MINUTES OF THE 26TH MEETING OF CLINICAL STUDY COMMITTEE (CSC), HELD ON 31ST MAY 2021.

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The 26th Meeting of the Clinical Study Committee (CSC) was held on 31st May 2021 through Zoom under the chairmanship of Dr. Abdur Rashid, Director Pharmacy Services Division / Chairman (CSC). at the Committee Room, Drug Regulatory Authority of Pakistan, 4th Floor, T.F. Complex, Islamabad.

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

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

3. Following members attended the meeting online through Zoom:

01	Prof. Dr. Javed Akram.	Professor of Medicine, Physician, Vice Chancellor, University of Health Sciences, Lahore.
02	Prof. Nadeem Irfan Bukhari.	Professor of Bio-Pharmaceutics & Pharmacokinetics, University of Punjab, Lahore.
03	Dr. Farhana Badar.	Biostatistician & Epidemiologist, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore.
04	Dr. Naseem Salahuddin.	Director Infectious Diseases Indus Hospital, Karachi Co-opted Member.
05	Dr. Aamir Jaffary	Sindh Institute of Urology & Transplantation (SIUT), Karachi Co-opted Member.
06	Prof. Dr. Rizwana Chaudhri	HOD Gynecologist, Holy Family Hospital, Rawalpindi Co-opted Member.
07	Prof: Dr. Mushtaq Ahmed	Professor of Cardiology, Bacha Khan Medical College, Mardan, KPK Co-opted Member.
08	Nadeem Alamgir	Representative of Pharma Bureau Observer

4. Meeting started with the recitation of holy verses of the Quran by Dr. Abdur Rashid. Chairman, CSC welcomed all the members & appreciated their active online participation through Zoom.

AGENDA ITEM - I: CONFIRMATION OF THE MINUTES OF THE 25TH CLINICAL STUDIES COMMITTEE MEETING.

1. Confirmation of Minutes of 25th CSC meeting, held on 28th April 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 perusal, discussion and decision of CSC.

Decision:

All the Members of the CSC unanimously confirmed the Minutes of 25th CSC meeting held on 28th April 2021.

AGENDA ITEM-II: APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, FROM REHMAN MEDICAL CENTER, PESHAWAR (F.No.15-24/2021 DD(PS)).

1. The case is an application from Dr. Mr. Muhammad Umar Farooq of M/s Rehman Medical Institute, Hayatabad, phase-v, Peshawar, wherein applicant has applied for clinical trial site for clinical trials of Phase III and 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 to pre- requisites as mentioned in Form-I of the Bio-Study Rules 2017, and after evaluation following panel was constituted by the Chairman CSC.

a. Prof. Dr. Mushtaq Ahmed, Professor of Cardiology, Bacha Khan Medical College, Mardan, KPK.
b. Dr. Abdur Rashid, Director Pharmacy Services Division, DRAP, Islamabad.
c. Mr. Faisal Shehzad, Additional Director, DRAP, Peshawar.
d. Prof. Fazal e Subhan, CECOS University, Peshawar.

3. Following members conducted inspection on 20.05.2021.

a. Prof. Dr. Mushtaq Ahmed, Professor of Cardiology, Bacha Khan Medical College, Mardan, KPK.
b. Mr. Faisal Shehzad, Additional Director, DRAP, Peshawar.
c. Prof. Fazal e Subhan, CECOS university, Peshawar.

4. Panel recommended for approval with following comments.

"Keeping in view the facilities provided in the institute, technical trained persons met, detailed review of documents provided by the institute, the panel unanimously recommends the facility (Rehman clinical Research center) for CRS"

Submitted for perusal, discussion and decision of CSC.

Decision:

After due discussion & pursuance to the recommendations of the inspection panel, CSC unanimously granted approval to issue licence in the name of Rehman Clinical Research Center of

M/s Rehman Medical Institute, Hayatabad, Phase-V, Peshawar to act as Clinical Trial Site for Phase-III & Phase-IV Clinical Trials.

AGENDA ITEM- III: APPLICATION FOR GRANT OF EXTENTION OF DURATION OF CLINICAL TRIAL BEYOND THREE MONTHS (ALREADY GRANTED), "A PHASE III RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED CLINICAL TRIAL IN 18 YEARS OF AGE AND ABOVE TO DETERMINE THE SAFETY AND EFFICACY OF ZF2001, A RECOMBINANT NOVEL CORONA VACCINE (CHO CELL) FOR PREVENTION OF COVID-19" (F.No.03-52/2020DD(PS)).

Mr. Asim Munir from DRK have submitted the request, wherein they have stated that DRK Pharma Solution the licensed Clinical Research Organization having License No CRO-001 dated 11 October 2019 had applied for approval for clinical trial to DRAP, titled as "A PHASE III RANDOMIZED, DOUBLE-BLIND, PARALLEL-CONTROLLED CLINICAL TRIAL IN 18 YEARS OF AGE AND ABOVE TO DETERMINE THE SAFETY AND EFFICACY OF ZF-2001, A RECOMIBINANT NOVEL CORONAVIRUS VACCINE (CHO CELL) FOR PREVENTION OF COVID-19" They further wrote that they were given permission to conduct the trial vide letter No. 03-5212021 DD (PS) Dated 15th February 2021 allotting under license No. 0023. Subsequently on their application for the change of Principal Investigator licenseNo.0033 was issued in March 2021. This application is being submitted in collaboration with the Principal Investigator Professor Javed Akram. The total number of subjects to be recruited (and approved) are 10,000. To date (l7th May 2021) 3804 subjects have been recruited. The trial protocol states that the subjects shall be given vaccine dosage at 0, I and 2 months. At the moment second dose has been started and soon the third dose shall also be given. To complete the total number of subjects' further time is required. They have requested for extension for further 6 months. Applicant has also submitted on this application with hand writing that since in this trial we are required to enroll 10,000 subjects from Pakistan. So, far we have screened9470 subjects, out of which 60% subjects are IgM/ IgG positive (60% screening failure). Therefore, it is requested to grant the approval to import additional 10,000 SARs CoV-2 IgM/IgG antibody detection kits to complete recruitment.

The request of the firm is submitted for perusal, discussion and decision of CSC.

Decision:

The CSC after detailed deliberation decided to approve extension in duration of clinical trial titled, "A PHASE III RANDOMIZED, DOUBLE-BLIND, PARALLEL-CONTROLLED CLINICAL TRIAL IN 18 YEARS OF AGE AND ABOVE TO DETERMINE THE SAFETY AND EFFICACY OF ZF-2001, A RECOMIBINANT NOVEL CORONAVIRUS VACCINE (CHO CELL) FOR PREVENTION OF COVID-19" for a further period of six (06) months and recommended the import of ten thousands (10,000/-) SARs CoV-2 IgM/IgG antibody detection kits , due to stated screening failure, to complete recruitment/ enrollment of required subjects, subject to submission of fee Rs.25000/-. The CSC also decided to ask the applicant to approach the MDMC Division/ QA&LT

Division for approval of import & Clearance of the said diagnostic Kits under provisions of relevant rules.

AGENDA ITEM-IV: CLINICAL VALIDATION REPORT OF INVESTIGATIONAL ICU VENTILATOR I-LIVE DEVELOPED BY PAKISTAN ATOMIC ENERGY COMMISSION (F.No.03-55/2020DD(PS)).

Dr. Hina Nabi Ahmed, Medical Expert of PEC/ Trials Team, Assistant Professor Anesthesia/ ICU, Jinnah Hospital, Lahore, has submitted the clinical validation report of investigational ICU ventilator I-Live developed by Pakistan atomic energy commission. The scanned repot is attached as annex. for screening, assessment, review and evaluation and consideration

Submitted for perusal, discussion and decision of CSC.

Decision:

The Clinical Studies Committee after detailed deliberation recommended to refer the Clinical Validation Report of I-LIVE ventilator for ICU, based on protocol version PEC-CVP-PMVS 001:2020, submitted by Dr. Hina Nabi Ahmed, Assistant Professor, AIMC/ Jinnah Hospital, Lahore, to Medical Devices Board (MDB) through Division of Medical Devices and Medicated Cosmetics.

AGENDA ITEM- V: APPLICATION FOR APPROVAL AND REGISTRATION OF CLINICAL TRIAL TITLED "A GLOBAL MULTICENTER, RANZOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED, ADAPTIVE DESIGNED PHASE III TRIAL TO EVALUATE THE EFFICACY, SAFETY AND IMMUNOGENICITY OF RECOMBINANT NOVEL CORONA VIRUS VACCINE (ADENOVIRUS TYPE 5 VECTOR) IN ADULTS 18 YEARS OF AGE AND OLDER" (F.No.03-69/2021DD(PS)).

Application submitted by Major General Prof. Dr. Aamer Ikram, Executive Director National Institute of Health, Islamabad, 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, Karachi.
ii. The Indus Hospital, Karachi.
iii. Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore.
iv. Shifa International Hospital, Islamabad.
v. University of Health Sciences, Lahore

2. Application is on prescribed Form-II, along with Prescribed fee of Rs.200000/-, deposited vide challan number 47124690320, dated 26th May 2021

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

S. No.	Document	Remarks

1	Application on prescribed Form-II	Attached.
2	Fee	Prescribed fee of Rs.200000/-, deposited vide challan number 47124690320, dated 26th May 2021
3	Investigator Brochure (s)	Attached
4	Final protocol	Attached.
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries	Mexico, Russia, Chile, Argentina & 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, 1976 and application for import of trial material.	16,560 of Vaccine (approx.).
9	Site of the trial	Aga Khan University Hospital, Karachi. The Indus Hospital, Karachi. Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore. Shifa International Hospital, Islamabad. University of Health Sciences, Lahore.
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	***IRB approval of proposed clinical trial sites has not been submitted.***
11	Approval of National Bio-ethics Committee (NBC)	NBC approval reference No.4-87/COVID-35/ Amendments/21/, dated 26 May 2021
12	CV's of the Investigators	Not provided but Major General Prof. Dr. Aamer Ikram was PI in

		previously approved trial on vaccine.
13	GMP certificate along with COPP & free sale certificate of the investigational product.	GMP certificate of CanSino Biologics Inc. is attached
14	Pre-clinical/clinical safety studies	Attached.
15	Summary of Protocol	Attached.
16	Summary of Investigator Brochure	
17	Adverse Event Reporting Form	Attached.
18	No of patients to be enrolled in each center.	This an end point case driven efficacy clinical trial, with the goal of 150 COVID-19 end point cases. About 40,000 total participants will be enrolled into four cohorts, based on the current attack rate of Covid-19 in the study areas. A subset approximately 3,000 participants (approximately 7% to 10 %) will comprise three of the cohorts. After the 2nd dose the objective of the study will be comparing the relative efficacy of single and second doses with target end point cases of approximately 83.
19	Name of Monitors & Clinical Research Associate	Muhammad Khurram Zaki Khan of M/s Dimension Research CRO.
20	Evidence of registration in country of origin.	Not provided
21	Copy of registration letter (if registered in Pakistan)	EUA certificate by DRAP is attached.
22	Sample of label of the investigational product / drug.	Attached.
22	Duration of trial	06 Months.
23	Undertaking on stamp paper	Not Attached.

5. In the view of above following shortcomings are recorded:

IRB approval of the following Institutes is required.

Aga Khan University Hospital, Karachi.

The Indus Hospital, Karachi.

Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore.

Shifa International Hospital, Islamabad.

University of Health Sciences, Lahore.

6. The soft copy of the study material has already been sent to all members of CSC through email on 27.05.2021 for screening, assessment, review and evaluation.

Submitted for the consideration of CSC.

Decision:

The CSC after detailed deliberation decided to approve clinical trial titled, "A Global Multicenter, Randomized, Double Blind, Placebo Controlled, Adaptive Designed Phase III Trial to Evaluate the Efficacy, Safety and Immunogenicity of Recombinant Novel Corona Virus Vaccine (Adenovirus Type 5 Vector) in Adults 18 Years of Age and Older" subject to submission of IRB approvals of the following Clinical Trial Sites:

i. Aga Khan University Hospital, Karachi.
ii. The Indus Hospital, Karachi.
iii. Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore.
iv. Shifa International Hospital, Islamabad.
v. University of Health Sciences, Lahore.

2. It is pertinent to mention that National Bioethics Committee has already approved this study.

ADDITIONAL AGENDA ITEM- VI

APPLICATION FOR REGISTRATION OF CLINICAL TRIAL OF ICU MEDICAL VENTILATOR ALNOVENT AVB-100 DEVELOPED BY ALSONS INDUSTRIES (Pvt.) Ltd, KARACHI (F. No.03-68/2021 DD (PS)).

Application submitted by Dr. Hina Nabi Ahmed CNIC No. 3840357848728 from M/s Jinnah Hospital, Lahore, wherein she has applied for clinical titles ICU 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 online vide Slip No. 9906480959 dated 19.05.2021.
3	Investigator Brochure (s)	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.	Clinical Trial will be conducted in three phases for around 96 hours. 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.	N/A
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)	Attached. Ref:No.4-87/EMD-VENT-0321/ dated 08th May, 2021.
12	CV's of the Investigators	Not Attached. Dr Hina Nabi Ahmed was PI in ILiveVent Study.
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	Not Attached
17	Adverse Event Reporting Form	Not Attached
18	No of patients to be enrolled in each center.	Not Attached
19	Name of Monitors & Clinical Research Associate	Not Attached

20	Evidence of registration in country of origin.	Not attached Newly manufactured Ventilator
21	Copy of registration letter (if registered in Pakistan)	NA
22	Sample of label of the investigational product / drug.	Not Attached
22	Duration of trial	Clinical Trial will be conducted in three phases for around 96 hours.
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 without signatures.

iii. Written Clinical Trial will be conducted in three phases for around 96 hours. needs to properly described i.e. Phase I, II, III or IV.

iv. Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members, is not attached.

v. CV's of the Investigators not attached.

vi. GMP certificate along with COPP & free sale certificate of the investigational product is not attached.

vii. Adverse Event Reporting Form not attached.

viii. Pre-clinical/clinical, safety studies are not attached.

ix. Summary of Protocol not attached.

x. Summary of Investigator Brochure not attached.

xi. No of patients to be enrolled in each center not described.

xii. Evidence of registration in country of origin not attached.

xiii. Name of Monitors & Clinical Research Associate not attached.

xiv. Sample of label of the investigational product / drug not attached.

xv. Undertaking on stamp paper not attached.

4. All above mentioned shortcomings were communicated to applicant vide letter no. F. No.03-68/2021 DD (PS), dated 28th May 2021. Response to the aforesaid letter is yet awaited.

Submitted for perusal, discussion and decision of CSC.

Decision:

The CSC after detailed deliberation decided to defer the case for fulfilment of all prerequisites as defined under the Bio-Study Rules 2017.

ADDITIONAL AGENDA ITEM- VII

APPROVAL OF REVISED GUIDELINES FOR CONDUCT OF CLINICAL TRIAL

Revised "Guidelines for Conduct of Clinical Trial" are attached as annexure-II. For technical evaluation, these revised guidelines forwarded to experts through email on 30th May 2021, for review & evaluation. Dr. Farhana Badar & Dr. Aamir Jaffary shared their comments. Comments/ input of both experts have been incorporated in the revised guidelines.

Submitted for perusal, discussion and decision of CSC.

The guidelines were not discussed by the CSC due to paucity of time.