not given sufficient time to review & verify the Clinical Study report & data, prima facie reliance has been based on the data provided by the applicant in his clinical study report & may be considered by the Registration Board after due diligence.

4. It is further decided by the committee that, if any AEFI/SAEs occur the said report shall be submitted to PNPC /CSC within 24 hours. Weekly updates shall be submitted up to one year to ensure the safety of the patients.