MINUTES OF 21ST MEETING OF CSC HELD ON 22ND March 2021.

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The 21st Meeting of the CSC was held on 22nd March 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	Prof. Brig. (R), Muzammil Hassan Najmi.	Professor of Pharmacology, Foundation University, 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.
05	Dr. Faiza Bashir.	Chairman, Pakistan Health Research Council or his nominee, Islamabad.
06	Prof. Dr. Sheikh Riaz-Ud-Din	Director of Center for Excellence in Molecular Biology (CEMB) in Lahore. Co-opted Member.
07	Dr. Aamir Jaffary	Sindh Institute of Urology & Transplantation (SIUT), Karachi Co-opted Member.
08	Prof: Dr. Mushtaq Ahmed	Professor of Cardiology, Bach Khan Medical College, Mardan, KPK Co-opted Member.

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 20TH CLINICAL STUDIES COMMITTEE MEETING.

1. Confirmation of Minutes of 20th CSC meeting, held on 10th March 2021. Since the occurrences of COVID pandemic majority of the meetings are being conducted online through Zoom.

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

Submitted for consideration of CSC.

Decision:

Minutes of the 20th meeting of CSC were confirmed by the committee.

AGENDA ITEM - II:

ADAPTATION OF ICH_GCP GUIDELINES UNDER THE BIO_STUDY RULES BY THE AUTHORITY.

1. Refer to "WHO global benchmarking tool (GBT) for evaluation of national regulatory system of medical products for Clinical trials oversight", as per tool CT01.03 following is need to be fulfilled:

"CT01.03: Legal provisions and regulations requiring research centers, researchers, sponsors, clinical research organizations (CROs) and all relevant institutions in the CT to comply with GCP"

2. It is submitted that refer to rule 15 of the Bio-Study Rules 2017, that ICH-GCP guidelines shall be adapted by the Authority. Rule 15 of the Bio-Study Rules 2017 is as follows:

"15. GCP, GLP and BA or BE guidelines.- The DRAP shall adapt the ICH-GCP guidelines and also the GLP, BA or BE guidelines as per WHO, ICH and other international standards, which describe the criteria for the conduct of clinical trials and BA or BE studies following good clinical practice and good laboratory practice principles:

Provided that the DRAP shall revise or upgrade these guidelines from time to time, in compliance with the international standards."

3. Agenda item was placed before the Authority in its 107th meeting held on 16th March 2021. The Authority decided the case as follows:

Decision:

The Authority referred back the agenda item to Pharmacy Services Division for placing before the Clinical Studies Committee for their recommendations before consideration by the Authority. The recommendations be made keeping in view of Section 7(c)(ix) of DRAP Act, 2012 on systemic implementation of these guidelines.

4. Refer to Section 7(c)(ix) of DRAP Act, 2012 describes as follows:

"Implementation of internationally recognized standards such as good laboratory practices, current good manufacturing practices, good distribution practices, cold chain management, bioequivalence studies, stability studies, anti-spurious codes, clinical trials, biosimilar evaluations, and endorsement and systematic implementation of World Health Organization, International Conference on Harmonizations and Food and Drug Administration guidelines etc."

Submitted for consideration of CSC.

Decision:

CSC unanimously granted approval for adaptation of the ICH-GCP GLP, & BA or BE guidelines as per WHO, ICH and other international standards.

AGENDA ITEM - III:

ADAPTATION OF U.S. NATIONAL TRIAL REGISTRY FOR APPROVED CLINICAL TRIALS BY DRAP.

1. It is submitted that refer to "WHO global benchmarking tool (GBT) for evaluation of national regulatory system of medical products for Clinical trials oversight", GBT-tool CT01.10 described as follows:

"CT01.10: There are guidelines on the format and content of clinical trial applications."

2. During discussion with QMS team, it is suggested that DRAP may adapt U.S. National Trial registry as an optional trial registry for trials approved by the DRAP.

3. It is a free trial registry and Principal Investigators & Responsible Party (Sponsors) may open a free account & may upload trial data. Some documents regarding the site are attached:

i. *How to apply for a PRS (Protocol Registration & Results System) account. (Flag-A).*
ii. *Application for a PRS account (Flag-B).*
iii. *How to register your study (Flag-C).*
iv. *Frequently asked questions*

4. Principal Investigators / Responsible parties (Sponsors) from Pakistan, already enlisting/uploading their approved studies on U.S. National Trial registry (https://clinicaltrials.gov/).

5. It is proposed that DRAP may adapt U.S. National trial registry at the moment till preparation of its own database for trials, as it is free and comprehensive trial registry already used by investigators of Pakistan.

6. Agenda item was placed before the Authority in its 107th meeting held on 16th March 2021. The Authority decided the case as follows:

Decision:

The Authority referred back the agenda item to Pharmacy Services Division for placing before the Clinical Studies Committee for their recommendations before consideration by the Authority.

7. It is also proposed that a separate Clinical Trial Registry for 57 Muslim countries of Organization for Islamic Cooperation (OIC), to strengthen the research on therapeutic goods. The request may be sent to division of MIS for preparation of Clinical Trial Registry. COMSTECH should also be taken onboard for preparation of Clinical Trial Registry.

Submitted for consideration of CSC.

Decision:

CSC after detailed discussion decided as follows:

- ***i. To adopt U.S. National Trial Registry at the moment.(https://clinicaltrials.gov/).***
- ***ii. Further it is decided that DRAP will prepare its own trial registry.***
- ***iii. Afterwards DRAP will try to constitute a clinical trial registry for Muslim countries & O.I.C. member countries.***

AGENDA ITEM - IV:

APPLICATION FOR LICENSE TO ACT AS CENTER, CLINICAL TRIAL SITE, CRO OR LABORATORY. F. No.15-20/2021 DD (PS).

Application submitted by Maj. Gen. Rao Ali Shan Khan M/s Combined Military Hospital (CMH) Rawalpindi with covering letter Project Management Organization (Manufacturer of PAKVENT-I), wherein Maj. Gen. Rao Ali Shan Khan has applied for Clinical trial Site for Phase I, II, III & IV. 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	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached.
2	Prescribed processing fee	Fee challan of Rs.100,000/- attached submitted vide slip No. 2107693 dated 23th February 2021.
3	Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and	Not attached. Combined Military Hospital is a Tertiary Care Military hospital in Rawalpindi. It provides specialized

	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).	treatment to the armed forces personals, their immediate families as well as civilians.
4	Details of premises including layout plan of the site.	CMH is an A Class Combined Military Hospital. It is chief medical hospital of cantonment area Rawalpindi, along with being a military hospital for the Armed Forces of Pakistan. This 2500 bed hospital mainly look after the surgical diseases and caters for all ranks of the Armed Forces. This hospital has the following healthcare units. General surgery, Spine Surgery Neuro Surgery, ENT, Eye, Thoracic surgery, Vascular Surgery, Laparoscopic surgery, Facio-maxillary surgery, Urology, Breast surgery, Burn Center, orthopedic, dental Surgery.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	**Surgical ICU Section** 8 x ICU Beds Cardiac Monitors, Hamilton Medical C2 ICU Ventilators O2 Supply, Portable Ventilators, Suction Machine, Portable X-Ray Machine, Portable Dialysis Machine, Portable Ultrasound and Echo Machine (Toshiba), Defibrillator and AED, TEG Machine, ABG Analyzer.
6	Names and qualifications of the above sections along with their staff.	Maj. Gen Rao Ali Khan- MBBS, FCPS (Aneas) Col. Prof. Ahmed Burki- FCPS (ANAES), FCPS (Critical care) Medicine
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Following names have been provided for allied facilities. Laboratory Operation Theater Radiology
8	Undertaking on stamp paper	Not Attached.

3. Evaluation of the application is placed in tabulated form. The Clinical Studies Committee decided following in its 19th meeting held on 12 February 2021;

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.*

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 which will be developed by sub-committee.

4. Panel of following experts conducted the inspection on 19th March 2021:

i.	*Brig. (Retd) Muzammil Hassan Najmi*
ii.	*Dr. Abdur Rashid, Chairman CSC-DRAP (Chairman)*
iii	*Dr. Afrasayab, Biomedical Engineer, NUST, Islamabad.*
iv	*Prof. Dr. Iqbal Memon, HOD Anesthesia, PIMS, Islamabad.*

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

Keeping in view the premises, ICU facilities, technical human resource, trainings, environmental control, experience on ventilator, standby generator, technical knowhow, IT facilities, emergency handling, panel recommends Combined Military Hospital, Rawalpindi Surgical ICU as Clinical Trial Site.

6. Concluding status / remarks of inspection panel:

Recommended for approval.

Submitted for consideration of CSC.

Decision:

CSC unanimously granted approval to issue licence to the M/s Combined Military Hospital (CMH), Rawalpindi, as Clinical Trial Site for ventilators clinical validation protocol, as per inspection panel recommendations.

AGENDA ITEM - V:

APPLICATION FOR LICENSE TO ACT AS CENTER, CLINICAL TRIAL SITE, CRO OR LABORATORY. F. No.15-03/2021 DD (PS)

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	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached
2	Prescribed processing fee	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 the site.	Not 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.	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. The case was presented in 19th CSC meeting and committee decided as following;

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.

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

III. 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.

IV. 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.

V. 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.

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

4. Panel of following experts conducted the inspection on 22nd March 2021:

i.	**Prof. Dr. Javed Akram.** Professor of Medicine, Physician, Vice Chancellor, University of Health Sciences, Lahore.
ii.	**Dr. Farhana Badar.** Biostatistician & Epidemiologist, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore.
iii	**Dr. Somia Iqtadar**
iv	**Dr. Sajjad Kazmi**.
V	**Abdul Rasheed Sheikh** *F.I.D. DRAP-Lahore*
vi	**Dr. Faheem M. Butt**
vii	**Dr. Munawar Hayat** Chief Pharmacist
viii	**M. Khawar** Biomedical Technician
ix	**Naeem**

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

Keeping in view the area inspected and meet the peoples in the organization (Jinnah Hospital). The panel of inspectors is of opinion to recommended the Jinnah Hospital Lahore as Clinical Trial Site (CTS) for the Clinical Trials of Ventilator with reference to DRAP Islamabad letter No. F.15-03/2021-DD (PS).

6. Concluding status / remarks of inspection panel:

Recommended for approval.

Submitted for consideration of CSC.

Decision:

CSC unanimously granted approval to issue licence to the M/s Jinnah Hospital, Lahore as Clinical Trial Site for ventilators clinical validation protocol, as per inspection panel recommendations.

AGENDA ITEM - VI:

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	Remarks
1	Application on prescribed Form-II	Attached
2	Prescribed processing fee	Fee of Rs.200,000/- submitted vide Challan No. 2077447 dated 14.01.2021.
3	Investigator Brochure (s)	Attached but not as per ICH guidelines.
4	Final protocol	Clinical validation protocol for Pakistan manufactured ventilator system (PMVS) prepared by PEC is attached.
5	Informed consent and participant information sheet (Urdu to English)	Attached.
6	List of participating countries	Pakistan.
7	Phase of trial.	**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.	01 ventilator
9	Site of the trial	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)	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	No clinical and safety studies Attached
15	Summary of Protocol	Not Attached
16	Summary of Investigator Brochure	Attached but not as per ICH guidelines.
17	Adverse Event Reporting Form	Attached
18	No of patients to be enrolled in each center.	Not Attached
19	Name of Monitors & Clinical Research Associate	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	03 Months
23	Undertaking on stamp	Not Attached

	paper.	

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.

6. 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.

7. 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".

8. 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.***

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

10. The application was presented before CSC in its 19th meeting held on 12th February 2021 & CSC decided as follows:

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.*

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

III. 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.*

IV. 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.*

V. 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.

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

Submitted before committee of clinical validation protocol as per Acceptance Test Procedure (ATP).

Decision:

CSC after detailed deliberation decided to deferred the case for further discussion after evaluation of trial protocol. Protocol will be shared with all CSC members for evaluation & review after which the application will discussed in the next CSC meeting which will be held on 23rd March 2021.

AGENDA ITEM - VII:

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	Remarks
1	Application on prescribed Form-II	Attached
2	Prescribed processing fee	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)	Only consent form in English is attached.
6	List of participating countries	Pakistan.
7	Phase of trial.	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.	01 ventilator
9	Site of the trial	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	Not Attached

	certificate of the investigational product.	
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 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	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. The application was presented before CSC in its 19th meeting held on 12th February 2021 & CSC decided as follows:

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.*

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

III. 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.*

IV. 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.*

V. 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.

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

Submitted before committee of clinical validation protocol as per Acceptance Test Procedure (ATP).

Decision:

CSC after detailed deliberation decided to deferred the case.

AGENDA ITEM - VIII:

REGULATORY APPROVAL FOR SCYNEXIS PROTOCOL NUMBER SCY-078-305, OPEN-LABEL STUDY TO EVALUATE THE EFFICACY, SAFETY, TOLERABILITY AND PHARMACOKINETICS OF SCY-078-305 (IBREXAFUNGERP) IN PATIENTS WITH FUNGAL DISEASES THAT ARE REFRACTORY TO OR INTOLERANT OF STANDARD ANTIFUNGAL TREATMENT (FURI). F. No.03-61/2021-DD (PS).

Application submitted by Dr. Faisal Mahmood (CNIC 42301-1116154-5), Associate Professor and Sec: Head Medicine, Aga Khan University, Karachi, wherein request has been made

for registration & approval of subject clinical trial, which will be carried out at Aga Khan University Hospital, Karachi. Application is on prescribed Form-II, along with a fee of Rs.200,000/- deposited vide challan no.2035424, dated 16th December 2020.

2. This is a multicenter, open label, non-comparator, single arm study to evaluate the efficacy and safety of Ibrexafungerp (SCY-078) in patients ≥ 18 years of age with a documented fungal disease that has been intolerant or refractory (rIFI) to Standard of Care (SoC) antifungal treatment, as per available record on U.S National Trial Registry with identification number ***NCT03059992***.

3. The study carried out under the supervision of Dr. Faisal Mahmood (PI). The trial comprises of following primary objective;

i. Assessment of Global Response [Time Frame: Up to 180 days of study treatment]
The proportion of subjects with a complete or partial Global Response (GR) at the End of Treatment Visit.

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached
2	Fee	Rs.200000/- deposited vide challan number: 2035424, dated 16th December 2020.
3	Investigator Brochure (s)	Attached. Edition 15.0, dated 12th August 2020.
4	Final protocol	Attached. Protocol SCY-078-301 Version 3.0, dated 13th August 2019.
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries	USA, Australia, Germany, Netherlands, Spain, United Kingdom & Pakistan.
7	Phase of trial.	Phase – III
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules,	SCY-078 Citrate-250mg Tablets. 150 Bottles for 15 subjects

	1976 and application for import of trial material.	
9	Site of the trial	M/s Aga Khan University Hospital, 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)	NBC-PHRC ethical approval letter Ref: No.4-87/NBC-546/20/748, dated 30th November 2021 is attached.
12	CV's of the Investigators	Attached.
13	GMP certificate along with COPP & free sale certificate of the investigational product.	Instead of GMP certificate applicant provided following documents: i. GMP inspection report. ii. Inspection exit notice. iii. CoA for IMPs. iv. Certificate of Manufacturing for IMPs.
14	Pre-clinical/clinical safety studies	Attached. Section 4 of the Investigators Brochure.
15	Summary of Protocol	Attached. Section 5 of the Protocol.
16	Summary of Investigator Brochure	Attached. Section 2 of the Investigators Brochure.
17	Adverse Event Reporting Form	Attached.
18	No of patients to be enrolled in each center.	15 subjects will be enrolled in Pakistan at Aga Khan University Hospital, Karachi
19	Name of Monitors & Clinical Research Associate	Dr. Nazish Urooj of M/s Metrics Research CRO, Karachi.
20	Evidence of registration in country of origin.	N/A as it's an investigational Medicinal Product manufactured by M/s Corealis Pharma Inc. Quebec.
21	Copy of registration letter (if registered in Pakistan)	N/A

22	Sample of label of the investigational product / drug.	Attached.
22	Duration of trial	Approximately 222 days.
23	Undertaking on Stamp paper	Copy attached.

5. 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.

Submitted for consideration of CSC.

Decision:

The CSC after detailed deliberation decided to grant approval for registration of the clinical trial titled "An Open-Label Study to Evaluate the Efficacy, Safety, Tolerability and Pharmacokinetics of Scy-078-305 (Ibrexafungerp) In Patients with Fungal Diseases That Are Refractory to Or Intolerant of Standard Antifungal Treatment (FURI)", subject to pharmacokinetic/ BA/BE studies facilities.