**MINUTES OF THE 31st MEETING OF CLINICAL STUDY COMMITTEE (CSC), HELD ON 26TH AUGUST 2021.**

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The 31st Meeting of the Clinical Study Committee (CSC) was held on 26th August 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. |
| 03 | Dr. Farhana Badar. | Biostatistician & Epidemiologist, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore. |
| 04 | Dr. Faiza Bashir. | Chairman, Pakistan Health Research Council or his nominee, Islamabad. |
| 06 | Prof. Dr. Rizwana Chaudhri | HOD Gynecologist, Holy Family Hospital, Rawalpindi<br>Co-opted Member. |
| 07 | Prof: Dr. Mushtaq Ahmed | Professor of Cardiology, Bacha Khan Medical College, Mardan, KPK<br>Co-opted Member. |
| 08 | Dr. Ahson Siddiqui | MBBS, DTCP, MCPS, MPH (London) as Chest Specialist, Karachi. |

4. Meeting started with the recitation of holy verses of the Quran by Mr. Ahmad Din Ansari. Chairman, CSC welcomed all the members & appreciated their active online participation through Zoom.

**AGENDA ITEM I: RATIFICATION OF THE MINUTES OF THE 30TH CSC MEETING HELD ON 12TH AUGUST 2021.**

***MINUTES OF THE 30TH CSC MEETING HELD ON 12TH AUGUST 2021.***

***Table of Contents:***

*The 30th Meeting of the CSC was held on 12th August 2021 through Zoom under the chairmanship of Dr. Abdur Rashid, Director Pharmacy Services Division / Chairman (CSC) in Committee Room-I, 4th Floor, Drug Regulatory Authority of Pakistan, Islamabad.*

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

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

*3. Following members attended the meeting online through Zoom:*

| | | |
|---|---|---|
| *01* | *Dr. Faiza Bashir.* | *Chairman, Pakistan Health Research Council or his nominee, Islamabad.* |
| *02* | *Dr. Farhana Badar.* | *Biostatistician & Epidemiologist, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore.* |
| *03* | *Dr. Naseem Salahuddin.* | *Director Infectious Diseases Indus Hospital, Karachi Co-opted Member.* |
| *04* | *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 Ahmad Din Ansari, Secretary CSC. The Chairman CSC welcomed all the members and asked the Secretary CSC to present agenda. The Secretary CSC informed the background of the meeting and presented the agenda. Mr. Muhammad Adnan Faisal Saim, Deputy Director (Pharmacy Services Division), Mr. Muhammad Ansar, Assistant Director and Mr. Ahsan AD were also present in the meeting.*

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***AGENDA ITEM I:***

***CONFIRMATION OF THE MINUTES OF THE 29TH CLINICAL STUDIES COMMITTEE MEETING.***

*1. Confirmation of Minutes of 29th CSC meeting held on 5th August 2021. Since, the occurrence of Covid-19 pandemic majority of the meeting are being conducted online through zoom.*

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

*Submitted for consideration of CSC.*

***Decision:** All the Members of the CSC unanimously confirmed the Minutes of 29th CSC meeting held on 05th August 2021.*

**Decision of 31st CSC meeting:**

*CSC ratified the decision of committee taken in its 30th meeting held on 12th August 2021.*

***AGENDA ITEM II:***

***TEMPORARY REGISTRATION OF ASPIRIN, TICAGRELOR AND PLACEBO FOR MULTI-CENTRE RANDOMIZED CONTROLLED TRIAL F. No. 03-16/2019-DD (PS).***

*The case vide letter No. EC-I/COVEERING/ PIC/19/34832 dated 19.11.2019 was received from Prof. Dr. Saqib Shafi Sheikh, Chief Executive, PIC, Lahore, Principal Investigator, Punjab Institute of Cardiology, Lahore dated 18.11.2019 addressed to the Director, Pharmacy Services, DRAP, Islamabad. Wherein he stated that three centers from Pakistan have been selected for a very innovative Multi-Centre randomized trial that might change the international guideline. This would be a great honor for Pakistan.*

*2. Since the trial is ready to start in other countries and high-volume centers in Pakistan can take a lead in trial subject to early participation. It is therefore requested to grant subject temporary registration of drug on fairly urgent basis so that leading role of Pakistan center is not jeopardized due to inordinate delay. Centers approved other than Punjab Institute of Cardiology (PIC) Lahore, for this trial are: Rawalpindi Institute of Cardiology (RIC) Rawalpindi and National Institute of Cardiovascular diseases (NICVD), Karachi.*

*3. This is a multicenter, randomized controlled research project titled "Comparison of 1-month versus Dual Antiplatelet Therapy after implantation of Drug-Eluting Stents Guided by either Intravascular Ultrasound or Angiography in Patients with Acute Coronary Syndrome" as per submitted documents (page 21/Corr.) by applicant, it is informed that the trial record is available on U.S National Trial Registry with identification number **NCT03971500.** Followings are details of contact and location as per the U. S. National Trial Registry.*

***Contacts***
*Shao-Liang Chen, MD, PhD +86-25-52208048 chmengx@126.com*
*Jing Kan, MPH +86-25-52271398 kanjingok@126.com*
***Locations***
***China, Jiangsu***
*Nanjing First Hospital* ***Recruiting***
*Nanjing, Jiangsu, China, 210006*
*Contact: Shaoliang Chen, MD +86 13605157029 chmengx@126.com*
*Contact: Jing Kan, MPH +86 15305140515 kanjingok@126.com*
***Sponsors and Collaborators***
*Nanjing First Hospital, Nanjing Medical University*
***Investigators***
*Study Chair: Shao-Liang Chen, MD, PhD Nanjing First Hospital, Nanjing Medical University*

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

| ***S. No.*** | ***Document*** | ***Remarks*** |
|---|---|---|
| *1* | *Application on prescribed Form-II* | *Application is not on prescribed Form* |
| *2* | *Fee* | *Not Attached* |
| *3* | *Investigator Brochure (s)* | *Not Provided* |
| *4* | *Final protocol* | *Attached* |

| | | |
|---|---|---|
| *5* | *Informed consent and participant information sheet (Urdu to English)* | *Not Attached* |
| *6* | *List of participating countries* | *Para 6/N as per US National Trial Registry.* |
| *7* | *Phase of trial.* | *Not Motioned* |
| *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.* | *Not mentioned* |
| *9* | *Site of the trial* | *Punjab Institute of Cardiology (PIC) Lahore.*<br><br>*Rawalpindi Institute of Cardiology (RIC) Rawalpindi.*<br><br>*National Institute of Cardiovascular diseases (NICVD), Karachi.*<br><br>***None of these trial sites is approved by CSC*** |
| *10* | *Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.* | *Attached but complete composition of committee i.e. names and designation of members are to be provided* |
| *11* | *Approval of National Bio-ethics Committee (NBC)* | *Not provided.* |
| *12* | *CV's of the Investigators* | *Not provided.* |
| *13* | *GMP certificate along with COPP & free sale certificate of the investigational product.* | *GMP certificate provided but COPP & Free Sale Certificate not attached* |
| *14* | *Pre-clinical/clinical safety studies* | *Not provided.* |
| *15* | *Summary of Protocol* | *Attached.* |
| *16* | *Summary of Investigator Brochure* | *Not Attached.* |
| *17* | *Adverse Event Reporting Form* | *Need to be elaborated* |
| *18* | *No of patients to be enrolled in each center.* | *Not Mentioned* |
| *19* | *Name of Monitors & Clinical Research Associate* | *Prof Dr. Saqib Shafi Sheikh (Principal Investigator Pakistan)*<br><br>*Dr. Muhammad Anjum (Co-Ordinator & Co-Investigator)* |
| *20* | *Evidence of registration in country of origin.* | *Not provided.* |
| *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* | *Not Clear from provided documents* |
| *23* | *Undertaking on Stamp paper* | *Not provided.* |

*08. In the view of above shortcomings, the applicant may be advised to submit application on prescribed Form along with prescribed fee documents as per checklist for clinical trial.*

*09. The shortcomings were communicated vide this office letter dated 3rd December 2021 and reminder dated 12th March 2020.*

*10. Dr. Asim Javaid, representative from Rawalpindi Institute of Cardiology, Rawalpindi visited DRAP on 09th March 2021and meeting regarding application status held in the office of Additional Director (PS). Application along with shortcomings were briefed to representative. A brief of the case was also forwarded to CEO-DRAP office for the Secretary M/o NHSR&C.*

*11. An application was received from Maj Gen (R) Dr. Azhar Mehmood Kayani, Executive Director, Rawalpindi Institute of cardiology, Rawalpindi in the name of CEO, DRAP, Islamabad in continuation to previously submitted application by Prof. Dr. Saqib Shafi Sheikh, Chief Executive, PIC, Lahore, Principal Investigator, Punjab Institute of Cardiology, Lahore dated 18.11.2019.*

*12. The details of the submitted documents are as under;*

| ***S. No.*** | ***Document*** | ***Remarks*** |
|---|---|---|
| *1* | *Application on prescribed Form-II* | *Application is on Form II* ***but without seal of the firm/ company*** |
| *2* | *Fee* | *Copy of fee challan attached* ***but original challan (DRAP Copy) required endorsed by Budget and Accounts Division.*** |
| *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* | *Para 6/N as per US National Trial Registry.*<br><br>*China, Indonesia, Thailand, Italy, Malaysia* |
| *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.* | *Tablet/ capsule Ticagrelor 90mg =36,000*<br><br>*Tablet/ capsule Aspirin 75mg =9,000*<br><br>*Tablet/ capsule Placebo =9,000*<br><br>*Boston Scientific IVUS Catheters =750* |
| *9* | *Site of the trial* | *Punjab Institute of Cardiology (PIC) Lahore.*<br><br>*Rawalpindi Institute of Cardiology (RIC) Rawalpindi.* |

| | | |
|---|---|---|
| | | *National Institute of Cardiovascular diseases (NICVD), Karachi.*<br><br>*CPE Institute of Cardiology, Multan*<br><br>***None of these trial sites is approved by CSC*** |
| *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* |
| *12* | *CV's of the Investigators* | *Attached* |
| *13* | *GMP certificate along with COPP & free sale certificate of the investigational product.* | *GMP certificate, COPP attached for Aspirin and Ticagrelor* |
| *14* | *Pre-clinical/clinical safety studies* | *In Clinical study protocol* |
| *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.* | *Not Mentioned* |
| *19* | *Name of Monitors & Clinical Research Associate* | *Attached.* |
| *20* | *Evidence of registration in country of origin.* | *COPP attached for Aspirin and Ticagrelor* |
| *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* | *4 years* |
| *23* | *Undertaking on Stamp paper* | *Not provided.* |

*13. Previously application was submitted by Prof. Dr. Saqib Shafi Sheikh, Chief Executive, PIC and now has been submitted by Maj Gen (R) Dr. Azhar Mehmood Kayani, Executive Director, Rawalpindi Institute of cardiology, Rawalpindi. Further applicant has requested CEO, DRAP to grant for the site Centers fee to help him to avoid unnecessary audit objection.*

*14. Applicant may be asked to submit undertaking on stamp paper along with name, signature and seal of the firm/ company. He may also be advised to submit fee for trial Centers along with necessary documents required for the approval of trial sites.*

*15. The applicant has submitted the prescribed Fee along with undertaking on stamp paper.*

*16. Rawalpindi Institute of Cardiology, Rawalpindi has been approved as CTS in 29th CSC meeting held on 05.08.2021.*

***SUBMITTED FOR CONSIDERATION OF CSC***

*17. Maj Gen (R) Dr. Azhar Mehmood Kayani, Executive Director, Rawalpindi Institute of cardiology, Rawalpindi joined the meeting virtually and briefed the CSC members regarding subject clinical trial and answered the questions raised by some of the CSC members.*

***Decision:***

*The CSC after detailed deliberation and discussion decided to approve the Clinical Trial/ Study titled "Comparison of l-month versus l2-month Dual Antiplatelet Therapy after implantation of Drug-Eluting Stents Guided by either Intravascular Ultrasound or Angiography in Patients with Acute Coronary Syndrome: The Prospective, Multicenter, Randomized, Placebo-controlled IVUS-ACS and ULTIMATE-DAPT trials" at following site;*

1. *M/s Rawalpindi Institute of Cardiology, Rawal Road, Rawalpindi.*

*The other three proposed sites will be considered to carry out this trial after inspection by the panel of experts and approval by CSC as CTS accordingly.*

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Discussion on the case:

Maj Gen (R) Dr. Azhar Mehmood Kayani, Executive Director, Rawalpindi Institute of cardiology, Rawalpindi joined virtually in the 30th CSC meeting and briefed the CSC members regarding subject clinical trial and answered the questions raised by some of the CSC members.

Secretary CSC presented the case along with its background, further appraised that the application is for Phase-III clinical trial site and that the panel has not mentioned the phase of trial in the inspection report. As the application is for Phase-III clinical trial so it is proposed for approval of Phase-III clinical trials & the committee may decide accordingly. Chairman CSC added that as per application it should be considered only for Phase-III Clinical Trial Site, further Chairman CSC directed that next time Phase/Phases of trial should be mentioned in the inspection letter so the site be inspected accordingly and contact numbers of PI of the site or contact person should also be included in the letter.

Dr. Mushtaq Ahmad, Co-Opted member CSC raised some concerns regarding clinical trial titled "Comparison of One Month Versus Dual Antiplatelet Therapy After Implantation of Drug Eluding Stunts Guided by Either Intravascular Ultrasound or Angiography in Patients with Acute Coronary Syndrome" & recommended that, as the trial is of critical nature so trial subjects should be in close vicinity of the Clinical Trial Site and in case of any emergency (i.e. blockage of arteries) trial subjects may get emergency/ambulatory services & intensive care promptly. Prof. Dr. Javed Akram also supported the concerns raised by Dr. Mushtaq Ahmad & added that PIs of all Clinical Trial Sites should develop a safety protocol so that being at high risk, the trial subjects may get 24/7 accessibility in case of any emergency or Serious Adverse Event. He further suggested that ADRs in this study should be reported within 24 hours & a weekly or fortnightly report in this regard should also be submitted to DRAP so that keeping in view the nature of ADRs the same may be forwarded to one or more members of CSC for review & in the light of input/comments/conclusion by the CSC member(s)/Expert(s) CSC may review its decision to halt the study/trial in best public interest if required so. It was also suggested that undertaking to implement these suggestions of the committee may also sought from the PIs & Co-PIs of all the four clinical trial sites.

**Decision of 31st CSC meeting:**

The committee ratified its decision regarding approval of subject trial/study taken in the in its 30th meeting with the addition of following more proposed Clinical Trial Sites that are approved by CSC in this meeting in the light of panel inspection report/recommendations.

i. National Institute of Cardiovascular Diseases, Karachi.
ii. Chaudhry Parvaiz Elahi Institute of Cardiology, Multan
iii. Punjab Institute of Cardiology, Lahore.

However, following additional measures will be taken by PI/Co-PI of each CTS while conducting the trial/study in the light of discussion made in the case:

i. *The proposed trial/study titled "Comparison of l-month versus l2-month Dual Antiplatelet Therapy after implantation of Drug-Eluting Stents Guided by either Intravascular Ultrasound or Angiography in Patients with Acute Coronary Syndrome: The Prospective, Multicenter, Randomized, Placebo-controlled IVUS-ACS and ULTIMATE-DAPT trials", is of critical nature so trail subjects should be in close vicinity of the Clinical Trial Site. So that, in case of any emergency/serious adverse events (i.e. Blockage of arteries) the trial subjects may get emergency/ambulatory services & intensive care promptly*
ii. *Principal Investigator of the Clinical Trial Site should develop a safety protocol so that being at high risk, the trial subjects may get 24/7 accessibility in case of any emergency or Serious Adverse Event.*
iii. *ADRs in the proposed study should be reported within 24 hours & a weekly or fortnightly report in this regard should also be submitted to DRAP.*
iv. *Undertaking for implementation of above-mentioned recommendations of the committee should be submitted to the Division of Pharmacy Services by PIs & Co-PIs of the clinical trial site.*

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***AGENDA ITEM II***

***APPROVAL OF ViDiSAM PROJECT i.e. TRIAL OF HIGH DOSE VITAMIN D IN THE TREATMENT OF COMPLICATED SEVERE ACUTE MALNUTRITION. F. No.03-53/2020 DD (PS)***

*The case is an application from Dr. Javeria Saleem CNIC No. 352102-9632593-0 from M/s University of the Punjab wherein the applicant has applied for approval or registration of clinical trial titled; Trial of high dose vitamin d in the treatment of complicated severe acute Malnutrition (ViDiSAM). 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*** | ***Remarks*** |
|---|---|---|
| *1* | *Application on prescribed Form-II* | *Attached.* |
| *2* | *Prescribed processing fee* | *Fee of Rs.200,000/- submitted vide Challan No. 2013290 dated 28.12.2020.* |

| | | |
|---|---|---|
| *3* | *Investigator Brochure (s)* | *Only label and promotional material attached instead of Investigator brochure.* |
| *4* | *Final protocol* | *Attached.* |
| *5* | *Informed consent and participant information sheet (Urdu to English)* | *Attached.* |
| *6* | *List of participating countries* | *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.* | *500 Ampoules (250 participants x 2 visits) with 10% Extra.*<br>*Locally Manufactured.* |
| *9* | *Site of the trial* | *Sir Ganga Ram Hospital, Lahore*<br>*The Children's Hospital & The Institute of Child Health (CH & ICH) Lahore.*<br>*Tehsil Headquarters (THQ), Hospital, Kahna Nau, Lahore.* |
| *10* | *Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.* | *IRB approval of Tehsil Headquarters (THQ), Hospital, Kahna Nau, Lahore along with complete composition of committee not attached.* |
| *11* | *Approval of National Bio-ethics Committee (NBC)* | *Attached.*<br>*Ref:No.4-87/NBC-516/20/477, Dated 12th October 2020.* |
| *12* | *CV's of the Investigators* | *Attached* |
| *13* | *GMP certificate along with COPP & free sale certificate of the investigational product.* | *Only GMP certificate attached.* |
| *14* | *Pre-clinical/clinical safety studies* | *Attached.* |
| *15* | *Summary of Protocol* | *Attached.* |
| *16* | *Summary of Investigator Brochure* | *Not Attached.* |
| *17* | *Adverse Event Reporting Form* | *Attached.* |
| *18* | *No of patients to be enrolled in each center.* | *250 subjects.* |
| *19* | *Name of Monitors & Clinical Research Associate* | *DRK Pharma Solution, Lahore.* |
| *20* | *Evidence of registration in country of origin.* | *Attached* |
| *21* | *Copy of registration letter (if registered in Pakistan)* | *Attached* |
| *22* | *Sample of label of the investigational product / drug.* | *Attached.* |
| *22* | *Duration of trial* | *Three years* |
| *23* | *Undertaking on stamp paper.* | *Not Attached.* |

*3. After evaluation following shortcomings were recorded:*

*i) Data of Phase I Trial may be provided.*
*ii) IRB approval from DHQ, Kahna Nau, Lahore 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) License to manufacture for experimental purposes is required under Chapter II Rule 3(v) & 21 of LRA Rules 1976 is required.*
*v) Investigator Brochure and summary of Investigator Brochure is 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 trial data required for onward submission to Expert under Rule 7(4) of Bio-Study rules 2017, is required.*
*viii) Undertaking of Stamp paper is required.*

*4. Shortcomings were communicated vide this office letter no. 03-53/2021 DD (PS) dated 19th January 2021.*

*5. The reply of the applicant in response to this office letter dated 19th January 2021 is as following;*

| *Documents Requested* | *Reply of the Firm* |
|---|---|
| *Data of Phase-I Trial may be provided* | *applicant has attached the article "A phase I/II dose escalation trial of vitamin D3 and calcium in multiple sclerosis"*<br>*High-dose vitamin D3 in the treatment of severe acute malnutrition: a multicenter double-blind randomized controlled trial.* |
| *IRB approval from DHQ, Kahna Nau, Lahore is required along with composition of committee i.e. names and designation of members.* | *Not Attached* |
| *Separate application for each clinical trial site is required on Form-I of Bio-Study Rules 2017.* | *Not received from Kahana Nau, DHQ, Lahore.* |
| *License to manufacture for experimental purpose is required under chapter II Rule 3(v) & 21 of Schedule G of LRA Rules 1976 is required.* | *Not Attached.* |

| | |
|---|---|
| *Investigator Brochure and summary of Investigator Brochure is required.* | *attached* |
| *Detailed CV of principal Investigator for each trial site is required.* | *Following CVs attached.*<br>*Dr. Rameeza Kaleem, Assistant Professor, FJMU/ Sir Ganga Ram Hospital.*<br>*Dr. Attia Bari, Associate Professor, The Children Hospital & The Institute of Child Health Lahore* |
| *Undertaking on stamp paper is required.* | *Attached.* |
| *Copy of ID Card and business Address of applicant is required.* | *Correct CNIC No.32102-9632593-0 and address is Department of Public Health, University of the Punjab, Quaid-e-Azam campus* |
| *Soft Copy Final protocol, Investigator Brochure, Pre-Clinical Data & Safety Studies and Phase-I trial data required for onward submission to Expert under Rule 7 (4) of Bio-Study Rules 2017.* | *Not Provided.* |

*6. Applicant has provided above mentioned documents but following required yet.*

*i. IRB approval from DHQ, Kahna Nau, Lahore is required along with composition of committee i.e. names and designation of members.*

*ii. Separate application for each clinical trial site is required on Form-I of Bio-Study Rules 2017 from DHQ, Kahna Nau, Lahore.*

*iii. License to manufacture for experimental purpose is required under chapter II Rule 3(v) & 21 of Schedule G of LRA Rules 1976 is required.*

*7. Shortcomings were communicated vide this office letter dated 2nd April 2021.*

*8. The reply from Dr Javeria Saleem, Principal investigator in response to this office letter dated 2nd April 2021 is as following;*

*9. A separate application has been made from CTS Kahana Nau on Form-I. Previously IRB approval was issued by IRD Global Limited, Singapore and now same has been edited and logo of IRD has been erased. Further, IRB approval has been issued to Public Health/ University of Punjab instead of THQ Kahna Nau. License to manufacture placebo for experimental purpose under chapter II Rule 3(v) & 21 of Schedule G of LRA Rules 1976 has not been provided.*

*10. It was proposed that applicant may be asked again to provide IRB approval from DHQ Kahna Nau to carry out the trial at DHQ Kahna Nau and license to manufacture placebo or the case may be placed before CSC along with shortcomings.*

*11. Following queries were asked from applicant vide this office letter dated 27th July 2021.*

*i) IRB approval from THQ, Kahna Nau, Lahore is required along with composition of committee i.e. names and designation of members.*

*ii) License to manufacture for experimental purposes is required under Chapter II Rule 3(v) & 21 of LRA Rules 1976 is required.*

*iii) Clarification is required for phase of trial as documents provided previously indicate that this trial is of Phase II while current documents submitted reveals that phase II trial has already been conducted by PI and paper has been published in American Journal of clinical Nutrition on 8th June 2010.*

*iv) The product, intended to be used as investigational product, is already registered in Pakistan and freely available in market, then why PI wants to conduct the trial of the same product? How the case for already registered product can be considered for Phase II trial.*

*12. A letter from PI and CRO was received respectively wherein they have addressed the queries of this office. PI has enclosed the IRB approval issued by IRB of Indus Hospital & Health Network under ICH guidelines for GCP E6, USFDA 21 CRF parts 50 and 56, US Department of health and Human Services (45 CFR part 46) etc. They have also enclosed the copy of Form 3 where in manufacturer i.e. M/s GT pharma has applied for grant of Drug Manufacturing License for experimental purposes. PI has explained that previous trial was on uncomplicated severe acute malnutrition children, community based conducted by lady health workers. Test conduct in that biochemical test were albumin, calcium and vitamin D, body composition was not measured and development assessment by DDST. The current applied trial is in complicated sever acute malnutrition children, hospital based to be conducted by pediatrician, blood tests to be conducted are calcium, albumin, CRP, 25 (OH)D, total alkaline, ferritin, Hepcidin, Urine examination include calcium, creatinine, osmolarity and stool examination include inflammatory market and microbiome. They have further stated that product intended to be used as investigational product is already registered in Pakistan and freely available but the safety of the product in the age group of 6-59 months with complicated severe acute malnutrition in the hospitalized children is not reported in the Pakistan population. The indication and dose being used in this age group and study is not available from previous study. Applicant has also attached PHCC registration certificate, DRAP license for Chughtai lab, MOU of Chughtai lab and Punjab university, SOP for albumin, calcium, CBC testing, SOP for handling and testing of samples, contract of PU with QMUL, material transfer agreement with QMUL.*

*13. It was proposed that application may be forwarded to Expert under rule 7 (4) of Bio-Study Rules 2017 or may be forwarded to CSC members and case may be placed in forthcoming CSC meeting.*

*14. Following proposed clinical trial sites applied for this trial have been approved by CSC in its 29th CSC meeting held on 05th August 2021.*

*i. Tehsil Headquarter (THQ), Kahna Nau, Lahore to carry out Phase III & IV clinical trials.*

*ii. Fatima Jinnah Hospital/ Sir Ganga Ram Hospital, Lahore to carry out Phase III & IV clinical trials.*

***SUBMITTED FOR CONSIDERATION OF CSC***

*15. Dr Javeria Saleem, Principal investigator and Mr. Asim Munir representative from M/s DRK Pharma Solutions, Lahore, joined the meeting virtually and briefed the CSC members regarding subject clinical trial and answered the questions raised by some of the CSC members.*

***Decision:***

*The CSC after detailed deliberation and discussion decided to approve the Clinical Trial/ Study titled "Trial of High Dose Vitamin D in The Treatment of Complicated Severe Acute Malnutrition (ViDiSAM)." Phase II at following sites subject to submission of license/ permission to manufacture Vitamin D and its placebo with the name of ViDiSAM from concerned DRAP's Directorate/Board.*

1. *M/s Tehsil Headquarter (THQ), Kahna Nau, Lahore*
2. *Department of Social & Preventive Pediatrics situated at M/s Fatima Jinnah Hospital/ Sir Ganga Ram Hospital, Lahore.*

*The CSC further deliberated and discussed in details that both sites mentioned above are allowed to carry out this specific study i.e. ViDiSAM clinical trial for Phase II as it was informed by the applicant that these sites will only collect samples while testing will be done/ performed at M/s Chughtai Lab. (DRAP approved Bio-analytical Lab), Lahore, University of East Anglia, Bioanalytical Facility, Norwich Research Park, Norwich, NR4 7UQ, UK and Blizzard Institute, Bart's and The London School of Medicine and Dentistry Queen Mary University of London.*

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**Decision of 31st CSC meeting:**

*CSC ratified the decision of committee taken in its 30th meeting held on 12th August 2021.*

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***ADDITIONAL AGENDA***

***AGENDA ITEM I: -***

*Subject:* ***APPLICATION FOR APPROVAL OF M/S SOUTH CITY HOSPITAL, KARACHI TO ACT AS CLINICAL TRIAL SITE. F. NO 15-33/2021-DD (PS).***

*Case is from Dr. Sadia Virk Rizvi (CNIC-42302-5833928-2), CEO, South City Hospital, Karachi, dated 17th May 2021, the site is situated at St-1, Block-3, Shahra-e-Firdousi, Clifton, Karachi. Wherein the request has been made to license the subject site to act as Clinical Trial Site for Phase I, II, III & IV Clinical Trials. Application is on prescribed form-I along with a prescribed fee of Rs.100000/- paid vide challan number 5500258312, dated 19th May 2021.*

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

| ***S. No.*** | ***Required Documents / Information*** | ***Page No.*** | ***Remarks*** |
|---|---|---|---|
| *1* | *Application on prescribed Form-I of The Bio-Study Rules 2017.* | *07-08* | *Attached.* |
| *2* | *Prescribed processing fee* | *02-03* | *Fee of Rs.100000/- paid vide challan number 5500258312, dated 19th May 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).* | *11-19* | *Provisional licence number SHCC/DLA/PL/0002/2019, dated 11/03/2019 is attached, issued by the Healthcare Commission Sindh.*<br>*Regular licence to be issued by the Healthcare Commission Sindh, needs to be provided.*<br>*SECP registration certificate need to be provided.* |
| *4* | *Details of premises including layout plan of the site.* | *21-30* | *Attached.* |
| *5* | *Details of the section-wise equipment and machinery required for the analytical or bio-analytical and clinical studies.* | *33-58* | *Attached list of equipment is not fulfilling the requirements of Phase-I & II clinical trials in which Pharmacokinetic studies are required.* |
| *6* | *Names and qualifications of the above sections along with their staff.* | *91-96* | *Attached.* |
| *7* | *Details of the allied facilities associated with the trial center including ambulatory services, emergency handling, etc.* | *---* | *Not provided.* |
| *8* | *Undertaking on stamp paper* | *08* | *Attached.* |

*3. Following shortcomings observed after initial scrutiny:*

*a. Regular licence issued by the Healthcare Commission Sindh, needs to be provided.*

*b. SECP registration certificate need to be provided.*

*c. Attached list of equipment is not fulfilling the requirements of Phase-I & II clinical trials in which Pharmacokinetic studies are required.*

*d. Details of the allied facilities associated with the trial center including ambulatory services, emergency handling, etc., need to be provided.*

*4. The following panel was constituted by chairman CSC to conduct the inspection of M/S South City Hospital, Karachi:*

i. *Prof. Dr. Aamir Jaffary, SIUT, Karachi;*
ii. *Dr. Ahson Siddiqi Karachi;*
iii. *Dr. Abdur Rashid, DRAP, Islamabad;*
iv. *Prof. Muhammad Raza Shah, HEJ, Karachi;*
v. *Dr. Saif Ur Rehman, CDL, DRAP, Islamabad*

***5.*** *However, the inspection was conducted by Prof. Dr. M. Iqbal Afridi, Prof Dr. M. Raza Shah, Dr. Abdur Rashid, Dr. Saif Ur Rehman Khattak and Dr. Naseem Salahuddin**.** Remarks of the Inspection Team are followings;*

*"Keeping in view the infrastructure, spacious space and environment, equipment, emergency and ambulatory services including ambulance, SOPs, documentation, archive room, human resource and training, the panel recommends the South City Hospital as clinical trial site for Phase III and IV."*

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

***Decision:***

*The CSC after due deliberation and discussion, in the light of panel inspection report and the recommendation of panel of experts/inspectors, unanimously decided to approve the Clinical Trial Site situated at M/s South City Hospital, Karachi as clinical trial site for Phase III and IV clinical trials."*

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**Decision of 31st CSC meeting:**

*CSC ratified the decision of committee taken in its 30th meeting held on 12th August 2021.*

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***AGENDA ITEM II***

***REQUEST FOR APPROVAL OF CHILDREN'S HOSPITAL KARACHI AND RESEARCH INSTITUTE FOR BLOOD, GENETIC & BONE MARROW TRANSPLANT, KARACHI TO ACT AS CLINICAL TRIAL SITE. F. No.15-47/2020 DD (PS)***

*Case is from Dr. Saqib Hussain Ansari, Children's Hospital Karachi and Research Institute for Blood, Genetic & Bone Marrow Transplant, Karachi and was presented in 15th CSC meeting, which decided as under:*

*"CSC after detailed deliberation decided to authorize the Chairman, CSC for constitution of an inspection panel for inspection of facilities at applied clinical trial site. The case will be again brought after before the CSC after deliberation and decision after inspection"*

*2. The Chairman, CSC constituted the following panel for re-inspection of M/s Children Hospital Karachi:*

i. *Dr. Abdur Rashid, DRAP, Islamabad;*
ii. *Prof. Dr. Aamir Jaffary, SIUT, Karachi;*

iii. *Dr. Ahson Siddiqui, Karachi;*
iv. *Dr. Najam Us Saqib; DRAP, Karachi*
v. *Prof. Dr. Nisar Hussain Shah, BZU, Multan.*

*3. However, the inspection was conducted by Prof. Dr. M. Iqbal Afridi, Prof Dr. M. Raza Shah, Dr. Abdur Rashid, Dr. Najam Us Saqib, and Dr. Naseem Salahuddin. The remarks are as under:*

*"This was the second visit of Children Hospital Karachi. Keeping in view the experienced and trained human Clinical Personnel, Children Bone Transplant facilities, approved site of HOTA, SOPs, documentation, archive facilities, IT facilities, hired biostatistician and other emergency and ambulatory services panel recommend Children Hospital, Karachi., St 2/2, Block 5, Gul-Shan-E Iqbal Karachi recommends Clinical Trial Site for Phase-III and IV."*

***3. SUBMITTED FOR CONSIDERATION AND DELIBERATION OF CSC.***

***Decision:***

*The CSC after due deliberation and discussion, in the light of panel inspection report and the recommendation of panel of experts/inspectors, unanimously decided to approve the Clinical Trial Site situated at M/s Children's Hospital Karachi and Research Institute for Blood, Genetic & Bone Marrow Transplant, Karachi., St 2/2, Block 5, Gul-Shan-E Iqbal Karachi as clinical trial site for Phase III and IV clinical trials."*

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**Decision of 31st CSC meeting:**

*CSC ratified the decision of committee taken in its 30th meeting held on 12th August 2021.*

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***AGENDA ITEM III***

***APPLICATION FOR THE GRANT OF GENERALIZED TRIAL SITE LICNSE TO DOW UNIVERSITY OF HEALTH SCIENCES, OJHA CAMPUS, KARACHI. F. No: 15-36/2021-DD (PS)***

*Case is from Prof. Badar Faiyaz Zuberi, CNIC No.42301-0868312-5, Dow University of Health Sciences, KDA Scheme 33, Gulzar-e-Hijri, SUPARCO Road, Ojha Campus, Karachi, dated 20th May 2021, wherein the request has been made for the grant of generalized Clinical Trial Site license to Dow University of Health Sciences, Ojha Campus, Karachi. The application is on prescribed Form-I of the Bio-Study Rules 2017, along with prescribed fee of Rs.100000/- deposited vide challan number 96509260264 dated 18th May 2021.*

*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*** | ***Page No.*** | ***Remarks*** |
|---|---|---|---|
| *1* | *Application on prescribed Form-I of The Bio-Study Rules 2017.* | *05* | *Attached*<br>*Not signed by applicant.* |
| *2* | *Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the* | *08* | *Attached.*<br>*It's a chartered university under the* |

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| | *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).* | | *Dow University of Health Sciences Act 2004.*<br>*Applied site is tertiary care Government Hospital.* |
| *3* | *Details of premises including layout plan of the site.* | *10-24* | *Attached.* |
| *4* | *Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.* | *26-55* | *Attached* |
| *5* | *Names and qualifications of the above sections along with their staff.* | *57-63* | *Attached* |
| *6* | *Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.* | *65-66* | *Attached* |
| *7* | *Affidavit on Stamp paper* | *68* | *Attached* |
| *8* | *Prescribed Fee* | *02* | *Rs.100000/- deposited vide challan number 96509260264 dated 18th May 2021.* |

*3. After initial scrutiny following shortcomings observed*

*i. Application form was not signed by the applicant.*
*ii. Phases of trial were not elaborated so that the application/inspection may be conducted accordingly.*

*4. Accordingly, the applicant submitted the signed Form-I and informed that site is for conduct of Phase-I, II, III, and IV. The subject applied site was approved for specific trial titled "Immunoglobulin Therapy for Passive Immunization of Critically Ill COVID-19 Patients", and licence to act as Clinical Trial Site (CTS) issued (CTS-0040). The organization (Dow University of Health Sciences, Ojha Campus, Karachi) is already licensed for BA/BE Studies Center. As the applied site is for conduct of Phase-I, II, III & IV Clinical Trials, the site was again inspected.*

*5. The Chairman, CSC constituted the following panel for inspection of Generalized Trial Site of Dow University of Health Sciences, Ojha Campus, Karachi:*

*i. Prof. Dr. Aamir Jaffary, SIUT, Karachi;*
*ii. Dr. Ahson Siddiqi Karachi;*
*iii. Dr. Abdur Rashid, DRAP, Islamabad;*
*iv. Dr. Najam Us Saqib, Additional Director, Karachi, DRAP; and*
*v. Prof. Dr. Nisar Hussain Shah, Faculty of Pharmacy, B.Z.U, Multan.*

*6. However, the inspection was conducted by Prof. Dr. M. Iqbal Afridi, Dr. Abdur Rashid, Dr. Naseem Salah Ud Din and Dr. Najam Us Saqib (no signature). The fee for generalized trial sites is submitted only for two i.e. Dow University of Health Sciences sites Gulzar-e- Hijri/ Suparco Road, KDA scheme-3 Karachi, and Dow Medical Hospital Sindh, The Remarks of Panel are as under:*

*" Keeping in view the whole infrastructure of Dow University of Health Sciences (Clinical Trial Unit), Trained professional Human resources, equipment, instruments, approved BA/BE studies, CRO, Clinical trial site for IVIG, SOPS for animal/ preclinical studies, Research Facilities for animal studies, biologicals, clinical research facilities in different departments, surgical operation theatres, OPD and indoor facilities, emergency and ambulatory services, waste management and other allied facilities, the Panel Unanimously recommends for Clinical Trial Site for zero (animal/ preclinical studies) Phase I, II, III, and IV at Gulzar-e- Hijri/ Suparco Road, KDA scheme-3 Karachi, including Dow Medical Hospital Sindh, Infectious Disease Hospital and Dental Hospital. They will use facilities jointly for research purpose."*

*7. Detailed Inspection Report signed by Dr. Abdur Rashid is under as under:*

i. *Dow University Karachi has very good facility for zero phase (animal studies / pre-clinical study) located at Ojha Campus near Dow University Hospital. Section wise equipment list is attached with the report. There is basic biological manufacturing facility central animal house research and development department allied facilities equipped with latest equipment instruments and machinery are available to conduct all phase zero studies. 23 technical human resources having expertise in Toxicology, molecular pathology immunology, microbiology, veterinarians, chemistry, animal nutrition and feed sciences, stem cells and regenerative medicines and other relevant expertise are available for zero phase studies. There is facility of advance research laboratory (Pre-clinical), Toxicity testing laboratory system, quality control system, QC equipment, basic biological manufacturing system (plasma processing) central animal house, QA along-with all SOP's are available.*

ii. *Dow University of Health Sciences have also facilities for phase-I and II. They have also ready approved Bioavailability / Bioequivalence Centre, contract research organization (CRO) and clinical trial site for COVID (IVIG) by Drug Regulatory Authority of Pakistan and license number are uploaded at DRAP website. They have the facility for pharmacokinetic and pharmacodynamics studies clinical trial unit can conduct Phase-I and Phase-II facilities for normal subjects and diseased subjects using BA/BE centre, CRO, COVID approved site, using Dow University Hospital, Sindh Infectious Disease Hospital, Dental Hospital, ICU, liver transplant facilities, Emergency and ambulatory services facilities in all departments, animal studies, research laboratories and other allied Testing facilities.*

iii. *Dow University of Health Sciences Clinical Trial Unit have also facilities for conduct of Phase-III and IV. As already mentioned they have approved license for BA/BE, CRO, Clinical Trial Site (IVIG) at Ojha Campus (Main Campus) and at Clinical Trial Site for COVID at Sindh Infectious Disease hospital (Nipa Churangi) and other facilities of Dow University Health Sciences, Dow University Hospital, Dow Dental Hospital Main Campus called Ohja Campus and Sindh Infectious*

*Disease Hospital (NIPA). The Clinical Trial Unit can conduct Phase-I and Phase IV trial.*

*iv. So, keeping in view the facilities at Dow University of Health Sciences, Clinical Trial Unit, Ojha Campus, Suparco Road, off main University Road, Gulzar-e- Hijri, Scheme 33, Karachi, along with allied hospitals are recommended for Phase I, II, III and IV clinical trials/ study.*

*8.* ***SUBMITTED FOR CONSIDERATION AND DELIBERATION OF CSC.***

***Decision:***

*The Secretary CSC pointed out the shortness of quorum and the case was deferred accordingly as advised the Chair.*

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**Decision of 31st CSC meeting:**

*CSC ratified the decision of committee taken in its 30th meeting held on 12th August 2021.*

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**AGENDA ITEM II: APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, FROM NATIONAL INSTITUTE OF CARDIOLOGY (NICVD) KARACHI. F. No.15-15/2021 DD (PS)**

Application is from Professor Syed Nadeem Hassan Rizvi, Director Interventional Cardiology Program & Cath Lab, M/s National Institute of Cardiovascular Diseases, Rafique (H.J) Shaheed Road, Karachi, has applied for license to act as Clinical Trial Site for Phase III clinical trials. The application is on Form-I of the Bio-Study Rules 2017 on stamp paper with fee of Rs.100,000/- submitted vide challan No. 2042302.

2. Details of attached documents as per prerequisites of the Bio-Study Rules 2017 is as follows:

| S. No. | Required Documents / Information | Remarks |
|---|---|---|
| 1 | Application on prescribed Form-I of The Bio-Study Rules 2017. | Form-I submitted on stamp paper. |
| 2 | Prescribed processing fee | Fee challan of Rs.100,000/- attached submitted vide slip No. 2042302. |
| 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 | Not Attached.<br>The National Institute of Cardiovascular Diseases is a government autonomous hospital and postgraduate teaching institute. |

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|---|---|---|
| | address of the company and its directors). | |
| 4 | Details of premises including layout plan of the site. | Layout Plan not attached.<br>Total Land. 460,000 sq. Ft (approximately)<br>Total Bed Capacity 650 Beds<br>Total Cath Labs 08<br>Total Surgical Operation Theater 07<br>Emergency Department 100<br>Well-equipped ICU & CCU |
| 5 | Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies. | Details of Machinery and Equipment;<br>Cath Labs 08<br>Toshiba Japan 07 Philips Netherland 01<br>IVUS Machine Volcano USA<br>IVUS Catheter Volcano USA<br>Stents All FDA Approved. |
| 6 | Names and qualifications of the above sections along with their staff. | Prof. (Dr.) Syed Nadeem Hassan Rizvi<br>Prof. (Dr.) Tahir Saghir<br>Dr. Muhammad Naeem Mengal |
| 7 | Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc. | Emergency Department:<br>Capacity 100 beds, fully equipped with 55 beds of intervention ward with CCU facility.<br>Timing 24/7<br>Cardiac Surgery Operation Theater:<br>Capacity 07 operation theaters, fully equipped<br>Timing 08am to 08pm the same timing while the trial patients will be enrolled for procedures. |
| 8 | Undertaking on stamp paper | Print of form 1 provided on stamp paper |

3. The following panel was constituted by Chairman CSC for inspection of subject clinical trial site:

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

4. Due to unavailability of nominated panel members and as powers conferred by CSC to Chairman CSC following new panel was constituted in reference to para 15/N.

i. Dr. Naseem Salahuddin, The Indus Hospital, Karachi.
ii. Dr Iqbal Afridi, Dean College of Physicians & Surgeons, Karachi.
iii. Dr. Saif Ur Rehman Khattak, Additional Director/In charge CDL, Karachi.
iv. Prof Dr. Raza Shah, HEJ, Karachi.

5. Inspection report forwarded by Chairman CSC through WhatsApp, original inspection report needs to be submitted formally. The panel conducted the inspection on 12th August, 2021 and submitted the report with following remarks;

> *"It is one of the largest cardiac institute of Pakistan serving the nation since 1956. Required facilities and structure for clinical trials are available. The management also has plans to improve the center further".*

- *Recommended for approval.*

6. It is submitted that as per record the applicant has applied for approval of site to conduct Phase III trials.

7. Submitted for perusal, discussion and decision of CSC.

8. Presentation & Discussion:

Maj Gen (R) Dr. Azhar Mehmood Kayani, Executive Director, Rawalpindi Institute of cardiology, Rawalpindi joined virtually in the 30th CSC meeting and briefed the CSC members regarding subject clinical trial and answered the questions raised by some of the CSC members.

Secretary CSC presented the case along with its background, further appraised that the application is for Phase-III clinical trial site and that the panel has not mentioned the phase of trial in the inspection report. As the application is for Phase-III clinical trial so it is proposed for approval of Phase-III clinical trials & the committee may decide accordingly. Chairman CSC added that as per application it should be considered only for Phase-III Clinical Trial Site, further Chairman CSC directed that next time Phase/Phases of trial should be mentioned in the inspection letter so the site be inspected accordingly and contact numbers of PI of the site or contact person should also be included in the letter.

Dr. Mushtaq Ahmad, Co-Opted member CSC raised some concerns regarding clinical trial titled "Comparison of One Month Versus Dual Antiplatelet Therapy After Implantation of Drug Eluding Stunts Guided by Either Intravascular Ultrasound or Angiography in Patients with Acute Coronary Syndrome" & recommended that, as the trial is of critical nature so trial subjects should be in close vicinity of the Clinical Trial Site and in case of any emergency (i.e. blockage of arteries) trial subjects may get emergency/ambulatory services & intensive care promptly. Prof. Dr. Javed Akram also supported the concerns raised by Dr. Mushtaq Ahmad & added that PIs of all Clinical Trial Sites should develop a safety protocol so that being at high risk, the trial subjects may get 24/7 accessibility in case of any emergency or Serious Adverse Event. He further suggested that ADRs in this study should be reported within 24 hours & a weekly or fortnightly report in this regard should also be submitted to DRAP so that keeping in view the nature of ADRs the same may be forwarded to one or more members of CSC for review & in the light of input/comments/conclusion by the CSC member(s)/Expert(s) CSC may review its decision to halt the study/trial in best public interest if required so. It was also suggested that undertaking to implement these suggestions of the committee may also sought from the PIs & Co-PIs of all the four clinical trial sites.

**Decision:**

*The CSC in pursuance to the recommendations of the inspection panel & in the light of discussion/deliberations unanimously decided to grant licence to M/s National Institute of Cardiovascular Diseases (NICVD), Rafique (H.J) Shaheed Road, Karachi to act as Clinical Trial Site for Phase-III Clinical Trials only subject to the following recommendations of CSC:*

*i. The proposed trial/study titled "Comparison of l-month versus l2-month Dual Antiplatelet Therapy after implantation of Drug-Eluting Stents Guided by either Intravascular Ultrasound*

*or Angiography in Patients with Acute Coronary Syndrome: The Prospective, Multicenter, Randomized, Placebo-controlled IVUS-ACS and ULTIMATE-DAPT trials" is of critical nature so trail subjects should be in close vicinity of the Clinical Trial Site. So that, in case of any emergency/serious adverse events (i.e. Blockage of arteries) the trial subjects may get emergency/ambulatory services & intensive care promptly*

ii. *Principal Investigator of the Clinical Trial Site should develop a safety protocol so that being at high risk, the trial subjects may get 24/7 accessibility in case of any emergency or Serious Adverse Event.*

iii. *ADRs in the proposed study should be reported within 24 hours & a weekly or fortnightly report in this regard should also be submitted to DRAP.*

iv. *Undertaking for implementation of above-mentioned recommendations of the committee should be submitted to the Division of Pharmacy Services by PIs & Co-PIs of the clinical trial site.*

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**AGENDA ITEM III: APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, FROM CHAUDHARY PERVAIZ ELLAHI INSTITUTE OF CARDIOLOGY, MULTAN (CPEIC), MULTAN. F. No.15-16/2021 DD (PS)**

Application is from Professor Dr. Muhammad Bilal Ahsan Qureshi, Ch. Pervaiz Elahi Institute of Cardiology, Abdali Road, Multan wherein he has applied for license to act as Clinical Trial Site for Phase III clinical trials. The application is on Form-I of the Bio-Study Rules 2017 on stamp paper with fee of Rs.100,000/- submitted vide challan No. 1981972.

2. Details of attached documents as per prerequisites of the Bio-Study Rules 2017 is as follows:

| S. No. | Required Documents / Information | Remarks |
|---|---|---|
| 1 | Application on prescribed Form-I of The Bio-Study Rules 2017. | Form-I submitted on stamp paper. |
| 2 | Prescribed processing fee | Fee challan of Rs.100,000/- attached submitted vide slip No. 21981972. |
| 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.<br>Chaudhary Pervaiz Elahi Institute of Cardiology, Multan is a tertiary care Government cardiology institute. Its services are free of cost, funded by Government of the Punjab, Health Department. |
| 4 | Details of premises including layout plan of the site. | Layout Plan not attached.<br>Total Land. 250 Kanals<br>Total Bed Capacity 260 Beds<br>Total Cath Labs 05<br>Total Surgical operation Theater 05<br>Emergency Department 60 |

| | | |
|---|---|---|
| | | Well-equipped ICU & CCU |
| 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. | Prof. (Dr.) Syed Nadeem Hassan Rizvi<br>Prof. (Dr.) Tahir Saghir<br>Dr. Muhammad Naeem Mengal |
| 7 | Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc. | Emergency Department:<br>Capacity 100 beds, fully equipped<br>Timing 24/7<br>Cardiac Surgery Operation Theater:<br>Capacity 07 operation theaters, fully equipped<br>Timing 08am to 08pm the same timing while the trial patients will be enrolled for procedures. |
| 8 | Undertaking on stamp paper | Print of form 1 provided on stamp paper |

3. After initial evaluation of the application shortcomings as mentioned in table were communicated to the applicant.

4. The following panel was constituted by Chairman CSC for inspection of subject clinical trial site:

i. Prof. Dr. Mehboob-e-Rabbani, Ex-Dean Faculty of Pharmacy, B. Z. U. Multan.
ii. Dr. Abdur Rashid (Coordinator), DRAP, Islamabad.
iii. Prof. Dr. Mushtaq Hussain Khan, (R) Cardiac Surgeon, Usama Medical Centre, Near Chungi No.1, Suraj, Miani Road, Multan.
iv. Prof. Dr. Nisar Hussain Shah, Faculty of Pharmacy, B.Z.U. Multan.
v. Dr Liaqat Ali, AP/Senior Registrar, Cardiology, Nishtar Medical College, Multan

5. Nominated panel members inspected the subject CTS on 16-08-2021and submitted the inspection report with following remarks:

> *"Keeping in view the cardiac facilities, 5 Cath-Labs, technical human resource, their expertize, trainings, SOP, documentations, archive room, waste management, IT facilities, pharmacy, and other facilities, the panel recommends Ch. Parvaiz Elahi Institute of Cardiology, Abdali Road Multan as Clinical Trial Site for Phase III and IV".*

- Recommended for approval.

6. It is submitted that as per record the applicant has applied for approval of site to conduct Phase III trials only.

7. <u>Submitted for perusal, discussion and decision of CSC.</u>

8. <u>Presentation & Discussion:</u>

Maj Gen (R) Dr. Azhar Mehmood Kayani, Executive Director, Rawalpindi Institute of cardiology, Rawalpindi joined virtually in the 30th CSC meeting and briefed the CSC members regarding subject clinical trial and answered the questions raised by some of the CSC members.

Secretary CSC presented the case along with its background, further appraised that the application is for Phase-III clinical trial site and that the panel has not mentioned the phase of trial in the inspection report. As the application is for Phase-III clinical trial so it is proposed for approval of Phase-III clinical trials & the committee may decide accordingly. Chairman CSC added that as per application it should be considered only for Phase-III Clinical Trial Site, further Chairman CSC directed that next time Phase/Phases of trial should be mentioned in the inspection letter so the site be inspected accordingly and contact numbers of PI of the site or contact person should also be included in the letter.

Dr. Mushtaq Ahmad, Co-Opted member CSC raised some concerns regarding clinical trial titled "Comparison of One Month Versus Dual Antiplatelet Therapy After Implantation of Drug Eluding Stunts Guided by Either Intravascular Ultrasound or Angiography in Patients with Acute Coronary Syndrome" & recommended that, as the trial is of critical nature so trial subjects should be in close vicinity of the Clinical Trial Site and in case of any emergency (i.e. blockage of arteries) trial subjects may get emergency/ambulatory services & intensive care promptly. Prof. Dr. Javed Akram also supported the concerns raised by Dr. Mushtaq Ahmad & added that PIs of all Clinical Trial Sites should develop a safety protocol so that being at high risk, the trial subjects may get 24/7 accessibility in case of any emergency or Serious Adverse Event. He further suggested that ADRs in this study should be reported within 24 hours & a weekly or fortnightly report in this regard should also be submitted to DRAP so that keeping in view the nature of ADRs the same may be forwarded to one or more members of CSC for review & in the light of input/comments/conclusion by the CSC member(s)/Expert(s) CSC may review its decision to halt the study/trial in best public interest if required so. It was also suggested that undertaking to implement these suggestions of the committee may also sought from the PIs & Co-PIs of all the four clinical trial sites.

**Decision:**

*The CSC in pursuance to the recommendations of the inspection panel & in the light of discussion/deliberations unanimously decided to grant licence to M/s Ch. Pervaiz Elahi Institute of Cardiology, Abdali Road, Multan to act as Clinical Trial Site for Phase-III Clinical Trials only subject to the following recommendations of CSC:*

i. *The proposed trial/study titled "Comparison of l-month versus l2-month Dual Antiplatelet Therapy after implantation of Drug-Eluting Stents Guided by either Intravascular Ultrasound or Angiography in Patients with Acute Coronary Syndrome: The Prospective, Multicenter, Randomized, Placebo-controlled IVUS-ACS and ULTIMATE-DAPT trials" is of critical nature so trail subjects should be in close vicinity of the Clinical Trial Site. So that, in case of any emergency/serious adverse events (i.e. Blockage of arteries) the trial subjects may get emergency/ambulatory services & intensive care promptly*
ii. *Principal Investigator of the Clinical Trial Site should develop a safety protocol so that being at high risk, the trial subjects may get 24/7 accessibility in case of any emergency or Serious Adverse Event.*
iii. *ADRs in the proposed study should be reported within 24 hours & a weekly or fortnightly report in this regard should also be submitted to DRAP.*
iv. *Undertaking for implementation of above-mentioned recommendations of the committee should be submitted to the Division of Pharmacy Services by PIs & Co-PIs of the clinical trial site.*

**AGENDA ITEM IV: APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, FROM PUNJAB INSTITUTE OF CARDIOLOGY (PIC), LAHORE. [F. No.15-60/2021 DD (PS)]**

Application is from Dr. Muhammad Anjum, Assistant professor of Cardiology, Punjab Institute of cardiology, jail Road Lahore, wherein he has requested for clinical trial site may be processed on priority basis. applicant has requested for grant of license to act as a Clinical Trial Site. The application is on Form-I of the Bio-Study Rules 2017 with fee of Rs.100,000/- submitted vide challan no. 2027386.

2. Details of attached documents as per prerequisites of the Bio-Study Rules 2017 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 | Fee challan of Rs.100,000/- attached submitted vide slip No. 2027386. |
| 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). | Punjab Institute of Cardiology is a tertiary care government cardiology institute. Its services are free of cost, funded by government of the Punjab, health department. |
| 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. | Prof. Dr. Saqib Shafi Sheikh<br>Prof. Dr. Shahid Hameed<br>Dr. Muhammad Anjum Rana<br>Dr. Muhammad Ammar Rashid |
| 7 | Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc. | Emergency<br>Capacity 200 bedded<br>Timing 24/7<br>Operation Theater (Cardiac Surgery)<br>Capacity 60 bedded<br>Timing 24/7 |
| 8 | Undertaking on stamp paper | Print of form 1 provided on stamp paper |

3. The following panel was constituted by Chairman CSC for inspection of subject clinical trial site:

i. Prof. Dr. Javed Akram, VC, UHS, Lahore.
ii. Prof. Dr. Farhana Badar, Biostatistician, SKMCH&RC, Lahore.
iii. Dr. Abdur Rashid (Coordinator), Director, DRAP, Islamabad.
iv. Prof. Dr. Nadeem Irfan Bukhari, College of Pharmacy, Punjab university, Lahore.
v. Dr. Javed Ashraf, one co-opted expert will be taken from Lahore with respect to cardiovascular drug, stents etc.

4. Nominated panel members inspected the subject CTS on 16-08-2021 and submitted the inspection report with following remarks:

> *"Keeping in view the tertiary care cardiac facility in Lahore, CCU, ICU, Cath-Labs, human resources, their expertize, trainings, IT system, record room, archive room, operation theater, standup generator, emergency handling and ambulance services, pharmacy etc., panel recommends Punjab Institute of Cardiology, Jail Road, Lahore as Clinical Trial Site for Phase III and IV".*

- Recommended for approval.

5. It is submitted that as per record the applicant has applied for approval of site to conduct Phase III trials only.

6. Submitted for perusal, discussion and decision of CSC.

7. Presentation & Discussion:

Maj Gen (R) Dr. Azhar Mehmood Kayani, Executive Director, Rawalpindi Institute of cardiology, Rawalpindi joined virtually in the 30th CSC meeting and briefed the CSC members regarding subject clinical trial and answered the questions raised by some of the CSC members.

Secretary CSC presented the case along with its background, further appraised that the application is for Phase-III clinical trial site and that the panel has not mentioned the phase of trial in the inspection report. As the application is for Phase-III clinical trial so it is proposed for approval of Phase-III clinical trials & the committee may decide accordingly. Chairman CSC added that as per application it should be considered only for Phase-III Clinical Trial Site, further Chairman CSC directed that next time Phase/Phases of trial should be mentioned in the inspection letter so the site be inspected accordingly and contact numbers of PI of the site or contact person should also be included in the letter.

Dr. Mushtaq Ahmad, Co-Opted member CSC raised some concerns regarding clinical trial titled "Comparison of One Month Versus Dual Antiplatelet Therapy After Implantation of Drug Eluding Stunts Guided by Either Intravascular Ultrasound or Angiography in Patients with Acute Coronary Syndrome" & recommended that, as the trial is of critical nature so trial subjects should be in close vicinity of the Clinical Trial Site and in case of any emergency (i.e. blockage of arteries) trial subjects may get emergency/ambulatory services & intensive care promptly. Prof. Dr. Javed Akram also supported the concerns raised by Dr. Mushtaq Ahmad & added that PIs of all Clinical Trial Sites should develop a safety protocol so that being at high risk, the trial subjects may get 24/7 accessibility in case of any emergency or Serious Adverse Event. He further suggested that ADRs in this study should be reported within 24 hours & a weekly or fortnightly report in this regard should also be submitted to DRAP so that keeping in view the nature of ADRs the same may be forwarded to one or more members of CSC for review & in the light of input/comments/conclusion by the CSC member(s)/Expert(s) CSC may review its decision to halt the study/trial in best public interest if

required so. It was also suggested that undertaking to implement these suggestions of the committee may also sought from the PIs & Co-PIs of all the four clinical trial sites.

**Decision:**

*The CSC in pursuance to the recommendations of the inspection panel & in the light of discussion/deliberations unanimously decided to grant licence to M/s Punjab Institute of Cardiology, jail Road Lahore to act as Clinical Trial Site for Phase-III Clinical Trials only subject to the following recommendations of CSC:*

i. *The proposed trial/study titled "Comparison of l-month versus l2-month Dual Antiplatelet Therapy after implantation of Drug-Eluting Stents Guided by either Intravascular Ultrasound or Angiography in Patients with Acute Coronary Syndrome: The Prospective, Multicenter, Randomized, Placebo-controlled IVUS-ACS and ULTIMATE-DAPT trials" is of critical nature so trail subjects should be in close vicinity of the Clinical Trial Site. So that, in case of any emergency/serious adverse events (i.e. Blockage of arteries) the trial subjects may get emergency/ambulatory services & intensive care promptly*
ii. *Principal Investigator of the Clinical Trial Site should develop a safety protocol so that being at high risk, the trial subjects may get 24/7 accessibility in case of any emergency or Serious Adverse Event.*
iii. *ADRs in the proposed study should be reported within 24 hours & a weekly or fortnightly report in this regard should also be submitted to DRAP.*
iv. *Undertaking for implementation of above-mentioned recommendations of the committee should be submitted to the Division of Pharmacy Services by PIs & Co-PIs of the clinical trial site.*

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**AGENDA ITEM V: APPLICATION FOR THE GRANT OF GENERALIZED TRIAL SITE LICNSE TO DOW UNIVERSITY OF HEALTH SCIENCES, OJHA CAMPUS, KARACHI. F. No: 15-36/2021-DD (PS)**

Case is from Prof. Badar Faiyaz Zuberi, CNIC No.42301-0868312-5, Dow University of Health Sciences, KDA Scheme 33, Gulzar-e-Hijri, SUPARCO Road, Ojha Campus, Karachi, dated 20th May 2021, wherein the request has been made for the grant of generalized (Phase-I,II,III & IV) Clinical Trial Site license to Dow University of Health Sciences, Ojha Campus, Karachi. The application is on prescribed Form-I of the Bio-Study Rules 2017, along with prescribed fee of Rs.100000/- deposited vide challan number 96509260264 dated 18th May 2021.

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<br>Not signed by applicant. |
| 2 | 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). | Attached.<br>It's a chartered university under the Dow University of Health Sciences Act 2004. |

| | | |
|---|---|---|
| | | Applied site is tertiary care Government Hospital. |
| 3 | Details of premises including layout plan of the site. | Attached. |
| 4 | Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies. | Attached |
| 5 | Names and qualifications of the above sections along with their staff. | Attached |
| 6 | Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc. | Attached |
| 7 | Affidavit on Stamp paper | Attached |
| 8 | Prescribed Fee | Rs.100000/- deposited vide challan number 96509260264 dated 18th May 2021. |

3. The Chairman, CSC constituted the following panel for inspection of Generalized Trial Site of Dow University of Health Sciences, Ojha Campus, Karachi:

i. Prof. Dr. Aamir Jaffary, SIUT, Karachi;
ii. Dr. Ahson Siddiqi Karachi;
iii. Dr. Abdur Rashid, DRAP, Islamabad;
iv. Dr. Najam Us Saqib, Additional Director, Karachi, DRAP; and
v. Prof. Dr. Nisar Hussain Shah, Faculty of Pharmacy, B.Z.U, Multan.

4. Due to unavailability of nominated panel members and as powers conferred by CSC to Chairman CSC following new panel was constituted:

i. Prof. Dr. M. Iqbal Afridi,
ii. Dr. Abdur Rashid,
iii. Dr. Naseem Salah Ud Din
iv. Dr. Najam Us Saqib

5. Nominated panel members inspected the subject CTS on 10th August 2021 and submitted the inspection report with following remarks:

" Keeping in view the whole infrastructure of Dow University of Health Sciences (Clinical Trial Unit), Trained professional Human resources, equipment, instruments, approved BA/BE studies, CRO, Clinical trial site for IVIG, SOPS for animal/ preclinical studies, Research Facilities for animal studies, biologicals, clinical research facilities in different departments, surgical operation theatres, OPD and indoor facilities, emergency and ambulatory services, waste management and other allied facilities, the Panel Unanimously recommends for Clinical Trial Site for zero (animal/ preclinical studies) Phase I, II, III, and IV at Gulzar-e- Hijri/ Suparco Road, KDA scheme-3 Karachi, including Dow Medical Hospital Sindh, Infectious Disease Hospital and Dental Hospital. They will use facilities jointly for research purpose."

6. Signatures of one of nominated inspection panel member (i.e. Dr. Najam Us Saqib) are missing on inspection report.

7. Detailed Inspection Report signed by Dr. Abdur Rashid is under as under:

i. Dow University Karachi has very good facility for zero phase (animal studies / pre-clinical study) located at Ojha Campus near Dow University Hospital. Section wise equipment list is attached with the report. There is basic biological manufacturing facility central animal house research and development department allied facilities equipped with latest equipment instruments and machinery are available to conduct all phase zero studies. 23 technical human resources having expertise in Toxicology, molecular pathology immunology, microbiology, veterinarians, chemistry, animal nutrition and feed sciences, stem cells and regenerative medicines and other relevant expertise are available for zero phase studies. There is facility of advance research laboratory (Pre-clinical), Toxicity testing laboratory system, quality control system, QC equipment, basic biological manufacturing system (plasma processing) central animal house, QA along-with all SOP's are available.

ii. Dow University of Health Sciences have also facilities for phase-I and II. They have also ready approved Bioavailability / Bioequivalence Centre, contract research organization (CRO) and clinical trial site for COVID (IVIG) by Drug Regulatory Authority of Pakistan and license number are uploaded at DRAP website. They have the facility for pharmacokinetic and pharmacodynamics studies clinical trial unit can conduct Phase-I and Phase-II facilities for normal subjects and diseased subjects using BA/BE centre, CRO, COVID approved site, using Dow University Hospital, Sindh Infectious Disease Hospital, Dental Hospital, ICU, liver transplant facilities, Emergency and ambulatory services facilities in all departments, animal studies, research laboratories and other allied Testing facilities.

iii. Dow University of Health Sciences Clinical Trial Unit have also facilities for conduct of Phase-III and IV. As already mentioned they have approved license for BA/BE, CRO, Clinical Trial Site (IVIG) at Ojha Campus (Main Campus) and at Clinical Trial Site for COVID at Sindh Infectious Disease hospital (Nipa Churangi) and other facilities of Dow University Health Sciences, Dow University Hospital, Dow Dental Hospital Main Campus called Ohja Campus and Sindh Infectious Disease Hospital (NIPA). The Clinical Trial Unit can conduct Phase-I and Phase IV trial.

iv. So, keeping in view the facilities at Dow University of Health Sciences, Clinical Trial Unit, Ojha Campus, Suparco Road, off main University Road, Gulzar-e- Hijri, Scheme 33, Karachi, along with allied hospitals are recommended for Phase I, II, III and IV clinical trials/ study.

8. It is submitted that Dow University of Health Sciences, Karachi submitted two separate applications along with prerequisites for generalized clinical trial sites for Phase-I, II, III & IV clinical trials at following sites:

i. Dow University of Health Sciences sites Gulzar-e- Hijri/ SUPARCO Road, KDA scheme-3 Karachi.
ii. Sindh Infectious Disease Hospital & Research Center, Nipa, Gulshan e Iqbal, Karachi.

9. Further above mentioned both sits are situated at different premises so both sites should be treated separately. Furthermore, Division of Pharmacy Services regulates Clinical Studies on Human Subjects under the Bio-Study Rules 2017 & animal studies or preclinical studies are not dealt under the Bio-Study Rules 2017. Short title and commencement are as under: -

*(1) These rules may be called the Bio-study Rules, 2017.*

*(2) They shall apply to all contract research organizations, laboratories for clinical research, bio-availability and 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.*

8. The subject application was discussed in the 30th CSC meeting & the CSC decided as follows:

**30th CSC Meeting Decision:**

*The Secretary CSC pointed out the shortness of quorum and the case was deferred accordingly as advised the Chair.*

9. Submitted for perusal, discussion and decision of CSC.

10. Discussion & presentation:

Dr. Abdur Rashid briefed the committee regarding the application along with its inspection. Afterwards Dr. Talat Roome joined the meeting & brief the CSC regarding their Phase-0/Preclinical/Animal research facility i.e. **Dow Institute for Advanced Biological & Animal Research and Advanced Research Laboratory, DUHS, Ojha Campus Karachi**). Then Dr. Sadia Asim joined the meeting & brief the CSC regarding their CTU facilities for Phase-I, II, III & IV Clinical Trials at CTU, Dow University, Ojha Campus, Karachi & CTU, Sindh Infectious Diseases Hospital & Research Center, NIPA, Karachi. CSC members asked many questions & are answered by the representative from DUHS, Karachi.

Mr. Ahmad Din Ansari, Secretary CSC appraised the committee that DUHS, Karachi submitted two separate applications for approval of generalized CTS. One is for DUHS, Ojha Campus Karachi & another for Sindh Infectious Diseases Hospital & Research Center, NIPA, Karachi. Further he elaborated that all prerequisites for these applications were already completed & after inspection of both sites a joint report has been submitted to the division along with recommendation for approval of Phase-I, II, III & IV Clinical Trails. Moreover, Phase-0 or preclinical studies are not covered under the Bio-Study Rules 2017 as per its preamble, that is reproduced as follows:

***Short Title and Commencement:***

***(1) These rules may be called the Bio-study Rules, 20 I 7.***
***(2) They shall apply to all contract research organizations, laboratories for clinical research, bio-availability and 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.***

Secretary CSC further added that it is not the mandate of CSC under the Bio-Study Rules 2017 to submit recommendations or approval about the Phase-0 or preclinical studies as these are not covered under the Bio-Study Rules 2017.

Chairman CSC appraised the committee that experts panel visited DUHS for many times and DUHS conducted Phase-I & Phase-II studies of IVIG clinical trials after CSC approval & paper also published in the Lancet and if the IMPs approved then it will be the 1st biological product of Pakistan. Further he added that as a regulatory body even in absence of any provisions regulatory bodies have to conclude any way forward in the situation like this. So as per DRAP act any situation regarding

Therapeutic Goods the Authority has the power to take up the matter. Chairman suggested that Clinical Trial Unit (CTU), DUHS, Ojha Campus, Karachi & Sindh Infectious Diseases Hospital & Research Center, NIPA, Karachi may be approved for Phase-I, II, III & IV clinical trials & the matter regarding Phase-0/preclinical studies may be referred to the Authority for consideration/discussion & decision by the Authority. The CSC will be apprised about the fate of case in the light of the decision of the Authority accordingly.

**Decision:**

*The CSC in pursuance to the recommendations of the inspection panel & in the light of discussion/deliberations unanimously decided to grant licence to following sites to act as generalized Clinical Trial Sites for Phase-I,II,II & IV Clinical Trials:*

i. *Clinical Trial Unit, Dow University of Health Sciences, Ojha Campus Karachi.*
ii. *Sindh Infectious Diseases Hospital & Research Center, NIPA, Gulshan e Iqbal, Karachi.*

*Further it is discussed that as there is no provision in the Bio-Study Rules 2017 to deal with the Phase-0 & preclinical studies and it is also not the mandate of CSC under the Bio-Study Rules 2017 to recommend or approve the site(s) for Phase-0 or preclinical studies. So, it was decided that, the matter regarding Phase-0/preclinical studies of M/s Dow Institute for Advanced Biological & Animal Research and Advanced Research Laboratory, DUHS, Ojha Campus Karachi be referred to the Authority for consideration/discussion & decision by the Authority.*

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**AGENDA ITEM VI: AMENDMENTS IN ALREADY APPROVED CLINICAL TRIAL TITLED "A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE-II CLINICAL TRIAL TO EVALUATE THE EFFICACY & SAFETY OF CBP-307 IN SUBJECTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS (UC)" F.NO.03-59/2021 DD (PS).**

Application submitted Dr. Saeed Hamid (PI), Director, Clinical Trial Unit, Professor & Consultant Gastroenterologist, Aga Khan University Hospital, Karachi, dated 28th June 2021, along with a fee of Rs.25000/- deposited vide challan no.7130454542 dated 25th June 2021. Wherein request has been made for amendments in already approved protocol of clinical trial titled "***A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase-II Clinical Trial to Evaluate the Efficacy & Safety Of CBP-307 in Subjects with Moderate to Severe Ulcerative Colitis (UC)".***

2. Applicant provided following documents along with softcopies received through email:

i. Application along with prescribed fee.
ii. AKUH-IRB approval for amendment of protocol version from 5.0 to 6.0.
iii. NBC- amendment approval letter reference No.4-87/NBC-591/21/1575, dated 11th June 2021.
iv. Amended protocol version 6.0 along with its summary.
v. Amended Investigator's Brochure version 6.0 along with its summary.
vi. Revised Informed Consent Form (English & Urdu with translation certificate).
vii. Updated Inflammatory Bowel Disease Questionnaire (IBDQ) (English & Urdu with translation certificate)
viii. NBC- protocol amendment approval letter reference No.4-87/NBC-591/21/1575, dated 16th June 2021.

3. For technical evaluation, technical documents already mentioned in para 2/N forwarded to CSC members/experts through email on 20th August 2021, for review & evaluation under sub-rule 4 of rule 7 of the Bio-Study Rules 2017. None of the expert member raised any queries.

4. Further, summary of amended protocol 6.0 & summary of amended Investigator's Brochure are also attached as Annex-I & Annex-II

5. Submitted for perusal, discussion and decision of CSC.

6. Discussion & presentation:

Secretary CSC presented the case along with its background, further appraised that the all prerequisites are submitted. Dr. Saeed Hamid (PI), Director, Clinical Trial Unit, Professor & Consultant Gastroenterologist, Aga Khan University Hospital, Karachi, joined the meeting & briefed the case of amendment in already approved Clinical Trial to the CSC members and answered the questions raised by the members.

**Decision:**

*The CSC after deliberation / detailed discussion decided to approve the proposed amendments in the protocol version 6.0 of already approved clinical trial titled "A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase-II Clinical Trial to Evaluate the Efficacy & Safety Of CBP-307 in Subjects with Moderate to Severe Ulcerative Colitis (UC)".*

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**AGENDA ITEM VII:**

**REQUEST FOR PROTOCOL AMENDMENT & CHANGE OF CLINICAL TRIAL SITE FOR 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).**

Application is from Prof. Dr. Muhammad Raza Shah, General Manager, CBSCR, International Center for Chemical & Biological Sciences, University of Karachi, dated 27th July 2021, wherein application is for protocol amendment & change of Clinical Trial Site from Jinnah Post Graduate Medical Center, Rafiqui Sarwar Shaheed Road, Karachi Cantonment, Karachi to CBSCR-ICCBS, Karachi applicant submitted following documents:

i. Application along with prescribed fee paid vide Fee challan number 0815333584, dated 30th June 2021.
ii. Copy of license of M/s CBSCR-ICCBS, Karachi (CTS-0046).
iii. CBSCR-ICCBS, Karachi-IRB/IEC approval letter for protocol amendment version 3.0. dated 15th June 2021.
iv. NBC- amendment for Clinical Trial Site change, approval letter reference No.4-87/NBC-565/21/48, dated 13th July 2021.
v. Amended protocol version 3.0.

2. It is submitted that, the subject Clinical Trial application was placed before CSC in its 19th meeting, held on 12th February 2021. CSC decided as follows:

**Decision:**

*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.*

3. Refer to the CSC decision applicant has provided photocopies of requisite documents and now applicant provided amended protocol & application for change of Clinical Trial Site from M/s Jinnah Post Graduate Medical Center, Rafiqui Sarwar Shaheed Road, Karachi to M/s CBSCR-ICCBS, Karachi

4. Submitted for perusal, discussion and decision of CSC.

5. Discussion & presentation:

Secretary CSC presented the case along with its background, further appraised that the application is now for amendment in protocol & the change of Clinical Trial Site from Jinnah Post Graduate Medical Center, Rafiqui Sarwar Shaheed Road, Karachi Cantonment, Karachi to CBSCR-ICCBS, Karachi. Prof. Dr. Muhammad Raza Shah, General Manager, CBSCR, International Center for Chemical & Biological Sciences, University of Karachi, joined the meeting & briefed the case to the CSC members and answered the questions raised by the members. Dr. Rizwana Chaudhry asked about the status of previously approved trial site & trial status, Secretary CSC informed that the trial was approved by the CSC in its 19th meeting subject to the provision of translated documents for CoPP & GMP certificate for IMPs as well as COA for IMPs. Now applicant provided photocopies of the requisite documents and also submitted an application for amendment/change in trial site. Chairman CSC further informed that, registration certificate for the trial was not issued due to submission of prerequisites and study is not started at JPMC yet. Now after approval registration letter will be issued to start trial at CBSCR-ICCBS, University of Karachi.

**Decision:**

The CSC after deliberation / detailed discussion decided to:

(i) Approve the proposed amendments in the protocol version 3.0 of already approved clinical trial protocol version 2.0 titled "Randomized, Double-Blind, Positive Controlled Study to Evaluate Efficacy & Safety of Fuke Qianjin Capsule in Patients with Pelvic Inflammatory Diseases", and

(ii) Approve the change of Clinical Trial Site from M/s Jinnah Post Graduate Medical Center, Rafiqui Sarwar Shaheed Road, Karachi Cantonment, Karachi to M/s Center for Bioequivalence Studies and Clinical Research (CBSCR)- International Center for Chemical and Biological Sciences (ICCBS), Karachi.

**AGENDA ITEM VIII:**

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

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

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

*Concluding the statement, he said that because of commission/ funding, the Doctors of Hameed Latif had made him a guinea pig for the testing of Eltrombopag by not considering the harmful effects of the drug. He said his life has changed as he cannot lift any weight, neither can he go upstairs because of shortness of breath. He also added that he had a running business in Kuwait before the start of that drug, but, he spent his entire asset on his treatment. He requested for help. He also said that the trial of that company should never have been allowed at that time in Pakistan as in 2007 and 2008, GSK was fined for 300 Billion Dollars by US Court due to death of 14 children in a trial with a drug of that company. Further, in China, that company was also fined for 490 million pounds because of*

*giving money to Doctors. Therefore, it would have been good, if that company had never been allowed for that trial in Pakistan. In the end, he said the doctors have ruined his life and future because he could not lift his children nor can he walk and earn for them. Therefore, he said that he needs justice to be done in the matter.*

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

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

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

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

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

I. The GSK Pakistan submitted that the subject matter with the complainant, Yasir Iqbal, is sub-judice in Consumer Court of Lahore and since the past few hearings the complainant hasn't been appearing before the concerned judge, despite several opportunities. Alongside, a civil suit was filed against the complainant in Civil Court Lahore, where an injunction order is passed against the complainant and is in a field whereby, the complainant is restrained from maligning the company, making derogatory comments or filing any frivolous complaints during the pendency of his complaint before Consumer Court Lahore. It was said that the complainant has undoubtedly violated the Court Order and the company reserves the right to initiate contempt of court proceedings against him.

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

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

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

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

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

the protocol of the study, the dose was increased by 25 mg after two weeks to 75mg once daily on 6th September, 2010.

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

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

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

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

5. Meanwhile, the complainant approached the Lahore court and filed a writ petition under Article 199 of the Constitution of the Islamic Republic of Pakistan in case W.P. No. 45033 of 2021 titled "Yasir Iqbal Versus Government of Pakistan", where he prayed that Respondent No. 2 i.e. Drug Regulatory Authority of Pakistan may kindly be directed to make arrangements for the petitioner to get treatment in a foreign country and to bear all the expenses of the treatment of the petitioner in foreign country expeditiously accordance with the law, to meet the end of justice. The Honorable court on 09th of July, 2021 ordered as under:

*"**Through instant petition, petition is seeking direction for decision on his pending application for making arrangements for petitioner to get treatment in foreign country and also compensate him for his treatment. Add that petitioner would be satisfied if a direction is issued to respondent No. 2 to decide the petitioner pending application strictly in accordance with law, after hearing petitioner and all concerned, through a well-reasoned***

***speaking order, preferably within a period of fifteen days from the date of receipt of certified copy of this order."***

6. In compliance with the decision of Honorable court the case was placed before CSC in its 29th meeting held on 05th August 2021. CSC decided as follows:

***Decision of 29th CSC meeting.***

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

7. Accordingly, the letters have been sent through WhatsApp & email on 24th August 2021.

8. List of respondents is as follows:

i. Mr. Yasir Iqbal S/o Zafar Iqbal (the petitioner/complainant/trial subject). Resident near Bismillah CNG & Bismillah Marriage Hall, GT Road, Muridke, District Sheikhu Pura.
ii. Dr. Yousaf Hasan Khan, Country Medical Director, **Glaxo Smith Kline**, Pakistan Ltd. 35-Dockyard Road West Wharf, Karachi.
iii. Dr. Irfan Ishaq, Additional Medical Director, M/s **Hamid Latif Hospital**, 14-Abu Bakr Block, New Garden Town, Lahore.
iv. Dr. Zeba Aziz, M/s **Hamid Latif Hospital**, 14-Abu Bakr Block, New Garden Town, Lahore.
v. Dr. Muhammad Akram, M/s Hamid Latif Hospital, 14-Abu Bakr Block, New Garden Town, Lahore.
vi. Dr. Abbas, M/s Hamid Latif Hospital, 14-Abu Bakr Block, New Garden Town, Lahore.

9. The complainant and Respondents have been also contacted telephonically for appearance/personal hearing before CSC in its 31st meeting.

10. Submitted for perusal, discussion and decision of CSC.

11. Discussion & presentation:

Secretary CSC past AD(IV) to present the case AD PS(IV) presented the case before the CSC and informed that trail titled "**,** LONGITUDINAL 2-YEAR BONE MARROW STUDY OF ELTROMBOPAG OLAMINE (SB-497115-GR) IN PREVIOUSLY TREATED ADULTS, WITH CHRONIC IMMUNE IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP)", which was approved by Ministry of Health in 2010 and was approved we conducted at following sites

1) National Institute of Blood Diseases Karachi.
2) Hameed Latif Hospital Lahore.

During the Trial one of the participant Mr M Yasir Iqbal submitted a complaint that in 2010 he was getting treatment from Hamid Latif Hospital for Chronic Immune thrombocytopenia and meanwhile during treatment Dr Zeba Aziz (PI) of Hameed Lateef Hospital informed the patient about drug and trial and started therapy with 25mg and next with 20mg and after 2 weeks with 75mg later on subject completed a based development of severe pain inflammation & vomiting in left legs he called Dr Zeba Aziz Dr Zeba Asked him to admit in the ICU later on it was informed that he has developed deep vein thrombosis he was started the warfarin treatment later on installed inferior vena cava filter now he has complained that his filler has been choked he is not fending any treatment blaming that hospital has not informed about this trial he also written application that this trial has been fined in US , China later on he went to the high court & High court decided the case & ordered as follow:

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

Copy of order received by the division. Chairman CSC invited the complainant Mr. M. Yasir Iqbal for personal hearing & presentation of his point of view before CSC. M.Yasir Iqbal joined the meeting in person & informed the committee that in March-2010 he was ill so he went to Hamid Latif Hospital Lahore from Gujranwala. Someone informed him to go to Hamid Latif Hospital Lahore for check-up because his platelets were at 15 percent (15000). At Hamid Latif Hospital, Dr. Zeba Aziz treated & admitted him in the hospital. He was hospitalized for 10-15 days, where he was treated. After discharge from the hospital, he was called 2-3 times a week with CBC report & also started Deltacortil and after 2-3 months, Dr. Zeba Aziz (PI) briefed regarding M/s GSK & its clinical trial & satisfied him regarding trial drug & the trial. It was also informed that during trial complete treatment will be given in case of any Serious Adverse Event. Inform Consent Form also shared. Afterwards trial started with 25mg of IMPs & after 2-3 days he complained regarding inflammation in left leg but the PI increased the dose up to 50mg. Besides to stop trial medication & care of adverse event, Dr. Zeba Aziz (PI) increased the dose up to 75mg. Mr. Yasir claimed that PI should not recruit him in the trial as at that time his platelets level was sufficient. He also claimed that the M/s GSK renowned all over the world for bribing doctors & in 10 countries they are fined. Due to Deep Vein Thrombosis (DVT) he went to all renowned specialists of Lahore including Dr. Javed Akram. At present IVC filter which was installed on advice of Dr. Zeba Aziz from Shaukat Khanum Hospital by Dr Ali Raza. IVC filter choked in 2015 then he went to Dr Zeba Aziz where a representative Doctor From M/s GSK was also available, after seeing reports they said that the reports are clear. But after 2015 IVC filter was choked and IVC vein is blocked. He got test from Al Noor Hospital, CMH, Shifa Hospital and visited to different surgeons for his health recovery. Due to illness he unable to perform normal functions even he barely can walk. Mr Yasir informed he had a business of tyre in Kuwait, statement of also be reproduced and due to trial and subsequent ADRs/ SAEs his business destroyed and he is now unable to do anything, he also informed that he was a married person and have three children's and unable to do for then. All the doctors he met said that there is no cure / treatment in Pakistan.

Dr Javed Akram said that our all sympathise are with Mr Yasir and informed that he chaired the disciplinary committee of PMDC for 10 years and also worked with health care commission and his opinion is that this forum have not any authority to proceed against any manufacturer on any medical specialist/ researcher and the study not approved by CSC. He further added that the proper forum for the case is Punjab Health Care Commission (PHCC) are Pakistan Medical Commission (PMC) because there is a proper infrastructure and proper follow up. He wonders that under which clause/ authority, the CSC is deal with this case and its hearing.

Chairman CSC appraised the members that there are directions form honourable Lahore high court and decision of the case within 15 days.

Dr Javed Akram added that we may write to High Court that DRAP has no power to help out in this case because CSC/DRAP can't proceed against any Dr and Hospital so if this forum can't proceed/ help out the complainant so why this forum is dealing with. We can only write the High Court in our drug law and per law we haven't authority proper forum was the case is PMC/PHCC. He further added that the CSC may use my name in reply as I was chaired disciplinary committee of PMDC

Chairman CSC informed the member that the personal hearing is given on direction of Lahore High Court and we are following court directions and that this trial was approved by Ministry of Health and files / records is present, and it is right that we can't proceed against Doctor and Hospital so the case may be forwarded to PMC and same report may be forwarded to the High Court.

Saeed Anjum Khokhar (Advocate M/s GSK Pakistan Ltd.) joint the meeting virtually and informed the members that the complainant had already filed the case at Lahore Consumer Court case and it is pending/sub-judice, another case files by the complainant is in civil court Lahore which is also pending. He further submitted that while hearing the said petition no notice is served by the Court and they have no idea regarding its content of petition. So, they are not in a position to appraise it. He also supported Dr Javed Akram's opinion regarding jurisdiction under the DRAP Act. He clarified that the direction passed by the High Court can't give/authorise jurisdiction to any organization. He further informed that in the first hearing of the petition the complainant requested to High Court that his application is pending so decide the application and, in the court, order it is clearly mention that "this learned authority is legally bond the decide the application strictly accordance with law" after hearing petition & all concerned through well-reasoned, and law is that DRAP has no jurisdiction in such cases. He further submitted that complainant had concealed the facts about his cases in consumer and civil court Lahore. The complainant should inform all facts in this hearing.

Mr Arslan Nadir (Advocate of Dr Zeba Aziz, Dr Abas Khokhar and Dr Akram of Hamid Latif Hospital Lahore) joint the meeting virtually and apprised the CSC about health care commission that complainant had already exhausted two forums (i.e. Consumer Court and Civil Court) and exhausted the third forum (i.e. Health Care Commission) vide complaint no 230 / 2021 (reference No of complaint in PHCC regarding negligence). All details are concealed here in the hearing by Lahore by the complainant. He further added that refer to writ petition no 45003/2021 there are 14 paras in the petition but complainant does not describe any details regarding civil court /consumer court and PHCC and after concealment of the facts on application is forwarded to this forum. Proper forum is consumer court where Mr Yasir filed in complaint 2015 which is still pending and its next hearing on 5th /7th September 2021, another forum used by the complainant his health care commission where detail reply his already filled and health care commission is right forum for the case as health care commission fined out the problem faced by the complainant is either from M/s GSK product or other aspects or involved. He further added that as the complainant concealed the facts it is difficult to sort out the matter on a zoom meeting and is unfair. DRAP has no jurisdiction to entertained this application thirdly consumer court is special law and special law prevails general laws fourthly PHCC is special law and after enactment if complainant has any complainant any hospital or negligence of Dr Zeba Aziz Dr Abbas Khokhar and Dr Akram's professional skills and complainant already exhausted the forum.so coming to the DRAP to just harass/blackmail as discussed matter may forwarded to PMC so it is suggested to ask from complainant at which forum he want to solve the matter as the same matter at 5 different forum is not the way to deal the case. Complainant already filed the case at consumer court and civil court and due to evidence submitted by the complainant and after submission of evidence production will cross the evidence after cross checking of evidences submitted by the complainant and respondents then any forum decides the case.
Chairman CSC asked the complainant regarding cases in consumer and civil court. Mr Yasir replied that it is to that he filed the cases in civil and consumer courts but these forums can't deal with manufacturer M/s GSK, so who will ask the manufacturer. he added that DRAP approved the medicines of M/s GSK so why not DRAP may ask from GSK about trial subject record.
Secretary CSC submitted that the case was also discussed in 29th CSC meeting and decided as follow:

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

Accordingly, letters were issued and also requested that if respondents intend make any submission, same may be furnished within 7 days positively along with mobile & landline numbers, time & date will be communicated later on and letters written on 6th august 2021. So, we should have some written argument or material this division to prepare the case in accordance with the law and submission of respondents.

Chairman CSC further added that biostudy rule 2018 any complaint regarding trials may be discussed by the CSC and even can be forward for persecution
Advocate M/s GSK replied that, they want to submit detail reply so the copy of writ petition and application may be supplied so they will submit their reply with evidence.
Chairman CSC asked the members to submit their opinion and informed that high court ordered to conclude the matter within 15 days and there is provision in the rules to decide any complaint. So, it may be decided as suggested by Dr Javed Akarma that court may be informed that as ordered the personal hearing was given to complainant and respondent and it is infirmed that the proper forum the case is Pakistan Medical Council (PMC) and Punjab Health Care Commission (PHCC) so it may be requested to High Court that direction may be passed to PHCC and PMC. Secondly it may be decided to refer the case to PMC to heir the complaint as per their rules and decide the case and the same may be informed to the court that the committee referred to matter to PMC.
Dr Javed Akram again apprised that the case is beyond the jurisdiction of this forum and as the court referred the case to CSC so the court may be guided that the case may be referred to the appropriate forum of jurisdiction. Further it may be informed that the committee take up the matter as per direction but we have no jurisdictions to take action against any hospital or professional.

Dr. Javed Akram added that the CSC has given hearing to the complainant & CSC also heard the respondents also. Members known about their powers. Mr. Yasir has complaints regarding Doctors, Hospital & Manufacturer and all three respondents can't be proceeded under the Bio-Study Rules 2017. Under the Drug Law manufacturer can't can be dealt but it is an imported drug & GSK Pakistan not manufacture it in Pakistan and a generic also available in market & the drug used in thrombocytopenia.
If an ADR in a study is observed it should be established that weather it is due to product or disease related. So, it is suggested that CSC has given opportunity to complainant of hearing as per orders of the Lahore High Court and given ample chance.
As per complaint there are thee respondent 1, Hameed Latif Hospital 2, Doctor and Manufacturer and for the case the two authorities have jurisdiction 1) PMC which can only able to proceed against their license holder (Doctors) and they can't proceed against any nurse or Hospital. Health Care commission can take action against Hospitals, so all the matter may be forwarded to the High court that the committee take up the matter and discussion may be forwarded that under the drug law it is not in our jurisdictions, under the Drug Act if a company manufacturer sub-standard drug so can be proceeded. It is an FDA approved drug & not manufactured in Pakistan and imported to Pakistan, he informed that he prescribes the drug under reference on daily basis it is not an experimental drug so far and it's a life saving drug, if some one gets ADRs we can't proceed against any one. So, it should be written to court that we hear out the case and this is not a proper forum and complainant already filed the case on proper forum PHCC, Civil Court, consumer court so it should not be prolonged and just to write back to the honourable Lahore High court that this case is not in our jurisdictions.
Dr Farhana Badar and Dr Rizwana Chaudhary agreed with Dr. Javed Akram point of view. Dr Rizwana added further that at this forum we can't decide these types of matters, even if it a trial related patient, he has given consent for that trial. so, this type of cases should be discouraged at this forum.
Chairman CSC concluded the case that we should submit the high court that CSC the matter and the relevant forum is PHCC and PMC so may be forwarded to appropriate forum.

**Decision:**

*The CSC after deliberation and detailed discussion decided to request the honorable Lahore High Court that, In this case the appropriate forum for redressal of grievances of the complaint is Punjab Health Care Commission (PHCC) or Pakistan Medical Commission (PMC).*

**AGENDA ITEM IX:**

**AMENDMENTS IN CLINICAL TRIAL TITLED, "A RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED, NON-INFERIORITY PHASE-II CLINICAL TRIAL ON THE EFFICACY & SAFETY OF HOUTOU JIANWEILING TABLET IN THE TREATMENT OF CHRONIC NON-ATROPIC GASTRITIS. F.No.03-19/2020 DD (PS)**

Application is from Prof. Dr. Muhammad Raza Shah, General Manager, CBSCR, International Center for Chemical & Biological Sciences, University of Karachi, dated 27th July 2021, wherein FR is for protocol amendment & change of Clinical Trial Site from the Indus Hospital Karachi to CBSCR-ICCBS, Karachi applicant submitted following documents:

ix. Application along with prescribed fee paid vide Fee challan number 0847570817, dated 30th June 2021.
x. Copy of license of M/s CBSCR-ICCBS, Karachi (CTS-0046).
xi. CBSCR-ICCBS, Karachi-IRB/IEC approval letter for protocol amendment version 2.0
xii. NBC- amendment & Clinical Trial Site change, approval letter reference No.4-87/NBC-465/21/47, dated 13th July 2021.
xiii. Amended protocol version 2.0.

2. Initially it was informed that, the following trial sites will participate in the trial but respective approval of the sites & IRB approval were not yet provided:

i. DOW University of Health Sciences, Karachi.
ii. The Indus Hospital, Karachi.

3. It is submitted that, the subject application was placed before CSC in its 20th meeting held on 10th March 2021and the CSC decided as follows:

***Decision of 20th CSC meeting:***

*CSC decided to grant registration for Phase-II Clinical Trial subject to the following:*

*i. IRB approval of the Indus Hospital Karachi.*
*ii. Formulation of the product to be tested in the clinical trial regarding all ingredients.*

4. Further, as per submitted NBC approval (amendment) M/s Center for Bioequivalence Studies and Clinical Research (CBSCR), will be an additional Clinical Trial Site for the trial, & as per provided revised protocol it will be a multicenter Clinical Trial. Clinical Trial Site will be M/s Center for Bioequivalence Studies and Clinical Research (CBSCR), Karachi & Source of subjects will be from following:

i. DOW University of Health Sciences, Karachi.
ii. The Indus Hospital, Karachi.
iii. Civil Hospital Karachi.

5. After initial scrutiny following shortcomings observed:

i. Applicant need to be asked for clarification regarding Clinical Trial Sites for the subject Clinical Trial.

ii. Evidence for approved Clinical Trial Sites for the trial need to be provided.

iii. IRB approval from each Clinical Trial Site need to be provided.

6. Accordingly, shortcoming letter number F.No.03-19/2020 DD (PS) dated 25th August 2021, response is yet awaited.

7. Submitted for perusal, discussion and decision of CSC.

8. Discussion & presentation:

Secretary CSC presented the case along with its background & appraised the committee that the case was presented in the 20th CSC meeting & it was decided to grant the registration for phase-II clinical trial subject to the following conditions:

i. IRB approval from the Indus Hospital Karachi.
ii. Formulation of the product to be tested in the clinical trial regarding all ingredients.

Secretary CSC added that, now the application is for change of clinical trial site from the Indus Hospital Karachi to CBSCR-ICCBS, Karachi. Whereas as per application/study protocol, the source of subjects will be the following centers:

i. DOW University of Health Sciences, Karachi.
ii. The Indus Hospital, Karachi.
iii. Civil Hospital Karachi.

Secretary CSC also informed about the shortcomings observed after evaluation. So, the clarification regarding shortcomings need to be submitted & clarified.

Chairman CSC invited Prof. Dr. Muhammad Raza Shah to join the meeting, defend the case & answer the question raised after evaluation. Prof. Dr. Muhammad Raza Shah replied that ingredients of the IMPs already analyzed/tested at Industrial analytical center. Further informed that the main site will be the CBSCR-ICCBS, Karachi whereas DOW, Indus & Civil Hospital will be utilized as source of subjects and ICCBS signed the MoUs with all subject source sites.

Chairman CSC raised reservations & asked the PI that at one application is for change of site & on other hand three different sites are mentioned in the protocol as source of subjects and in protocol it's a multicenter trial. So, PI is asked for clarification, Prof. Dr. Raza Shah informed that the main trial site will be CBSCR-ICCBS whereas as they have MoU with these hospitals so the OPDs of the hospitals will be utilized for subjects' recruitments. Chairman CSC suggested that a new amended protocol in which CBSCR-ICCBS mentioned as a single site, along with IRB & NBC approval need to be provided. Prof. Dr. Raza Shah claimed that IRB & NBC approvals are already submitted. Assistant Director (PS) clarified the matter that, previously the site for the trial was the Indus Hospital, Karachi but due to non-submission of the IRB approval of the Indus Hospital registration letter was not issued. So now if PI wants to add the sites he should submit IRB approval

from all Clinical Trial Sites or if PI wants to retain CBSCR-ICCBS as an exclusive site so he should submit a revised/amended protocol along with revised IRB & NBC approvals. CSC member also suggested that MoU/agreements with source sits should also be submitted. Chairman CSC concluded the matter that CSC may to approve the change/transfer of Clinical Trial Site from the Indus Hospital Karachi to CBSCR-ICCBS, Karachi subject to submission of IRB & NBC approval along with revised/amended protocol. In case PI want to retain sites (i.e. The Indus Hospital, Karachi, DOW University of Health Sciences, Karachi & Civil Hospital Karachi, as source of trial subjects. So, MoUs with source sites need to be provided along with IRB approval from each site.

**Decision:**

*The CSC after deliberation / detailed discussion decided to approve the change/transfer of Clinical Trial Site from the Indus Hospital Karachi to CBSCR-ICCBS, Karachi subject to submission of IRB & NBC approval along with revised/amended protocol. In case PI want to retain sites (i.e. The Indus Hospital, Karachi, DOW University of Health Sciences, Karachi & Civil Hospital Karachi, as source of trial subjects). So, MoUs/agreements with trial subjects source sites need to be provided along with IRB approval from each site.*

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**AGENDA ITEM - X:**

**APPLICATION FOR APPROVAL OF CLINICAL TRIAL TITLED "A GLOBAL, MULTICENTER, RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED, PHASE-III CLINICAL STUDY TO EVALUATE THE PROTECTIVE EFFICACY, SAFETY & IMMUNOGENOCITY OF SARS-CoV-2 MESSENGER RIBONUCLEIC ACID (mRNA) VACCINE IN POPULATION AGED 18 YEARS & OLDER "F.NO.03-66/2021 DD (PS).**

The case is an application from Mr. Asim Munir, Project Manager, CNIC No 35202-4375948-5 of M/s DRK, Pharma Solution, Lahore wherein the applicant has requested for approval or registration of clinical trial titled A Global, Multi-center, Randomized, Double-Blind, Placebo-Controlled, Phase III Clinical Study to Evaluate the Efficacy, Safety, and Immunogenicity of Sequential Immunization of Recombinant SARS-CoV-2 Fusion Protein Vaccine (V-01) Against COVID-19 in Healthy Adults Aged 18 Years and Older after the Vaccination of 2 Doses of Inactivated Vaccines. 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 | Remarks |
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| 1 | Application on prescribed Form-II | Attached |
| 2 | Prescribed processing fee | Fee of Rs.200,000/- submitted Slip No. 59705338481 dated 02.08.2021. |
| 3 | Investigator Brochure (s) | Attached |
| 4 | Final protocol | Attached. |

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| 5 | Informed consent and participant information sheet (Urdu to English) | Attached. |
| 6 | List of participating countries | Pakistan, Turkey, Mexico, Malaysia. |
| 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. | Vaccine recombinant SARs COV 2 fusion protein vaccine (V-01) 4,800 vials<br>Placebo 4,800 vials<br>Total 9600 vials |
| 9 | Site of the trial | Agha Khan Hospital Karachi<br>Dow University of Health Sciences<br>Central Park Medical College and Hospital, Lahore.<br>Sindh Infectious Diseases Centre, Dow University CTU<br>Shifa International Hospital, Islamabad<br>SKMCH&RC, Lahore,<br>Al Khidmat Foundation, Surayya Azeem Waqaf Hospital, Lahore,<br>Central Hospital Gujranwala. |
| 10 | Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members. | IRB approval SKMCH&RC, Lahore not attached. |
| 11 | Approval of National Bio-ethics Committee (NBC) | Attached.<br>Ref:No.4-87/COVID-79/21/129, Dated 30th July 2021. |
| 12 | CV's of the Investigators | CV of<br>Syed Faisal Mehmood, Associate professor, Principal Investigator.<br>Dr. Shoba Luxmi, Associate Prof. at Dow university of Health Sciences<br>Dr. Muneeba Ahsan, Assistant Professor at Sindh Infectious Diseases Hospital and Research Center,<br>Dr. Mian Amjad Sohail, Director Shifa research Centre, |

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| | | Dr. Salman Athar, Anesthetist, Central Hospital Gujranwala, Dr. Muhammad Ahmad, Central Park Medical college and Hospital, Dr. Muhammad Asif Naveed, Associate Professor, |
| 13 | GMP certificate along with COPP & free sale certificate of the investigational product. | GMP certificate and DML attached of M/s Livzon Mabpharm Inc. is attached in Chinese language and translation by Delsalt Consulting Co. ltd. |
| 14 | Pre-clinical/clinical safety studies | Attached |
| 15 | Summary of Protocol | Attached. |
| 16 | Summary of Investigator Brochure | Attached. |
| 17 | Adverse Event Reporting Form | Attached. |
| 18 | No of patients to be enrolled in each center. | Total 8,000 subjects and 1000 in each site will be recruited. |
| 19 | Name of Monitors & Clinical Research Associate | DRK Pharma Solution, Lahore. Manisha Lohano, Yusra Maryam, Saad Ali Shah, Roha Badar, Fatima Aleem, Bakhtawar Abid, Mohsin Ali, Salman Tariq, Abdullah Mir, Khizar Hayat, Haina Sarwar, Hasnain Hashmi, Ali Faizan, Sana Rafique. |
| 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. | Attached. |
| 22 | Duration of trial | 20 months. |
| 23 | Undertaking on stamp paper. | Attached. |

3. After evaluation following shortcomings were recorded:

   i) IRB approval SKCMH&RC and Avicenna Hospital, Lahore not attached.

   ii) Al-Khidmat Foundation, Surayya Azeem Waqaf Hospital, Lahore and

Central Hospital Gujranwala are not approved as CTS by CSC.

iii) Clarification required regarding CTS, is it SKCMH&RC or Avicenna Hospital, Lahore

4. Case is placed before CSC for review, assessment, evaluation and decision.

5. Discussion & deliberations:

Secretary CSC presented the case before committee & briefed regarding application and its shortcomings (already mentioned above). Dr. Javaid Akram in the very beginning added that application should be completed and then be placed before the CSC and suggested that case may be deferred at the moment, Secretary CSC invited Dr. Faisal Mehmood (PI) to present the case before CSC. Mr. Faisal Mehmood Joined the meeting virtually and briefed the committee regarding trial. He informed that it's a global vaccine booster dose trial. All the subjects recruited in this trial will already be fully vaccinated and in this trial a booster dose of the vaccine will be administered, the trial is already in progress in Philippines.

Dr. Javaid Akram asked the applicant to confirm about the subject vaccination that if subjects are already vaccinated then in this trial protocol mRNA vaccine booster dose will be administered? Dr. Faisal Mehmood replied that subjects recruited in this trial will be fully vaccinated and the booster vaccine is not an mRNA vaccine, it's a fusion protein/ protein subunit vaccine and initially subjects will be vaccinated with inactive SARS-COV-2 vaccine (either Sinopharm or SinoVac vaccines)

Dr. Javaid Akram informed that it's a mix and match trial and WHO/FDA does not know whether mix and match vaccine trial is a safe phenomenon or not? Right now, UHS is starting a registry, not a trial, where thousands of volunteers are registered who have done mix and match. They have initially been vaccinated with one type of vaccine and due to travel reasons, they got another type of vaccine as second dose/booster dose. WHO on its website still says that this is not safe because there is no safety data. It may be safe but due to lack of data no one can be sure about mix and match vaccine results. We are collecting data from all over the world for polyvac and polyvac browser, UHS has developed polyvac browser. At the browser, anyone can register himself and enter the details of vaccines type & doses. It is a best thing that we must have some safety data that mixing of two different vaccine is safe or not?

Dr. Faisal Mahmood replied that some data is available from mRNA Astra Zeneca Vaccine which shows safety and this is the very reason we are doing this trial for a booster dose in a mix and match in which third dose will be of different type. So, for we have not received safety signals and through this trial safety can be evaluated.

Dr Javed Akram addressing Dr Fasial Mehmood said that it's a mix and match trial because after two doses of vaccine, a 3rd dose of different vaccine will be administered; booster dose of same vaccine is a different scenario. It is a mix and match trial so there are concerns as there is no sufficient safety data, (at UHS data of thousands of volunteers is available and data is compiled in real time). We have already thousands of volunteers enrolled from US, UK, Pakistan and Dubai, we are not only enrolling them but also following them every month whether they have got suspected/ expected SAEs after 3rd dose of different vaccine with dedicated call agents. Dr Javed Akram support this idea of mix & match vaccine trial, but the only concern at the moment that, WHO on its website say that there is no safety data and discourage it, it may be dangerous and yes it may be dangerous unless we prove it but we are at UHS not doing trial we were offered this trial to do but we said no, let's see people we are done what happen to them. Let interim release will be soon available by suggested let complete all the formalities, we come with safety data ( Short time safety data). Now people who mix and match they could have adverse event one year later or two year later we will be following

then and we will give three-month safety data would be tell. Moreover, Dr Javed Akram suggested that Dr. Faisal Mehmood may collaborate with UHS & may also communicate telephonically & that further collaborator from UHS may share link also where mix and match data may be found. So, we can get as much data from all over the world. We need a press conference to release this link on the press newspaper so the people who have mix and match with or without medical advice , whatever the reason they should just registered. UHS already have one thousand volunteer and can give the interim but this data valid for one month, the ADRs can occur after one year also so we are unpredicted. PI may complete the formalities and we complete safety data and shared it PI and hope fully we go thorough it but the concern is that mix and match is safe or not because nobody can tell it right now.

Dr. Faisal also added that they will also look for safety data that may have come, Dr Javed Akram suggested to share link by messages. Chairman CSC concluded the matter and said as this is mix and match trial and it is the first case for CSC so if any member has question He / she may ask and input from every member is required for decision, any query/ question may also be shared through Email.

Dr Farhana Badar shared her comments and observation that in Bahrain her relatives are there, they have got 2 doses of Sinopharm in February/March and after 5 to 6 months a shot of Pfizer administered and there is no data for safety for side effects but it is in practice. Ministry of Bahrain may do it upon recommendation from the west and don't know it was from CDC or WHO.

In this particular case it seems similar that was done over there if anyone have contacts so the data may be ask from CDC or data as Dr Javed Akram recommended to be used as it is a multi-country and multi-center0 trial

**Decision:**

*The CSC after deliberation / detailed discussion decided to defer the case till fulfilment of all prerequisites of the application as briefed by Secretary CSC & further review of the trail application by expert members of CSC as per international practices & WHO recommendations and in the light of safety data worldwide regarding mix & match vaccine trial/study.*

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