MINUTES OF THE 14TH MEETING OF CSC, HELD ON 21st SEPTEMBER 2020.

Table of Contents:

1. The 14th CSC Meeting was held on 21st August 2020 through Zoom under the chairmanship of Dr. Abdur Rashid, Director Pharmacy Services Division / Chairman (CSC). At the Committee Room, 4th Floor, Drug Regulatory Authority of Pakistan, Islamabad.

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

Sr. No.	Name	Designation
01	Dr. Abdur Rashid.	Chairman CSC / Director Pharmacy Services.
02	Muhammad Arif Chaudhry.	Secretary CSC / Additional Director, Pharmacy Services.

3. Following members attended the meeting online through Zoom:

01	Prof. Nadeem Irfan Bukhari.	Professor of Bio-Pharmaceutics & Pharmacokinetics, University of Punjab, Lahore.
02	Dr. Faiza Bashir.	Chairman, Pakistan Health Research Council or his nominee, Islamabad.
03	Dr. Farhana Badar.	Biostatistician & Epidemiologist, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore. Member CSC.
04	Dr. Naseem Salahuddin.	Director Infectious Diseases Indus Hospital, Karachi Co-opted CSC Member.
05	Prof. Dr. Rizwana Chaudhri	HOD Gynecologist Holy Family Hospital, Rawalpindi Co-opted Member.

3. Chairman, CSC welcomed all the members. He briefed members of meeting regarding the meeting agenda. Chairman, CSC also thanked members for their active participation online through Zoom.

4. Meeting started with recitation of holy verses of Quran by Muhammad Arif Chaudhry, Secretary CSC/Additional Director, Division of Pharmacy Services.

AGENDA ITEM - I: CONFIRMATION OF THE MINUTES OF THE 13TH CLINICAL STUDIES COMMITTEE MEETING.

Minutes of 13th CSC meeting held on 11th August 2020, are placed for confirmation of CSC members.

Decision of 14th CSC meeting:

All the members confirmed the minutes of 13th CSC which was held on 11th August 2020.

AGENDA ITEM - 2: **LICENSING & REGISTRATION OF CLINICAL TRIAL SITE & CLINICAL TRIALS / STUDIES IN RESPECT OF COVID-19.**

APPLICATION FROM PAKISTAN KIDNEY & LIVER INSTITUTE & RESEARCH INSTITUTE, LAHORE TO ACT AS CLINICAL TRIAL SITE. F.No.15-53/2020 DD (PS)

Application is from Prof. Dr. Hafiz Ijaz Ahmed, Dean Pakistan Kidney & Liver Institute & Research Institute, Lahore, wherein the application has requested for grant of licence to act as a Clinical Trial Site. The application is on Form-I of the Bio-Study Rules 2017 without fee.

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

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached
2	Prescribed processing fee	Not provided.
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).	Corporate body working as non-profit organization.
4	Details of premises including layout plan of the site.	Attached
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached
6	Names and qualifications of the above sections along with their staff.	Attached
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Not provided.
8	Undertaking on stamp paper	Not provided.

After evaluation following shortcomings were recorded:

i) **Prescribed processing fee of Rs.100000/-, is not provided.**
ii) Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc, need to be provided.
iii) Undertaking on stamp paper is not provided.

Applcant informed regarding shortcomings vide letter even number dated 20th August 2020, but still response is awaited.

Decision of 14th CSC meeting:

A team comprises of Dr. Ammara & others, from Pakistan Kidney & Liver Institute & Research Institute, Lahore, joined the meeting through Zoom and presented a brief regarding their facilities & status of their organization before CSC. CSC after detailed deliberation decided to approve "PAKISTAN KIDNEY & LIVER INSTITUTE & RESEARCH INSTITUTE, LAHORE", to act as a clinical trial site, subject to fulfilment of all prerequisites as per Bio-Study Rules 2017.

AGENDA ITEM - 3:

APPLICATION FOR APPROVAL OF CLINICAL TRIAL TITLED "A SINGLE CENTER PROSPECTIVE RANDOMIZED CONTROL TRIAL TO EVALUATE EFFICACY OF TOCILIZUMAB WITH & WITHOUT STEROIDS IN COVID-19 PNEUMONIA WITH FEATUTRES OF HYPER INFLAMMATION", BY PAKISTAN KIDNEY & LIVER INSTITUTE & RESEARCH CENTER, LAHORE.F.No.03-45/2020 DD (PS)

Application is from Dr. Naveed Rashid, Consultant Infectious Diseases Dean Pakistan Kidney & Liver Institute & Research Institute, Lahore, Pakistan Kidney & Liver Institute & Research Center, Lahore wherein the application has requested for approval of subject Clinical Trial. The application is on Form-II of the Bio-Study Rules 2017 without fee.

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	Not provided.
3	Investigator Brochure (s)	Attached, not as per ICH-GCP guidelines.
4	Final protocol	Attached, not as per ICH-GCP guidelines.
5	Informed consent and participant information	Attached.

	sheet (Urdu to English)	
6	List of participating countries	Pakistan.
7	Phase of trial.	Not described
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.	88 Vials of 200mg.
9	Site of the trial	M/s Pakistan Kidney & Liver Institute & Research Center, Lahore.
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Approval letter is attached, without complete composition of committee i.e. names and designation of members.
11	Approval of National Bio-ethics Committee (NBC)	Attached. Ref:No.4-87/NBC-COVID-19-14/20/, Dated 23rd May 2020.
12	CV's of the Investigators	Attached.
13	GMP certificate along with COPP & free sale certificate of the investigational product.	Certificate of Medicinal Product issued by European Medicines Agency is attached. Whereas GMP Certificate is not provided.
14	Pre-clinical/clinical safety studies	Product information attached instead of its pre-clinical studies.
15	Summary of Protocol	Attached, not as per ICH-GCP guidelines.
16	Summary of Investigator Brochure	Attached, not as per ICH-GCP guidelines.
17	Adverse Event Reporting Form	Attached.
18	No of patients to be enrolled in each center.	22 subjects. 11 in Arm A and 11 in Arm B.
19	Name of Monitors & Clinical Research Associate	Dr. Asim Idrees, Senior Registrar ICU
20	Evidence of registration in country of origin.	Certificate of Medicinal Product issued by European Medicines

		Agency is attached.
21	Copy of registration letter (if registered in Pakistan)	Attached.
22	Sample of label of the investigational product / drug.	Not provided.
22	Duration of trial	Three months.
23	Undertaking on stamp paper.	Not provided.

After evaluation following shortcomings were recorded:

i) **Prescribed processing fee of Rs.200000/-, is not provided.**
ii) Phase of trial is not described.
iii) IRB approval letter issued by PKLI is attached, without complete composition of committee i.e. names and designation of members.
iii) Product information attached instead of pre-clinical/clinical safety studies.
iv) Investigator brochure along with its summary need to be provided as per ICH-GCP guidelines.
v) Protocol along with its summary need to be provided as per ICH-GCP guidelines.
vi) Sample of label of the investigational product needs to be provided.
vii) Undertaking on stamp paper is not provided.

Applcant informed regarding shortcomings vide letter even number dated 25th August 2020, but still response is awaited.

Decision of 14th CSC meeting:

A team comprises of Dr. Ammara & others, from Pakistan Kidney & Liver Institute & Research Institute, Lahore, joined the meeting through Zoom and informed that they want to withdraw their application for the clinical study at the moment, due to decrease in COVID-19 cases. CSC after application detailed deliberation accept their request and allow the withdrawl of Clinical Studies titled "A SINGLE CENTER PROSPECTIVE RANDOMIZED CONTROL TRIAL TO EVALUATE EFFICACY OF TOCILIZUMAB WITH & WITHOUT STEROIDS IN COVID-19 PNEUMONIA WITH FEATUTRES OF HYPER INFLAMMATION".

AGENDA ITEM - 4

APPLICATION FOR LICENSE TO ACT AS CRO, BY M/S CYNTAX HEALTH PROJECTS ISLAMABAD. F.No.15-52/2020 DD (PS)

Application from Madeeha Malik of M/s Cyntax health Projects PVT LTD Apartment No. 6, 4th Floor, Plaza No. 129, Civic center, Phase IV, Bahria town Islamabad, wherein the request has been made to license their company with DRAP to work as Clinical Research Organization (CRO). The application is on prescribed Form-I of the Bio-Study Rules 2017 along with fee of Rs.300000/- deposited for CRO vide challan no.2039292.

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

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached
2	Fee	Attached
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).	Attached
4	Details of premises including layout plan of the site.	Layout plan does not justify sitting capacity of provided staff.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Applied for CRO.
6	Names and qualifications of the above sections along with their staff.	Attached staff is not as per decision of 2nd CSC meeting.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Applied for CRO.
8	Undertaking on stamp paper	Attached.

Applcant informed regarding shortcomings vide letter even number dated 09th September 2020, but still response is awaited.

Decision of 14th CSC meeting:

CSC after detailed deliberation decided to authorize the Chairman CSC for constitution of inspection panel for the inspection of facilities as per criteria laid down CSC in its 2nd meeting. The case will be again brought before the CSC for further delibration and decision after inspection.

AGENDA ITEM - 5

EMPAGLIGLOZIN SAFETY & EFFICACY IN TREATMENT OF T2DM OTHER ORAL ANTIDIABETIC AGENT WITH AF. A PAKISTANI PERSPECTIVE.

Application is from Prof. Dr. Aziz-Ul-Hassan Aamir, Head of Department of Diabetes, at KGMC/ Hayatabad Medical Complex, Peshawar, dated 13th August, 2020, wherein the applicant has applied for clinical trial study titled as Empagliflozin safety & efficacy in treatment of T2DM other oral anti diabetic agents with AF. A Pakistani perspective

2.4.2. After scrutiny as per Checklist for Form-II of the Bio-Study Rules 2017, the details of submitted documents is as follows:

S. No.	Required Documents	Remarks
1.	Application on prescribed Form-II	Application is not applied on prescribed Form – II
2.	Investigator Brochure	Not provided
3.	Final Protocol	ESTAR-PAK study v4.0 MA (not as per ICH-GCP)
4.	Informed consent form (English & Urdu)	Attached
5.	List of participating countries (If applicable)	Pakistan.
6.	Phase of trial	Post marketing Phase IV
7.	Quantity of Drug(s) to be imported/procured/manufactured for the trial	Not Applicable
8.	Site(s) of the trial	Trial will be conducted at following sites. 1. Hayatabad Medical Complex, Peshawar. 2. Lady reading Hospital Peshawar. 3. National Institute of Cardiovascular disease

		(NICVD) Karachi. 4. Alkhaliq Hospital Multan. 5. Shifa International Hospital Islamabad. 6. Shaukat Khanam Hospital. Lahore.
9.	C.Vs of investigator(s)	CV attached.
10.	Ethical committee approval with complete composition of committee i.e. Name and designations of the members	Not Attached
11.	Approval from National Bio-ethics Committee (PHRC)	Not Attached
12.	GMP certificate along with Free Sale Certificate/Certificate of Pharmaceutical Product (Note: For locally manufactured product GMP Cert., COA of the Product and Registration Letter will be required)	M/s CCL Pharmaceuticals (Pvt.) Ltd., Lahore. GMP Certificate attached.
13.	Pre-clinical, clinical data and safety studies.	The article published on 16 January 2014 with open success at Springerlink.com provided.
14.	Summary of the protocol	Not Provided
15.	Summary of the Investigator Brochure	Not provided
16.	Adverse Event Reporting form	Not Provided
17.	No. of Patients to be enrolled in each center	380 Approximately
18.	Name of monitors/clinical research associate	Attached
19.	Evidence of registration of study drug in country of origin	Not attached
20.	Copy of registration letter (if drug is registered in Pakistan)	Registration certificates attached.
21.	Sample of label of drug	Not Attached
22.	Duration of trial	36 weeks
23.	**Prescribed Fee**	**Rs.50,000 submitted instead of Rs.200,000/-**
24.	Undertaking on Stamp paper	Not Provided

Applcant informed regarding shortcomings vide letter even number dated 09th September 2020, but still response is awaited.

Discussion: *All the members emphasized for submission of complete cases before the Committee. And insisted the incomplete cases should not be included in the agenda. Secondly agenda may be sent well before the meeting.*

Decision of 14th CSC meeting:

CSC after detailed deliberation decided to defer the instant application & advised applicant for fulfilment of all prerequisites as per the Bio-Study Rules 2017.

AGENDA ITEM - VI:

PERMISSION FOR CONDUCTION OF CLINICAL TRIAL AS A PART OF SHIFA CLINICAL RESEARCH CENTER(DRAP REGISTERED CLINICAL TRIAL SITE)

Dr. Rizwana Chaudhry has submitted letter reference No. PNCC/LSHTM/GIHD-STMU/07/2020/02, dated 27th July 2020 along with fee of 25000 Rupees. Her request to Director Pharmacy Services, DRAP-Islamabad is reproduced as under:

Subject: Change in University affiliation and postal address of Pakistan National Coordinating Centre (PNCC).

Dear Sir

I am writing to bring into your kind notice the change in university affiliation and postal address of Pakistan National Coordinating Centre (PNCC). Initially PNCC was established as a result of memorandum of understanding between London School of Hygiene and Tropical Medicine (LSHTM) and Rawalpindi Medical University (RMU). Myself, serving as head of Obstetrics and Gynecology RMU, is appointed as Director of PNCC and National Coordinator of clinical trials. The primary objective behind PNCC inception is to coordinate and facilitate the Clinical trials of LSHTM at different hospitals, across Pakistan and hence bringing quality research to the country. Aa integral part of its policy, we strictly adhere to the standards and requirements of existing regulatory and ethics bodies, governing the conduct of research in the country. At PNCC, clinical trials are coordinated, only after sorting the favorable opinions/ approvals from concerned bodies. However, after my retirement from RMU, the legal contract between LSHTM and RMU was suspended. The new MOU is endorsed between Global Institute of Human Development, Shifa

Tameer - e. Millat University and LSHTM on 18 March 2020 (Section 2.1). According to Terms of Reference laid in MOU, PNCC is now working under the Umbrella of GIHD-STMU and I have charges of Principal Scientist at GIHD - STMU (Section 2.2) and Director of PNCC. The office of PNCC is also shifted from its previous location. Kindly note the change in Postal Address and ensure that all the future correspondence should be made to following address:

Prof Rizwana Chaudhri Director Pakistan National Coordinating Centre Global Institute of Human Development, Shifa Tameer -e. Millat University (GIHD-STMU) F-759, Said Pur Road Rawalpindi, Pakistan Landline no: 0092 51 8444512 Cell no: 0320 551496.

Dr. Prof Rizwana Chaudhri, made another request to the Director Pharmacy Services, DRAP-Islamabad vide letter No. PNCC/LSHTM/GIHD-STMU/08/2020/01, dated 1st September 2020, without any fee, is reproduced as under:

SUBJECT: Change in Physical Location and University affiliation of approved Clinical Trial site.

Dear Sir,

We are immensely thankful to your support for all our clinical trials conducted/coordinate at Pakistan National Coordinating Center (PNCC), initially established at Holy Family Hospital Rawalpindi. After my retirement I have joined Shifa Tameer-e-Millat University (STMU), as head of Translational Research Department and PNCC comes under this department. All PNCC staff working at Holy Family Hospital are also appointed officially at STMU (please find the official appointment letters along with the allocation of physical space for PNCC). Sir, Shifa Clinical Research Center at Shifa International Hospital Ltd, is already approved as clinical trial site by DRAP (please see copy of approval letter). Both the Clinical Research Center at Shifa International hospital and Translational Research department share the same resources and are working under the umbrella of Shifa Tameer-e-Millat University (STMU). Therefore, we request DRAP to grant permission to Translational Research department for conduction/coordination of clinical trials in this new capacity. We are currently coordinating Woman 2 trial at twenty-five hospitals across country. Almost all of them are tertiary care public hospitals and are approved as clinical trial sites by DRAP. Owing to Covid-19 pandemic however we have stopped all sites from recruiting patients since 25" March 2020. The reason was primarily taken, to ensure the safety of non-essential health care workers. Currently our country demonstrated remarkable decline in Covid-19 infection rates. Therefore, all our sites have put forth formal request to restart the Woman 2 trial. The main hurdles

in the resumption of Woman 2 is that, all trial drugs from our previously imported batch, have expired on 31st August. We need to import new batch of drugs immediately in order to resume Woman 2 Trial. To make this happen we need your approval of change in the physical location/ address, in the original Woman 2 Approval (Attached). Once this change is endorsed by DRAP, we will then apply for the new Import license for Woman 2 Trial, from drug importation and licensing department of DRAP. Looking forward to your support.

Many Thanks

Prof Rizwana Chaudhri Director Pakistan National Coordinating Centre Global Institute of Human Development, Shifa Tameer -e. Millat University (GIHD-STMU).

Dr. Prof Rizwana Chaudhri, made third request to the Director Pharmacy Services, DRAP-Islamabad vide letter No. PNCC/LSHTM/GIHD-STMU/09/2020/01, dated 15th September 2020, without any fee, is reproduced as under:

Subject: Permission for the conduction of clinical trials as a part of Shifa Clinical Research Centre (DRAP registered Clinical Trial Site)

Dear Sir,

I am writing to bring into your kind notice, I was previously working as Dean and Professor of Obstetrics & Gynecology, at Holy Family Hospital. The Holy Family Hospital is a constituent hospital of Rawalpindi Medical University. Holy Family Hospital has been approved as registered clinical trial site, by Drug Regulatory Authority of Pakistan (CTS-0001). After my retirement from Holy Family Hospital, I have joined Shifa Tameer Millat University (STMU), as Head of Translational Research Department. STMU is a recognized Medical University, and its constituent Hospital, Shifa international Hospital, is a tertiary care hospital. Shifa Clinical Research Centre, based at Shifa international Hospital, is also registered as Clinical trial site by DRAP, with license number CTS-0026. Under my new designation at STMU, kindly allow me to conduct clinical trials under the Shifa Clinical Trial site.

Many Thanks

Prof Rizwana Chaudhri Director Pakistan National Coordinating Centre Global Institute of Human Development, Shifa Tameer -e. Millat University (GIHD-STMU).

After evaluation following shortcomings were recorded:

i. Processing fee for request submitted on 1st & 15th September 2020, under heading of miscellaneous request vide SRO 1047(I)/2019, dated 12th September 2019.

ii. Application for Clinical Trial Site on prescribed Form-I of the Bio-Study Rules 2017 along with all prerequisites & ethical approval from IRB & NBC-PHRC.

Decision of 14th CSC meeting:

CSC after detailed deliberation decided to approve the Shifa International Hospital, Islamabad (An already approved site by CSC) as a Clinical Trial Site and decided to close Holy Family Hospital, Rawalpindi for Woman-II Clinical Trial. Further applicant will provide IRB approval.

AGENDA ITEM - VII:

APPLICATION FOR LICENSE FOR CHUGHTAI LAB, LAHORE, TO ACT AS BIO-ANALYTICAL LABORATORY FOR CLINICAL TRIALS.

Application on Form-I of the Bio-Study Rule 2017, from Dr. Omar Rasheed Chughtai, Chughtais Lahore Lab (Pvt) Ltd, 7-Jail Road Main Gulberg, Lahore, dated 15th January 2020, along with fee of Rs.50,000/-, deposited vide challan number 1927647, dated 15th January 2020.

After initial evaluation as per prerequisites of Form-I of the Bio-Study Rules 2017, the details of the submitted documents are as under:

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached,
2	Prescribed fee	Rs.50000/- & Rs. 250000/- submitted vide challan number 1927647 & 1980787 dated 15th & 28th January, 2020 respectively.
3	Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).	SECP Registration certificate attached. Certificate No.007795. Punjab Healthcare Commission Certificate No. REG.No-R-09524

		attached
4	Details of premises including layout plan of the site.	Only layout plan is attached.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	List of equipment along with calibration certificate is attached.
6	Names and qualifications of the above sections along with their staff.	A brief detail is provided regarding officers & staff serving in the Gynae Ward 08 & 09 of JPMC, Karachi.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Not provided. Not Applicable for Bio-Analytical Laboratory.
8	Undertaking on stamp paper	Attached.

It is submitted that the subject application was discussed in the 7th CSC meeting & CSC decided as follows:

Decision of 7th CSC Meeting: -

The CSC after deliberations decided to conduct the inspection of Chughtai Lab Lahore (Pvt) Ltd, 7-Jail Road Main Gulberg Lahore (applied for Bio Analytical Lab). The team, comprising of the following experts will inspect. In case any member is not available the committee authorized its chairman to add another suitable member of the relevant expertise from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly. -

i.	Dr. Masud Ur Rehman (Coordinator).
ii.	Prof. Dr. Javed Akram.
iii.	Dr. Farhana Badar
Iv	Dr. Rizwana Choudhry.
v	Dr. Najam Us Saquib.

Due to unavailability of Dr. Najam Us Saquib, Chairman CSC replaced him with Rana Ahsan Ul Haq Athar, Assistant Director, Division of Pharmacy Services, DRAP. And following inspection panel conducted inspection:

i.	Dr. Masud Ur Rehman (Coordinator).
ii.	Prof. Dr. Javed Akram.
iii.	Dr. Farhana Badar
Iv	Dr. Rizwana Choudhry.
v	Rana Ahsan Ul Haq Ather

Inspection conducted on 24th July 2020, Dr. Rizwana Choudhry could not joined the panel due to her health issue (COVID-19) and after inspection, panel "**Recommended for Approval"**, and submitted report with following remarks:

Remarks of inspection team:

Panel advised the management of Chugtai Lahore Lab to strengthen the their Institutional Review Board, to get a certificate from Rescue 1122 for Safety and Disaster management plan. The management of M/s Chugtai Lab agreed with suggestions of panel. Panel further suggested that there should be more relavent person in panel and members having conflict should be avoided. keeping in view the SOPS, Qualification of Staff, Management, Machinery/ equipment premises, layout plan, panel recommended the laboratory for approval.

Decision of 14th CSC meeting:

CSC deferred the case due to shortage of time, the case will be decided in the next CSC meeting.
