Minutes of the 4th CSC Meeting held on 17th July, 2019.

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1. The 4th Meeting of CSC held on 17.07.2019 at the Committee Room of DRAP, Islamabad under chairmanship of Dr. Abdur Rashid, Chairman, Clinical Studies Committee (CSC).

2. The following members attended the meeting:-

Ser.	Name	Designation
1.	Dr. Abdur Rashid	Chairman CSC / Director Pharmacy Services.
2.	Dr. Masud ur Rehman	Secretary CSC / Additional Director, Pharmacy Services.
3.	Prof. Dr. Javed Akram	VC, University of Health Sciences, Lahore
4.	Dr. Faiza Bashir	Nominee of Chairman NBC-PHRC
5.	Ms.Salwa Ahsan	Chief of Pharmacy, Shifa Intl Hospital, Islamabad.
6.	Prof. Brig. (R), Muzammil Hassan Najmi.	Professor of Pharmacology, Foundation University, Islamabad.
7.	Prof. Dr. Nadeem Irfan Bukhari	Principal Institute of Pharmaceutical Sciences, University of Punjab, Lahore.
8.	Dr. Farhana Badar.	Biostatistician & Epidemiologist, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore.
9.	Dr. Nadeem	Nominee of Pharma Bureau As Observer

The Meeting started with the Holy Verses of Quran, narrated by Prof. Nadeem Irfan Bukhari. After introduction of the members the Chairman CSC welcomed all the participants and appraised about the proceedings of previous meeting and elaborated the outcome of that decisions.

The general discussion ensued Prof. Dr. Javed Akram raised the issue of fee, which is too much exorbant and non-conducive for clinical research. He also emphasized that the process is over regulated. He reiterated the previous decisions of the meeting that Phase-IV clinical trials are needed to be non-regulated. He also argued about the decisions of the Honourable Supreme Court that DRAP should ease the process. He also recommended that DRAP should take fee only for Primary Clinical Trial Sites, whereas the secondary trial sites or clinics where patients are procured for the clinical studies, there should be no fee or may be only nominal fee.

Dr. Faiza Bashir and Dr. Abdur Rashid Chairman CSC added that there should be some nominal fee for application process, it should not free for secondary Clinical Trial Sites. As everyone will apply without any rhyme and reasons and DRAP shall be unable to cater the influx of such applications.

Discussing about delay in approval process, Prof. Dr. Javed Akram said that due to inordinate delay in approval process, the international Clinical Trials are transferred to India & other countries, and this causes huge loss to country.

About over regulation by DRAP he deliberated that there should be no need for Phase-IV clinical Studies which are post marketing open trials. Dr Faiza Bashir added that all ICH-GCP guidelines should be followed and protocol should be submitted to the DRAP for all Phase-IV Clinical Studies, Prof. Dr. Javed Akram further added that Protocol, guidelines and all required documents should be submitted to DRAP for review of CSC. Investigator initiated trials as or non-commercial and facilitation to the post graduate researcher in Medicine & Pharmacy so the intimation to the DRAP be made and Investigators may allowed to start their Clinical Studies.

Dr. Masud Ur Rehman, Secretary CSC, suggested that Clinical studies done by students should be without fee to introduce the culture of clinical research in Pakistan, and Prof. Dr. Javed Akram also suggested that P.I initiated Clinical Studies approval should be free of the cost or with nominal fee of 5000-10000.

It is decided all the matter deliberated will be conveyed to the Competent Authority for approval and implementation.

After discussion the agenda items were presented by the Secretary of the Committee and their decisions are recorded, at the end of each agenda item.

AGENDA ITEM - I: CONFIRMATION OF THE MINUTES OF THE 3rd CLINICAL STUDIES COMMITTEE MEETING.

The CSC confirmed the minutes of 3rdMeeting of Clinical Studies Committee (CSC) held on 16th May, 2019, at Committee Hall, DRAP Headquarter, TF Complex, Islamabad, and signed on the hard copy of minutes for record.

AGENDA ITEM - II: HONORARIUM FOR MEMBERS OF THE CLINICAL STUDIES COMMITTEE.

2.1 Chairman Clinical Studies Committee (CSC) proposed that honorarium as given to members of registration Board and Licensing Board equivalent to Rs. 5000/- may also be paid / granted by the DRAP for each CSC Meeting to the Chairman, Secretary and all members of CSC, who attends the meeting.

- **Decision of CSC:-**

  CSC after discussion unanimously approved the proposal of Honorarium for Chairman, Secretary and all Members of the Clinical Studies Committee, as prevalent practice of Licensing Board & Registration Board, and recommended for further approval from the Competent Authority.

AGENDA ITEM - III: **SUBMISSION OFCERTIFICATE OF NON CONFLICT OF INTEREST BY THE ALL BOARD AND COMMITTEE MEMBERS CONSTITUTED UNDER DRAP ACT, 2012, FOR ATTATINING REQUIREMENTS OF WHO LEVEL III.**

3.1 Drug Regulatory Authority of Pakistan (DRAP) is endeavouring to adopt international best practices. In this context DRAP is currently working to attain maturity level III in WHO NRA Global Benchmarking tool, which is considered as baseline for stringent regulatory authorities. DRAP has successfully submitted revised WHO Global Benchmarking Self-Assessment Tool. During this self-assessment, strengths and areas for improvements were identified. And CEO-DRAP assigned tasks to Shafqat Hussain Danish, AD-II, Pharmacy Services Division, to develop required guidelines, SOPs, Databases and fulfilment of required tasks to achieve WHO level III.

3.2 In this context to achieve WHO level III, there is a requirement that committee on clinical studies (i.e. Clinical Studies Committee (CSC)) are independent, in this regards H.R, Administration Division, DRAP, vide letter no.F.No.12-1/2019-ADMN-I, dated 12th April, 2019, desired that all the members of Boards & Committees need to undertake and submit a certificate of Non Conflict of interest to DRAP.

3.3 **Proforma for Non Conflict of interest is attached (Annex-I)**

- ***Members of CSC present in the 4th CSC Meeting Signed the Non Conflict of Interest Forms, as per proforma sent by the Admin & H.R. Division DRAP, If any member could not signed the non-Conflict of interest form, it will be sent to the members on his official address.***

AGENDA ITEM - IV: **LICENSING OF CRO, CLINICAL TRIAL SITE AND BA/BE CENTRE UNDER THE BIO STUDY RULES, 2017. (Discussed in previous CSC Meetings, Ongoing cases)**

4.1) APPLICATION FOR APPROVAL OF HOLY FAMILY HOSPITAL TO ACT AS CLINICAL TRIAL SITE. (F.No.15-13/2019).

Application is from Medical Superintendent, Holy Family Hospital, Rawalpindi, dated 4thApril, 2019, wherein the request has been made to license their Hospital Gynae Unit-I with the DRAP. To act as a Clinical Trial Site, the application is on prescribed Form-I of the Bio-Study Rules 2017 with fee.

4.1.2. It is submitted that application evaluated according pre- requisites as mentioned in Form-I of the Bio-Study Rules 2017, and remarks are placed against each quarry:

Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	The firm is a Tertiary care Provincial Government Public Hospital.
4	Details of premises including layout plan of the site.	Only Layout is 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 for only Obstetrics & Gynecology section.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Applied site is a Tertiary care Provincial Government Public Hospital.
8	Undertaking on stamp paper	Attached.

4.1.3. Decision of 3rd CSC Meeting: - **"***The CSC after deliberations decided to conduct the inspection of Clinical Trial Site from team of Pool C comprising of the following experts. These experts shall get training at UHS, Lahore prior to moving for inspection. In case any member is not available the committee authorized its chairman to add another suitable member of the relevance expertise from the pool of experts. The applicant shall be inform for the proposed date of inspection accordingly. The CSC also directed the applicant to remove the shortcomings, which have been described in agenda:-*

i.	Dr. Masud ur Rehman
ii.	Dr. Uzma Malik
iii.	Dr. Nazli Hameed
iv.	Dr. Farhana Badar
v.	Dr. Sidra

4.1.4. The CSC has been decided in its 3rd meeting, that incase of unavailability of any member of the panel constituted by the committee, CSC delegated power to the Chairman CSC to include experts from the pool approved in 2nd CSC meeting and may adopt any other relevant expert member from the pool.

4.1.5. Due to availability of some members and non-availability of other members, Chairman CSC, exercising the power delegated by the CSC in its 3rd meeting, added the inspection pool members for the inspection, and following expert's panel inspected the facility on 14th June, 2019:

i.	Dr. Abdur Rashid
ii.	Dr. Masud ur Rehman
iii.	Dr. Salwa Ahsan
iv.	Dr. Uzma Malik

4.1.6. Remarks of inspection team: P.I. has a good experience of running trials. Infra-structure is available. London school of Hygiene is conducting this trial. Regulatory frame work is existing. IRB is regular, safety reporting, ADR reporting is present. Waste disposal through incinerator is existing.

Drugs (trials) storage, distribution, numbering and returning of unused medicine is there. Supply chain is established. Electronic system is present, access control is regulated.

4.1.7. Concluding status of inspection / application:

Recommended for approval

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

- **Decision of 4th CSC Meeting:-**

The CSC unanimously approved the Gynae Unit-I& II, Holy Family Hospital, Rawalpindi, as Clinical Trial Site, under the Bio Study Rules 2017, to Conduct Women-II Clinical Studies.
The CSC directed to issue the approval of trial and its site immediately after the meeting and without any further delay.

4.2) APPLICATION FOR APPROVAL OF INDUS HOSPITAL TO ACT AS CLINICAL TRIAL SITE, (F.No. 15-05/2019).

Application is from Prof. Abdul Bari Khan, CEO, The Indus Hospital, Karachi, dated 25th January, 2019, wherein the request has been made to license their firm with DRAP to act as a Clinical Trial Site. The application is on prescribed Form-I of the Bio-Study Rules 2017.

4.2.2. Application evaluated according to prerequisites as mentioned in Form-I of the Bio-Study Rules 2017, after scrutiny status of application is as follows:

Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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 is 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.	Applied site is a Private Charity Hospital. Details of its facilities are attached.
8	Undertaking on stamp paper	Attached

4.2.3. Description of shortcomings

i) Applied for the Indus Hospital & Delhi Medical Center, as per the Bio-Study Rules 2017, separate application for Delhi Medical Center has not been submitted.

4.2.4. Decision of 3rdCSC Meeting: - *The CSC after deliberations decided to conduct the inspection of Clinical Trial Site from team of Pool-B comprising of the following experts. These experts shall get training at UHS, Lahore prior to moving for inspection. In case any member is not available the committee authorized its chairman to add another suitable member of the relevance experties from the pool of experts. The applicant shall be inform for the*

proposed date of inspection accordingly. The CSC also directed the applicant to remove the shortcomings, which have been described in agenda:-

i.	Prof. Dr. Ali Jawa
ii.	Prof. Dr. Nadeem Afzal
iii.	Mr. Waqas from UHS as Biostatistician
iv.	Dr. Faiza
v.	Dr. Masud ur Rehman (**Coordinator**)

4.2.5. Due to availability of some members and non-availability of other members, Chairman CSC, exercising the power delegated by the CSC in its 3rd meeting, added the inspection pool members for the inspection, and following expert's panel inspected the facility on 01st July, 2019:

i.	Dr. Masud ur Rehman (**Coordinator**)
ii.	Prof. Dr. Ali Jawa
iii.	Mr. Waqas Latif

4.2.6. Remarks of inspection team:

Best facility for TB patients. Out patient, Lab, In-patient, Pharmacy all available. Non-profit charity organization. Well established system & protocol. Well builted as trial site for Anti TB trial at Ghouri Clinic.

4.2.7. Concluding status of inspection / application:

Recommended for approval

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

- **Decision of 4th CSC Meeting:-**

The CSC unanimously approved the Ghouri Clinic ofThe Indus Hospital, Karachi, as Clinical Trial Site, under the Bio Study Rules 2017, to conduct endTB Clinical Studies.

4.3) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT AGA KHAN UNIVERSITY, KARACHI. (F.No.15-11/2019).

Application is from Dr. Saeed Hamid, Director, Clinical Trail Unit, Professor and Consultant Gastroenterologist, Department of Medicine, Aga Khan University, Karachi, dated 7th March, 2019, wherein the request has been made to license their firm with DRAP to act as a Clinical Trial Site, the application is not on prescribed

Form-I of the Bio-Study Rules 2017 along with fee of Rs.50000/- submitted vide challan number 0819383 dated 07.03.2019, whereas differential fee of Rs.50000/- paid vide challan number 0798343dated 29.04.2019. Another challan of Rs.200000/- submitted vide challan no.0819384 dated 21.05.2019.

4.3.2. It is submitted that application evaluated according pre- requisites as mentioned in Form-I of the Bio-Study Rules 2017, status after scrutiny of application is as follows:

Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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.	Attached.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Attached.

4.3.3. Decision of 3rdCSC Meeting: - **"***The CSC after deliberations decided to conduct the inspection of Clinical Trial Site from team of comprising of the following experts. In case any member is not available the committee authorized its chairman to add another suitable member of the relevance experties from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly. The CSC also directed the applicant to remove the shortcomings, which have been described in agenda*:-
The CSC after deliberations decided to conduct evaluation from the following panel:-

i. Dr. Masud ur Rehman, Chairman
ii. Dr. Najam Us Saqib, Additional Director, Karachi, Coordinator
iii. Dr. Mehwish FID, Karachi

4.3.4. As per discussion of Pool Chairman / Secretary CSC with Chairman CSC, following expert's panel inspected the facility on 3rd July, 2019:

i.	Dr. Masud ur Rehman (Chairman)
ii.	Prof. Dr. Ali Java
iii.	Mr. Waqas Latif
iv.	Dr. Najam Us Saqib, Additional Director, Karachi
v.	Dr. Mehwish FID, Karachi

4.3.6. Remarks of inspection team:

State of the art facility. Best of human resources available, responsibility and ownership at maximum available. Ideally as per international norms are all systems protocol, procedure & SOPs developed. Implementation is guaranteed. Neat & clean, HVAC facility.

4.3.7. Concluding status of inspection / application:

Recommended for approval

- Submitted for perusal, discussion and decision of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC unanimously approved the Aga Khan Hospital CTU, as Clinical Trial Site, under the Bio Study Rules 2017.

4.4) APPLICATION FOR LICENSE TO ACT AS CRO, BA/BE STUDIES SITE, AND LABORATORY AT INSTITUTE OF BIOLOGICAL BIOCHEMICAL & PHARMACEUTICAL SCIENCES (IBBPS), AT DOW UNIVERSITY OF HEALTH SCIENCES, KARACHI. (F.No.15-06/2019).

Application is from Mr. Munawar Ali, Additional Director, Institute of Biological, Biochemical & Pharmaceutical Sciences (IBBPS), At Dow University of Health Sciences, Karachi, dated 28th September, 2018, wherein the request has been made to license their firm with DRAP to act as a Contract Research Organization (CRO), BA/BE Studies Center and Bio Analytical Laboratory, on prescribed Form-I of the Bio-Study Rules 2017 without fee.

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

4.4.3 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached, But applied for Contract Research Organization (CRO), BA/BE Studies Center and Bio-Laboratory, on same application form.
2	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).	Not Provided.
4	Details of premises including layout plan of the site.	Layout of ground & first floor 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.	No details provided
8	Undertaking on stamp paper	Not on Stamp paper

4.4.4. Description of shortcomings

i) Particulars regarding the legal status of the applicant are not provided.
ii) Details of the allied facilities associated with center are not provided.
iii) Fee not submitted.
iv) Undertaking is not on stamp paper.

4.4.5. Applicant in reply of letter number F.No.15-06/2019 DD (PS), dates 08th March, 2019 applied for Bio analytical Laboratory and CRO on separate applications, included in the agenda as per application number F.No.15-15/2019 and F.No.15-16/2019 respectively.

4.4.6. This application may be considered for BA/BE Studies Centre

4.4.7. <u>Decision of 3rdCSC Meeting</u>: - *"The CSC after deliberations decided to conduct the inspection of CRO from team of Pool-C comprising of the following experts. These experts shall get training at UHS, Lahore prior to moving for inspection. In case any member is not available the committee authorized its chairman to add another suitable member of the relevance expertise from the pool of experts. The applicant shall be inform for the proposed date of inspection accordingly. The CSC also directed the applicant to remove the shortcomings, which have been described in agenda:-*

i.	Dr. Uzma Malik
ii.	Dr. Nazli Hameed
iii.	Dr. Farhana Badar
iv.	Dr. Sidra
v.	Dr. Masud ur Rehman (**Coordinator**)

4.4.8. The firm informed regarding shortcomings through letter no.F.No.15-08/2019 DD (PS), dated 08thJuly, 2019, still response is awaited.

4.4.9. As per discussion of Pool Coordinator / Secretary CSC with Chairman CSC, following expert's panel inspected the facility on 3rd July, 2019. Dr. Saif Ur Rehman Khattak being expert was given duty from DRAP as liaison officer on volunteer basis to help Dow University in the improvement and development of their BA/BE Centre:

i.	Dr. Masud ur Rehman (**Coordinator**)
ii.	Prof. Dr. Ali Java
iii.	Mr.Waqas Latif
iv.	Dr. Saif Ur Rehman Khattak

4.4.10. Remarks of inspection team:

The infra-structure and human resources is not sufficient for BA/BE centre. HVAC is not available. Safety of staff and trial subject is compromised. Safe disposal of labs waste is not available. Training manuals, validation of available equipment, log books, moisture/ temperature control is lacking. Need gross improvements & interaction with regulators. DRAP will extend technical help for this purpose.

4.4.11. Concluding status of inspection / application:

Provisionally approved for improvements.

4.4.12. <u>Submitted for perusal, discussion and consideration of CSC.</u>

➢ **Decision of 4th CSC Meeting:-**

The CSC after deliberation, deferred the application for six months for improvements, and after the six months when the firm submit compliance report then re-inspected by the same panel of inspectors as nominated in the 3rd CSC meeting.

4.5) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT SHAUKAT KHANUM MEMORIAL CANCER HOSPITAL & RESEARCH CENTER, LAHORE. (F.No.15-12/2019).

Application is from Dr. Faisal Sultan, Chief Executive Officer, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore, Pakistan, dated 15thMarch, 2019, wherein the request has been made to license their firm with DRAP to act as a Clinical Trial Site, the application is not on prescribed Form-I of the Bio-Study Rules 2017.

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

Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached.
2	Fee	Rs.100000/- deposited vide challan number 1921859, dated 08.07.2019, Unverified photocopy 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).	Attached.
4	Details of premises including layout plan of the site.	Attached.
5	Details of the section wise equipment and	Attached.

	machinery required for the analytical or bio-analytical and clinical studies.	
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Attached.

4.5.3. <u>Decision of 3rdCSC Meeting</u>: - ***"****The CSC after deliberations decided to conduct the inspection of Clinical Trial Site from team of Pool D comprising of the following experts. These experts shall get training at UHS, Lahore prior to moving for inspection. In case any member is not available the committee authorized its chairman to add another suitable member of the relevance experties from the pool of experts. The applicant shall be inform for the proposed date of inspection accordingly. The CSC also directed the applicant to remove the shortcomings, which have been described in agenda:-*

i.	Prof. Dr. Javed Akram
ii.	Prof. Saqib Mahmood
iii.	Dr. Uzma Malik
iv.	Dr. Nadeem Irfan Bukhari
v.	Mr. Waqas from UHS as Biostatistician
vi.	Dr. Abdur Rashid (**Coordinator**)

4.5.4. The CSC has been decided in its 3rd meeting, that in case of unavailability of any member of the panel constituted by the committee, CSC delegated power to the Chairman CSC to include experts from the pool approved in 2nd CSC meeting and may adopt any other relevant expert member from the pool.

4.5.5. Due to unavailability of pool members Chairman CSC, exercising the power delegated by the CSC in its 3rd meeting, replaced the inspection pool members for the inspection, and following expert's panel inspected the facility on 08th July, 2019:

i.	Dr. Abdur Rashid (**Coordinator**)
ii.	Prof. Saqib Mahmood
iii.	Dr. Beenish Pervaiz
iv.	Mr.Waqas Latif
v.	Dr. Nadeem Irfan Bukhari

4.5.6. Remarks of inspection team:

Keeping in view the premises, technical personnel and their expertize, equipment, record, documentation, SOPs, Records, Clinical & emergency aspect, pharmacy, calibration, waste management, disaster management and other facilities to conduct the clinical studies, panel unanimously recommends the Clinical Trial Site of Shaukat Khanum Memorial Cancer Hospital & Research Centre, Lahore.

4.5.7. Concluding status of inspection / application:

Recommended for approval

4.5.8. Submitted for the approval of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberation approved the Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore, Pakistan, as Clinical Trial Site, under the Bio Study Rules 2017, subject to submission of verified Fee Challan of remaining fee.

4.6) M/s Pakistan Drug Testing & Research Center (PDTRC), For Bio-Lab, F.15-2/2018-DD (PS)

Application is from Dr. Shafiq-Ur-Rehman Chief Operating Officer, Pakistan Drug Testing and Research Center (PDTRC), Commercial Area (North), Sundar Industrial Estate, Sundar- Raiwind Road, Lahore dated 22nd October, 2018, wherein the request has been made to register their Lab with DRAP as Clinical Research Lab / Analytical Lab, wherein the request has been made to register their Lab with DRAP as Clinical Research Lab / Analytical Lab.

4.6.2. After evaluation observations were communicated as per prerequisites of prescribed Form-I of the Bio-Study Rules 2017 on 08-01-2019 and subsequent reminder also sent on 28th January, 2019, but still response is awaited.

4.6.3 After scrutiny the status of application is as follows:

Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

S.No.	Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017	Provided	Not Provided
1	Application on prescribed Form-I	Yes	--

2	Description regarding applicant and the firm	Yes	--
3	Type of the site meant for (whichever is applicable) (i)Bio-equivalence and Bio-availability studies (ii)CRO (iii)Laboratory (iv)Clinical trials- (a) Phase I (b) Phase II (c) Phase III (d) Phase IV	Laboratory	--
4	Particulars regarding the legal status of the applicant	Yes	--
5	Details of premises including layout plan of the site	Yes	--
6	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Yes	--
7	Names and qualifications of the above sections along with their staff.	Yes	--
8	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	As per reply Not applicable.	Not Provided
9	Undertaking	--	Not Provided
10	Prescribed Fee	--	Not Provided

4.6.4. Description of shortcomings:

i) Scope of lab is not described properly, as the lab previously was working as third-party drug testing lab, it should be properly mentioned that under the Bio-Study Rules which services provided by the lab.

ii) Details of the allied facilities associated with the trial center including ambulatory services, emergency handling not provided.

iii) Processing fee of Rs.300000/- is not provided.

iv) Undertaking on stamp paper is not provided.

4.6.5. <u>Decision of 3rdCSC Meeting</u>: - *"The CSC after deliberations decided to conduct the inspection of Clinical Research Lab / Analytical Lab from team of Pool A comprising of the following experts. These experts shall get training at UHS, Lahore prior to moving for inspection. In case any member is not available the committee authorized its chairman to add another suitable member of the relevance expertise from the pool of experts.*

The applicant shall be inform for the proposed date of inspection accordingly. The CSC also directed the applicant to remove the shortcomings, which have been described in agenda:-

i.	Prof. Dr. Javed Akram
ii.	Dr. Salva
iii.	Prof. Dr. Nadeem Afzal
iv.	Dr. Farhana Badar
v.	Dr. Abdur Rashid (**Coordinator**)

4.6.6. **The firm informed regarding shortcomings through letter no.F.No.15-02/2019 DD (PS), dated 8thJuly, 2019, but still response is awaited.**

4.6.7. The CSC has been decided in its 3rd meeting, that in case of unavailability of any member of the panel constituted by the committee, CSC delegated power to the Chairman CSC to include experts from the pool approved in 2nd CSC meeting and may adopt any other relevant expert member from the pool.

4.6.8. Due to unavailability of pool members Chairman CSC, exercising the power delegated by the CSC in its 3rd meeting, replaced the inspection pool members for the inspection, and following expert's panel inspected the facility on 08th July, 2019:

i.	Dr. Abdur Rashid (**Coordinator**)
ii.	Prof. Dr. Nadeem Afzal
iii.	Prof. Saqib Mahmood
iv.	Dr. Beenish Pervaiz
v.	Mr.Waqas Latif

4.6.9. Remarks of inspection team:

Keeping in view the premises, technical expertise, Pre-qualification from WHO, documentation, equipment, record, training, SOPs, QA system, Calibration, Validation and other facilities, the panel recommends the Pakistan Drug Testing and Research Centre, Sundar Industrial Estate, Lahore for the Clinical Research Laboratory / Analytical Laboratory.

4.6.10. Concluding status of inspection/ application:

Recommended for approval

4.6.11

Processing fee of Rs.300000/- approved by the Authority is still not provided, and Undertaking on stamp paper is also not provided.

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

➢ **Decision of 4th CSC Meeting:-**

The CSC after deliberations approved the Pakistan Drug Testing & Research Center, Lahore, as Bio-analytical Laboratory, under the Bio Study Rules 2017, subject to fulfilment of all codal requirements and fee approved by the Authority.

4.7) M/S DRK Pharma Solutions (Pvt) Ltd, For CRO, F.3-13/2017.

Application is from Azam Shahid Jafri, Director Commercial and Operation, M/s DRK Pharma Solutions (Private) Ltd., 15 KM Multan road, Lahore dated 3rd October 2018, to work as Clinical Research Organization.

4.7.2. After evaluation some observations were communicated as per prerequisites of prescribed Form-I of the Bio-Study Rules 2017 on 12-12-2018, Firm replied as following:

S.No.	Observations	Comments / Reply
1	The firm is applying for license of both CRO and Clinical Trial Site, However, for each category a separate application is required.	We as the subject specifies have applied only for CRO. As given above in the "*Independent ethics committee (IEC)"* definition and explanation IEC is responsible to ensure the protection of the rights, safety and well-being of human subjects involved in a trial protocol and to provide public assurance of that protection by among other thing, reviewing and approving or providing favorable opinion on the trial protocol, the suitability of the investigators, facilities, methods and material to be used in obtaining and documenting informed consent of the trial subjects.
2	Details of premises including layout plan not provided.	The layout plan of our office has been attached as Annex 3.
3	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies is not provided.	We shall not be required to do these as sponsor of clinical trial Phase II, III and IV. These are required by Bioequivalence centers and for Phase-I trials. As per our application on Form-I (attached) we have applied for organizing and monitoring Phase II, III and IV.
4	Names and qualifications of the section wise staff not provided.	The document attached as Annexure 2, contains the CVs of the employees required for conduct of clinical trial and monitoring.
5	Details of the allied	The trial sites to be monitored by us are hospitals

	facilities associated with the trial center including ambulatory services, emergency handling not provided.	which has all the facilities required for any emergency and is reviewed and approved by IEC.
6	Deposited fee will be adjusted after notification by the Authority.	Shall be done as required.

4.7.3. After submission of reply and clarification regarding observations, it is clear that the applicant firm only work as CRO and provide services to conduct clinical trial, and not conduct clinical trial itself, Differential fee of Rs.250000/- also paid vide challan number 0796399 dated 08.03.2019.

4.7.4. After scrutiny status of application is as follows:

Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

S.No.	Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017	Provided	Not provided
1	Application on prescribed Form-I	Yes	--
2	Description regarding applicant and the firm	Yes	--
3	Type of the site meant for (whichever is applicable) (i)Bio-equivalence and Bio-availability studies (ii)CRO (iii)Laboratory (iv)Clinical trials- (a) Phase I (b) Phase II (c) Phase III (d) Phase IV	In recent submission "CRO" is ticked.	--
4	Particulars regarding the legal status of the applicant	Yes	--
5	Details of premises including layout plan of the site	Yes	--
6	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	As per reply Not applicable as they will not conduct any studies.	--
7	Names and qualifications of the above sections along with their staff.	Yes	--
8	Details of the allied facilities associated with the trial center including ambulatory services, emergency	As per reply Not	--

	handling etc.	applicable as they will not conduct any studies.	
9	Undertaking	Provided on stamp paper.	--
10	Prescribed Fee	Rs.300000/- submitted.	--

4.7.5. **<u>Decision of 3rdCSC Meeting</u>: -** **"**The CSC after deliberations decided to conduct the inspection of CRO and its clinical sites from team of Pool A comprising of the following experts. These experts shall get training at UHS, Lahore prior to moving for inspection. In case any member is not available the committee authorized its chairman to add another suitable member of the relevance experties from the pool of experts. The applicant shall be inform for the proposed date of inspection accordingly. The CSC also directed the applicant to remove the shortcomings, which have been described in agenda:-

i.	Prof. Dr. Javed Akram
ii.	Dr. Salva
iii.	Prof. Dr. Nadeem Afzal
iv.	Dr. Farhana Badar
v.	Dr. Abdur Rashid (**Coordinator**)

4.7.6. The CSC has been decided in its 3rd meeting, that in case of unavailability of any member of the panel constituted by the committee, CSC delegated power to the Chairman CSC to include experts from the pool approved in 2nd CSC meeting and may adopt any other relevant expert member from the pool.

4.7.7. Due to unavailability of pool members Chairman CSC, exercising the power delegated by the CSC in its 3rd meeting, replaced the inspection pool members for the inspection, and following expert's panel inspected the facility on 19th June, 2019:

i.	Dr. Abdur Rasheed (Coordinator)
ii.	Prof. Dr. Nadeem Afzal
iii.	Dr. Farhana Badar
iv.	Dr. Beenish Pervaiz.
v.	Dr. Zaman Khan

4.7.8. Remarks of inspection team:

Keeping with human resource, their technical expertise& experience, training, SOPs, documentation, record, equipment's for IT, archive, safety arrangements recommends the approval of CRO of DRK Solution, Raiwind Road Lahore.

4.7.9. Concluding status of inspection / application:

Recommended for approval

- Submitted for perusal, discussion and decision of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC unanimously approved the M/s DRK Pharma Solutions (Private) Ltd., 15 KM Multan road, Lahore, as Contract Research Organization (CRO), under the Bio Study Rules 2017.

4.8) M/s Pioneer Research Solutions (Pvt) Ltd, For CRO, F.3-5/2017(Old) F.15-3/2017(New)

Application is from Tanweer Ahmed CEO, Pioneer Research Solutions (Pvt.) Ltd, House No. 20 St. No.29, Sector F-8/1 Islamabad dated 20th April, 2017, to work as Clinical Research Organization.

4.8.2. After evaluation following observations were communicated as per prerequisites of prescribed **Form-I** of the **Bio-Study Rules 2017** on **12-12-2018**, and three reminders also sent on **7th,11th and 28th January, 2019**, but still response is awaited.

4.8.3. After scrutiny status of application is as follows

Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

S.No.	Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017	Provided	Not Provided
1	Application on prescribed Form-I	--	Not Provided
2	Description regarding applicant and the firm	Yes	--
3	Type of the site meant for (whichever is applicable) (i)Bio-equivalence and Bio-availability studies (ii)CRO (iii)Laboratory (iv)Clinical trials-	--	Application is not on prescribed Form-I.

	(a) Phase I (b) Phase II (c) Phase III (d) Phase IV		
4	Particulars regarding the legal status of the applicant	Yes	--
5	Details of premises including layout plan of the site	--	Not Provided
6	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	--	Not Provided
7	Names and qualifications of the above sections along with their staff.	--	Not Provided
8	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	--	Not Provided
9	Undertaking	--	Not Provided
10	Prescribed Fee	--	Not Provided

4.8.4. Description of shortcomings:

i) Application is not on prescribed Form-I of the Bio-Study Rules 2017.

ii) Submission of fee pending as per approval and notification by Policy Board DRAP.

ii) Undertaking on stamp paper is not provided.

iv) Details of premises including layout plan not provided.

v) Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies is not provided.

vi) Names and qualifications of the section wise staff not provided.

vii) Details of the allied facilities associated with the trial center including ambulatory services, emergency handling not provided.

4.8.5. <u>Decision of 3rd CSC Meeting</u>: - *"The CSC after deliberations decided to conduct the inspection of CRO from team of Pool B comprising of the following experts. These experts shall get training at UHS, Lahore prior to moving for inspection. In case any member is not available the committee authorized its chairman to add another suitable member of the relevance expertise from the pool of experts. The applicant shall be inform for the proposed*

date of inspection accordingly. The CSC also directed the applicant to remove the shortcomings, which have been described in agenda:-

i.	Prof. Ali Jawa
ii.	Prof. Nadeem Afzal
iii.	Mr.Waqas from UHS as Biostatistician
iv.	Dr. Faiza
v.	Dr. Masud ur Rehman (**Coordinator**)

4.8.6. The firm informed regarding shortcomings through letter no.F.No.15-03/2017 DD (PS), dated 8thJuly, 2019, but still response is awaited.

4.8.7. Inspection of the firm was scheduled on 08.07.2019, When firm representative Mr.Tanweer Ahmed CEO, M/s Pioneer Research Solution Pvt Ltd, contacted through office phone for inspection, then He informed that, the firm is closed and not in operation, and will also inform in written, but still written reply is awaited.

- Submitted for perusal, discussion and decision of CSC.

- **Decision of 4th CSC Meeting:-**

  The CSC after deliberations deferred the case.

4.9) M/s Metrics Research (Pvt) Ltd, For CRO & SMO and Clinical Trial Site, F.3-7/2018

Application is from Syed Muhammad Iftikhar Zaidi, CEO Metrics Research (Pvt) Ltd, Plot No. 23-C, 3rd Floor, Old Sunset Boulevard, DHA Phase-II, Karachi, dated 10th September, 2018, wherein the request has been made for license of their company with DRAP to work as Clinical Research Organization (CRO) and Clinical Trial Site

4.9.2. After evaluation observations were communicated as per prerequisites of prescribed **Form-I** of the **Bio-Study Rules 2017** on **12-12-2018**, and **two reminders also sent on 09th and 28th January, 2019**, but still response is awaited, after scrutiny the status of application is as follows:

Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

S.No.	Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017	Provided	Not Provided
1	Application on prescribed Form-I	Yes	--
2	Description regarding applicant and the firm	Yes	--

3	Type of the site meant for (whichever is applicable) (i)Bio-equivalence and Bio-availability studies (ii)CRO (iii)Laboratory (iv)Clinical trials- (a) Phase I (b) Phase II (c) Phase III (d) Phase IV	Nothing ticked on Form-I.	--
4	Particulars regarding the legal status of the applicant	Yes	--
5	Details of premises including layout plan of the site	--	Not Provided
6	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	--	Not Provided
7	Names and qualifications of the above sections along with their staff.	Provided	
8	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	--	Not Provided
9	Undertaking	--	Not on stamp paper
10	Prescribed Fee	--	Not provided

4.9.3. Description of shortcomings:

i) Application to issue license for CRO and Clinical Trial Site is submitted on same application without fee.
ii) Details of premises including layout plan of the clinical trial site is not provided.
iii) Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies not provided.
iv) Details of the allied facilities associated with the trial center including ambulatory services, emergency handling not mentioned.
v) Undertaking should be on stamp paper.
vi) Fee not provided.

4.9.4. <u>Decision of 3rd CSC Meeting</u>: - *"The CSC directed the applicant for clarification of 'SMO' as the term is not permissible in Bio-studies rules. The CSC after deliberations decided to conduct the inspection of CRO and Site from team of Pool B comprising of the following experts. These experts shall get training at UHS, Lahore prior to moving for inspection. In case any member is not available the committee authorized its*

chairman to add another suitable member of the relevance expertise from the pool of experts. The applicant shall be inform for the proposed date of inspection accordingly. The CSC also directed the applicant to remove the shortcomings, which have been described in agenda:-

i.	Prof. Dr. Ali Jawa
ii.	Prof. Dr. Nadeem Afzal
iii.	Mr. Waqas from UHS as Biostatistician
iv.	Dr. Faiza
v.	Dr. Masud ur Rehman (**Coordinator**)

4.9.5. Inspection of the firm was scheduled on 4th July, 2019, when the firm contacted regarding inspection, the firm representative informed telephonically, that they are unavailable on the scheduled date of 4th July, 2019, Later on when panel team returned on3rd July, 2019, asked for their inspection on 4th July, 2019.

4.9.6. Written application from Syed Muhammad Iftikhar Zaidi, CEO Metrics Research (Pvt) Ltd, received on 24th June, 2019, wherein it is informed that due to time constraints their scheduled inspection on 4th July, 2019 was declined upon their request, and it is informed now they are ready for inspection, and requested to schedule inspection plan for their firm.

- Submitted for perusal, discussion and decision of CSC.

- **Decision of 4th CSC Meeting:-**

  The CSC deferred the case for inspection by the same panel constituted in the 3rd CSC meeting. The CSC also directed the applicant to remove the shortcomings.

4.10) M/s Pharma Professional Services (Pvt) Ltd, For the License of BA/BE Centre F.No. 15-1/2018 DD (PS)

Application is from Prof. Dr. Tasneem Ahmed, CEO, Pharma Professional Services (Pvt.) Ltd, A-93 Ettawah society, Ahsan Abad, [near Gulshan-e-Maymar], Gadap Town, Karachi, wherein the request has been made to register their company with DRAP as BA/BE Studies Center and Clinical Research Organization (CRO), dated 18th October, 2018.

4.10.2. After evaluation observations were communicated as per prerequisites of prescribed **Form-I** of the **Bio-Study Rules 2017** on **07-01-2019**, and reminders were also sent on **11th and 23rd January, 2019**. The firm in its recent communication dated 26th January, 2019 submitted application on Prescribed Form-I for the BA/BE Centre, dully singed and stamped by the firm along with fee and undertaking on stamp paper.

4.10.3. After scrutiny the status of application is as follows:

Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

S.No.	Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017	Provided	Not Provided
1	Application on prescribed Form-I	Yes	--
2	Description regarding applicant and the firm	Yes	--
3	Type of the site meant for (whichever is applicable) (i)Bio-equivalence and Bio-availability studies (ii)CRO (iii)Laboratory (iv)Clinical trials- (a) Phase I (b) Phase II (c) Phase III (d) Phase IV	As per the most recent submission, application is submitted on Form-I for BA/BE Centre	--
4	Particulars regarding the legal status of the applicant	Yes	--
5	Details of premises including layout plan of the site	Yes	--
6	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Yes	--
7	Names and qualifications of the above sections along with their staff.	Yes	--
8	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Yes	--
9	Undertaking	Yes	--
10	Prescribed Fee	Fee of Rs.300000/- submitted vide challan no.0808271, dated 15.05.2019 for BE/BA Centre. & Rs.200000/- for their BA/BE Studies Clarithro.	

4.10.4. **Decision of 3rdCSC Meeting: -** "*The CSC after deliberations decided to conduct the inspection of BA/BE Center from team of Pool A comprising of the following experts along with Prof. Dr. Afzal, Ex, VC, UVAAS, Lahore. These experts shall get training at UHS, Lahore*

prior to moving for inspection. In case any member is not available the committee authorized its chairman to add another suitable member of the relevance expertise from the pool of experts. The applicant shall be inform for the proposed date of inspection accordingly. The CSC also directed the applicant to remove the shortcomings, which have been described in agenda:-

i.	Prof. Dr. Javed Akram
ii.	Dr. Salva
iii.	Prof. Dr. Nadeem Afzal
iv.	Dr. Farhana Badar
v.	Dr. Abdur Rashid (**Coordinator**)

4.10.5. The CSC has been decided in its 3rd meeting, that in case of unavailability of any member of the panel constituted by the committee, CSC delegated power to the Chairman CSC to include experts from the pool approved in 2nd CSC meeting and may adopt any other relevant expert member from the pool.

4.10.6. Due to unavailability of pool members Chairman CSC, exercising the power delegated by the CSC in its 3rd meeting, replaced the inspection pool members for the inspection, and following expert's panel inspected the facility on02ndJuly, 2019:

i.	Dr. Abdur Rashid (**Coordinator**)
ii.	Prof. Dr. Nadeem Afzal
iii.	Dr. Salwa Ahsan
iv.	Dr. Farhana Badar

4.10.7. Remarks of inspection team:

Keeping in view technical expertise, equipment, SOPs, documentation, IT facilities, statistical parameters and other facilities, Pharma Professional Services, Karachi, recommended for the application of BA/BE Studies Centre.to conduct the clinical studies, panel unanimously recommends the Clinical Trial Site of Shaukat Khanum Memorial Cancer Hospital & Research Centre, Lahore.

4.10.8. Concluding status of application:

Recommended for approval

- Submitted for perusal, discussion and decision of CSC.

- **<u>Decision of 4th CSC Meeting</u>:-**

The CSC unanimously approved the Pharma Professional Services (Pvt.) Ltd, A-93 Ettawah society, Ahsan Abad, [near Gulshan-e-Maymar], Gadap Town, Karachi, as BA/BE Studies Center, under the Bio Study Rules 2017. The CSC also decided that the Site will be inspected surprisingly when in operation and Prof. Brig. (R), Muzammil Hassan Najmi will be member of that panel.

4.11) M/s Dimension Research CRO & SMO, For and Clinical Trial Site, F.11-2/2018-DD (PS)

Application is from Muhammad Khurram Zaki Khan, CEO of M/s Dimension Research CRO & SMO, Gulistan-e-Jauhar, Scheme-36, Karachi, Pakistan, dated 6th of August, 2018, wherein the request has been made for license of their company with DRAP to work as Clinical Research Organization (CRO) and for management service provider for Clinical Trial Sites.

4.11.2 After evaluation observations were communicated as per prerequisites of prescribed **Form-I** of the **Bio-Study Rules 2017** on **12-12-2018**. The firm accordingly submitted some documents. In addition, two **reminders also sent on 11th and 28th January**, 2019, but still response is awaited. After scrutiny status of application is as follows:

4.11.3 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

S.No.	Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017	Provided	Not Provided
1	Application on prescribed Form-I	Yes	--
2	Description regarding applicant and the firm	Yes	--
3	Type of the site meant for (whichever is applicable) (i)Bio-equivalence and Bio-availability studies (ii)CRO (iii)Laboratory (iv)Clinical trials- (a) Phase I (b) Phase II (c) Phase III (d) Phase IV	Both CRO and Clinical Trial Center are Ticked. But the Firm in response letter confirmed it is a "CRO".	--
4	Particulars regarding the legal status of the applicant	Yes	--
5	Details of premises including layout plan of the site	As per reply Not applicable for the services they are offering.	Not Provided
6	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	As per reply Not applicable for the services they are	Not Provided

		offering.	
7	Names and qualifications of the above sections along with their staff.	Yes	--
8	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	As per reply Not applicable for the services they are offering.	Not Provided
9	Undertaking	Yes	--
10	Prescribed Fee	Fee of Rs.100000/- deposited vide Challan No.0781309 dated 03.08.2018, remaining fee of Rs.200000/- deposited vide Challan No. 1945214 dated 08.07.2019	--

4.11.4. **Decision of 3rdCSC Meeting: -** ***"****The CSC directed the applicant for clarification of 'SMO' as the term is not permissible in Bio-studies rules. The CSC also directed the applicant to remove the shortcomings and the case was deferred.*

4.11.5. The firm has submitted all requisite documents and differential fee also submitted, Firm clarified that they work only as CRO& Management Services Provider for Clinical Trial Sites.

4.11.6 Submitted for perusal, discussion and decision of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberations decided to conduct the inspection of Contract Research Organization (CRO) from team, comprising of the following experts. In case any member is not available the committee authorized its chairman to add another suitable member of the relevant experties from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly:-

i.	Prof. Nisar Hussain Shah
ii.	Dr. Ali Jawa
iii.	Dr. Najam Us Saqib
iv.	Dr. Salwa Ahsan

AGENDA ITEM - V: LICENSING OF CRO, CLINICAL TRIAL SITE AND BA/BE CENTRE UNDER THE BIO STUDY RULES, 2017. (New Cases)

5.1) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, ATM/s SHIFA CLINICAL RESEARCH CENTER (SCRC), SHIFA INTERNATIONAL HOSPITAL LTD, ISLAMABAD. (F. No.15-14/2019-DD (PS)

Application is from Dr. Mian Amjad Sohail, Director Medical Services, Shifa Clinical Research Center, Shifa International Hospital Ltd, Islamabad. Dated 20th May, 2019, wherein the request has been made to license their firm to act as a Clinical Trial Site, the application is on prescribed Form-I of the Bio-Study Rules 2017, along with fee of Rs.100000/- deposited vide challan number 1943309.After scrutiny status of application is as follows:

5.1.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached
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
3	Details of premises including layout plan of the site.	Layout plan not provided. Applied facility is a Tertiary Care Private Hospital.
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 for only Obstetrics & Gynecology section.
6	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Applied site is a Tertiary care private Hospital.
7	Affidavit on Stamp paper	Attached.
8	Fee	Attached

5.1.3. They had also applied for the "POISE" Clinical Study, and had requested that their trial may be considered in this meeting.

- Submitted for perusal, discussion and consideration of CSC.
- **Decision of 4th CSC Meeting:-**

The CSC after deliberations decided to conduct the inspection of Clinical Trial Site (CTS) from team, comprising of the following experts. In case any member is not available the committee authorized its chairman to add another suitable member of the relevant experties from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly:-

i.	Dr. Abdur Rashid
ii.	Dr. Farhana Badar
iii.	Dr. Gul Majeed
iv.	Dr. Rizwana Choudhry

5.2) APPLICATION FOR LICENSE TO ACT AS CRO AT INSTITUTE OF BIOLOGICAL BIOCHEMICAL & PHARMACEUTICAL SCIENCES (IBBPS), AT DOW UNIVERSITY OF HEALTH SCIENCES, KARACHI.(F.No.15-16/2019 - DD (P.S))

Application is from Dr. Sadia Asim, Director, Institute of Biological, Biochemical & Pharmaceutical Sciences (IBBPS), At Dow University of Health Sciences, Karachi, dated 26thApril, 2019, wherein the request has been made to license their firm with DRAP to act as a CRO, on prescribed Form-I of the Bio-Study Rules 2017, with fee OF Rs.300000/- submitted Vide challan no. 1932881. After scrutiny status of application is as follows:

5.2.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached.
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).	Not Provided.
3	Details of premises including layout plan of the site.	Not Provided.
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	Fee	Attached
8	Undertaking	Attached

5.2.3. Description of shortcomings:

i) Particulars regarding the legal status of the applicant/firm are not provided.

ii) Details of premises including layout plan is not provided.

5.2.4. Applicant informed regarding shortcoming vide letter no. F.No.15-16/2019-DD (PS), dated 04th July, 2019, response is still awaited.

- Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberation, decided that the panel constituted for BA/BE Center will also inspect the Contract Research Organization (CRO).

5.3) APPLICATION FOR LICENSE TO ACT AS BIO ANALYTICAL LAB AT INSTITUTE OF BIOLOGICAL BIOCHEMICAL & PHARMACEUTICAL SCIENCES (IBBPS), AT DOW UNIVERSITY OF HEALTH SCIENCES, KARACHI.(F. No.15-15/2019-DD (PS)

Application is from Dr. Sadia Asim, Director, Institute of Biological, Biochemical & Pharmaceutical Sciences (IBBPS), At Dow University of Health Sciences, Karachi, dated 26thApril, 2019, wherein the request has been made to license their firm with DRAP to act as a Bio Analytical Laboratory, on prescribed Form-I of the Bio-Study Rules 2017, with fee OF Rs.300000/- submitted Vide challan no. 1932881. After scrutiny status of application is as follows:

Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached.
2	Particulars regarding the legal status of the	Not Provided.

	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).	
3	Details of premises including layout plan of the site.	Not Provided.
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
	Fee	Attached
	Undertaking	Attached

5.3.2. Following deficiencies were identified:

i) Particulars regarding the legal status of the applicant/firm are not provided.

ii) Details of premises including layout plan is not provided.

5.3.3. Applicant informed regarding shortcoming vide letter no. F.No.15-15/2019-DD (PS), dated 04th July, 2019, response is still awaited.

- Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberation, decided that the panel constituted for BA/BE Center will also inspect the Bio Analytical Laboratory.

5.4) APPLICATION FOR LICENSE TO ACT AS CRO, AT M/S OLIVE WORLDWIDE (SMC-PVT) LTD. (F.No.15-17/2019-DD (PS))

Application is from Mohsin Ali Jawa CEO, M/s Olive Worldwide (SMC-PVT) Ltd, 3-4-5 M, Model Town Extension, Lahore, wherein the request has been made to license their company with DRAP to work as Clinical Research Organization (CRO) (M/s Olive Worldwide (SMC-PVT) Ltd), 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.0846246.After scrutiny status of application is as follows:

Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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.	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. Applied for CRO.
8	Undertaking on stamp paper	Attached.

- Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberations decided to conduct the inspection of Contract Research Organization (CRO) from team, comprising of the following experts. In case any member is not available the committee authorized its chairman to add another suitable member of the relevant experties from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly:-

i.	Prof. Dr. Javed Akram
ii.	Dr. Abdur Rashid
iii.	Dr. Masud Ur Rehman
iv.	Dr. Gul Majeed
v.	Dr. Farhana Badar

5.5) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, BY M/S OLIVE WORLDWIDE (SMC-PVT) LTD, WILCARE POLY CLINIC, LAHORE. (F.No.15-18/2019 DD (PS).

Application is from Mohsin Ali Jawa CEO, M/s Olive Worldwide (SMC-PVT) Ltd, 3-4-5 M, Model Town Extension, Lahore, wherein the request has been made to license their company with DRAP to work as Clinical Trial Site at (M/s Wilcare Hospital), the application is on prescribed Form-I of the Bio-Study Rules 2017 along with fee of Rs.100000/- deposited vide challan no.0846246.After scrutiny status of application is as follows:

Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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.	Attached.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Attached.

- Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberations decided to conduct the inspection of Clinical Trial Site (CTS) from team, comprising of the following experts. In case any member is not available the committee authorized its chairman to add another suitable member of the relevant experties from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly.-

i.	Prof. Dr. Javed Akram
ii.	Dr. Abdur Rashid

iii.	Dr. Masud Ur Rehman
iv.	Dr. Gul Majeed
v.	Dr. Farhana Badar

➢ Secondary Trial Sites for Women-II Clinical Trial:

➢ **Note:-**

The following 17 Clinical Trial Site are peripheral Trial Sites, to recruit the Human Subjects for the Composite Site of The Holy Family Hospital, to conduct Women-II Clinical Studies.

The CSC in its 3rd Meeting decided that detail inspection of composite site where P.I is based shall be subject to detailed inspection and its peripheral trial sites shall be inspected randomly by a small panel, to negate the existence of ghost trial sites.

➢ **Decision of 4th CSC Meeting:-**

As decided in the 3rd CSC meeting, a composite inspection carried out at the principle site (i.e. The Holy Family Hospital, Rawalpindi), for conducting Women-II Clinical Studies, whereas for the rest of secondary clinical trial sites shall be inspected randomly to negate the existence of any ghost sites and confirmation of documented trial sites.

The CSC after deliberations decided that some secondary Clinical Trial Sites shall be inspected, and nominated the inspection panel for them separately, case to case as following:-

5.6 APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT BENAZIR BHUTTO HOSPITAL, RAWALPINDI. (F.No.15-19/2019 DD (PS).

Application is from Prof. Dr. Shugufta Saeed Sial, Professor of Gynae and Obs, at Benazir Bhutto Hospital, Rawalpindi, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960628. After scrutiny status of application is as follows:

5.6.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	Not Provided Facility applied for Clinical Trial Site is a Public Hospital.
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 Applied site is a Private Hospital.
8	Undertaking on stamp paper	Attached.

5.6.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

CSC after deliberations decided that, as the applied site is a tertiary care Government Hospital, hence decided to approve the Clinical Trial Site, to conduct Women-II Clinical Studies.

5.7) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT SERVICES INSTITUTE OF MEDICAL SCIENCES. (F.No.15-20/2019 DD (PS).

Application from Prof. Dr. Rubina Sohail, dated 07th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960629. After scrutiny status of application is as follows:

5.7.2. **Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017**

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	Not Provided Facility applied for Clinical Trial Site

	case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).	is a Public Hospital.
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 Applied site is a Private Hospital.
8	Undertaking on stamp paper	Attached.

5.7.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

CSC after deliberations decided that, as the applied site is a tertiary care Government Hospital, hence decided to approve the Clinical Trial Site, to conduct Women-II Clinical Studies.

5.8) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT BOLAN MEDICAL COMPLEX, QUETTA. (F.No.15-21/2019 DD (PS).

Application is from Prof. Dr. Uzma Sohail Afridi, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960627. After scrutiny status of application is as follows:

5.8.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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	Not Provided Facility applied for Clinical Trial Site is a Public Hospital.

	name and address of the company and its directors).	
4	Details of premises including layout plan of the site.	Not Provided. Facility applied for Clinical Trial Site is a Public Hospital.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not Provided Facility applied for Clinical Trial Site is a Public Hospital.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Attached.

5.8.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberations decided to conduct the inspection of Clinical Trial Site (CTS) from team, comprising of the following experts. In case any member is not available the committee authorized its chairman to add another suitable member of the relevant experties from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly.-

i.	Muhammad Adnan Faisal Saim Deputy Director Pharmacy Services, DRAP.
ii.	Area F.I.D

5.9) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT NISHTER MEDICAL UNIVERSITY & HOSPITAL, MULTAN. (F.No.15-22/2019 DD (PS).

Application is from Prof. Dr. Huma Quddusi, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960632. After scrutiny status of application is as follows:

5.9.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	Facility applied for Clinical Trial Site is a Public Hospital.
4	Details of premises including layout plan of the site.	Layout plan Not Provided. Facility applied for Clinical Trial Site is a Public Hospital.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not Provided Facility applied for Clinical Trial Site is a Public Hospital.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Attached.

5.9.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

CSC after deliberations decided that, as the applied site is a tertiary care Government Hospital, hence decided to approve the Clinical Trial Site, to conduct Women-II Clinical Studies.

5.10) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT SIR GANGA RAM HOSPIATAL, FATIMA JINNAH MEDICAL UNIVERSITY, LAHORE. (F.No.15-23/2019 DD (PS).

Application is from Prof. Dr. Shamsa Humayun, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960631. After scrutiny status of application is as follows:

5.10.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	Not Provided Facility applied for Clinical Trial Site is a Public Hospital.
4	Details of premises including layout plan of the site.	Not Provided. Facility applied for Clinical Trial Site is a Public Hospital.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not Provided Facility applied for Clinical Trial Site is a Public Hospital.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Attached.

5.10.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

CSC after deliberations decided that, as the applied site is a tertiary care Government Hospital, hence decided to approve the Clinical Trial Site, to conduct Women-II Clinical Studies.

5.11) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT ALLAMA IQBAL MEDICAL COLLEGE, JINNAH HOSPITAL, LAHORE. (F.No.15-24/2019 DD (PS).

Application is from Prof. Dr. Arif Tajammul, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960630. After scrutiny status of application is as follows:

5.11.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	Not Provided Facility applied for Clinical Trial Site is a Public Hospital.
4	Details of premises including layout plan of the site.	Attached.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Attached.

5.11.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

CSC after deliberations decided that, as the applied site is a tertiary care Government Hospital, hence decided to approve the Clinical Trial Site, to conduct Women-II Clinical Studies.

5.12) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT PAK-EMIRATES MILITARY HOSPITAL, RAWALPINDI. (F.No.15-25/2019 DD (PS).

Application is from Prof. Dr. Shehla Baqai, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960634. After scrutiny status of application is as follows:

5.12.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	Facility applied for Clinical Trial Site is a Public Military Hospital.
4	Details of premises including layout plan of the site.	Layout Plan not provided. Facility applied for Clinical Trial Site is a Public Military Hospital...
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not Provided Facility applied for Clinical Trial Site is a Public Military Hospital...
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Attached.

5.12.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

CSC after deliberations decided that, as the applied site is a tertiary care Government Hospital, hence decided to approve the Clinical Trial Site, to conduct Women-II Clinical Studies.

5.13) **APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT SHAIKH ZAID WOMEN HOSPITAL, CHANDKA MEDICAL COLLEGE, SHAHHED BENAZIR BHUTTO MEDICAL UNIVERSITY, LARKANA. (F.No.15-26/2019 DD (PS).**

Application from Prof. Dr. Shahida Shaikh, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960643. After scrutiny status of application is as follows:

5.13.2 **Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017**

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).	Facility applied for Clinical Trial Site is a Public Hospital.
4	Details of premises including layout plan of the site.	Layout plan not provided, Facility applied for Clinical Trial Site is a Public Hospital.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not Provided Facility applied for Clinical Trial Site is a Public Hospital.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Attached.

5.13.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

CSC after deliberations decided that, as the applied site is a tertiary care Government Hospital, hence decided to approve the Clinical Trial Site, to conduct Women-II Clinical Studies.

5.14) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT FEDERAL GOVT POLY CLINIC HOSPITAL, ISLAMABAD. (F.No.15-27/2019 DD (PS).

Application is from Dr. Naila Israr, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960637. After scrutiny status of application is as follows:

5.14.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached, but not signed or stamped
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).	Facility applied for Clinical Trial Site is a Public Hospital.
4	Details of premises including layout plan of the site.	Layout plan not provided. Facility applied for Clinical Trial Site is a Public Hospital.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not Provided Facility applied for Clinical Trial Site is a Public Hospital.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Color copy Attached.

5.14.3 Submitted for perusal, discussion and consideration of CSC.

➢ **Decision of 4th CSC Meeting:-**

CSC after deliberations decided that, as the applied site is a tertiary care Government Hospital, hence decided to approve the Clinical Trial Site, to conduct Women-II Clinical Studies.

5.15) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT KOOHI GOTH WOMEN HOSPITAL, KARACHI. (F.No.15-28/2019 DD (PS).

Application is from Dr. Shershah Syed, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960640. After scrutiny status of application is as follows:

5.15.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	Not Provided Facility applied for Clinical Trial Site is a Charitable Hospital. Affiliated with Malir University.
4	Details of premises including layout plan of the site.	Not Provided. Facility applied for Clinical Trial Site is a Charitable Hospital.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Facility applied for Clinical Trial Site is a Charitable Hospital.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Not Provided.

5.15.3 Submitted for perusal, discussion and consideration of CSC.

➢ **Decision of 4th CSC Meeting:-**

The CSC after deliberations decided to conduct the inspection of Clinical Trial Site (CTS) from team, comprising of the following experts. In case any member is not available the committee authorized its chairman to add another suitable member of the relevant experties. The applicant shall be informed for the proposed date of inspection accordingly.-

i.	Dr. Najam Us Saqib. Additional Director, DRAP-Karachi
ii.	Area F.I.D

5.16) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT AYUB MEDICAL TEACHING INSTITUTION, ABBOTABAD. (F.No.15-29/2019 DD (PS).

Application is from Prof. Dr. Aziz Un Nisa Abbasi, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960626. After scrutiny status of application is as follows:

5.16.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	Facility applied for Clinical Trial Site is a Public Hospital.
4	Details of premises including layout plan of the site.	Layout plan is not provided. Facility applied for Clinical Trial Site is a Public Hospital.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Facility applied for Clinical Trial Site is a Public Hospital.
6	Names and qualifications of the above sections along with their staff.	Attached.

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

5.16.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberations decided to conduct the inspection of Clinical Trial Site (CTS) from team, comprising of the following experts. In case any member is not available the committee authorized its chairman to add another suitable member of the relevant experties from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly.-

i.	Dr. Masud Ur Rehman. Secretary CSC / Additional Director, Pharmacy Services-DRAP.
ii.	Prof. Dr. Nadeem Irfan Bukhari Principal Institute of Pharmaceutical Sciences, University of Punjab, Lahore.
iii.	Area F.I.D

5.17) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT BAHAWAL VICTORIA HOSPITAL, BAHAWALPUR. (F.No.15-30/2019 DD (PS).

Application is from Prof. Dr. Naheed Fatima, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960639. After scrutiny status of application is as follows:

5.17.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	Facility applied for Clinical Trial Site is a Public Hospital.

4	Details of premises including layout plan of the site.	Facility applied for Clinical Trial Site is a Public Hospital.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Facility applied for Clinical Trial Site is a Public Hospital.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Attached.

5.17.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

CSC after deliberations decided that, as the applied site is a tertiary care Government Hospital, hence decided to approve the Clinical Trial Site, to conduct Women-II Clinical Studies.

5.18) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT MCH CENTRE, PAKISTAN INSTITUTE OF MEDICAL SCIENCES (PIMS). (F.No.15-31/2019 DD (PS).

Application is from Prof. Dr. Nasira Tasnim, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960627. After scrutiny status of application is as follows:

5.18.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	Facility applied for Clinical Trial Site is a Public Hospital.
4	Details of premises including layout plan of the	Layout plan not

	site.	provided. Facility applied for Clinical Trial Site is a Public Hospital.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Facility applied for Clinical Trial Site is a Public Hospital.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Color copy Attached.

5.18.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

CSC after deliberations decided that, as the applied site is a tertiary care Government Hospital, hence decided to approve the Clinical Trial Site, to conduct Women-II Clinical Studies.

5.19) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT DOW UNIVERSITY OF HEALTH SCIENCES / DR RUTH KM PFAU CIVIL HOSPITAL, KARACHI.(F.No.15-32/2019 DD (PS).

Application is from Prof. Fouzia Parveen, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960635. After scrutiny status of application is as follows:

5.19.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	Facility applied for Clinical Trial Site is a Public Hospital.
4	Details of premises including layout plan of the	Layout plan not

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

5.19.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

CSC after deliberations decided that, as the applied site is a tertiary care Government Hospital, hence decided to approve the Clinical Trial Site, to conduct Women-II Clinical Studies.

5.20) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT JINNAH POSTGRADUATE MEDICAL CENTRE, KARACHI .(F.No.15-33/2019 DD (PS).

Application is from Prof. Dr. Khadija Bano, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960633. After scrutiny status of application is as follows:

5.20.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	Facility applied for Clinical Trial Site is a Public Hospital.
4	Details of premises including layout plan of the	Attached.

	site.	
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Attached.

5.20.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

CSC after deliberations decided that, as the applied site is a tertiary care Government Hospital, hence decided to approve the Clinical Trial Site, to conduct Women-II Clinical Studies.

5.21) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT AZIZ BHATTI SHAHEED TEACHING HOSPITAL, BHIMBAR ROAD GUJRAT, NAWAZ SHARIF MEDICAL COLLEGE, UNIVERSITY OF GUJRAT. (F.No.15-34/2019 DD (PS).

Application from Dr. Shazia Syed, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960638. After scrutiny status of application is as follows:

5.21.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	Facility applied for Clinical Trial Site is a Public Hospital.
4	Details of premises including layout plan of the	Layout plan not

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

5.21.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

CSC after deliberations decided that, as the applied site is a tertiary care Government Hospital, hence decided to approve the Clinical Trial Site, to conduct Women-II Clinical Studies.

5.22) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT BOLAN MEDICAL COMPLEX UNIT-I & UNIT-II, SANDEMAN PROVINCIAL HOSPITAL, QUETTA. (F.No.15-35/2019 DD (PS).

Application is from Prof. Dr. Uzma Sohail Afridi, dated 08th July, 2019, wherein the request has been made to license their Public Hospital with DRAP to work as Clinical Trial Site, to conduct Women-II Clinical Studies, the application is accompanied with fee of Rs.100000/- for Clinical Trial Site vide challan no.1960627. After scrutiny status of application is as follows:

5.22.2 Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	Facility applied for Clinical Trial Site is a Public Hospital.
4	Details of premises including layout plan of the site.	Layout plan not provided.

		Facility applied for Clinical Trial Site is a Public Hospital.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not Provided Facility applied for Clinical Trial Site is a Public Hospital.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Color copy attached.

5.22.3 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberations decided to conduct the inspection of Clinical Trial Site (CTS) from team, comprising of the following experts. In case any member is not available the committee authorized its chairman to add another suitable member of the relevant experties. The applicant shall be informed for the proposed date of inspection accordingly.-

i.	Muhammad Adnan Faisal Saim Deputy Director Pharmacy Services, DRAP.
ii.	Area F.I.D

AGENDA ITEM NO. VI: CLINICALTRIALS/STUDIESREGISTRATION. (Discussed in previous CSC Meeting, Ongoing Cases)

All the following cases for registration of Clinical Studies under agenda item no. VI were discussed in the 3rd CSC meeting and most of them were deferred due to Clinical Trial Site approval from DRAP, Clinical Trial Sites of some clinical studies were inspected by experts of National Inspection Pool and already discussed in Agenda Item-I

6.1) **APPLICATION FOR APPROVAL OF CLINICAL STUDIES TRANEXAMIC ACID (TXA) FOR REDUCINGPOSTPARTUM BLEEDING IN WOMEN WITH ANEMIA: AN INTERNATIONAL, RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED TRIAL (WOMEN-II TRIAL), F.No.03-03/2019 DD (PS).**

Application is from Prof. Dr. Rizwana Chaudhri, Dean of Obstetrics & Gynecology, Rawalpindi Medical University, Head of department Gynae Unit-I, Hospital, Rawalpindi, dated 8thFebruary, 2019, wherein request has been made for registration & approval of subject clinical trial, which will be carried out on following sites:

S.No.	Site Name	Investigators
01	Ayub Teaching Hospital, Abbottabad (Units A,B,C,D)	Prof. Azizunisa Abbasi Dr. Ruqia Sultana Dr. Sadia Habib Dr. Shehla Noor
02	Azad Jammu Kashmir Medical College, Muzaffarabad	Dr. Nosheen Akhter Shabbir
03	Aziz Bhatti Teaching Hospital, Gujrat	Dr. Shazia Saeed
04	Bahawalpur Victoria Hospital (Unit I, II)	Prof. Naheed Fatima Prof. Bushra Sher Zaman
05	Baqai Medical University, Karachi	Prof. Farrukh Naheed
06	Benazir Bhutto Shaheed Hospital, Rawalpindi	Prof Shugufta Sial
07	Bolan Medical Complex Unit, Quetta (Unit I, II, III, IV)	Prof. Naila Ehsan Prof. Aysha Siddiqa Prof. Uzma Sohail Prof. Najma Ghaffar
08	Chandka Medical College, Shaheed Mohtarma Benazir Bhutto Medical University, Larkana (Unit I, II, III)	Prof. Rafia Baloch Prof. Shahida Sheikh Prof. Fozia Kashif
09	Civil Hospital Bahawalpur	Prof. Sohail Chaudhry
10	Civil Hospital Karachi (Unit I, II, III)	Prof. Fauzia Parveen Prof. Nazli Hossain Prof. Nusrat Shah
11	DHQ Rawalpindi	Dr. Attiya Begum
12	Federal Government Polyclinic Hospital, Islamabad	Dr. Naila Israr
13	Holy Family Hospital Unit, Rawalpindi (Unit I, II)	Prof. Rizwana Chaudhri
14	Junnah Hospital Lahore (Unit I, II)	Prof. Tayyab Prof. Arif Tajamal
15	Jinnah Post Graduate Medical Centre, Karachi (Wards 8 & 9)	Prof. HaleemaYaseen Prof. Khadija Bano
16	KEMC, Lady Willington Hospital, Lahore (Units I, II, V)	Prof. Arshad Chohan Prof. Aysha Malik Prof. Abida Sajid
17	Koohi Goath Women's Hospital, Karachi	Dr. Mubasshra Samina
18	Lady Reading Hospital, Peshawar Gynecology A	Prof. Sadaqat Jabeen
19	Liaquat University of Medical & Health Sciences	Prof. Sajida Yousfani

	Hyderabad (Units I, II, III)	Prof. Raheel Sikander Prof. Seema Bibi Qureshi
20	MCH Centre PIMS, Islamabad (Units I, II)	Prof. Sayyeda Batool Mazhar Prof. Nasira Tasneem
21	Military Hospital Rawalpindi	Prof. Shehla Baqai
22	Murshid Hospital Larkana	Dr. Tayyaba Naseer
23	Nishtar Hospital, Multan (Units I, II, III)	Prof. Huma Quddusi Prof. Mehnaz Khakwani Dr. Shahid Irshad Rao
24	Services Hospital Lahore (Units I, II)	Prof. Rubina Sohail Prof. Tayyiba Wasim
25	Sir Ganga Ram Hospital Lahore (Units I, II, III, IV)	Prof. Shamsa Humayun Prof. Zohra Khanum Prof. Noreen Akmal Prof. Shamila Ijaz
26	Ziauddin University Hospital, Karachi	Prof. Rubina Hussain

6.1.2. The trial comprises of primary objective;

i. Proportion of women with a clinical diagnosis of primary PPH. The cause of PPH will be described.

6.1.3. After scrutiny following observations were recorded as per prerequisites of prescribed **Form-II** of the **Bio-Study Rules 2017.**

S. No.	**Document**	**Remarks**
1	Application on prescribed form along with Fee	Attached.
2	Fee	Attached
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	Uganda, Nigeria and Pakistan
7	Phase of trial.	Phase – III
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for	Not Provided

	import of trial material.	
9	Site of the trial	26 Clinical Trial Sites, in Pakistan, applications for Clinical Trial Sites not yet received.
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Approval from Ethics Review Committees of Clinical Trial Sites with Composition not provided.
11	Approval of National Bio-ethics Committee (NBC)	Attached, dated 27th November, 2018
12	CV's of the Investigators	Attached
13	GMP certificate along with COPP & free sale certificate of the investigational product.	GMP for the Manufacturer is Attached. COPP & Free Sale Certificate are not provided.
14	Pre-clinical/clinical safety studies	Not provided. Claimed that as the product is already a registered product, its safety profile is well established.
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 Described
19	Name of Monitors &Clinical Research Associate	Dr. Aasia Kayani, RMU-LSHTM Research Collaboration Centre, Holy Family Hospital, Rawalpindi, Pakistan. Dr. Kiran Javaid Research Collaboration Centre, Holy Family Hospital, Rawalpindi, Pakistan.
20	Evidence of registration in country of origin.	Not Provided
21	Copy of registration letter (if registered in Pakistan)	Not registered in Pakistan
22	Sample of label of the investigational product /	Attached.

	drug.	
23	Duration of trial	38 Months
24	Undertaking	Undertaking is not provided.

6.1.4. **Decision of 3rd CSC Meeting:** - *The CSC directed the applicant to remove the shortcomings. In principle it was decided to approve the clinical trial. Meanwhile, CSC decided to defer the case till the approval of study sites.*

The CSC after deliberations decided to conduct the inspection of clinical trial site from team of Pool C comprising of the following experts. These experts shall get training at UHS, Lahore prior to moving for inspection. In case any member is not available the committee authorized its chairman to add another suitable member of the relevance expertise from the pool of experts. The applicant shall be inform for the proposed date of inspection accordingly. The CSC also directed the applicant to remove the shortcomings, which have been described in agenda:-

i.	Dr. Masud ur Rehman
ii.	Dr. Uzma Malik
iii.	Dr. Nazli Hameed
iv.	Dr. Farhana Badar
v.	Dr. Sidra

A composite inspection shall be carried out at the principle site whereas for the rest of the small trial sites a small teams comprising of the coordinator and local inspector of drugs shall visit the other sites randomly to negate the existence of any ghost sites and confirmation of documented trial sites.

6.1.5. As per direction of the CSC, Inspection Pool C of experts has been inspected the Clinical Trial Site for conducting Women-II Clinical Studies and recommended for approval.

6.1.6 Submitted for perusal, discussion and consideration of CSC.

6.1.7 Dr. Rizwana Choudhry presents before the CSC, clarified and answered the questions raised by the CSC members.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberation unanimously approved the Women-II Clinical studies, under the Bio Study Rules 2017, to be conducted only approved Clinical Trial Sites.

6.2) **APPLICATION FOR APPROVAL AND REGISTRATION OF CLINICAL TRIAL FOR THE endTB (EVALUATING NEWLY APPROVED DRUGS FOR MULTIDRUG RESISTANT TB) PHASE-III CLINICAL TRIAL, AT THE INDUS HOSPITAL KARACHI, F.No.03-04/2019 DD (PS).**

Application is from Prof. Dr. Abdul Bari Khan, CEO, The Indus Hospital, Karachi, dated 25th January, 2019, wherein request has been made for registration & approval of subject clinical trial, which will be carried out mainly at The Indus Hospital, Karachi, whereas Delhi Medical Center (DMC) and Jinnah Post Graduate Medical Center (JPMC) will also be partially involved in the studies but their role in the study is not described. It is a Randomized, Controlled, Open label, Multicounty Phase-III clinical trial.

6.2.2. The study carried out under the supervision of Dr. Naseem Salahuddin M.D (PI), and in the partnership between Partners In Health (PIH), Médecins sans Frontières (MSF), and Interactive Research & Development (IRD) and has a financial partner UNITAD.

The trial comprises of two primary objectives;

i. To evaluate the efficacy of new combination regimens for the treatment of Multi Drug Resistant-Tuberculosis (MDR-TB).
ii. To assess whether the efficacy of experimental regimens at 73 weeks is non-inferior to that of the control.

6.2.3. After scrutiny following observations were recorded as per prerequisites of prescribed **Form-II** of the **Bio-Study Rules 2017.**

S. No.	Document	Remarks
1	Application on prescribed Form-I	Attached
2	Fee	Attached
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	Georgia, Lesotho, Kazakhstan, Kyrgyzstan, Peru, South Africa and Pakistan
7	Phase of trial.	Phase – III
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for import of trial material.	Attached
9	Site of the trial	The Indus Hospital. Application for Site approval, applied but not approved yet.
10	Institutional Review Board (IRB)	Approval from Ethics Review Committee

	approval of sites with complete composition of committee i.e. names and designation of members.	of The Indus Hospital is not provided.
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.	Attached. Explanatory note regarding two ancillary medicine attached regarding their GMP status
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.	108
19	Name of Monitors & Clinical Research Associate	Attached
20	Evidence of registration in country of origin.	Attached. Explanatory note regarding two ancillary medicine attached regarding their GMP status
21	Copy of registration letter (if registered in Pakistan)	Not registered in Pakistan
22	Sample of label of the investigational product / drug.	Attached
22	Duration of trial	48 Months
23	Undertaking on stamp	Attached

6.2.4. It is pertinent to mention here that duration of trial is "**48 Months",** and the applicant provided a list of medicine they will utilized during the clinical studies, provided by the Sponsor, Doctors Without Borders (MSF-France), The Investigational Products (TB drugs) and ancillary medicines supplied by the Sponsor to The Indus Hospital are with **short shelf life** intended to be used in this clinical trial only and NOT FOR SALE, details are as follows:

International Nonproprietary Names (INN) for Pharmaceutical Products	**Manufacturer**	**Country of origin**	**Shelf life (months)**
Investigational Medicinal Products (IP) TB Drugs			
AMIKACIN sulfate, eq.	**MEDOCHEMIE**	CYPRUS	48

250 mg/ml base, 2 ml, amp.			
BEDAQUILINE, 100 mg, tab.	**JANSSEN**	BELGIUM	36
CLOFAZIMINE, 100 mg, soft caps.	**NOVARTIS**	SWITZERLAND/FRANCE	60
CYCLOSERINE 250 mg caps.	**MACLEODS**	INDIA	36
DELAMANID, 50mg, tab., blister	**OTSUKA**	GERMANY	60
ETHIONAMIDE, 250 mg, tab., blister	**MACLEODS**	INDIA	48
LEVOFLOXACIN hemihydrate, eq. 250 mg base, tab.	**HETERO**	SPAIN	36
LEVOFLOXACIN hemihydrate, eq. 500 mg base, tab.	**MACLEODS**	INDIA	48
LINEZOLID, 600 mg, coated tab.	**HETERO**	INDIA	36
MOXIFLOXACIN hydrochloride eq. to 400 mg base , tab.	**HETERO**	INDIA	36
PARA-AMINOSALICYLIC acid (PAS),del.rel.gran, 4g, sach.(25°C)	**JACOBUS**	US	24
ETHAMBUTOL hydrochloride (E), eq. 400 mg base, tab. blister	**MACLEODS**	INDIA	36
ISONIAZID (H), 300 mg, tab., blister	**MACLEODS**	INDIA	36
PYRAZINAMIDE (PZA), 400 mg, tab., blister	**MACLEODS**	INDIA	48
Ancillary medicines			
AMITRIPTYLINE hydrochloride, 25 mg, tab.	**REMEDICA LTD**	CYPRUS	60
BECLOMETASONE dipropionate, 0.10mg/puff, 200 puffs,aerosol	**LABORATORIO ALDO-UNION S.L.**	SPAIN	36
TRIHEXYPHENIDYL hydrochloride, 2 mg, tab.	**REMEDICA LTD**	CYPRUS	60
CARBAMAZEPINE, 200 mg, tab.	**MEDOCHEMIE**	CYPRUS	60

CHLORPHENAMINE maleate, 4 mg, tab.	**CADILA**	INDIA	48
FLUOXETINE, 20mg, caps.	**MYLAN**	FRANCE	48
HALOPERIDOL, 5 mg, tab.	**REMEDICA LTD**	CYPRUS	60
IBUPROFEN, 400 mg, tab.	**REMEDICA LTD**	CYPRUS	60
LEVOTHYROXINE SODIUM, 0.025 mg, tab.	**Mercury Pharmaceuticals Ltd**	UK	24
LOPERAMIDE hydrochloride, 2 mg, tab.	**REMEDICA LTD**	CYPRUS	60
MAGNESIUM OXIDE 270 mg, eq. to 150 mg Magnesium, efferv. tab	**ARROW GENERIQUE**	FRANCE	36
METOCLOPRAMIDE hydrochloride anhydrous, 10 mg, tab.	**REMEDICA LTD**	CYPRUS	60
OMEPRAZOLE 20 mg, enteric caps.	**MEDOCHEMIE**	CYPRUS	36
ONDANSETRON hydrochloride, eq. 8 mg base, tab.	**PLIVA**	UK	60
PARACETAMOL (acetaminophen), 500 mg, tab.	**REMEDICA LTD**	CYPRUS	60
POTASSIUM chloride, 600 mg, sustained release tab.	**LABORATOIRE LEO**	FRANCE	60

6.2.5. <u>Decision of 3rd CSC Meeting</u>:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

6.2.6. Applicant submitted all requisite documents and clarification as per direction of CSC. Inspection of the site also carried out by the experts of inspection Pool-B, and recommended for approval.

6.2.7 Submitted for perusal, discussion and consideration of CSC.

6.2.8 Dr. Mehrun Nisa Hameed, representative from The Indus Hospital, delivered the presentation of the endTB Clinical Studies before CSC.

6.2.9 After presentation Prof. Dr. Javed Akram, asked for scientific data about drugs used in the study and Clinical study protocol, required data shall be provided and will be reviewed by experts & if found satisfactory, then approval granted.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberation deferred the case, till the satisfactory results of scientific data about drugs used in the study and Clinical study protocol, which will be provided by the applicant and reviewed by the experts.

- ***Applicant sent the data asked by the expert members in the 4th meeting of the CSC, Secretary CSC sent the data to the Prof. Brig. (R), Muzammil Hassan Najmi, for review, vide letter numberF.No.03-04/2019 DD (PS) dated 22nd July, 2019.***

6.3) An International, Multi-Centre Controlled Randomized Clinical Trial to Evaluate Rifampicin 1200 Mg and 1800 Mg Daily in the Reduction of Treatment Duration for Pulmonary Tuberculosis from 06 Months to 04 Months. (F.No.03-06/2018 DD (PS)).

Application is from Dr. Bushra Jamil, Agha Khan University, Karachi, wherein the request has been made for approval of clinical trial, which will be carried out at Agha Khan University Hospital, Karachi and Shaukat Khanum Memorial Cancer Hospital, Lahore.

6.3.2. After evaluation following observations were recorded as per prerequisites of prescribed **Form-IIA** of the **Bio-Study Rules 2017.**

6.3.3. The details of the submitted documents as per checklist are as under;

S. No.	Required Documents	Remarks
1.	Application along with Fee	Attached
2.	Fee	Attached Rs.50000/- deposited vide challan No.0798342 dated 11.09.2018 & differential amount of Rs.150000/- deposited vide challan No.1963577, dated 22.05.2019.
3.	Investigator Brochure	Attached
4.	Final Protocol	Protocol Version 6.0 dated 15th June, 2017, has been provided.
5.	Informed consent form (English & Urdu)	Attached

6.	List of participating countries (If applicable)	07 countries including Botswana, Peru, Uganda, Nepal, Mexico, Republic of Guinea and Pakistan.
7.	Phase of trial	Phase – III
8.	Quantity of Drug(s) to be imported/procured/manufactured for the trial	Attached
9.	Site(s) of the trial	Trial will be conducted at following two sites in Pakistan; The Aga Khan University Hospital, Karachi. Shaukat Khanum Memorial Cancer Hospital, Lahore.
10.	C.Vs of investigator(s)	CVs of both Investigators are attached.
11.	Ethical committee approval with complete composition of committee i.e. Name and designations of the members	Attached
12.	Approval from National Bio-ethics Committee (PHRC)	NBC Approval vide letter No.4-87/NBC-329/18/337, dated 10th August, 2018, is attached.
13.	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)	GMP Certificates of M/s Macleods Pharmaceuticals Limited, India and M/s SW Pharma GmbH, Germany have been provided.
14.	Pre-clinical, clinical data and safety studies.	Attached
15.	Summary of the protocol	Attached
16.	Summary of the Investigator Brochure	Not provided
17.	Adverse Event Reporting form	Attached
18.	No. of Patients to be enrolled in each center	It is mentioned that a total of 100 patients will be enrolled in Pakistan.
19.	Name of monitors/clinical research associate	Attached
20.	Evidence of registration of study drug in country of origin	Not provided.
21.	Copy of registration letter (if drug is registered in Pakistan)	The investigational material will be imported from India and Germany
22.	Sample of label of drug	Attached

23.	Duration of trial	Months
24.	Undertaking	Attached

6.3.4. Decision of 2nd CSC Meeting

A four member Sub-committee was constituted to evaluate the trial, as the dose prescribed for Rifampicin was higher than normal dose. The committee comprised of (i) Dr. Javaid Akram, (ii) Prof. Dr. Muzammil Hassan Najmi, (iii) Dr. Masud-ur-Rehman, (iv) Dr. Shahzad, UHS and Prof. Aftab Mohsin, Iqbal Medical College, Lahore.

As Asiatic by genetic build up are slow acetylators and are quite different from others Caucasian. The dose is so high to cause liver damage. The PI will prove that the phase-I studies has been carried out in this dose on Asiatic population or not. It was also advised to PI to conduct Phase-I trial if not available in its preliminary studies. The subcommittee shall evaluate the use of high dose in this studies and will submit its recommendations.

The site will be inspected after the decision of the committee and the case was deferred.

6.3.5. Decision of 3rdCSC Meeting:-

The CSC after deliberations decided to defer the case. The CSC also directed the applicant to remove the shortcomings. The panel will be constituted after submission of report by subcommittee decided in the 2nd CSC Meeting.

6.3.6 The P.I has not contacted the sub-committee, nor provided any literature to its members for evaluation.

6.3.6 Submitted for perusal, discussion and consideration of CSC.

6.3.7 **4th CSC Meeting:**

Dr. Summaeya on the behalf of P.I. attended the 4th CSC meeting and presented the Clinical Studies before CSC, Clinical Studies were also presented in the UHS to the expert, Prof. Dr. Javed Akram, and He said after presentation Clinical Studies found satisfactory.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberation conditionally approved the Rifa-Shot Clinical studies, under the Bio Study Rules 2017. Applicant directed to fulfill all requirements as per Form-II of the Bio-Study Rules 2017. To be conducted only at approved Clinical Trial Sites.

6.4) **APPLICATION FOR IMPORT OF NUTRITIONAL SUPPLEMENT, BOVINE LACTOFERRIN (bLF) 150MG AND 300MG AND PLACEBO D GLUCOSE FOR CLINICAL TRIAL, F.No.03-02/2019 DD (PS).**

Application is from Prof. Dr. Shabina Ariff, Associate Professor, Consultant Pediatrician& Neonatologist, Department of Pediatrics, Aga Khan University Hospital, Karachi, dated 22nd February, 2019, wherein request has been made to import and for startup of subject clinical trial at Aga Khan University Hospital, Karachi, under the supervision of principal investigator Dr. Shabina Ariff and Sajid Soofi co-investigator.

6.4.2. The purpose of this study is to evaluate the effectiveness of bovine Lactoferrin (bLF) to prevent late onset neonatal sepsis in low birth weight infants in Pakistan, It's "A Three-Arm Double Blind Individual RCT.

6.4.3. After scrutiny following observations were recorded as per prerequisites of prescribed **Form-II** of the **Bio-Study Rules 2017.**

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached
2	Fee	Rs.50000/- deposited instead of Rs.200000/- Approved amount of fee by the Authority
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	The study is Pakistan specific only
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.	Bovine Lactoferrin (150mg)=3150 Bovine Lactoferrin (300mg)=3150 Placebo D-Glucose=3150 Sachets
9	Institutional Review Board (IRB) approval with complete composition of committee i.e. names and designation of members.	Attached
10	National Bioethics Committee approval	Attached

11	CV's of the Investigators	Attached.
12	GMP certificate along with COPP & free sale certificate of the investigational product.	Attached.
13	Pre-clinical/clinical safety studies	Attached.
14	Summary of Protocol	Not provided.
15	Safety and progress report	Not provided.
16	Adverse Event Reporting Form	Attached
17	No of patients to be enrolled in each center.	Attached. Three Arms: 100 patients in each. **Total 300 Patients.**
18	Name of Monitors & Clinical Research Associate	Attached
19	Evidence of registration in country of origin.	Registration certificate for Glucose –D is not provided.
20	Evidence of registration in Pakistan.	Not registered in Pakistan
21	Sample of label of the investigational product / drug.	Attached
22	Duration of trial	24 Months

6.4.4. Description of shortcomings:

i) Differential fee of Rs.150000/- is not deposited yet.
ii) Undertaking on stamp paper is not provided.
iii) CoPP and free sale certificates for the investigational product are not provided.

6.4.5. <u>Decision of 3rd CSC Meeting</u>:-

The CSC also discussed in detail that lactoferrin is a food product and is not drug or therapeutic good, so its approval from DRAP is not mandatory, nor it comes in the category of clinical trial. If the applicant has any relevant clinical trial approval from any SRA they may share with the CSC for further proceeding. The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

6.4.6. Applicant informed regarding shortcoming vide letter no. F.No.03-02/2019-DD (PS), dated 04th July, 2019, response is still awaited.

6.4.7 Submitted for the consideration of CSC.

➢ **Decision of 4th CSC Meeting:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. The case was so deferred. Applicant directed to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

6.5) APPLICATION FOR THE APPROVAL OF CLINICAL STUDY "LACTOFERRIN EVALUATION IN ANEMIA IN PREGNANCY (LEAP-1) – A MULTICOUNTRY RANDOMIZED CONTROL CLINICAL TRIAL", F.No.03-02/2017 DD (PS).

Application is from Dr. Sajid Soofi, Associate Professor, Department of Pediatrics& Child Health, Aga Khan University Hospital, Karachi, submitted the application to import Lactoferrin Capsules 200mg & Ferrous Sulphate 80mg for clinical trials on 6th March, 2017 (page 01-12/corr), after evaluation of application this division issued a letter, dated 8th March 2017 for submission of formal application along with required documents refer to para 4-10/N. After submission of firm reply refer to para 17 & 27/N, application was placed before Registration Board in its 276th meeting dated 22nd to 24th November, 2017, As before notification of the Bio-Study Rules 2017 all cases regarding clinical studies were placed before Registration Board as per practice at that time, Registration Board decided the matter as under:

"Decision:In the light of discussion and deliberation, Registration Board deferred the case for provision of following information and documents:

a) CoPP or Free sale certificate of investigational product.
b) Pharmacological data of Bovine Lactoferrin
c) Results of Phase I clinical trials and animals studies on Bovine Lactoferrin.
d) Data regarding safety of Bovine Lactoferrin in pregnant women and children.
e) Proof of Halal source of Bovine Lactoferrin"

6.5.2. After scrutiny following observations were recorded as per prerequisites of prescribed **Form-II** of the **Bio-Study Rules 2017.**

S. No.	Document	Remarks
1.	Application on prescribed Form-II	Attached
2.	Fee	Rs.50000/- submitted instead of Rs.200000.
3.	Investigator Brochure (s)	Not provided
4.	Final protocol	Attached
5.	Informed consent and participant information sheet (Urdu to English)	Attached
6.	List of participating countries	Pakistan, Australia and New Zealand
7.	Phase of trial.	Phase – II trial

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.	Lactoferrin Capsules 200mg: 840 bottles x 30 Capsules = 25,200 Capsules FeSO4 Capsules 80mg: 840 bottles x 30 Capsules = 25,200 Capsules (Mfg. by M/s Pharmaceutical Packaging Professionals, Pty Ltd, 3/31, Sabre Drive, Port Melbourne VIC 3207, Australia)
9.	Independent Ethics Committee (IEC)/Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Attached
10.	Approval of National Bio-ethics Committee	Attached.
11.	CV's of the Investigators	Attached.
12.	GMP certificate along with COPP & free sale certificate of the investigational product.	GMP Certificate is attached
13.	Pre-clinical/clinical safety studies	Although few study reports have been provided by the applicant but no comprehensive data has been furnished regarding the safety of Lactoferrin in pregnant women and children.
14.	Summary of Protocol	Attached
15.	Adverse Event Reporting Form	Attached
16.	No of patients to be enrolled in Pakistan.	Attached 240 Patients (120 in each group)
17.	Name of Monitors & Clinical Research Associate	Attached
18.	Evidence of registration in country of origin.	Not provided
19.	Evidence of registration in Pakistan.	N/A
20.	Sample of label of the investigational product / drug.	Attached
21.	Duration of trial	02 Years
22.	Undertaking on stamp paper	Not provided

6.5.3. Description of shortcomings:

i) Rs.50000/- deposited instead of Rs.200000/-, differential Fee of Rs.150000/- need to be paid.
ii) Undertaking on stamp paper is not provided.
iii) Evidence of registration in country of origin is not provided.

6.5.4. <u>Decision of 3rdCSC Meeting</u>:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings already pointed out by the Division of Pharmacy Services.

6.5.5. Applicant informed regarding shortcoming vide letter no. F.No.3-2/2017-DD (PS), dated 04th July, 2019, response is still awaited.

6.5.6 Submitted for perusal, discussion and consideration of CSC.

6.5.7 **4th CSC Meeting:**

Dr. Laila on behalf of P.I presented the Clinical Studies before the CSC experts.

- **<u>Decision of 4th CSC Meeting</u>:-**

The CSC after deliberation conditionally approved the Clinical studies, under the Bio Study Rules 2017. Applicant directed to fulfill all requirements as per the Bio-Study Rules 2017, to be conducted only at approved Clinical Trial Site.

6.6) <u>A Randomized Double-Blind, Clinical Trial on the Efficacy and Safety of "Yinhuang Qinfei Capsule" in the Treatment of Acute Exacerbation of Chronic Simple Bronchitis,F.No.03-05/2018-DD (PS).</u>

Application is from Prof. M. Iqbal Chaudhary, Director, International Center for Chemical and Biological Sciences (ICCBS), University of Karachi, wherein request has been made for approval of "Clinical Trial On The Efficacy And Safety Of "Yinhuang Qinfei Capsule" In The Treatment Of Acute Exacerbation Of Chronic Simple Bronchitis", which will be carried out by Principal Investigator Prof. M. Iqbal Chaudhary and Dr. Kausar Aamir Co-Principal Investigator.

6.6.2. After evaluation following observations were recorded as per prerequisites of prescribed Form-II of the Bio-Study Rules 2017.

S. No.	Document	Remarks
1	Application on prescribed Form-II	Not provided
2	Fee	Rs.50000/- provided only.
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	Pakistan and China.
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.	Not provided
9	Site approval of the trial and sites	Not provided
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Not provided
11	Approval of National Bio-ethics Committee (NBC)	Not provided
12	CV's of the Investigators	Attached
13	GMP certificate along with COPP & free sale certificate of the investigational product.	Valid GMP Certificate of M/s Hunan Anbang Pharmaceutical Co. Ltd., has been furnished.
14	Pre-clinical/clinical safety studies	Reports of animal studies are attached. However, no data regarding the Phase – I studies has been provided.
15	Summary of the Protocol	Attached
16	Summary of the Investigator Brochure	Attached
17	Adverse Event Reporting Form	Attached
18	No of patients to be enrolled in each center.	Attached. 212 patients. (106 in each group)
19	Name of Monitors & Clinical Research Associate	Attached
20	Evidence of registration in country of origin.	Attached
21	Evidence of registration in Pakistan.	Not registered in Pakistan.
22	Sample of label of the investigational product / drug.	Attached
23	Duration of trial	12 Months

6.6.3 Description of Shortcomings:

i. Application is not on prescribed Form-II of the Bio-Study Rules 2017.
ii. The submitted Investigator's Brochure and Final Protocol of the trial is not in line with the ICH – GCP Guidelines and do not contain sufficient information.
iii. The qualitative and quantitative composition of the investigational product has not been furnished.
iv. The results of previously conducted Phase – I studies and Pharmacokinetic/ Pharmacodynamic studies on human subjects, have not been provided.
v. Approval from National Bioethics Committee (NBC) of Pakistan Health Research Council (PHRC), Islamabad, has not been provided.
vi. CoPP and Free Sale Certificate of the investigational product has not been submitted.
vii. The registration/marketing authorization letter of the investigational product is in Chinese language and therefore not readable. A duly attested translated copy of the said letter in English language, should be provided.
viii. The proposed clinical trial site i.e. Jinnah Post-graduate Medical Center (JPMC), Karachi, is not licensed by DRAP.
ix. It is mentioned in the protocol that Amoxicillin Potassium Clavulanate 375mg capsules will be administered to the enrolled patients in both Control Group as well as in the Treatment Group, whereas on the same page in section 9.4.5 of the protocol, it is mentioned that during the trial no any medication having therapeutic effects on the indications of the study, will be administered to the patients. The justification for use of Amoxicillin Potassium Clavulanate in the trial and the source of manufacturing and procurement of the said drug should be provided.
x. Processing Fee for approval of each clinical studies is Rs.200000/- , only Rs.50000/- are submitted, differential amount is not provided.
xi. Undertaking on stamp paper is not provided.

6.6.4. <u>Decision of 3rd CSC Meeting</u>:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

6.6.5. The deficiencies observed in the application was communicated to the applicant through letter number F.3-5-2018 dated 10th October, 2018, 05th March, 2019, and 08th July, 2019 but still response is awaited.

6.6.6 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. The case was so deferred. Applicant directed to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

6.7) Open Label, Non-Randomized, Multi-Center Investigator Initiated Study to Evaluate Effectiveness of Generic Velpatasvir and Sofosbuvir in Hepatitis-C with or without Ribavirin among Pakistani Population, F.No.03-03/2018-DD (PS)

Application is from Prof. Syed Muhammad Zahid Azam, Dow University Hospital, Karachi, for approval of "OPEN LABEL, NON-RANDOMIZED, MULTI-CENTER INVESTIGATOR INITIATED STUDY TO EVALUATE EFFECTIVENESS OF GENERIC VELPATASVIR AND SOFOSBUVIR IN HEPATITIS-C WITH OR WITHOUT RIBAVIRIN AMONG PAKISTANI POPULATION", Phase-IV clinical trial.

6.7.2. After evaluation following observations were recorded as per prerequisites of prescribed Form-II of the Bio-Study Rules 2017.

S. No.	Document	Remarks
1	Application on prescribed Form-II	Not provided
2	Fee	Rs.50,000 has been deposited as processing fee
3	Investigator Brochure (s)	Not provided. Prescribing Information of International brand of M/s Gilead Sciences, USA, has been furnished.
4	Final protocol	Attached Protocol Version 3.0,
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries	The study is Pakistan specific only
7	Phase of trial.	Phase – IV Post – marketing observational study
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.	1300 Packs, each containing 28 tablets of Velpatasvir/Sofosbuvir 100mg/400mg) Applicant has informed that the study drug will be provided by the M/s

		CCL Pharma, Lahore which has submitted that their product is pending for approval in Registration Division, DRAP. Whereas they have the registration of the same product for export purpose only and they can supply the same for study purpose. **Information regarding quantities and source of other trial material i.e. Ribavirin has not been disclosed.**
9	Site approval of the trial and sites	Anwar Riyaz-I-Qadeer Diabetes Institute Lahore. Not approved yet.
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Applicant has provided the approval of Institutional Review Committee, Dow University, Karachi.
11	Approval of National Bio-ethics Committee (NBC)	Not provided
12	CV's of the Investigators	Attached.
13	GMP certificate along with COPP & free sale certificate of the investigational product.	In-valid GMP Certificate of M/s CCL Pharmaceuticals (Pvt.) Ltd., has been furnished which has expired on 30-03-2018
14	Pre-clinical/clinical safety studies	Not provided
15	Summary of the Protocol	Attached.
16	Summary of the Investigator Brochure	Attached
17	Adverse Event Reporting Form	Attached
18	No of patients to be enrolled in each center.	Attached. 30 to 40 patients at each site. Total 300 Patients approximately.
19	Name of Monitors & Clinical Research Associate	Attached
20	Evidence of registration in country of origin.	Not provided.
21	Evidence of registration in Pakistan.	Registration letter of Abriva Forte Tablet (Velpatasvir/Sofosbuvir 100mg/400mg) for Export Purpose, is attached.
22	Sample of label of the investigational	Attached

	product / drug.	
23	Duration of trial	12 Months

6.7.3. Following deficiencies were identified:

i) Application is not on prescribed Form-II of the Bio-Study Rules 2017.

ii) Product registration certificates used during Clinical studies not provided.

iii) Related to study title "Effectiveness of Generic Velpatasvir/Sofosbuvir…" license to manufacture drug for experimental purposes or drug registration certificate is required.

iv) Complete information regarding quantities and source of Zovirin is required.

v) GMP, CoPP and free sale certificate for the investigational products is required.

vi) Approval of National Bioethics Committee (PHRC) and Institutional Review Board of study sites is required.

vii) Processing Fee for approval of each clinical studies is Rs.200000/- , only Rs.50000/- are submitted, differential amount is not provided

viii) Undertaking on stamp paper is not provided.

6.7.4. <u>Decision of 3rdCSC Meeting</u>:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

6.7.5. The shortcomings were communicated to the firm through letter no. F.No.3-3/2018 DD (PS), dated 06th June, 2018, 05th March, 2019 and 08th July, 2019, but still response is awaited.

6.7.5 Submitted for perusal, discussion and consideration of CSC.

- **<u>Decision of 4th CSC Meeting</u>:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. The case was so deferred. Applicant directed to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

6.8) **REQUEST FOR THE APPROVAL OF OBSERVATIONAL STUDY PROGRAM ASSESSING EFFECTIVENENSS AND TOLERABILITY OF GLICLAZIDE 60 mg MODIFIED RELEASE TABLET IN PATIENTS WITH TYPE-II DIABETES FASTING DURING RAMADAN, (F. No. 03-01/2019).**

Application is from Dr. Shoaib Mushtaq (Head of Medical Affairs), M/s Servier Research and Pharmaceuticals Pakistan (Pvt) Ltd., wherein request has been made for approval of subject clinical trial, which was being carried out at following centres:

i) Baqai Institute of Diabetes and Endocrinology, Karachi.

ii) National Defence Hospital, Lahore.

iii) University of Health Sciences, Lahore.

iv) Diabetes Institute of Pakistan, Jail Road, Lahore.

v) Hayatabad Medical Complex (Medical Teaching Institute), Peshawar.

6.8.2. After scrutiny following observations were recorded as per prerequisites of prescribed **Form-II** of the **Bio-Study Rules 2017.**

S. No.	Required Documents	Remarks
1.	Application on prescribed Form-II	Attached
2.	Fee	Not provided
3.	Investigator Brochure	Not provided & claimed that it's an observational study.
4.	Final Protocol	Protocol Version 1.1.0 dated 20th November, 2017.
5.	Informed consent form (English & Urdu)	Attached
6.	List of participating countries (If applicable)	09 countries including Bangladesh, India, Indonesia, Malaysia, Saudi Arab, United Arab Emirates, Kuwait, Egypt and Pakistan.
7.	Phase of trial	Phase-IV
8.	Quantity of Drug(s) to be imported/procured/manufactured for the trial	Details not provided. Applicant claimed as it is an observational study, there is no need to import medicines.
9.	Site(s) of the trial	Trial will be conducted at following five sites in Pakistan; 1. Baqai Institute of Diabetes and Endocrinology, Karachi.

		2. National Defence Hospital, Lahore. 3. University of Health Sciences, Lahore. 4. Diabetes Institute of Pakistan, Jail Road, Lahore. 5. Hayatabad Medical Complex (Medical Teaching Institute), Peshawar.
10	C.Vs of investigator(s)	Attached.
11	Ethical committee approval with complete composition of committee i.e. Name and designations of the members	Ethical Committee Composition and approval from each Clinical trial Site is not provided.
12	Approval from National Bio-ethics Committee (PHRC)	NBC Approval vide letter No.4-87/NBC-302(2nd yrExten+Amed/19/360) Dated 4th January, 2019, is attached.
13	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)	Not Provided.
14	Pre-clinical, clinical data and safety studies.	Not provided & claimed that it's an observational Study.
15	Summary of the protocol	Attached
16	Summary of the Investigator Brochure	Not provided.
17	Adverse Event Reporting form	Attached
18	No. of Patients to be enrolled in each center	20 patients at each site.
19	Name of monitors/clinical research associate	Mr. Faheem Shehzad.
20	Evidence of registration of study drug in country of origin	Not provided.
21	Copy of registration letter (if drug is registered in Pakistan)	Attached.
22	Sample of label of drug	Not provided, and claimed that the product is already registered in Pakistan, so Not applicable
23	Duration of trial	06 Months
24	Undertaking on stamp paper	Not provided

6.8.3. Shortcomings were communicated through letter number F.No.03-01/2019 dated 8th March, 2019, and reply is as follows:

S.No.	Shortcomings	Reply

01	Investigator Brochure is not provided and claimed that it is an observational studies.	Investigators Brochure is the requirement for an Investigational Drug (Phase II-III). For phase IV studies already available product leaflet is used.
02	Quantity of Drug(s) to be imported/procured/manufactured for the trial, is not described.	As this is an observational (Phase IV) study using the already available medicines in the market (having being prescribed and patient already using) and since we are not going to import any medicines hence the quantity of the medicines were not mentioned.
03	Ethical committee approval with complete composition of committee i.e. Name and designations of the members for the clinical trial sites are not provided.	Complete composition of the IRB with names and designations were attached as Appendix B (the checklist given in the Bio-Study Rules 2017 at number 10). This is being provided again. (Annexure 1)
04	Approval from NBC attached, but it is for second year extension and amendments, previous approval is not provided.	The initial approval by the NBC is being provided. (Annexure 2)
05	GMP Certificate and Free Sale Certificates are not provided, and claimed that as the drug registered in Pakistan so not applicable.	Gliclazide 60 mg MR (Diamicron 60 mg MR) was registered in Pakistan in 2009 (as per the registration letter dated 9th September 2009-copy attached). The GMP certificate of the production facility is attached. This is a locally manufactured drug and hence does not require a free sale certificate.
06	Pre-clinical, clinical data and safety studies are not provided and claimed it is an observational study.	Pre-clinical, clinical data and safety studies again is a requirement for investigational drug and if the drug is registered and marketed (as is the case with Gliclazide 60 mg MR since 2009) and its pharmacology is widely understood by medical practitioners, an extensive IB is not necessary and the leaflet suffices.
07	Summary of Investigator brochure is not provided.	Not required for a registered and marketed drug (as given above)
08	Evidence of registration in country of origin is not provided, as the drug registered in the Pakistan	The requirement of registration in the country of origin is also for an unapproved investigational drug. This is an approved drug in Pakistan since 2009 and is being locally manufactured since then hence this is not required. (Registration letter attached—Annexure 3)

09	Sample of label of drug is not provided.	This (leaflet of the drug) was provided and is being sent again. (Annexure 4)

6.8.4 Description of shortcomings:

i) Clinical Trial Sites mentioned in the application are neither licensed, nor applied for licensing from the DRAP.

6.8.5. Decision of 3rdCSC Meeting:-

The CSC after deliberations decided to defer the case till approval of study site. The CSC also directed the applicant for submission of fee required for clinical trial site (s). Clinical trial site need approval from DRAP.

6.8.6. The firm was communicated through letter no. F.No.03-04/2019 DD (PS), dated 08th, 2019, but still response is awaited.

6.8.7 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. The case was so deferred. Applicant directed to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

6.9) REQUEST FOR THE APPROVAL FOR IMPORT OF STUDY MEDICINES FOR RESEARCH PROJECT ENTITLED "ANTIBIOTICS FOR CHILDERN WITH SEVERE DIARRHEA (ABCD) TRIAL". (F. No. 03-02/2019).

Application is from Dr. Farah Qamar, Associate Professor Department of Pediatrics and Child Health, Aga Khan University, Karachi, wherein request has been made for approval for import of study medicine for subject clinical trial, which was being carried out by the Aga Khan University Hospital, at following seven different sites in the Karachi:

i) Ali Akber Shah.
ii) Ibrahim Hyderi.
iii) Bhains Colony.
iv) Shireen Jinnah Colony.
v) Machar Colony.
vi) Sindh Govt: Hospital Ibrahim Hyderi.
vii) Sindh Govt: Hospital Korangi No.5.

6.9.2. After scrutiny following observations were recorded as per prerequisites of prescribed **Form-II** of the **Bio-Study Rules 2017.**

S. No.	Required Documents	Remarks
1.	Application on prescribed Form-II	Application is not applied on prescribed Form – II
2.	Investigator Brochure	Not provided & claimed that it's not a Trial for Licensure.
3.	Final Protocol	ABCD Protocol Version 9.0 dated 21st December, 2018, has been provided.
4.	Informed consent form (English & Urdu)	Attached
5.	List of participating countries (If applicable)	07 countries including Bangladesh, India, Kenya, Malawi, Mali, Tanzania and Pakistan.
6.	Phase of trial	Not provided & claimed that it's a clinical Trial of already marketed drug.
7.	Quantity of Drug(s) to be imported/procured/manufactured for the trial	Details not provided
8.	Site(s) of the trial	Trial will be conducted at following seven sites in Pakistan; 1. Ali Akber Shah. 2. Ibrahim Hyderi. 3. Bhains Colony. 4. Shireen Jinnah Colony. 5. Machar Colony. 6. Sindh Govt: Hospital Ibrahim Hyderi. 7. Sindh Govt: Hospital Korangi No.5.
9.	C.Vs of investigator(s)	CVs of both Investigators are attached.
10.	Ethical committee approval with complete composition of committee i.e. Name and designations of the members	Attached
11.	Approval from National Bio-ethics Committee (PHRC)	NBC Approval vide letter No.4-87/NBC-249-Yr II Exten. With Amend. /181/67, Dated 24th July, 2018, is 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)	GMP Certificates of M/s Universal Corporation Limited, **Kenya** Expired on 30th September 2017 However, no CoPP or Free Sale Certificates of the investigational products, have been furnished.
13.	Pre-clinical, clinical data and safety studies.	Not provided & claimed that it's an already registered & marketed.
14.	Summary of the protocol	Attached
15.	Summary of the Investigator Brochure	Not provided & claimed that it's an already registered & marketed.
16.	Adverse Event Reporting form	Attached
17.	No. of Patients to be enrolled in each center	It is mentioned that a total of 1650 patients will be enrolled, approximately 15 Children per week from study sites within the study period.
18.	Name of monitors/clinical research associate	Not provided & claimed that it's an already registered & marketed.
19.	Evidence of registration of study drug in country of origin	Not provided.
20.	Copy of registration letter (if drug is registered in Pakistan)	Not provided. But alternate Brands are Registered & Marketed in Pakistan.
21.	Sample of label of drug	Attached
22.	Duration of trial	43Months
23.	Prescribed Fee	Not provided
24.	Undertaking on stamp paper	Not provided

6.9.3. The firm was communicated shortcomings through letter no. F.No.03-02/2019 DD (PS), dated 12thApril, 2019, and reply is as follows:

S.No.	Shortcomings	Reply
1	Trial drug which is imported in the Brand Name of "Throza" from Kenya is not registered in Pakistan and not imported with due process.	Trial drug which was imported from Kenya by the brand name of "Throza" is Azithromycin and this generic Azithromycin is registered in Pakistan with a different brand name available most commonly as "Zetro". It is widely used among children and adults. Proof of

		registration of Azithromycin in Pakistan is provided with previous response letter dated 19th March, 2019. Registration certificate from country of origin is attached again for your reference.
2	As mentioned in the reply that the drug "Zetro (Azithromycin)" is registered and widely used in Pakistan, so why you are importing unregistered drug "Throza" from Kenya, It should be clear that, if a generic drug like "Azithromycin" is registered in Pakistan, it doesn't means to allow its import from any country or any drug containing "Azithromycin", without due process.	The trial is being conducted by (WHO) in 7 countries in Asia and Africa (Pakistan, India, Bangladesh, Kenya, Tanzania, Mali and Malawi). For the purpose of standardization among all participating countries the trial medication was centrally procured and distributed to all sites by WHO, purchased from Universal Corporation, Kenya with the brand name of "Throza and imported to all sites.
3	Exemption approval from Ministry of Foreign Affairs, as mentioned in the emails, is not attached with reply.	We had received the exemption from Ministry of Foreign Affairs (MOFA) for the release of shipment and the trial medications were delivered to WHO office in Islamabad and subsequently to AKU.
4	Application for licensing of the Aga Khan Clinical Trial Unit, to work as clinical Trial Site was received to this division on 07th March, 2019, whereas you received trial drugs on 03rd July, 2017, and continued the Clinical Trial.	The clinical trial unit of Aga khan university has already applied for a license to drug regulatory authority of Pakistan and the application with fee has been submitted. As per DRAP response, representative from DRAP will visit CTU.
5	Clarification regarding starting the clinical studies without prior approval from DRAP, and consumption of unregistered medicines in clinical trial is not submitted.	Nil
6	Despite all above shortcoming, you are applying for approval, for import of study medicines for research project.	Nil

6.9.4. After evaluation of the reply following shortcomings were recorded:

i) Applicant is not for approval of Clinical Studies.

ii) Applied for approval of medication import for trial.

iii) No evidence is provided for exemption, granted by Ministry of Foreign Affairs, as per your own claim.

iv) No clarification submitted regarding conducting clinical trial without prior approval from DRAP.

6.9.5. Decision of 3rdCSC Meeting:-

The CSC after deliberations decided to defer the case till the response received from the applicant. The applicant was directed to proceed as per established norms for the import of unregistered clinical trial material and avoid illegal procedures as were adopted previously. They may contact the local DRAP office, Karachi for any such import applications.

6.9.6. The firm was communicated through letter no. F.No.03-02/2019 DD (PS), dated 08th, 2019, but still response is awaited.

6.9.7. Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. The case was so deferred. Applicant directed to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

6.10) A MULTI-COUNTRY, MULTI-CENTER, TWO ARM, PARALLEL, DOUBLE BLIND, PLACEBO CONTROLLED, RANDOMIZED TRIAL OF ANTENATAL CORTICOSTEROIDS (DEXAMETHASONE) FOR WOMEN AT RISK OF IMMINENT BIRTH IN THE EARLY PRE-TERM PERIOD (ACTION – I TRIAL) AND LATE PRE-TERM PERIOD (ACTION – II TRIAL) IN HEALTH FACILITIES IN LOW-RESOURCE SETTINGS TO IMPROVE NEWBORN OUTCOMES, F.No.03-01/2018 DD (PS).

Application is from Dr. Shabina Ariff, Assistant Professor, Department of Pediatrics, Aga Khan University, Karachi, wherein request has been made for approval of subject clinical trial, which will be carried out at Sheikh Zaid Hospital, Rahim Yar Khan and Liaquat University Hospital, Hyderabad.

6.10.2. The trial comprises of two primary objectives;

i. To compare the effect of Dexamethasone to placebo, on stillbirth and neonatal survival when given to women at risk of imminent preterm birth in facilities.

ii. To compare the effect of Dexamethasone to placebo on possible maternal bacterial infections when given to women at risk of imminent preterm birth in facilities.

6.10.3. This trial is sponsored and funded by the World Health Organization (W.H.O), Geneva. In Pakistan, Department of Pediatrics and Child health, Aga Khan University, Karachi, is the national trial coordinator.

6.10.4. After scrutiny following observations were recorded as per prerequisites of prescribed **Form-II** of the **Bio-Study Rules 2017.**

S. No.	**Document**	**Remarks**
1	Application on prescribed Form-II	Attached
2	Fee	Rs.50000/- deposited instead of Rs.200000/-
3	Investigator Brochure (s)	Attached
4	Final protocol	Attached Action – I (Version 1.9.2) Action – II (Version 1.5)
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries	Bangladesh, India, Kenya, Nigeria and Pakistan
7	Phase of trial.	Phase – IV
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for import of trial material.	**ACTION – I Trial** Dexamethasone Injection 4mg/ml = 5760 ampoules Placebo (Sodium chloride 0.9%) = 5,760 ampoules **ACTION – II Trial** Dexamethasone Injection 4mg/ml = 10,800 ampoules Placebo (Sodium chloride 0.9%) = 10,800 ampoules
9	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names	Approval from Ethics Review Committee of Aga Khan University is attached

	and designation of members.	
10	Approval of National Bio-ethics Committee (NBC)	Attached
11	CV's of the Investigators	Attached
12	GMP certificate along with COPP & free sale certificate of the investigational product.	GMP Certificate of the manufacturer i.e. M/s Fresenius Kabi Manufacturing SA (Pty) Ltd., South Africa and Registration Certificate of Dexamethasone Injection 4mg/ml is attached.
13	Pre-clinical/clinical safety studies	Attached
14	Summary of Protocol and Investigator Brochure	Attached
15	Adverse Event Reporting Form	Attached
16	No of patients to be enrolled in each center.	**Liaquat University Hospital, Hyderabad** ACTION – I Trial = 120 ACTION – II Trial = 480 **Sheikh Zaid Hospital, RYK** ACTION – I Trial = 600 ACTION – II Trial = 2220 **Total:** **ACTION – I Trial = 720** **ACTION – II Trial = 2700**
17	Name of Monitors & Clinical Research Associate	Attached
18	Evidence of registration in country of origin.	Registration Certificate of Dexamethasone Injection 4mg/ml is attached.
19	Evidence of registration in Pakistan.	N/A
20	Sample of label of the investigational product / drug.	Attached
21	Duration of trial	24 Months
22	Undertaking on stamp	Not provided

	paper	

6.10.5. Description of shortcomings:

i) Applied Clinical trial sites are not licensed from DRAP.
ii) Applicant deposited Rs.50000/-, whereas, fee approved by the Authority for clinical studies is Rs.200000/-.
iii) Undertaking on stamp paper is not provided.

6.10.6. <u>Decision of 3rd CSC Meeting</u>:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

6.10.7. The firm was communicated through letter no. F.No.03-01/2018 DD (PS), dated 03rd May, 2019 and 08th July, 2019, but still response is awaited.

6.10.8 Submitted for perusal, discussion and consideration of CSC.

6.10.9 **4th CSC Meeting**:

Dr. Summaeya on the behalf of P.I. attended the 4th CSC meeting and presented the Clinical Studies before CSC.

- **<u>Decision of 4th CSC Meeting</u>:-**

The CSC after deliberation conditionally approved the Clinical studies, under the Bio Study Rules 2017. Applicant directed to fulfill all requirements as per the Bio-Study Rules 2017, and after approval of Clinical Trial Site approval.

6.11) <u>APPLICATION FOR THE APPROVAL OF CLINICAL STUDY "ACCURACY OF BODY COMPOSITION MONITORS IN ASSESSMENT OF FLUID STATUS IN THE CHRONIC KIDNEY DISEASE [CKD] PATIENTS ON HEMODIALYSIS VERSUS CLINICAL ASSESSMENT", F.No.03-05/2019 DD (PS).</u>

Application is from Javaid Nasir Qureshi, Managing Director Pakistan & Afghanistan for M/s Fresenius Medical Care Pakistan (Pvt) Ltd., wherein request has been made for approval of subject clinical assessment studies, which was being carried out at

Fatima Memorial Hospital College of Medicine & Dentistry, Karachi. Under supervision of Dr. Hafiz Usman (PI) and Dr. Nauman Tarif (Co-Investigator).

6.11.2. After scrutiny following observations were recorded as per prerequisites of prescribed **Form-II** of the **Bio-Study Rules 2017.**

S. No.	Required Documents	Remarks
1.	Application on prescribed Form-II	Attached
2.	Fee	Not provided.
3.	Investigator Brochure	Not provided.
4.	Final Protocol	Not provided.
5.	Informed consent form (English & Urdu)	Not provided.
6.	List of participating countries (If applicable)	Nil
7.	Phase of trial	Not provided.
8.	Quantity of Drug(s) to be imported/procured/manufactured for the trial	01 Body Composition Machine (BCM) (Medical Device) & 600 electrodes for 150 patients.
9.	Site(s) of the trial	8. Fatima Memorial Hospital College of Medicine & Dentistry, Karachi.
10.	C.Vs of investigator(s)	CVs of both Investigators are attached.
11.	Ethical committee approval with complete composition of committee i.e. Name and designations of the members	Attached
12.	Approval from National Bio-ethics Committee (PHRC)	Not provided.
13.	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)	Not provided.
14.	Pre-clinical, clinical data and safety studies.	Not provided.
15.	Summary of the protocol	Not provided.
16.	Summary of the Investigator Brochure	Not provided.
17.	Adverse Event Reporting form	Not provided.

18.	No. of Patients to be enrolled in each center	150 patients.
19.	Name of monitors/clinical research associate	Not provided & claimed that it's an already registered & marketed.
20.	Evidence of registration of study drug in country of origin	Not provided.
21.	Copy of registration letter (if drug is registered in Pakistan)	Not provided.
22.	Sample of label of drug	Attached
23.	Duration of trial	Not provided.
24.	Undertaking on Stamp Paper	Not provided

6.11.3. Description of shortcomings:

i) Investigators brochure, final protocol, and informed consent form is not provided.
ii) Clinical trial site is not approved from DRAP.
iii) Approval from National Bio-ethics Committee (PHRC), is not provided.
iv) GMP certificate along with Free Sale Certificate/Certificate of Pharmaceutical Product is not provided.
v) Pre-clinical, clinical data and safety studies is not provided.
vi) Summary of protocol and summery of investigators brochure is not provided.
vii) Adverse Event Reporting form is not attached.
viii) Evidence of registration of study drug in country of origin is not provided.
ix) Copy of registration letter (if drug is registered in Pakistan), is not provided.
x) Sample of label of drug is not attached
xi) Duration of trial is not described.
xi) Processing Fee is not provided.
xii) Undertaking on Stamp paper is not provided.

6.11.4. **Decision of 3rd CSC Meeting:-**

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings. The applicant shall be informed to apply for approval of trial site first and then its clinical trial.

6.11.5. The firm was communicated through letter no. F.No.03-05/2019 DD (PS), dated 11th April, 2019 and 08th July, 2019, firm replied through letter no. T010719-BCM-DRAP01L, dated 09th July, 2019, due to financial reasons and approval for Clinical Trial Sites by Principal Investigator, they are termination of the project and will not conduct the said studies.

6.11.6 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. The case was so deferred. Applicant directed to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

6.12) M/s Origin Pharma (Pvt) Ltd, For Clinical Trial on Insugin (Recombinant Human Insulin) 25IU Mouth rinse solution 5ml, F.No.03-08/2018-DD (PS)

Application is from Muhammad Farooq (MD), M/s Origin Pharma Pvt Ltd, 41-Baber Block, New Garden Town Lahore-Pakistan, for approval of Multicentre Observational Study For the drug **Insugin** (Recombinant Human Insulin) 25IU Mouth rinse solution 5ml, for clinical trial (Phase-III), East gate Pharmaceuticals Inc,2203-65, Harbour Square, Toronto Canada, Another application attached from Muhammad Farooq (MD),), M/s Origin Pharma Pvt Ltd, 41-Baber Block, New Garden Town Lahore-Pakistan, on Form-4 of rule 6 (30) of the Drugs (import & export) rules, 1976, For import of 2000 boxes of the drug for the study

6.12.2. After evaluation following observations were recorded as per prerequisites of prescribed **Form-II** of the **Bio-Study Rules 2017.**

S. No.	Document	Remarks
1	Application on prescribed Form-II	Not provided
2	Fee	Not provided
3	Investigator Brochure (s)	Not provided
4	Final protocol	Not provided
5	Informed consent and participant information sheet (Urdu to English)	Not provided
6	List of participating countries	Not provided
7	Phase of trial.	Phase-III (Details not provided)
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.	10*2000 Boxes
9	Site approval of the trial and sites	Anwar Riyaz-I-Qadeer Diabetes Institute Lahore. (Not approved yet by the DRAP)
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names	Not provided

	and designation of members.	
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.	Not provided
14	Pre-clinical/clinical safety studies	Not provided
15	Summary of the Protocol	Not provided
16	Summary of the Investigator Brochure	Not provided
17	Adverse Event Reporting Form	Not provided
18	No of patients to be enrolled in each center.	200 Patients, Details not provided
19	Name of Monitors & Clinical Research Associate	Principal Investigator: Dr. Arif Riaz Qadeer
20	Evidence of registration in country of origin.	Not provided
21	Evidence of registration in Pakistan.	Not provided
22	Sample of label of the investigational product / drug.	Not provided
23	Duration of trial	66 Months

6.12.3. Description of shortcomings:

i) Application is for import of the drug for clinical trial, where clinical trial site and clinical trial is not approved from the DRAP.
ii) Application for clinical trial approval is not on prescribed form-II of the Bio-Study Rules 2017.
iii) Fee not provided.
iv) Prerequisite information as per form-II of the bio-Study rules 2017 are not provided
v) The firm was advised to apply on prescribed form-I of the Bio-Study Rules 2017 for approval of Clinical Trial Site before applying for clinical trial approval.

6.12.4. <u>Decision of 3rdCSC Meeting</u>:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

6.12.5. The deficiencies observed in the application was communicated to the applicant on 7th January, 2019 and subsequent reminder was also sent on 11th& 30th January, 2019, and

after 3rd CSC meeting shortcoming along with CSC decision sent on 08th July, 2019, but still response is awaited.

6.12.6 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. The case was so deferred. Applicant directed to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

6.13) CLINICAL TRIAL OF SUBBETTA (ORAL SUB-UNIT INSULIN RECEPTOR 6MG SUBLINGUAL TABLET), BY M/s Origin Pharma (Pvt) Ltd, F.No.03-04/2018-DD (PS)

Application is from Mr. Muhammad Farooq, Managing Director, M/s Origin Pharma (Pvt.) Ltd., regarding the conduct of subject clinical trial.

6.13.2. M/s Origin Pharma (Pvt.) Ltd., is the sponsoring firm of the trial and the investigational product i.e. Subetta (oral sub-unit insulin receptor 6mg sublingual tablet) will be manufactured by Materia Medica Holdings, Moscow Russia. Investigational product contains affinity purified antibodies to C-terminal fragment of beta-subunit of insulin receptor and affinity purified antibodies to endothelial NO (nitric oxide) synthase.

6.13.3. Dr. Arif Riaz Qadeer is the Principal Investigator and the trial is planned to be conducted at Anwar Riyaz-I-Qadeer Diabetes Institute, Lahore.

6.13.4. After evaluation following observations were recorded as per prerequisites of prescribed **Form-II** of the **Bio-Study Rules 2017.**

S. No.	Document	Remarks
1	Investigator Brochure (s)	Not provided. Prescribing Information of the investigational product has been furnished
2	Final protocol	Not provided.
3	Informed consent and participant information sheet (Urdu to English)	Attached
4	Fee	Rs.50,000 has been deposited as processing fee
5	List of participating countries	Not provided.

6	Phase of trial.	Phase – III
7	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.	5000 boxes containing 40 tablets each.
8	Independent Ethics Committee (IEC)/National Bioethics Committee/Institutional Review Board (IRB) approval with complete composition of committee i.e. names and designation of members.	Not provided.
9	Trial Site	Applied Clinical Trial Site is not licensed from DRAP, and also not applied yet.
10	CV's of the Investigators	Attached.
11	GMP certificate along with COPP & free sale certificate of the investigational product.	Two GMP certificates have been provided. One issued by MoH Russia dated 10-12-2007 which was valid for 03 years and expired in 2010. Other GMP certificate is issued by Govt of Ukraine dated 21-10-2012 which expired on 21-10-2015
12	Pre-clinical/clinical safety studies	Data of a safety and efficacy study has been provided but the applicant has not furnished any comprehensive information about pre-clinical / animal studies and Phase – I and Phase – II studies.
13	Summary of Protocol	Not provided.
14	Safety and progress report	Not provided.
15	Adverse Event Reporting Form	Not provided
16	No of patients to be enrolled at each center.	5000 patients.
17	Name of Monitors & Clinical Research Associate	Not provided.
18	Evidence of registration in country of origin.	The provided document is in Russian language and therefore not readable.
19	Evidence of registration in Pakistan.	Not provided.
20	Sample of label of the investigational product / drug.	Outer label of commercial pack has been submitted.

21	Duration of trial	01 year.
22	Undertaking on stamp paper	Not provided.

6.13.5. Description of shortcomings:

i) Protocol of the trial is not attached with the application, which should be provided in a format as defined under Good Clinical Practice (GCP) Guidelines of International Council for Harmonization (ICH).
ii) Investigator's brochure should be provided as per Good Clinical Practice (GCP) Guidelines of International Council for Harmonization (ICH).
iii) Pharmacological data of investigational drug should be submitted in detail.
iv) Names of other countries participating in this trial needs to be provided.
v) Approval from Institutional Review Board (IRB) / Independent Ethics Committee (IEC) should be furnished along with composition and names of the members of the IRB / IEC as per ICH GCP guidelines.
vi) Approval from National Bioethics Committee (NBC), Pakistan Health Research Council should be provided.
vii) Applied Clinical Trial Site is not licensed from DRAP, and also not applied yet.
viii) The submitted GMP certificates are expired. Valid GMP certificate of the manufacturer needs to be provided.
ix) Comprehensive information about previously conducted pre-clinical safety studies / animal studies, Phase – I and Phase – II studies on the investigational drug should be submitted.
x) Adverse Event Reporting form and trial monitoring mechanism should be revealed.
xi) Registration certificate / marketing authorization of the investigational product in the country of origin along with certified translated copy in English language (if the document is in any other foreign language).
xii) Processing fee deposited is less than approved by the Authority.
xiii) Undertaking on stamp paper is not provided.

6.13.6. <u>Decision of 3rd CSC Meeting</u>:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

6.13.7. Deficiencies observed in the application was communicated to the applicant on 2nd July, 2019 and subsequent reminder was also sent on 3rd May, 2019, and after 3rd CSC meeting applicant again informed regarding deficiencies through letter number F.No.3-4/2018 dated 08th July, 2019, but still reply is awaited.

6.13.8 Submitted for perusal, discussion and consideration of CSC.

- **<u>Decision of 4th CSC Meeting</u>:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. The case was deferred. Applicant directed to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

AGENDA ITEM - VII: CLINICAL TRIALS/STUDIES REGISTRATION (New Cases)

7.1) APPLICATION FOR ISSUANCE OF INVOICE OF PAYMENT FOR THE APPROVAL OF NEW CLINICAL TRIAL, ENTITLED PERIOPERATIVE ISCHEMIC EVALUATION-3 (POISE-3), SPONSERED BY POPULATION HEALTH RESEARCH INSTITUTE, HAMILTON CANADA.

Application is from Dr. Sumeyya Azam, Senior clinical research associate, Shifa Clinical Research Center (SCRC), Shifa International Hospital Ltd, Islamabad, dated 23rdApril, 2019, wherein request has been made for issuance of invoice for fee payment along with application for registration of clinical studies on prescribed Form-II of the Bio-Study Rules 2017, and fee of Rs.200000/- submitted vide challan No1943310, dated 15.05.2019.

7.1.2. The study is sponsored by **Population Health Research Institute Hamilton Canada,** The aim of the study to determine Tranexamic Acid (TXA) is superior to placebo for the occurrence of life-threatening, major and critical organ bleeding and non- inferior to placebo for the occurrence of major arterial and venous thrombotic events.

7.1.3. As per Population Health Research Institute trial will recruit from following 27 countries:

01	Australia	10	Germany	19	Poland
02	Austria	11	Hong Kong	20	Romania
03	Belgium	12	India	21	Russia
04	Brazil	13	Ireland	22	South Africa
05	Canada	14	Italy	23	Spain
06	Chile	15	Malaysia	24	Uganda
07	China	16	Netherland	25	United Arab Emirates
08	Denmark	17	New Zealand	29	United Kingdom

09	France	18	Pakistan	27	United States of America

7.1.3. In Pakistan 180 subjects will recruited for POISE-3 Clinical studies.

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

S. No.	Document	Remarks
1	Application on prescribed form	Attached
2	Fee	Attached
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	27 countries including Pakistan, as mentioned in para 03/N
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.	Locally manufactured & registered product will be used in the trial.
9	Site of the trial	i- Shifa Int. Hospital Ltd, Islamabad.(Site#520) ii- Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore. (Site#521) iii- Aga Khan University Hospital, Karachi. (Site#522)
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	IRB approval for Shifa International Hospital & Aga Khan Hospital is attached. Approval from Ethics Review Committee of Shaukat Khanum Memorial Cancer Hospital is not provided.
11	Approval of National Bio-ethics Committee (NBC)	Not Provided
12	CV's of the Investigators	i- Prof. Dr. Mohammad Aamir (PI), Shifa Int. Hospital Ltd, Islamabad.(Site#520)

		ii- Dr. Faisal Hanif (PI), Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore. (Site#521) iii-Dr. Mohsin Nazir Butt (PI), Aga Khan University Hospital, Karachi. (Site#522) **(CVs Attached)**
13	GMP certificate along with COPP & free sale certificate of the investigational product.	Attached
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.	10000 in all 27 Countries. 180 Subject recruited in Pakistan.
19	Name of Monitors & Clinical Research Associate	Attached
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.	Not Provided
23	Duration of trial	48 Months
24	Undertaking on stamp paper	Not Provided

7.1.5. After evaluation shortcoming were communicated to the applicant, reply dated 6th July, 2019, in reference to the short comings is as follows:

S.No.	Shortcomings	Reply
01	Approval from Ethics Review Committee of Shaukat Khanum Memorial Cancer Hospital is not provided.	Shifa International Hospital terminated Shaukat Khanum Memorial Cancer Hospital from the Clinical Studies.

02	Approval of National Bio-ethics Committee (NBC) is not provided.	Provided.
03	Sample of label of the investigational product not provided.	Provided.
04	Undertaking on stamp paper.	Provided.

7.1.6 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberations decided to defer the case till the approval of the Clinical Trial Site.

7.2) REQUEST TO CONDUCT CLINICAL TRIAL "PREVENTION OF METRNAL & NEONATAL DEATH/INFECTIONS WITH A SINGLE ORAL DOSE OF AZITHROMYCIN IN WOMEN IN LABOR (IN LOW & MIDDLE INCOME COUNTRIES), A RANDOMIZED CONTROLLED TRIAL.(F.No.03-09/2019-DD (PS))

Application is from Prof. Dr. Sarah Saleem, Principle Investigator Aspirin Trial, Department of Community Health Sciences, Aga Khan University, dated 22nd May, 2019, wherein request has been made for registration & approval of subject clinical trial, which will be carried out at Jinnah Post Graduate Medical Center (JPMC). It is a Randomized, Controlled, Phase-III clinical trial, Application is not on prescribed Form-I, and along with a fee of Rs.50000/- deposited vide challan no.1943654.

7.2.2. The study carried out under the supervision of Prof. Dr. Sarah Saleem (PI), along with Dr. Saleem Jessani (Co-PI).

7.2.3. The trial comprises of two primary objectives;

i. To test the effectiveness of a single dose of prophylactic intrapartum Azithromycin compared to placebo in reducing the risk of composite outcome of following:
   a) Maternal death or sepsis and,
   b) Intrapartum /neonatal death or sepsis.

7.2.4. The details of the submitted documents as per checklist are as under:

S. No.	Document	Remarks
1	Application on prescribed Form-II	Not provided.
2	Fee	Only Rs.50000/- deposited instead of

		Rs.200000/-
3	Investigator Brochure (s)	Not Provided.
4	Final protocol	Attached
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries	Bangladesh, Democratic Republic of Congo, Guatemala, Kenya, India, Zambia and Pakistan
7	Phase of trial.	Phase – III
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for import of trial material.	10000 Tablets (Azithromycin 500mg Tablet, Blister pack of 4s) 10000 Identical Placebo Tablet, with identical packaging.
9	Site of the trial	Jinnah Post Graduate Medical Center (JPMC). Application for Site approval, applied but not approved yet.
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Approval from Ethics Review Committee of Aga Khan Hospital is provided, but Ethics Review Committee of JPMC is not provided.
11	Approval of National Bio-ethics Committee (NBC)	Not provided.
12	CV's of the Investigators	Attached.
13	GMP certificate along with COPP & free sale certificate of the investigational product.	Attached.
14	Pre-clinical/clinical safety studies	Articles Attached.
15	Summary of Protocol	Attached.
16	Summary of Investigator Brochure	Not provided.
17	Adverse Event Reporting Form	Attached.
18	No of patients to be	4250

	enrolled in each center.	
19	Name of Monitors & Clinical Research Associate	Attached.
20	Evidence of registration in country of origin.	Web page address with snapshot is attached. Also verified online, details are as under: **AZITROMICINA CINFA 500 mg** **MANUFACTURED BY:** **LABORATORIOS CINFA, S.A.** Active Ingredients(Azithromycine Dihidrate) Marketing Authorization No.65600. Registration certificate is not provided.
21	Copy of registration letter (if registered in Pakistan)	Product used in the trial is not registered in Pakistan
22	Sample of label of the investigational product / drug.	Attached.
22	Duration of trial	36 Months
23	Undertaking on Stamp paper	Not provided.

7.2.5. Description of shortcomings:

i) Application is not on prescribed Form-II of the Bio-Study Rules 2017.

ii) Only Rs.50000/- submitted as processing fee, instead of Rs.200000/-, which is approved by the Authority.

iii) Investigator Brochure & its summary are not provided.

iv) Approval from National Bio-ethics Committee (NBC) is not provided.

v) Undertaking on stamp paper is not provided.

vi) Applied Clinical Trial Site not yet approved from DRAP, even application for the site is not received yet.

7.2.6 The firm was communicated through letter no. F.No.03-09/2019 DD (PS), dated 11th April, 2019 and 08th July, 2019, but still response is awaited.

7.2.7 Submitted for the consideration of CSC.

7.2.8 Dr. Saleem Jessani on behalf of the P.I presented the Studies before the CSC, Prof. Dr. Javed Akram asked for BA/BE Studies and study protocol.

- **Decision of 4th CSC Meeting:-**

After deliberations CSC deferred the case till experts review of the scientific data and BA/BE studies data, which shall be provided by the applicant. And applicant directed to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

7.3) **REGULATORY APPROVAL FOR EIGER BIOPHARMACEUTICAL, INC. PROTOCOL EIG-LNF-011, FOR A PHASE-III, MATRIX DESIGN, PARTIALLY DOUBLE BLIND, RANDOMIZED STUDY OF THE EFFICACY AND SAFETY OF 50mg LONAFARNIB / 100mg RITONAVIR BID WITH & WITHOUT 180mcg PEG IFN-ALFA-2A FOR 48 WEEKS, COMPARED WITH PEG IFN-ALFA-2A MONOTHERAPY AND PLACEBO TREATMENT IN PATIENT CHRONICALLY INFECTED WITH HEPATITIS DELTA VIRUS BEING MAINTAINED ON ANTI-HBV NUCLEOS (T) IDE THERAPY (D-LIVR).(F.No.03-08/2019-DD (PS))**

Application is from Dr. Saeed Hamid, Director Clinical Trial Unit, Professor & Consultant Gastroenterologist, Aga Khan University, dated 6thMay, 2019, wherein request has been made for registration & approval of subject clinical trial, which will be carried out at Jinnah Post Graduate Medical Center (JPMC). It is a Randomized, Controlled, Phase-III clinical trial, Application is not on prescribed Form-I, and along with a fee of Rs.50000/- deposited vide challan no.1943654.

7.3.2. The study carried out under the supervision of Prof. Dr. Sarah Saleem (PI),

7.3.3. The primary objective of the trial is to evaluate the efficacy and safety of LNF 50mg/RTV 100mg BID with and without PEG-IFN-alfa-2a 180mcg QW for 48 weeks compared to no treatment (placebo LNF and Placebo RTV) in patients chronically infected with HDV and receiving anti-HBV nucleos (t) ide maintenance therapy &to compare the composite virologic and biochemical response rate at (end-of-treatment (EOT) (week 48)

i) In patients who receive LNF 50mg/RTV 100mg BID vs patients receive placebo.

ii) In patients who receive LNF 50mg/RTV 100mg BID with PEG-IFN-alfa-2a 180mcg QW vs patients who receive placebo.

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached.
2	Fee	Only Rs.50000/- deposited instead of Rs.200000/-
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	USA, Belgium, France, Canada, Bulgaria, Germany, Greece, Israel, Italy, Moldova, New Zealand, Romania, Spain, Switzerland, Turkey, UK, Taiwan, Vietnam Sweden and Pakistan
7	Phase of trial.	Phase – III
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for import of trial material.	Attached.
9	Site of the trial	M/s Aga Khan University Hospital Karachi.
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Attached.
11	Approval of National Bio-ethics Committee (NBC)	Attached.
12	CV's of the Investigators	Attached.
13	GMP certificate along with COPP & free sale certificate of the investigational product.	GMP Certificate are attached, COPP & Free Sale Certificate are not provided.
14	Pre-clinical/clinical safety studies	Attached.
15	Summary of Protocol	Attached.
16	Summary of Investigator	Not provided.

	Brochure	
17	Adverse Event Reporting Form	Attached.
18	No of patients to be enrolled in each center.	80
19	Name of Monitors & Clinical Research Associate	Attached.
20	Evidence of registration in country of origin.	Not provided.
21	Copy of registration letter (if registered in Pakistan)	Not registered in Pakistan
22	Sample of label of the investigational product / drug.	Attached.
22	Duration of trial	24 Months
23	Undertaking on Stamp paper	Not provided.

7.3.5. Description of shortcomings:

i) Only Rs.50000/- submitted as processing fee, instead of Rs.200000/-, which is approved by the Authority.

ii) COPP & Free Sale Certificate of investigational drugs are not provided.
iii) Evidence of registration in country of origin is not provided.
iv) Undertaking on stamp paper is not provided.

7.3.6. The firm was communicated through letter no. F.No.03-08/2019 DD (PS), dated 04th July, 2019, but still response is awaited.

7.3.7. Submitted for the consideration of CSC.

7.3.8. Dr. Saeed Hamid presented the case before CSC.

- **Decision of 4th CSC Meeting:-**

After deliberations CSC conditionally approved the Clinical Studies, subject to fulfilment of the requirements as per the Bio-Study Rules 2017.

7.4) APPLICATION FOR THE USE OF GRANULOCYTE COLONY STIMULATING FACTOR (GCSF) FOR BILIARY ATRESIA AS PART OF A PHASE-II CLINICAL TRIAL.

Application is from Dr. Saqib Hamid Qazi, Assistant Professor & Head – Section of Pediatric Surgery, Director Pediatric Sugary Residency Program, Co-Chief – Children Hospital Service Line (Pediatric Surgery), Aga Khan University Hospital, Karachi, dated 16thMay, 2019, wherein request has been made for registration & approval of subject clinical trial, which will be carried out at Aga Khan University Hospital, Stadium Road, Karachi.

7.4.2. The study carried out under the supervision of Dr. Saqib Qazi (P.I) and Dr. Abeer Aziz (Co-P.I)

7.4.3. The primary objective is aim to assess the hypothesis that GCSF therapy improves the short term clinical outcome of biliary atresia in a multi institutional trial and to prospectively evaluate, using the parameters mentioned within the study endpoints, the safety and efficacy of GCSF in each of two groups of newly diagnosed patients.

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached.
2	Fee	Not provided.
3	Investigator Brochure (s)	Not provided.
4	Final protocol	Not provided.
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries	USA, Vietnamand 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.	Not provided.
9	Site of the trial	M/s Aga Khan University Hospital Karachi.
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names	Attached.

	and designation of members.	
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.	Not provided.
14	Pre-clinical/clinical safety studies	Not provided.
15	Summary of Protocol	Not provided.
16	Summary of Investigator Brochure	Not provided.
17	Adverse Event Reporting Form	Not provided.
18	No of patients to be enrolled in each center.	Not provided.
19	Name of Monitors & Clinical Research Associate	Dr. Saqib Qazi (P.I) Dr. Abeer Aziz (Co-P.I)
20	Evidence of registration in country of origin.	Not provided.
21	Copy of registration letter (if registered in Pakistan)	Not registered in Pakistan
22	Sample of label of the investigational product / drug.	Not provided.
22	Duration of trial	48 Months
23	Undertaking on Stamp paper	Not provided.

7.4.5. Description of shortcomings:

i) Processing Fee of Rs.100000/- , approved by the Authority is not provided.
ii) Investigator's Brochure and Final protocol are not provided.
iii) Quantity of drug / trial material to be imported is not described.
iv) Approval from National Bio-ethics Committee (NBC) is not provided.
v) CV's of the Investigators are not provided.
vi) GMP certificate along with COPP & free sale certificate of the investigational product.
vii) Pre-clinical/clinical safety studies are not provided.
viii) Summary of Protocol & Summary of Investigator Brochure are not provided.

ix) Adverse Event Reporting Form is not attached.
x) No of patients to be enrolled in each center is not explained.
xi) Evidence of registration in country of origin.
xii) Sample of label of the investigational product / drug is not provided.
xiii) Undertaking on Stamp paper.

7.4.6. The firm was communicated through letter no. F.No.03-08/2019 DD (PS), dated 08th July, 2019, but still response is awaited.

7.4.7. Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. The case was so deferred. Applicant directed to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

AGENDA ITEM - VIII: BA/BE Studies Registration (Old cases)

All the following cases for registration of BA/BE studies under agenda item-VII were discussed in the previous CSC meetings. All the applicants required licensing of their BA/BE Centre from DRAP.

8.1) Application of M/s Pharma Professional for Approval and Registration of Comparative Clinical Study of Irpo-Fa ® Tablets, F.No.14-12/2018 DD (PS).

Application is from Professor Dr. Tasneem Ahmed, CEO M/s Pharma Professional Services Pvt Ltd, PPS House A-93, Ettawah Cooperative Housing Society, Gadap Town, Near Gulshan-e-Maymar, Karachi, wherein request has been made to register a comparative clinical study to determine the efficacy and tolerability of combination tablets of Iron Polymaltose and Folic Acid of test product **Irpo-FA ® tablets** manufactured by M/s Nabiqasim Industries (PVT) Ltd, Karachi compared with reference product **MaltoferFol® tablets,** manufactured under license of M/s (Vifor International) Inc, in woman with Iron deficiency Anaemia(IDA) including pregnant woman.

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

i. **Study title:** A comparative, open labelled, multicentre, double arm, controlled, and randomized study in iron deficient anaemic women including pregnant woman to compare the efficacy and tolerability of test product Irpo-FA ® tablets manufactured by M/s Nabiqasim Industries (PVT) Ltd, Karachi with reference product MaltoferFol® tablets, manufactured under license of M/s (Vifor International) Inc.

ii. **Investigational Product:** Irpo-FA ® (Iron Polymaltose and Folic Acid) tablets manufactured by M/s Nabiqasim Industries (PVT) Ltd, Karachi.
iii. **Reference Product:** MaltoferFol® (Iron Polymaltose and Folic Acid) tablets**,** manufactured under license of M/s (Vifor International) Inc.
iv. **Sponsor & Manufacturer:** M/s Nabiqasim Industries (PVT) Ltd, Karachi
v. **CRO:** M/s Pharma Professional Services (Pvt) Ltd, Karachi.
vi. **Study Sites:**
    a. Department of Gynaecology, JPMC, Karachi;
    b. Sobhraj Maternity Hospital Karachi; and
    c. Karachi Medical Complex.
vii. **Principal Investigator:** Dr. Haleema Yasmin.
viii. **Funding Source**: The sponsor
ix. **Cost of the Project**: 4,000,000 PKRs (approximately).

8.1.3. The details of the submitted documents as per checklist are as under:

S. No.	**Document**	**Remarks**
1	Application on prescribed Form-II	Application submitted as per Form-II of the Bio study Rules, 2017.
2	Fee	Not provided
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 if applicable	Conduct in Pakistan
7	Phase of trial.	Post-marketing study (Phase-IV).
8	Quantity of drug / trial material to be imported/ procured.	Reference Product: *Total 19380 tablets (14400 tablets for 80 subjects and remaining to be retained as per GCP standards).* Test Product: *Total 19380 tablets (14400 tablets for 80 subjects and remaining to be retained as per GCP standards).*
9	Site (s) of the trial.	a. Department of obstetrics and Gynaecology, JPMC, Karachi; b. Sobhraj Maternity Hospital Karachi; and

		c. Karachi Medical Complex. (All the three sites are not licensed by the DRAP neither the firm has applied for it.)
10	CVs of the Investigators	Attached
11	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Approval of trial and composition of the IRB provided; but the approval of the site by the IRB is not attached with application.
12	Approval of National Bio-ethics Committee (NBC)	Not attached.
13	GMP certificate along with COPP & free sale certificate of the investigational product. (For Local Manufacturer GMP or Registration letter)	Attached
14	Pre-clinical/clinical safety studies	Provided as in Investigator Brochure.
15	Summary of the Protocol	Attached
16	Summary of the Investigator Brochure	Provided as in Investigator Brochure
17	Adverse Event Reporting Form	Attached
18	No of patients to be enrolled in each center.	Total of 160 IDA subject (woman patient). 80 subjects for test product and 80 for reference product.
19	Name of Monitors & Clinical Research Associate.	Provided as in Final Protocol.
20	Evidence of registration in country of origin.	Not Attached
21	Evidence of registration in Pakistan.	Attached
22	Sample of label of the investigational product / drug.	Attached
23	Duration of trial	8 months for completion of clinical part of the trial; whereas, estimated one month would be required for analysis of data.
24	Undertaking on stamp paper	Not provided

8.1.4. Following deficiencies were identified:

i. The clinical trial sites of Department of obstetrics and Gynaecology, JPMC, Karachi; Sobhraj Maternity Hospital Karachi; and Karachi Medical Complex are not licensed with DRAP neither the hospitals have applied for their license;

ii. The approval from the National Bioethics Committee has not been attached with the application;

iii. The sites are not approved by the IRB/ethics committee; and

iv. Undertaking on stamp paper is not provided.

v. Fee not provided.

8.1.5. Decision of 3rdCSC Meeting:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

8.1.6. The decision of CSC along with deficiencies, communicated to the firm on 8th July, 2019, but still response is awaited.

8.1.7. Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. Accordingly the case was deferred. It was decided to direct the applicant to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

8.2) Application of M/s Pharma Professional for Approval and Registration of Comparative Clinical Study of Injection Megafer, F.No.14-10/2018 DD (PS).

Application is from Prof. Dr. Tasneem Ahmed, CEO M/s Pharma Professional Services Pvt Ltd, PPS House A-93, Ettawah Cooperative Housing Society, Gadap Town, Near Gulshan-e-Maymar, Karachi, wherein request has been made to register a comparative clinical study to determine the efficacy and safety of test product **Megafer Injection ®** manufactured by M/s Surge Laboratories (PVT) Ltd, Karachi, compared with reference product **Venofer Injection ®,** manufactured by M/s (Vifor International) Inc, in woman with Iron deficiency Anaemia (IDA).

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

i. **Study title:** A comparative, open labelled, multicentre, parallel arm, controlled, and randomized study with 2 parallel groups to compare the efficacy and safety of test drug (Megafer Injection) with reference (Venofer Injection) in outpatient woman with Iron deficiency anaemia (IDA).
ii. **Investigational Product:** Megafer Injection ® (Iron Sucrose) manufactured by M/s Surge Laboratories (PVT) Ltd, Karachi.
iii. **Reference Product:** Venofer Injection ® (Iron Sucrose), manufactured by M/s (Vifor International) Inc.
iv. **Sponsor & Manufacturer:** M/s Surge Laboratories (PVT) Ltd, Karachi.
v. **CRO:** M/s Pharma Professional Services (Pvt) Ltd, Karachi.
vi. **Study Sites:**
    a. Department of Obstetrics and Gynaecology, JPMC, Karachi; and
    b. Sobhraj Maternity Hospital Karachi.
vii. **Principal Investigator:** Dr.Haleema Yasmin.
viii. **Funding Source**: The sponsor
ix. **Cost of the Project**: 3,000,000 PKRs (approximately).

8.2.3. The details of the submitted documents as per checklist are as under:

S. No.	Document	Remarks
1	Application on prescribed Form-II	Application submitted as per Form-II of the Bio study Rules, 2017.
2	Fee	Not provided
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 if applicable	Conduct in Pakistan
7	Phase of trial.	Post-marketing study (Phase-IV)
8	Quantity of drug / trial material to be imported/ procured.	Reference Product: *Total 550 ampoules (400 ampoules for 40 subjects and remaining to be retained as per GCP standards)* Test Product: *Total 550 ampoules (400 ampoules for 40 subjects and remaining to be retained as*

		per GCP standards)
9	Site (s) of the trial.	i. Department of Obstetrics and Gynaecology, JPMC, Karachi; and ii. Sobhraj Maternity Hospital Karachi. *Both the sites are not yet licensed by the DRAP neither the firm had applied for it.*
10	CVs of the Investigators	Attached
11	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Approval of trial and composition of the IRB provided; but the approval of the site by the IRB is not attached with application.
12	Approval of National Bio-ethics Committee (NBC)	Not attached.
13	GMP certificate along with COPP & free sale certificate of the investigational product. (For Local Manufacturer GMP or Registration letter)	Attached
14	Pre-clinical/clinical safety studies	Provided as in Investigator Brochure.
15	Summary of the Protocol	Attached
16	Summary of the Investigator Brochure	Attached
17	Adverse Event Reporting Form	Attached
18	No of patients to be enrolled in each center.	80 woman subjects with iron deficiency anaemia (40 subjects for test and 40 subject for reference product).
19	Name of Monitors & Clinical Research Associate.	Provided as in Investigator Brochure
20	Evidence of registration in country of origin.	Not Attached
21	Evidence of registration in Pakistan.	Attached
22	Sample of label of the investigational product / drug.	Attached
23	Duration of trial	Clinical part of the trail will be completed in 6 months; whereas, for the analysis of date estimated one month would be required.
24	Undertaking on stamp paper	Not provided

8.2.4. Following deficiencies were identified:

i. The clinical trial sites of Department of Obstetrics and Gynaecology, JPMC, Karachi and Sobhraj Maternity Hospital Karachi are not licensed with DRAP neither the hospitals have applied for their license;

ii. The approval from the National Bio Ethic committee has not been attached with the application,

iii. The sites are not approved by the IRB/ ethics-committee; and

iv Undertaking on stamp paper is not provided.

v. Fee not provided.

8.2.3. Decision of 3rdCSC Meeting:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

8.2.4. The decision of CSC along with deficiencies, communicated to the firm on 8th July, 2019, but still response is awaited.

8.2.5 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. Accordingly the case was deferred. It was decided to direct the applicant to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

8.3) Application of M/s Pharma Professional for Approval and Registration of Comparative Clinical Study of *Rexyl*® Cough SyrupF.No.14-11/2018 DD (PS).

Application is from Prof. Dr. Tasneem Ahmed, CEO M/s Pharma Professional Services Pvt Ltd, PPS House A-93, Ettawah Cooperative Housing Society, Gadap Town, Near Gulshan-e-Maymar, Karachi, wherein request has been made to register a comparative clinical study to determine the efficacy and safety of test product **Rexyl® cough syrup** manufactured by M/s Nabiqasim Industries (Pvt) Ltd, Karachi, compared with reference product **Hydryllin® cough syrup,** Manufactured by M/s The Searle Company Ltd in adult outpatients with productive cough.

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

i. **Study title:** An open labelled, controlled, and randomized study with 2 parallel groups to compare the efficacy and safety of test drug (Rexyl cough syrup) with reference (Hydryllin cough syrup) in adult outpatients with productive cough.
ii. **Investigational Product:** Rexyl ® cough syrup (Aminophylline, Ammonium Chloride, Diphenhydramine and menthol), manufactured by Nabiqasim Industries (Pvt) limited, Karachi.
iii. **Reference Product:** Hydryllin ® cough syrup (Aminophylline, Ammonium Chloride, Diphenhydramine and Menthol) manufactured by the Searle Company Ltd.
iv. **Sponsor & Manufacturer:** M/s Nabiqasim Industries (Pvt) Ltd, Karachi.
v. **CRO:** M/s Pharma Professional Services (Pvt) Ltd, Karachi.
vi. **Study Site:** Karachi Medical Complex, Gulshan-e- Iqbal, Karachi.
vii. **Principal Investigator:** Prof Dr. M. Rafiq Khanani.
viii. **Funding Source**: The sponsor
ix. **Cost of the Project**: 20,000,00 PKRs (approximately)

8.3.3. The details of the submitted documents as per checklist are as under:

S. No.	Document	Remarks
1	Application on prescribed Form-II	Application submitted as per Form-II of the Bio study Rules, 2017.
2	Fee	Not provided
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 if applicable	Conduct in Pakistan.
7	Phase of trial.	Post-marketing study (Phase-IV)
8	Quantity of drug / trial material to be imported/ procured.	Reference Product: *Total 600 Bottles (300 for 100 subjects and 300 would be retained as per GCP standards).* Test Product: Total 600 bottles (*300 for 100 subjects and 300 would be retained as per GCP standards).*
9	Site (s) of the trial.	Karachi Medical Complex, Karachi

		(Not approved by the CSC)
10	CVs of the Investigators	Attached
11	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Approval of trial and composition of the IRB provided; but the approval of the site by the IRB is not attached with application.
12	Approval of National Bio-ethics Committee (NBC)	Not attached.
13	GMP certificate along with COPP & free sale certificate of the investigational product. (For Local Manufacturer GMP or Registration letter)	Attached
14	Pre-clinical/clinical safety studies	Provided as in Investigator Brochure.
15	Summary of the Protocol	Attached
16	Summary of the Investigator Brochure	Provided as in Investigator Brochure.
17	Adverse Event Reporting Form	Attached
18	No of patients to be enrolled in each center.	Total of 200 subject (100 subjects for test and 100 subjects for reference drug)
19	Name of Monitors & Clinical Research Associate.	Provided as in Investigator Brochure
20	Evidence of registration in country of origin.	NA
21	Evidence of registration in Pakistan.	Attached
22	Sample of label of the investigational product / drug	Attached
23	Duration of trial	Clinical part will be completed in 6 months; whereas, 1 month would be required for analysis of data.
24	Undertaking on stamp paper	Not provided

8.3.4. Following deficiencies were identified:

i. The clinical trial site of Karachi Medical Complex is not licensed with DRAP neither the hospital had applied for its license;

ii. The approval from the National Bio Ethic committee has not been attached with the application;
iii. The clinical site is not approved by the IRB (ethics-committee); and
iv. Undertaking on stamp paper is not provided and fee is not submitted.
v. Fee not provided.

8.3.5. Decision of 3rd CSC Meeting:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

8.3.6. The decision of CSC along with deficiencies, communicated to the firm on 8th July, 2019, but still response is awaited.

8.3.7. Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. Accordingly the case was deferred. It was decided to direct the applicant to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

8.4) Bioequivalence Study of Moksi (Moxifloxacin) 400mg Tablet, of M/s Searle Company Ltd, at Center for Bioequivalence Study and Clinical Research (CBSCR), (ICCBS), F. No. 14-3/2018 DD (PS)

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

8.4.2. After evaluation following observations were recorded as per prerequisites of prescribed **Form-IIA** of the **Bio-Study Rules 2017.**

The short summary of the proposed study is as under;

i. **Study title:** A Single Center, Open Label, Randomized, Single Dose, Two way Cross-over Study to explore the Relative Bioavailability of **Moksi (Moxifloxacin) 400mg Tablet** of M/s Abbott Laboratories and **Avelox (Moxifloxacin) 400mg Tablet** of M/s Bayer Pharmaceuticals under the fasting conditions in Healthy Male Pakistani Subjects.
ii. **Investigational Product:** Moksi (Moxifloxacin) 400mg Tablet
iii. **Reference Product:** Avelox (Moxifloxacin) 400mg Tablet of M/s Bayer Pharma
iv. **Sponsor & Manufacturer:** M/s Abbott Laboratories (Pakistan) Ltd., Karachi.
v. **CRO and Study Site:** Center for Bioequivalence Studies and Clinical Research (CBSCR), University of Karachi.

vi. **Principal Investigator:** Dr. Muhammad Raza Shah
vii. **Co-Principal Investigator:** Dr.Naghma Hashmi
viii. **Funding Source**: The sponsor
ix. **Cost of the Project**: Rs.3, 800, 000 (approximately).

8.4.3. The details of the submitted documents as per checklist are as under;

S. No.	Document	Remarks
1	Application	Application has been submitted on prescribed Form – IIA, under the Bio-study Rules, 2017
2	Fee	Rs.50000/- deposited instead of Rs.200000
3	Formulation of Investigational Product	Attached
4	Purpose of Study along with its cost and source of fund	Attached
5	Proposed center for study	CBSCR, ICCBS Not yet approved
6	Investigational Design and Study Plan	Attached
7	Pre-clinical or clinical data or safety studies	Not applicable
8	Final protocol	Attached
9	Detail of Investigators	Attached
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	The applicant has informed that the IRB approval is still under process.
11	Approval of National Bio-ethics Committee (NBC)	Not attached.
12	Informed consent and participant information sheet (Urdu to English)	Attached
13	Summary of Protocol and Investigator Brochure	Attached
14	Adverse Event Reporting Form	Attached
15	Name of Monitors & Clinical Research Associate	Attached
16	Proof of Registration of Investigational Product in Pakistan	Attached

17	Quantity of Investigational Product	Reference Product: 350 Tablets Test Product: 350 Tablets
24	Undertaking on stamp paper	Not provided

8.4.4. Description of shortcomings:

i) Rs.50000-/ submitted instead of Rs.200000/-, approved by the Authority for approval of BA/BE Studies.

ii) The approval of Institutional Review Board (IRB) and NBC has not yet been provided yet.

iii) Undertaking on stamp paper is not provided.

8.4.5. Decision of 3rd CSC Meeting:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

8.4.6. The decision of CSC along with deficiencies, communicated to the firm on 8th July, 2019, but still response is awaited.

8.4.7 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. Accordingly the case was deferred. It was decided to direct the applicant to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

8.5) Bioequivalence Study of Xorban (Rivaroxaban) 20mg Tablet, of M/s Searle Company Ltd, at Center for Bioequivalence Study and Clinical Research (CBSCR), (ICCBS), F. No. 14-4/2018 DD (PS)

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

8.5.2. After evaluation following observations were recorded as per prerequisites of prescribed **Form-IIA** of the **Bio-Study Rules 2017.**

The short summary of the proposed study is as under;

i. **Study title:** A Single Center, Open Label, Randomized, Single Dose, Two way Cross-over Study to explore the Bioequivalence of Xaroban 20mg (Rivaroxaban)

tablet Manufactured by The Searle Company Limited, with reference product Xarelto 20mg (Rivaroxaban) Tablet manufactured by Bayer Healthcare Pharmaceuticals under Fed conditions in Healthy male Pakistani Subjects.

ii. **Investigational Product:** Xaroban 20mg (Rivaroxaban) tablet Manufactured by The Searle Company Limited

iii. **Reference Product:** Xarelto 20mg (Rivaroxaban) Tablet manufactured by Bayer Healthcare Pharmaceuticals

iv. **Sponsor & Manufacturer:** M/s the Searle Company Limited, Karachi.

v. **CRO and Study Site:** Center for Bioequivalence Studies and Clinical Research (CBSCR), University of Karachi.

vi. **Principal Investigator:** Dr. Muhammad Raza Shah

vii. **Co-Principal Investigator:** Dr.Naghma Hashmi

viii. **Funding Source**: The sponsor

ix. **Cost of the Project**: Rs.22, 00,000 (approximately).

8.5.3. The details of the submitted documents as per checklist are as under;

S. No.	Document	Remarks
1	Application	Application has been submitted on prescribed Form – IIA, under the Bio-study Rules, 2017
2	Fee	Rs.50000/- deposited instead of Rs.200000
3	Formulation of Investigational Product	Attached
4	Purpose of Study along with its cost and source of fund	Attached
5	Proposed center for study	CBSCR, ICCBS Not approved yet
6	Investigational Design and Study Plan	Attached
7	Pre-clinical or clinical data or safety studies	Not applicable
8	Final protocol	Attached
9	Detail of Investigators	Attached
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	The applicant has informed that the IRB approval is still under process.
11	Approval of National Bio-ethics Committee (NBC)	Attached.

12	Informed consent and participant information sheet (Urdu to English)	Attached
13	Summary of Protocol and Investigator Brochure	Attached
14	Adverse Event Reporting Form	Attached
15	Name of Monitors & Clinical Research Associate	Attached
16	Proof of Registration of Investigational Product in Pakistan	Attached
17	Quantity of Investigational Product	Reference Product: 110 Tablets Test Product: 110 Tablets

8.5.4. Description of shortcomings:

i) Rs.50000-/ submitted instead of Rs.200000/-, approved by the Authority for approval of BA/BE Studies.

ii) The approval of Institutional Review Board (IRB) has not yet been provided.

iii) Undertaking on stamp paper is not provided.

8.5.5. Decision of 3rd CSC Meeting:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

8.5.6. The decision of CSC along with deficiencies, communicated to the firm on 8th July, 2019, but still response is awaited.

8.5.7 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. Accordingly the case was deferred. It was decided to direct the applicant to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

8.6) Bioequivalence Study of Vaptor (Rosuvastatin) 20mg Tablet, of M/s Searle Company Ltd, at Center for Bioequivalence Study and Clinical Research (CBSCR), (ICCBS), F. No. 14-5/2018 DD (PS)

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

8.6.2. After evaluation following observations were recorded as per prerequisites of prescribed **Form-IIA** of the **Bio-Study Rules 2017.**

The short summary of the proposed study is as under;

i. **Study title:** A Single Center, Open Label, Randomized, Single Dose, Two way Cross-over Study to explore the Bioequivalence Vaptor (Rosuvastatin) 20mg Tablet manufactured by the Searle Company Pakistan Limited with reference product Crestor 20mg (Rosuvastatin) Tablet manufactured by AstraZeneca Pharmaceuticals under the fasting conditions in Healthy Male Pakistani Subjects.
ii. **Investigational Product:** Vaptor (Rosuvastatin) 20mg Tablet of M/s Searle Company Ltd.
iii. **Reference Product:** Crestor (Rosuvastatin) 20mg Tablet of M/s AstraZeneca Pharmaceuticals
iv. **Sponsor & Manufacturer:** M/s the Searle Company Limited, Karachi.
v. **CRO and Study Site:** Center for Bioequivalence Studies and Clinical Research (CBSCR), University of Karachi.
vi. **Principal Investigator:** Dr. Muhammad Raza Shah
vii. **Co-Principal Investigator:** Dr. Naghma Hashmi
viii. **Funding Source**: The sponsor
ix. **Cost of the Project**: Rs.30, 00,000 (approximately).

8.6.3. The details of the submitted documents as per checklist are as under;

S. No.	**Document**	**Remarks**
1	Application	Application has been submitted on prescribed Form – IIA, under the Bio-study Rules, 2017
2	Fee	Rs.50000/- deposited instead of Rs.200000
3	Formulation of Investigational Product	Attached
4	Purpose of Study along with its cost and source of fund	Attached
5	Proposed center for study	CBSCR, ICCBS Not approved yet
6	Investigational Design and Study Plan	Attached
7	Pre-clinical or clinical data or safety studies	Not applicable.
8	Final protocol	Attached
9	Detail of Investigators	Attached

10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	The applicant has informed that the IRB approval is still under process.
11	Approval of National Bio-ethics Committee (NBC)	Provided
12	Informed consent and participant information sheet (Urdu to English)	Attached
13	Summary of Protocol and Investigator Brochure	Attached
14	Adverse Event Reporting Form	Attached
15	Name of Monitors & Clinical Research Associate	Attached
16	Proof of Registration of Investigational Product in Pakistan	Attached
17	Quantity of Investigational Product	Reference Product: 80 Tablets Test Product: 80 Tablets

8.6.4. Description of shortcomings:

i) Rs.50000-/ submitted instead of Rs.200000/-, approved by the Authority for approval of BA/BE Studies.
ii) The approval of Institutional Review Board (IRB) has not yet been provided.
iii) Undertaking on stamp paper is not provided.

8.6.5 Decision of 3rd CSC Meeting:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

8.6.6. The decision of CSC along with deficiencies, communicated to the firm on 8th July, 2019, but still response is awaited.

8.6.7 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. Accordingly the case was deferred. It was decided to direct the applicant to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

8.7) Bioequivalence Study of Lamnet (Lamotrigine BP) 100mg Tablet of M/s Searle Company Ltd, at Center for Bioequivalence Study and Clinical Research (CBSCR), (ICCBS), F. No. 14-6/2018 DD (PS).

Application is from General Manage Dr. Raza Shah, Center for Bioequivalence Study and Clinical Research (CBSCR), University of Karachi, for approval of subject Bioequivalence Study, under the Bio-study rules, 2017 dated 19-01-2018.

8.7.2. After evaluation following observations were recorded as per prerequisites of prescribed **Form-IIA** of the **Bio-Study Rules 2017.**

The short summary of the proposed study is as under;

i. **Study title:** A Single Center, Open Label, Randomized, Single Dose, Two way Cross-over Study to explore the Bioequivalence Lamnet (Lamotrigine) 100mg Tablet with reference product Lamictal (Lamotrigine) 100mg Tablet under the fasting conditions in Healthy Male Pakistani Subjects.
ii. **Investigational Product:** Lamnet (Lamotrigine) 100mg Tablet of M/s Searle Company Ltd.
iii. **Reference Product:** Lamictal (Lamotrigine) 100mg Tablet of M/s GlaxoSmithKline Pakistan, Limited
iv. **Sponsor & Manufacturer:** M/s the Searle Company Limited, Karachi.
v. **CRO and Study Site:** Center for Bioequivalence Studies and Clinical Research (CBSCR), University of Karachi.
vi. **Principal Investigator:** Dr. Muhammad Raza Shah
vii. **Co-Principal Investigator:** Dr.Naghma Hashmi
viii. **Funding Source**: The sponsor
ix. **Cost of the Project**: Rs.20,00,000 (approximately)

8.7.3. The details of the submitted documents as per checklist are as under;

S. No.	Document	Remarks
1	Application	Application has been submitted on prescribed Form – IIA, under the Bio-study Rules, 2017
2	Fee	Rs.50000/- deposited instead of Rs.200000
3	Formulation of Investigational Product	Attached
4	Purpose of Study along with its cost and source of fund	Attached
5	Proposed center for study	CBSCR, ICCBS Not yet approved by the DRAP.
6	Investigational Design and Study Plan	Attached
7	Pre-clinical or clinical data or safety studies	Not applicable.
8	Final protocol	Attached
9	Detail of Investigators	Attached

10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	The applicant has informed that the IRB approval is still under process.
11	Approval of National Bio-ethics Committee (NBC)	Provided
12	Informed consent and participant information sheet (Urdu to English)	Attached
13	Summary of Protocol and Investigator Brochure	Attached
14	Adverse Event Reporting Form	Attached
15	Name of Monitors & Clinical Research Associate	Attached
16	Proof of Registration of Investigational Product in Pakistan	Attached
17	Quantity of Investigational Product	Reference Product: 80 Tablets Test Product: 110 Tablets

8.7.4. Description of shortcomings:

i) The approval of Institutional Review Board (IRB) has not yet been provided.

ii) Rs.50000-/ submitted instead ofRs.200000/-, approved by the Authority for approval of BA/BE Studies.

ii) Undertaking on stamp paper is not provided.

8.7.5. <u>Decision of 3rd CSC Meeting:-</u>

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

8.7.6. The decision of CSC along with deficiencies, communicated to the firm on 8th July, 2019, but still response is awaited.

8.6.7. Submitted for perusal, discussion and consideration of CSC.

- **<u>Decision of 4th CSC Meeting</u>:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. Accordingly the case was deferred. It was decided to direct the applicant to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

8.8) Bioequivalence Study of Dextop (Dexlansoprazole) 60mg Tablet, of M/s Searle Company Ltd, at Center for Bioequivalence Study and Clinical Research (CBSCR), (ICCBS), F. No. 15-1/2018 DD (PS)

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

8.8.2. After evaluation following observations were recorded as per prerequisites of prescribed **Form-IIA** of the **Bio-Study Rules 2017.**

8.8.3 The short summary of the proposed study is as under;

i. **Study title:** A Single Center, Open Label, Randomized, Single Dose, One Period Study to explore the Pharmacokinetics of Dextop (Dexlansoprazole) 60mg Capsules under the fasting conditions in Healthy Male Pakistani Subjects.
ii. **Investigational Product:** Dextop (Dexlansoprazole) 60mg Capsules of M/s Searle Company Ltd.
iii. **Sponsor & Manufacturer:** M/s The Searle Company Limited, Karachi.
iv. **CRO and Study Site:** Center for Bioequivalence Studies and Clinical Research (CBSCR), University of Karachi.
v. **Principal Investigator:** Dr. Muhammad Raza Shah
vi. **Co-Principal Investigator:** Dr.Naghma Hashmi
vii. **Funding Source**: The sponsor
viii. **Cost of the Project**: Rs.15, 00,000 (approximately).
ix.

8.8.4. The details of the submitted documents as per checklist are as under;

S. No.	Document	Remarks
1	Application	Application has been submitted on prescribed Form – IIA, under the Bio-study Rules, 2017
2	Fee	Rs.50000/- deposited instead of Rs.200000
3	Formulation of Investigational Product	Attached
4	Purpose of Study along with its cost and source of fund	Attached
5	Proposed center for study	CBSCR, ICCBS Not approved yet
6	Investigational Design and Study Plan	Attached
7	Pre-clinical or clinical data or safety studies	Not applicable.

8	Final protocol	Attached
9	Detail of Investigators	Attached
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	The applicant has informed that the IRB approval is still under process.
11	Approval of National Bio-ethics Committee (NBC)	Provided
12	Informed consent and participant information sheet (Urdu to English)	Attached
13	Summary of Protocol and Investigator Brochure	Attached
14	Adverse Event Reporting Form	Attached
15	Name of Monitors & Clinical Research Associate	Attached
16	Proof of Registration of Investigational Product in Pakistan	Attached
17	Quantity of Investigational Product	100 Capsules

8.8.5. Description of shortcomings

i) Rs.50000-/ submitted instead of Rs.200000/-, approved by the Authority for approval of BA/BE Studies.

ii) The approval of Institutional Review Board (IRB) has not yet been provided.

iii) Undertaking on stamp paper is not provided.

8.8.6. Decision of 3rd CSC Meeting:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

8.8.7. The decision of CSC along with deficiencies, communicated to the firm on 8th July, 2019, but still response is awaited.

8.8.8. Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. Accordingly the case was deferred. It was decided to direct the applicant to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

8.9) Bioequivalence Study of *Clarithro*® (Clarithromycin) 500mg Tablet, of M/s Nabiqasim Industries Ltd, at Pharma Professional Services, F. No. 14-7/2018 DD (PS)

Application is from Prof. Dr. Tasneem Ahmed, CEO M/s Pharma Professional Services Pvt Ltd, PPS House Ettawah Cooperative Housing Society, Gadap Town, Near Gulshan-e-Maymar, Karachi, for approval of subject Bioequivalence Study, under the Bio-study rules, 2017.

8.9.2. After evaluation following observations were recorded as per prerequisites of prescribed **Form-IIA** of the **Bio-Study Rules 2017.**

The short summary of the proposed study is as under;

i. **Study title:** An open labelled Two period, Two Treatments, Two Sequences, Single Dose, Single Dose, Randomized, Crossover Bioequivalence Study Of Clarithromycin (Clarithro) 500mg Tablets in Healthy Volunteers, Compared to equivalent drug dose in reference formulation of KLARICID 500mg Tablets under fasting condition.
ii. **Investigational Product:** Clarithro® (Clarithromycin) 500mg Tablets of M/s NabiQasim (Pvt) Ltd and Klaricid® (Clarithromycin) 500mg Tablets of M/s Abbott Laboratories, Karachi
iii. **Sponsor &Manufacturer:** M/s Nabiqasim Industries (Pvt) Ltd, Karachi.
iv. **CRO and Study Site:** M/s Pharma Professional Services (Pvt) Ltd, Karachi.
v. **Principal Investigator:** Prof. Dr. Tasneem Ahmad
vi. **Funding Source**: The sponsor
vii. **Cost of the Project**: Rs.3, 000,000 (approximately).

8.9.3. The details of the submitted documents as per checklist are as under;

S. No.	Document	Remarks
1	Application	Application has been submitted on prescribed Form – IIA, under the Bio-study Rules, 2017
2	Fee	Not Provided
3	Formulation of Investigational Product	Attached
4	Pharmacodynamics and Pharmacokinetics of Investigational Product	Attached
5	Purpose of Study along with its cost and source of fund	Study Objective: To determine the Bioequivalence of Test Product Clarithro® 500mg Tablets, manufactured by M/s Nabiqasim Industries (Pvt) Ltd, Karachi, Pakistan, in healthy Adult Human Subjects, compared with Reference Product: Klaricid® 500mg Tablet, manufactured by Abbott Laboratories, Karachi, Pakistan.

		Study Purpose: To evaluate the bioequivalence of test product (Clarithro®) as a generic replacement for the reference product (Klaricid®) Anticipated Cost of Project PKR 3,000,000/-
6	Proposed center for study	M/s Pharma Professional Services (Pvt) Ltd, Karachi.
7	Investigational Design and Study Plan	To investigate average bioequivalence in a 2x2 Crossover design in humans. Attached
8	Investigational design and study plan	Attached
9	Pre-clinical or clinical data or safety studies	Attached
10	Final protocol	Attached
11	Detail of the investigator (Principal investigator, analysts and others along with CV)	Attached
12	IRB approval	Attached
13	Ethical committee composition (names and designations)	Attached
14	Site approval by the Ethics committee	Attached
15	Informed consent (English and Urdu)	Attached
16	Summary of the protocol or synopsis (Investigational Product)	100 Capsules
17	Adverse Event Reporting Form	Attached
18	Name of the monitor or clinical research associate	Attached
19	Evidence of registration in country of origin (GMP certificate along with CoPP or Free sale certificate)	Attached
20	Copy of registration letter if registered in Pakistan	Attached
21	Proposed label of	Attached

	investigational product	
22	Quantity of investigational product to be used in the study along with justification (Note: All the quantities of the each of investigational product should be procured from one single source)	Reference Product: 120 Tablets Test Product: 120 Tablets

8.9.4. Description of shortcomings:

Following deficiencies were identified:

i) Applicant advised to apply for BA/BE Studies Center approval on prescribed Form-I of the Bio-Studies Rules along with prerequisites.

ii) Applicant advised to submit prescribed fee for processing of application apply for BA/BE Studies Center approval on prescribed Form-I of the Bio-Studies Rules along with prerequisites.

iii) The approval of Institutional Review Board (IRB) of medical teaching institutions and National Bioethics Committee (NBC) of Pakistan, is prerequisite to conduct above mentioned studies under the Bio Study Rules, 2017.

iv) Fee of Rs.200000/- approved by the Authority for Clinical Studies/ BA/BE Studies is not provided.

8.9.5. Decision of 3rd CSC Meeting:-

The CSC after deliberations decided to defer the case till the approval of study site. The CSC also directed the applicant to remove the shortcomings.

8.9.6. The decision of CSC along with deficiencies, communicated to the firm on 8th July, 2019, but still response is awaited.

8.9.7. Submitted for perusal, discussion and consideration of CSC.

- **Decision of CSC:-**

No representative of the firm / institution appeared before the CSC for presentation of the studies. Accordingly the case was deferred. It was decided to direct the applicant to fulfil all requirements as per Form-II of the Bio-Study Rules 2017.

AGENDA ITEM - IX: **CHECKLISTS FOR INSPECTION OF CROs, BA / BE STUDIES CENTER, CLINICAL TRIAL SITE, AND BIOANALYTICAL LAB FOR CLINICAL TRIAL CONDUCT AND EVALUATION.**

1) Inspection Checklists for CROs:

CONTRACT RESEARCH ORGANIZATION INSPECTION CHECKLIST

Name of facility: _____

Address: _____

Organization Type: - Public ☐ Not For Profit ☐ Private ☐Other- _____

Name of Owner / Proprietor: _____

Date of inspection: _____

(dd/mm/yyyy)

i. Organization and personnel	Yes	No	NA	Observations / Recommendations
Organizational chart exists and accurately represents the organization? The following departments are needed: • Clinical Operations • Regulatory • IT Support Departments • HR • Finance • QC				
Are Job Descriptions Available for all personnel?				
Are training records Available?				
Are there personnel curricula (training, matrix/plan) established and documented for each individual?				
Does the training program include new hire training ‘and re-qualification training for personnel?				
Has personnel been Appropriately trained to perform functions required by job descriptions?				
Is there a procedure to assess and document personnel competency on				

an annual basis?				
Has personnel received regulatory training? GCP ☐ Others:_____				
Is there a system in place for personnel to report any safety concerns or incidents?				
Are external contractors/vendors utilized? Are they qualified/ approved for use? Is there an SOP that outlines this process?				
Is there a Quality Assurance Unit?				
If yes, what are the roles of the Quality Control and the Quality Assurance group?				
Does the Quality Assurance Unit perform audits, trend metrics and report the results to the Senior Management?				
Is the Quality Assurance Unit independent from the personnel engaged in the direction or conduct of a clinical trial?				
ii. Standard Operating Procedures / Methods	**Yes**	**No**	**NA**	**Observations / Recommendations**
Is there a governing SOP that outlines the creation, revision, approval, distribution, document control and retirement of SOPs?				
Is there a current index listing of the SOPs available?				
Is there a schedule for review of the SOPs?				
Are the SOPs in locations where they are used?				
Is there a system for documenting and handling SOP/method deviations and CAPAs?				
Is there a change control system for SOP/Methods?				
Does the Organization have SOPs to cover all the aspects of Clinical Operations e.g., Study start up, Study Conduct and Study				

Closeout/Completion?				
iii. Facility	**Yes**	**No**	**NA**	**Observations / Recommendations**
Is security and Confidentiality adequate so as to prevent unauthorized access to records?				
Is there sufficient space to store materials, archive records and for equipment to function properly?				
Is the facility reasonably maintained and clean?				
Is safety equipment (e.g. fire extinguishers etc.) available?				
If yes, is the equipment maintained?				
Does the Organization have a disaster recovery plan that covers all areas of the facility including computer systems and equipment?				
Are generators utilized at the facility?				
iv. Data handling Procedures and Computer Validation	**Yes**	**No**	**NA**	**Observations / Recommendations**
Is access to computers limited by an individual username and password system (Organization members cannot share a username)?				
How is the computed network arid--computer systems maintained, if applicable?				
Are there a computer validation master plan and/or SOPs?				
List computers systems and software utilized. Validated?				
Are changes to computer systems controlled and documented?				
Are records of computer system errors maintained and investigated?				
Are records of hardware maintenance and repairs maintained?				
Are computers backed up routinely to prevent loss of data? Is there a backup log?				
Is there a preventative maintenance program for computer systems?				
vii. Records and Reports	**Yes**	**No**	**NA**	**Observations / Recommendations**
Does a documentation control system exists and is functional?				

Is there a SOP or a system for the retention, storage, and destruction of records?				
How does the site ensure the sponsor's proprietary information is not disclosed to unauthorized personnel or external organizations?				
viii. Record Retention and Archival	**Yes**	**No**	**NA**	**Observations / Recommendations**
Is there a dedicated facility/area for the archival of records?				
Is there controlled access to the archival facility?				
Is the environment of the facility monitored and controlled?				
Is the procedure for archiving records outlined in an SOP?				
Is the retention time for records stated in the SOP?				
Is there a method of electronic data archival?				
ix. Clinical Study Site (IRB/IEC approval is necessary for conducting the clinical trial at a site. If local IRB/IEC is not available NBEC approval shall cover the site)	**Yes**	**No**	**NA**	**Observations / Recommendations**
Does the facility have an IRB/IEC available?				

Remarks of inspection team:

_____

_____

_____

_____

Concluding status of inspection / application :(Circle One)

Recommended for Approval

Recommended for Rejection

Recommended for Provisional approval for improvements

Name **Signature**

Inspector: _____ _____

Inspector: _____ _____

Inspector: _____ _____

Inspector: _____ _____

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2) Inspection Checklists for Clinical Trial Sites (CTS):

CLINICAL TRTAL SITE (CTS) TNSPECTION CHECKLIST

Name of facility: _____
Address: _____
Organization Type: - Public ☐ Not For Profit ☐ Private ☐Other- _____
Name of Owner / Proprietor: _____
Date of inspection: _____
(dd/mm/yyyy)

i. General Information	**Yes**	**No**	**NA**	**Observations / Recommendations**
Is this CTS a primary care, secondary care or tertiary care facility? (Record one in observations section)				
Is this the Composite CTS (Where Principal investigator is located)?				
Is the facility registered with the Healthcare Commission?				
If yes, is the certificate, available for review and is valid?				
Is there enough space available for proper functioning 'for clinical trials?				
Is there an outpatient facility?				
If yes, On an average how many patients visit per day?				
Is there an inpatient facility?				
If yes, how many beds?				
Have any clinical trials been conducted at this CTS in the past?				
If yes, how many clinical trials were conducted?				

Give details of the Pl as well as nature and duration of the clinical trials.				
How many other studies currently on going at the site? If yes, how many clinical trials were conducted? Give details of the Pl as well as nature and duration of the clinical trials.				
Is there a pharmacy / dedicated investigational Medicine dispensing area?				
If yes, does the CTS have required storage facility for routine operations?				
If yes, does the CTS I have required trial related Investigational Product storing facility? (Investigational Product Provided by the sponsor as per requirements of the protocol).				
Does the CTS have Laboratory services?				
If yes, is in house or central?				
Is there an X-Ray facility?				
If yes, is it on-house or central?				
Does the facility have an incinerator? If yes, document the average weight of Hospital waste disposed of per month.				
If No, does the facility', have a contract with a Hospital waste management Company?				
ii. Study Related Staff	**Yes**	**No**	**NA**	**Observations / Recommendations**
Does the CTS have, any of the study related personnel on staff? -Principal Investigator (Pl) -Sub-Investigator (Sub-Pt) -Coordinator -Nurses -Pharmacists. *Give details in remarks Section				
Are CVs available for Key staff members (Pl, Sub-PI, Coordinator)				
iii Education and Training	**Yes**	**No**	**NA**	**Observation / Recommendations**
Have CTS personnel received or are scheduled to receive any of following trainings?				

o GCP o Trial related o Safety reporting o Pharmacovigilance Training o Other				
Are training records available for study related staff?				
Security and confidentiality is adequate to prevent unauthorized access to records?				
Is there sufficient space to store materials, archive records, equipment to function properly?				
Are generators and/or UPS available utilized at the facility?				
iv. Safety	**Yes**	**No**	**NA**	**Observation / Recommendations**
Is there a system in place for personnel to report any safety concern or Incidents?				
v. Data Handling procedures and Computer Validation	**Yes**	**No**	**NA**	**Observation / Recommendations**
Does the CTS have adequate IT facilities e.g. Computers, internet available?				
Is access to computers limited by an individual username and password system (Clinical Research team members cannot share a username)?				
vi. Records and Reports	**Yes**	**No**	**NA**	**Observation / Recommendations**
Is there space available for document storage?				
If yes, do access control systems to the area exist and are functional?				
Is there a SOP or a system for the retention, storage, and destruction of records?				
How does the site ensure the sponsor's proprietary information is not disclosed to unauthorized personnel or external organizations?				
vii. Records Retention and Archival	**Yes**	**No**	**NA**	**Observation / Recommendations**
Is there a dedicated facility/area for the archival of records?				
Is there control access to the archival facility?				
Is the environment of the facility				

monitored and controlled?				
Is the retention time for records agreed with the sponsors?				
Is there a method of electronic data archive (if required)?				

Remarks of inspection team:

_____
_____
_____
_____
_____
_____
_____

Concluding status of inspection / application :(Circle One)

Recommended for Approval

Recommended for Rejection

Recommended for Provisional approval for improvements

	Name	**Signature**
Inspector:	_____	_____
Inspector:	_____	_____
Inspector:	_____	_____
Inspector:	_____	_____
Inspector:	_____	_____

3) Inspection Checklists for Bio analytical Laboratories:

LABORATORIES FOR CLINICAL RESEARCH (LAB) INSPECTION CHECKLIST

Name of facility: _____
Address: _____
Organization Type: - Public ☐ Not For Profit ☐ Private ☐ Other- _____
Name of Owner / Proprietor: _____
Date of inspection: _____
(dd/mm/yyyy)

i. General organization of the site Activity	**Yes**	**No**	**NA**	**Observations / Recommendations**
Is the scope of lab functions well defined?				
Is the site already well equipped and has adequate facilities?				
Are the algorithms for analysis well defined in any manual or SOP?				
Is the facility registered with the Healthcare Commission?				
If yes, is the certificate available for review and is valid?				
ii. Personnel	**Yes**	**No**	**NA**	**Observations / Recommendations**
Are Organization charts, valid at the time of the inspection and at the time when the inspected study was conducted?				
Is there documentation of the number and qualifications of people employed?				
Is the training and experience of the personnel, individual work load of people involved, documented?				
Are CVs available for key staff members (Lab Director, Lab Manager Pathologists etc.)				
iii. Education and Training	**Yes**	**No**	**NA**	**Observations / Recommendations**
Have Lab personnel received or are scheduled to receive any of following trainings? • GLP • Trial related • Safety reporting • Other				
iv. Quality assurance system	**Yes**	**No**	**NA**	**Observations / Recommendations**
Is there a quality assurance system in place at the laboratory?				

Do they have SOPs that are available, accessible and valid for laboratory operation?				
Are people in charge aware of the SOPs?				
Is there a change control system for SOP/Methods?				
v. Installations and equipment	**Yes**	**No**	**NA**	**Observations / Recommendations**
Is the facility suitable, equipment available and appropriate for the activity of the laboratory? (This includes energy sources, environment, lighting, test equipment and its calibration)				
vi. Archiving of documentation	**Yes**	**No**	**NA**	**Observations / Recommendations**
What is the nature of the documents kept?				
Is there dedicated place of archiving documents?				
Is there access control to that archiving place?				
Is there adequate? Protection of the documents?				
Is there person responsible for the archives identified and documented?				
Is there documentation of file movements?				
Is there an SOP as to how long the records will be maintained .State in remarks the average retention time?				
vii. Sample tracking Receipt	**Yes**	**No**	**NA**	**Observations / Recommendations**
Is there a responsible person identified and documented for receipt and handling of biological samples?				
Is there an organized receipt system, and tracking of samples?				
Is there a sample registration system?				
Are dates and times of receipt of the samples, and acknowledgement of receipt documented?				
Is there a list of samples received for				

each dispatch?				
Is there any protocol of maintaining and monitoring shipment conditions?				
Are there any anomalies noted?				
Is the condition of the samples on receipt documented?				
viii. Storage	**Yes**	**No**	**NA**	**Observations / Recommendations**
Are storage conditions of the study samples satisfactory?				
Do the storage conditions of the samples comply with the protocol?				
Is there assessment of the risk of confusion between samples?				
Is there Identification of the freezer(s) used including model #?				
Are there temperature records of the freezer?				
Is there calibration of the thermometer and its traceability to national/international Standards?				
Are there alarms and other surveillance measures?				
Are the samples labeled, if they are still available?				
Is there documentation of freeze / thaw cycles undergone by the samples?				
ix. Equipment	**Yes**	**No**	**NA**	**Observations / Recommendations**
Is there Identification of the equipment (make, model)?				
Is equipment for the study available at the site at the time of inspection?				
Are instructions for equipment use available?				
Does the equipment comply with specific conditions necessary for the clinical studies?				
Is there documentation relating to the qualification, checks, and maintenance of the equipment available?				
x. Calibration of Equipment	**Yes**	**No**	**NA**	**Observations / Recommendations**
Is the equipment compared and calibrated by a 3rd party?				

Remarks of inspection team:

_____
_____
_____
_____
_____
_____
_____

Concluding status of inspection / application :(Circle One)

Recommended for Approval

Recommended for Rejection

Recommended for Provisional approval for improvements

	Name	**Signature**
Inspector:	_____	_____
Inspector:	_____	_____
Inspector:	_____	_____
Inspector:	_____	_____
Inspector:	_____	_____

3) Inspection Checklists for BA / BE Studies Centers:

BIO-AVAILABILITY OR BIO-EQUIVALENCE STUDIES CENTER (CENTER) INSPECTION CHECKLIST

Name of facility: _____
Address: _____
Organization Type: - Public ☐ Not For Profit ☐ Private ☐ Other-_____
Name of Owner / Proprietor: _____
Date of inspection: _____
(dd/mm/yyyy)

A. CONDUCT OF INSPECTION OF CLINICAL PART OF BIO-WQUIVALENCE STUDIES

i. **Organizational Aspects: Implementation of the BE studies at the clinical site**	**Yes**	**No**	**NA**	**Observations/Recommendations**
Are organization charts (facility management and scientific organization charts) available?				
Is there documentation of delegation of responsibilities by the principal investigator?				
Are there systems for QA and QC in place?				
Are disaster plans (e.g. handling of defective equipment and consequences} including first aid in place?				
Is staff qualification, responsibilities, experience, availability, training programs, training records, CV available for review?				
Have any BE studies already been performed here? If yes, what are their number, nature and records if any?				
What proportion of time is allocated to BE study work? (Enter in remarks section)				
Are there contracts between the sponsor or sponsor's representative and the investigator?				
Does the investigator/s tenant have qualifications and experience in the considered clinical area?				
Is there documentation describing the distribution of duties and functions for the conduct of the BABE study?				
Is there compatibility of the workload of the investigator				

and the staff with the requirements of the study?				
Is the site organized for the study (organization chart, specific training, specific equipment, specific Procedures)?				
Does the site comply with planned time schedule for the study?				
Are correct versions of the protocol and its amendments implemented Correctly?				
ii. Facilities and equipment	**Yes**	**No**	**NA**	**Observations/Recommendations**
What equipment is being used? List in detail in remarks section or provide list.				
Are investigation up-to-date?				
Are the facilities suitable for the protocol requirements and the characteristics of the study being inspected?				
iii. Management of biological samples	**Yes**	**No**	**NA**	**Observations/Recommendations**
Is there documentation available for person in charge of collecting biological samples with dates and handling procedures?				
Is there devised protocol and documentation for storage of the samples before analysis or shipping?				
Are the shipping conditions for biological samples maintained and monitored to prevent degradation?				
iv. Organization of the Documentation	**Yes**	**No**	**NA**	**Observations/recommendations**
Are the medical reports (Patient's charts, X-ray, etc.)Available, complete and archived?				
Are there informed consent documents available?				
Are there Case Report Forms				

(CRF) in records?				
v. Monitoring and auditing	**Yes**	**No**	**NA**	**Observations/recommendations**
Is there monitoring and follow up by the sponsor?				
Is SOP and method of study monitoring available by the sponsor?				
Are there QA certificates from research organization available?				
vi. Use of computerized systems	**Yes**	**No**	**NA**	**Observations/recommendations**
Is a computerized systems being used for the BE study? If yes, what is its validation status, version and mode				
vii. Informed consent of subjects	**Yes**	**No**	**NA**	**Observations/recommendations**
Are the signed and self-dated (by the subject and by the person who conducted the informed consent discussion) consent form actually used and approved by the IEC/IRB?				
Is the patient information sheet actually used and approved by the IEC/IRB?				
Does the center give copy of the informed consent to the patient/attendant?				
viii.Characteristics of the subjects included in the BA/BE study	**Yes**	**No**	**NA**	**Observations/recommendations**
Are the subjects nominated for the study actually on board and participating in study?				
Is the subjects participation recorded in their medical records				
Do the subjects included fulfill the inclusion criteria and none of the exclusion criteria stated in protocol?				
ix. Subject's Visits Calendar	**Yes**	**No**	**NA**	**Observations/recommendations**
Is there subjects visits calendar available for review and is compiled				

x. Efficacy and safety assessment data	**Yes**	**No**	**NA**	**Observations/recommendations**
Is the efficacy and safety data recorded in the CRF in agreement with the source medical data obtained during the BE study				
Are adequate data management procedures in place?				
Is the protocol established for reporting the adverse and side reactions? Mention reporting channel in remarks				
xi. Concomitant therapy and intercurrent illness	**Yes**	**No**	**NA**	**Observations/recommendations**
Were concomitant therapy and intercurrent illnesses managed in compliance with the protocol and recorded in the CRF and source medical documents				
xii. Management Of The investigational products	**Yes**	**No**	**NA**	**Observations/Recommendations**
Are there instructions for handling of investigational product(s) and study related materials (if not included in protocol or investigators brochure)?				
Are shipping records for investigational product(s) and study related material available? (Receipt, date(s) of product delivery and quantity, batch (or lot) numbers {check correspondence with the information kept at the sponsor site}, expiration dates and codes assigned to the product and the subject)				
Is there documentation regarding allocation of treatment, randomization and code braking available?				
Is there investigational product(s) accountability at site (pharmacy or investigator)?				
is the date and quantity of				

investigational Product dispensed or returned, identification of recipients (patient's code or authorized Persons) documented? (Should also contain batch (or lot) numbers, expiration dates and codes assigned to the product and the subject)				
Is there documentation about relabeling, if Applicable?				
Is there documentation on date and quantity of investigational product returned to the sponsor? (Return receipt, batch (or lot) numbers, Expiration dates and codes assigned to the product and the subject)				
Is there documentation of dates, batch (or lot) numbers and quantity of investigational product (s) destruction? (if destroyed at the site)				
Is there documentation of treatment compliance?				
Is there a check on suitability of storage conditions and their records (fridge, freezer and controlled substances, etc?)				
If yes to above, are there specific SOP's for this activity from the pharmacy or institution?				
Is there documentation whether there was controlled access to the investigational product(s) from reception to dispensing?				
Is there documentation of certification of the labeling for compliance with applicable regulations?				

B. **CONDUCT OF INSPECTION OF BIOANALYTICAL PART OF BIO-EQUIVALENCE STUDIES**

i. General organization of the site Activity	**Yes**	**No**	**NA**	**Observations/Recommendations**
Is the scope of laboratory and functions well defined?				
Is the site already well-equipped and has adequate facilities?				
Are the algorithms for analysis well defined in any manual or SOP?				
ii. Personnel	**Yes**	**No**	**NA**	**Observations/Recommendations**
Are organization charts, valid at the time of the inspection and at the time when the inspected study was conducted?				
Is there documentation of the number and qualifications of people employed?				
Is the training and experience of the personnel, individual work load of people involved documented?				
iii. Quality assurance system	Yes	No	NA	Observations/Recommendations
Is there a quality assurance system in place at the laboratory?				
Does the center have SOP's that are available, accessible and valid for study?				
Are people in charge aware of the SOPs is there a change control system for SOP/Methods?				
iv. Installations and equipment				
Is the facility suitable, equipment available and appropriate for the activity of the laboratory and for the Bio-equivalence study to be inspected during the inspection? (This includes energy sources, environment and its calibration)				
v. Archiving of documentation	**Yes**	**No**	**NA**	**Observations/Recommendations**
What is the nature of the				

documents kept				
Is there dedicated place of archiving documents?				
Is there access control to that archiving documents				
Is there adequate protection of the documents				
Is there person responsible for the archives identified and documents?				
Is there documentation of file movements?				
Is there an SOP as to how long the records will be maintained State in remarks the average retention time.				
vi. Sample tracking receipt	**Yes**	**No**	**NA**	**Observations/Recommendations**
Is there a responsible person identified and documented for receipt and handling of biological samples?				
Is there an organized receipt system, and tracking of samples?				
Is there a sample registration system?				
Are controls performed on receipt?				
Are dates and times of receipt of the samples, and acknowledgement of receipt documented?				
Is there a list of samples received for each dispatch?				
Is there any protocol of maintaining and monitoring shipment conditions?				
Are there any anomalies noted?				
Is the condition of the samples on receipt documented?				
vii. Storage	**Yes**	**No**	**NA**	**Observations/Recommendations**
Are storage conditions of the BE study samples satisfactory?				
Do the storage conditions of the samples comply with the protocol and the conditions used during BE study				

inspected?				
Is there assessment of the risk of confusion between samples?				
Is there identification of the freezer(s) used including model#				
Are there temperature records of the freezer?				
Is there calibration of the thermometer and its trace ability to national international standards?				
Are there alarms and other surveillance measures?				
Are the samples labeled, if they are still available?				
Is there documentation of freeze/thaw cycles undergone by the samples				
viii. Destruction	**Yes**	**No**	**NA**	**Observations/Recommendations**
Is there documentation of date of destruction or return of the samples				
ix. Sample analysis Bio analytical method used	**Yes**	**No**	**NA**	**Observations/Recommendations**
Is the BE study report consistent with the SOP describing the bio analytical methods and other documents?				
If yes to above are documents available?				
x. Equipment	**Yes**	**No**	**NA**	**Observations/Recommendations**
Is there identification of the equipment (make, model)?				
Is equipment for the study available at the site at the time of inspection?				
Are instructions for equipment use available				
Does the equipment comply with specific conditions necessary for the BE study?				
Is there documentation relating to the qualification checks and maintenance of the equipment available?				
xi. Reagents	**Yes**	**No**	**NA**	**Observations/Recommendations**

Are the reagents labeled properly including the expiry date?				
Is there traceability of the reagents use?				
Is there compliance with specific conditions? if any				
xii. Reference standard	**Yes**	**No**	**NA**	**Observations/Recommendations**
Are contents of the certificates of analysis and expiry dates documented and available				
Are the storage conditions optimal?				
Are the conditions for access to reference standard optimal?				
xiii. Calibration ,control samples	**Yes**	**No**	**NA**	**Observations/Recommendations**
Are there dates and conditions of preparation of the stock and working solutions and of the calibration and control samples and the number of aliquots prepared for each sample documented?				
Are the Conditions and duration of storage of the stock solutions, working solutions optimal?				
Are calibration and control samples, compared to their stability, as described in the validation report?				
Is there any matrix used? Mention details if applicable				
Is the number of calibration samples documented? Mention number for each run.				
Is the response function used, including weighting used for each run, if any?				
Is there an acceptance criteria for the calibration curve?				
Is there a criterion for exclusion of calibration samples?				
xiv. Development of the method	**Yes**	**No**	**NA**	**Observations/Recommendations**
Is there a quick overview of the origin and of the				

development of the Bio analytical method can be helpful to identify critical steps in the procedure?				
xv. method validation	**Yes**	**No**	**NA**	**Observations/Recommendations**
Is there method validation protocol?				
Are there dates of the validation documented?				
Is there adequate documentation of all operations?				
Is there completeness of the validation report, when compared to the various experiments performed?				
Is there consistency of the validation report with the source documents?				
Is there Chromatogram integrations?				
Is there exclusion of calibration samples, if any?				
Is there stability of: 1. The stock solutions? 2. The samples (bench-top, freeze/thaw cycles, long term)? 3. Extracted samples before their injection, if applicable?				
Is there Specificity / selectivity?				
Is there accuracy?				
Is there Limit of quantification?				
Is there Response function Carry-over?				
In case of mass spectrometric methods: matrix?				
Is there Effect of a dilution, if applicable?				
Is there effect of the anticoagulant, if the anticoagulant used for the preparation of the calibration and/or QC samples is different from the anticoagulant used to collect samples during the				

study?				
xvi. Assays	**Yes**	**No**	**NA**	**Observations/Recommendations**
Is nature and completeness of the documentation available?				
Is there adequacy of the documentation of all operations?				
Is there completeness of the analytical report?				
Is there number, date and composition of the analytical runs?				
Is there Identification of samples and tubes?				
Is there any method for the Assessment of the risk of sample mix-ups?				
Is there any method for assessment of the risk of sample cross contamination?				
Are there Chromatogram integrations?				
Is there Calculation of the concentrations?				
Is there Compliance with pre-defined criteria for the exclusion of calibration samples?				
Are there Criteria of acceptance of the runs, and compliance with pre-established criteria?				
Is there audit trail settings and information recorded in the audit trails?				
Is there Maintenance of blinding, if required by the protocol?				
Are there practicalities of data transfer?				
Is there consistency of the analytical report with the source documents?				
C. CONDUCT OF INSPECTION OF PHARMACOKINETIC AND STATISTICAL ANALYSES PART OF BIO-EQUIVALANCE STUDIES				
i. Pharmacokinetics	**Yes**	**No**	**NA**	**Observations/Recommendations**
Is there a quality system in place?				

Are personnel involved identified, their qualifications documented and responsibilities clearly stated?				
Is software used?				
Is there software validation system documented?				
Is the software practical and has enough controls of data entry?				
Are sampling times used?				
Is data selected for the calculation of the terminal half-life, if applicable?				
Is the raw data consistent with study report?				
ii. Statistics	**Yes**	**No**	**NA**	**Observations/Recommendations**
Is there a quality system in place?				
Are personnel involved identified, their qualifications documented and responsibilities clearly stated?				
Is software used?				
Is the software practical and has enough controls of data entry?				
Are sampling times used?				
Are there Data line listings and tables of results?				
Is there consistency of the raw data with the calculated pharmacokinetic parameters and with the study report?				

Remarks of inspection team:

_____

_____

_____

_____

_____

Concluding status of inspection / application :(Circle One)

Recommended for Approval

Recommended for Rejection

Recommended for Provisional approval for improvements

Name	**Signature**
Inspector: _____	_____
Inspector: _____	_____
Inspector: _____	_____
Inspector: _____	_____
Inspector: _____	_____

- **Decision of 4th CSC Meeting:-**

The CSC unanimously approved all the checklists for inspection of CROs, Clinical Trial Site, BA/BE Studies Center, and Bio-analytical Laboratories.

AGENDA ITEM - X: **NRA SELF ASSESSMENT- DEVELOPMENT OF NOTIFICATION / GUIDELINES / SOPs / DATABASES FOR ATTATINING REQUIREMENT OF WHO LEVEL III.**

Drug Regulatory Authority of Pakistan (DRAP) is endeavouring to adopt international best practices. In this context DRAP is currently working to attain maturity level III in WHO NRA Global Benchmarking tool, which is considered as baseline for stringent regulatory authorities. DRAP has successfully submitted revised WHO Global Benchmarking Self-Assessment Tool. During this self-assessment, strengths and areas for improvements were identified. And CEO-DRAP assigned tasks to Shafqat Hussain Danish, AD-II, Pharmacy Services Division, to develop required guidelines, SOPs, Databases and fulfilment of required tasks to achieve WHO level III.

In this context Guidelines, SOPs, and required consent are placed before CSC for approval.

- **Attached at Annex-II**

- **Decision of 4th CSC Meeting:-**

The CSC in principle approved the guidelines for the conduct of clinical trial, any quarries will be shared by email.

Minutes of 4th Meeting of CSC (Additional Agenda) Scheduled on 17th July, 2019.

As per direction & permission of the Chairman CSC Additional agenda presented before the CSC

ADDITIONAL AGENDA ITEM - I: LICENSING OF CRO, CLINICAL TRIAL SITE AND BA/BE CENTRE UNDER THE BIO STUDY RULES, 2017. (Discussed in previous CSC Meetings, ongoing cases).

1.1. A) M/S IQUVIA SOLUTIONS PAKISTAN (PVT) LTD, APPLICATION FOR LICENSE TO ACT AS CRO AND CLINICAL TRIAL MONITORING SERVICES (F.No.15-09/2019).

Application is from Dr. Aman Ullah Khan CEO, M/s IQUVIA Solutions Pakistan (Pvt) Ltd. Karachi, wherein the request has been made to license their company with DRAP to work as Clinical Research Organization (CRO) and Clinical Trial Monitoring Services, the application is on prescribed Form-I of the Bio-Study Rules 2017, without fee.

1.1.2. After initial evaluation the firm was informed regarding shortcomings through letter no. F.No.15-09/2019 DD (PS), dated 07th March, 2019, and firm submitted their reply, which is re-evaluated according to prerequisites as mentioned in Form-I of the Bio-Study Rules 2017, after scrutiny status of application is as follows:

Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached.
2	Fee	Not Provided. Firm Reply: While we understand that no formal approval has been made in term of the applicable fee for the CRO license, we understand that previously PKR 50,000 was proposed as the fee for application.

		In this regard, we have submitted PKR 50,000 as the applicable fee. In the event that a revised applicable fee is notified, we will submit the remainder amount once it is notified. Please find the challan evidencing the submission of the above mentioned fee attached herewith.
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 of ground & first floor attached, same premises will be also be utilized for BA/BE Site &Clinical Trial Site.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not Provided
6	Names and qualifications of the above sections along with their staff.	Attached
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Firm Reply: Please note that the ambulatory services are not required in relation to Contract Research Organization license application, hence we understand that such information is not required along with the application. IQVIA will manage study with in the approved hospital/clinical site by DRAP under the supervision on local EC and NBC with qualifies investigators as per ICH-GCP guidelines and Patient Wellbeing.
8	Undertaking	Attached

1.1.3 Applicant informed that they will conduct/monitor Clinical Trials activities in following tertiary care hospitals:

i) Aga Khan University Hospital (Karachi).

ii) Shifa International Hospital (Islamabad).
iii) Shaukat Khanum Memorial Cancer Hospital and Research Centre (Lahore).

1.1.4 Description of shortcomings:

i) Fee approved by the Authority for CRO is Rs.300000/-, only Rs.50000/ submitted.

1.1.5. <u>Decision of 3rdCSC Meeting</u>: - *The CSC after deliberations decided to conduct the inspection of CRO from team of Pool-A comprising of the following experts. These experts shall get training at UHS, Lahore prior to moving for inspection. In case any member is not available the committee authorized its chairman to add another suitable member of the relevance experties from the pool of experts. The applicant shall be inform for the proposed date of inspection accordingly. The CSC also directed the applicant to remove the shortcomings, which have been described in agenda:-*

i.	Prof. Dr. Javed Akram
ii.	Dr. Salwa Ahsan
iii.	Prof. Dr. Nadeem Afzal
iv.	Dr. Farhana Badar
v.	Dr. Abdur Rashid (**Coordinator**)

1.1.6. The firm informed regarding shortcomings through letter no.F.No.15-03/2017 DD (PS), dated 8thJuly, 2019, but still response is awaited.

1.1.7 The CSC has been decided in its 3rd meeting, that in case of unavailability of any member of the panel constituted by the committee, CSC delegated power to the Chairman CSC to include experts from the pool approved in 2nd CSC meeting and may adopt any other relevant expert member from the pool.

1.1.8. Due to unavailability of pool members Chairman CSC, exercising the power delegated by the CSC in its 3rd meeting, replaced the inspection pool members for the inspection, and following expert's panel inspected the facility on July, 2019:

i.	Dr. Abdur Rashid (**Coordinator**)
ii.	Prof. Dr. Javed Akram
iii.	Dr. Salwa Ahsan
iv.	Prof. Dr. Nadeem Afzal
v.	Dr. Farhana Badar

1.1.9. Remarks of inspection team:

Keeping in view the human resources in HR, Clinical Operation, Finance, separate premises (need), training of human resource, defer the case for improvement.

1.1.10 Concluding status of application:

Recommended for provisional approval for improvements.

1.1.11 Submitted for perusal, discussion and decision of CSC.

- **Decision of 4thCSC Meeting:-**

The CSC after deliberations decided to defer the case for re-inspection by the same panel nominated in the 3rd CSC meeting after fulfilment of all requirements as per the bio-Study Rules 2017 & intimation by the applicant. CSC further directed the applicant for development of separate infra-structure& H.R.

1.2. A) APPLICATION FOR THE LICENSE OF THE CENTER FOR BIOEQUVALANCE STUDIES AND CLINICAL RESEARCH (CBSCR) FOR BA/BE SITE, CRO AND CLINICAL TRIAL SITE AT INTERNATIONAL CENTER FOR CHEMICAL AND BIOLOGICAL SCIENCES (ICCBS), UNIVERSITY OF KARACHI, (F. No.15-07/2019).

Application is from Prof. Dr. M. Iqbal Choudhary, Director, Center for Bioequivalence Studies and Clinical Research (CBSCR), dated 8th February, 2019, wherein the request has been made to license their firm with DRAP to act as a BA/BE Site, the application is on prescribed Form-I of the Bio-Study Rules 2017.

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

Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017

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).	It's a Government organization working under the University of Karachi, No evidence provided for its legal status.
4	Details of premises including layout plan of	Layout of ground &

	the site.	first floor attached, same premises will be also be utilized for Clinical Trial Site &CRO.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached
6	Names and qualifications of the above sections along with their staff.	Attached
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached (Copy)
8	Undertaking on stamp paper	Not provided

1.2.3. Description of shortcomings

i) Undertaking on stamp paper is not provided.

1.2.4. <u>Decision of 3rdCSC Meeting</u>: - ***"****The CSC after deliberations decided to conduct the inspection of BA/BE Studies Center from team of Pool-A comprising of the following experts. These experts shall get training at UHS, Lahore prior to moving for inspection. In case any member is not available the committee authorized its chairman to add another suitable member of the relevance experties from the pool of experts. The applicant shall be inform for the proposed date of inspection accordingly. The CSC also directed the applicant to remove the shortcomings, which have been described in agenda:-*

i.	Prof. Dr. Javed Akram
ii.	Dr. Salva
iii.	Prof. Dr. Nadeem Afzal
iv.	Dr. Farhana Badar
v.	Dr. Abdur Rashid (**Coordinator**)

1.2.5. The firm informed regarding shortcomings through letter no.F.No.15-07/2019 DD (PS), dated 08th July, 2019, still response is awaited.

1.2.6 The CSC has been decided in its 3rd meeting, that in case of unavailability of any member of the panel constituted by the committee, CSC delegated power to the Chairman CSC to include experts from the pool approved in 2nd CSC meeting and may adopt any other relevant expert member from the pool.

1.2.7. Due to unavailability of pool members Chairman CSC, exercising the power delegated by the CSC in its 3rd meeting, replaced the inspection pool members for the inspection, and following expert's panel inspected the facility on 1st July, 2019:

i.	Dr. Abdur Rashid (**Coordinator**)
ii.	Prof. Dr. Javed Akram
iii.	Dr. Salwa Ahsan
iv.	Prof. Dr. Nadeem Afzal
v.	Dr. Farhana Badar

1.2.8. Remarks of inspection team:

Keeping in view the human resources, their training, SOPs revision, panel recommended for provisional approval and advised to the applicant for improvements.

1.2.9. Concluding status of application:

Recommended for provisional approval for improvements.

1.2.10 Submitted for perusal, discussion and decision of CSC.

- **Decision of 4thCSC Meeting:-**

The CSC after deliberations decided to deferred for re-inspection of the BA/BE Site.

ADDITIONAL AGENDA ITEM - II: LICENSING OF CRO, CLINICAL TRIAL SITE AND BA/BE CENTRE UNDER THE BIO STUDY RULES, 2017. (New Cases)

2.1) REQUEST FOR APPROVAL OF OBSERVATIONAL STUDY PROGRAM ASSESSING EFFECTIVENESS AND TOLERABILITRY OF GLICLAZIDE 60mg MODIFIED RELEASE TABLET IN PATIENTS WITH TYPE II DIABETES FASTING DURING RAMADAN, TO BE CONDUCTED AT MTI/HAYATABAD MEDICAL COMPLEX, PESHAWAR.

Application is from Prof. Dr. Abbas Raza, MTI/Hayatabad Medical Complex, Peshawar., submitted by Dr. Ahmed Atif Mirza, President Clinical Operations M/s DRK

Pharma Solution, Lahore on behalf of Sponsor M/s Servier Research and Pharmaceuticals (Pvt) Ltd, dated 12th July, 2019, wherein the request is in reply of this division letter number F.No.03-01/2019-DD (PS), to license their Public Hospital with DRAP to work as Clinical Trial Site (CTS), to conduct the clinical studies mentioned in subject cited above.

2.1.2. The application is on prescribed Form-I of the Bio-Study Rules 2017 along with fee of Rs.100000/- for Clinical Trial Site vide challan no.0550723, 11th July, 2019.

2.1.3. 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).	Applicant is Professor of Medicine and working at Public Hospital
4	Details of premises including layout plan of the site.	Not provided.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not provided. Applied site is a Public Hospital.
6	Names and qualifications of the above sections along with their staff.	Not provided.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Applied site is a Public Hospital.
8	Undertaking on stamp paper	Attached.

2.1.4. After evaluation following shortcomings were recorded:

i) Details of premises including layout plan of the site is not provided.

ii) Details of the section wise equipment is not provided.

iii) Names and qualifications of the section wise staff is not provided.

2.1.5 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberations decided to conduct the inspection of Clinical Trial Site (CTS) from team, comprising of the following experts. In case any

member is not available the committee authorized its chairman to add another suitable member of the relevant experties from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly.-

i.	Muhammad Adnan Faisal Saim Deputy Director Pharmacy Services.
ii.	Dr. Gul Majeed
iii.	Dr. Faiza Bashir

2.2) **REQUEST FOR APPROVAL OF OBSERVATIONAL STUDY PROGRAM ASSESSING EFFECTIVENESS AND TOLERABILITRY OF GLICLAZIDE 60mg MODIFIED RELEASE TABLET IN PATIENTS WITH TYPE II DIABETES FASTING DURING RAMADAN, TO BE CONDUCTED AT AKRAM MEDICAL COMPLEX, LAHORE.**

FR (page 01 – 19/corr.) is an application from Dr. Ayesha Nasir, Akram Medical Complex, Lahore, submitted by Dr. Ahmed Atif Mirza, President Clinical Operations M/s DRK Pharma Solution, Lahore on behalf of Sponsor M/s Servier Research and Pharmaceuticals (Pvt) Ltd, dated 12th July, 2019, wherein the request is in reply of this division letter number F.No.03-01/2019-DD (PS), to license their Private Hospital with DRAP to work as Clinical Trial Site (CTS), to conduct the clinical studies mentioned in subject cited above.

2.2.2. The application is on prescribed Form-I of the Bio-Study Rules 2017 along with fee of Rs.100000/- for Clinical Trial Site vide challan no.0550727, 11th July, 2019.

2.2.3. 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.	03	Attached
2	Fee	02	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).	05	Applicant is Professor of Medicine and working at Private Hospital
4	Details of premises including layout plan of the site.	---	Not provided.
5	Details of the section wise equipment and machinery required for the analytical or bio-	---	Not provided. Applied site is a

	analytical and clinical studies.		Private Hospital.
6	Names and qualifications of the above sections along with their staff.	---	Not provided.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	---	Applied site is a Private Hospital.
8	Undertaking on stamp paper	04	Attached.

2.2.4. After evaluation following shortcomings were recorded:

i) Details of premises including layout plan of the site is not provided.

ii) Details of the section wise equipment is not provided.

iii) Names and qualifications of the section wise staff is not provided.

- Submitted for perusal, discussion and consideration of CSC.\

- **Decision of 4th CSC Meeting:-**

The CSC after deliberations decided to conduct the inspection of Clinical Trial Site (CTS) from team, comprising of the following experts. In case any member is not available the committee authorized its chairman to add another suitable member of the relevant experties from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly.-

i.	Dr. Abdur Rashid
ii.	Dr. Nadeem Irfan
iii.	Dr. Farhana Badar
iv.	Dr. Ali Jawa

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2.3 REQUEST FOR APPROVAL OF OBSERVATIONAL STUDY PROGRAM ASSESSING EFFECTIVENESS AND TOLERABILITRY OF GLICLAZIDE 60mg MODIFIED RELEASE TABLET IN PATIENTS WITH TYPE II DIABETES FASTING DURING RAMADAN, TO BE CONDUCTED AT BAQAI INSTITUTE OF DIBETOLOGY & ENDOCRINOLOGY, KARACHI.

Application is from Dr. Muhammad Yaqoob Ahmedani, Baqai Institute Of Dibetology & Endocrinology, Karachi, submitted by Dr. Ahmed Atif Mirza, President Clinical Operations M/s DRK Pharma Solution, Lahore on behalf of Sponsor M/s Servier Research and Pharmaceuticals (Pvt) Ltd, dated 12th July, 2019, wherein the request is in reply of this division letter number F.No.03-01/2019-DD (PS), to license their Public Hospital with DRAP to work as Clinical Trial Site (CTS), to conduct the clinical studies mentioned in subject cited above.

2.3.2. The application is on prescribed Form-I of the Bio-Study Rules 2017 along with fee of Rs.100000/- for Clinical Trial Site vide challan no.0550723, 11th July, 2019.

2.3.3. 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).	Applicant is Professor of Medicine and working at Private Hospital
4	Details of premises including layout plan of the site.	Not provided.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not provided. Applied site is a Private Hospital.
6	Names and qualifications of the above sections along with their staff.	Not provided.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Applied site is a Private Hospital.
8	Undertaking on stamp paper	Attached.

2.3.4. After evaluation following shortcomings were recorded:

i) Details of premises including layout plan of the site is not provided.

ii) Details of the section wise equipment is not provided.

iii) Names and qualifications of the section wise staff is not provided.

2.3.5 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberations decided to conduct the inspection of Clinical Trial Site (CTS) from team, comprising of the following experts. In case any member is not available the committee authorized its chairman to add another suitable member of the relevant experties from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly.-

i.	Dr. Najam Us Saqib
ii.	Dr. Mehboob Rabbani

iii.	Dr. Saif Ur Rehman Khattak

2.4) **REQUEST FOR APPROVAL OF OBSERVATIONAL STUDY PROGRAM ASSESSING EFFECTIVENESS AND TOLERABILITRY OF GLICLAZIDE 60mg MODIFIED RELEASE TABLET IN PATIENTS WITH TYPE II DIABETES FASTING DURING RAMADAN, TO BE CONDUCTED AT DIABETES INSTITUTE OF PAKISTAN, Lahore.**

Application is from Dr. Muhammad Imtiaz Hassan, Diabetes Institute of Pakistan, Lahore, submitted by Dr. Ahmed Atif Mirza, President Clinical Operations M/s DRK Pharma Solution, Lahore on behalf of Sponsor M/s Servier Research and Pharmaceuticals (Pvt) Ltd, dated 12th July, 2019, wherein the request is in reply of this division letter number F.No.03-01/2019-DD (PS), to license their Public Hospital with DRAP to work as Clinical Trial Site (CTS), to conduct the clinical studies mentioned in subject cited above.

2.4.2. The application is on prescribed Form-I of the Bio-Study Rules 2017 along with fee of Rs.100000/- for Clinical Trial Site vide challan no.0550724, 11th July, 2019.

2.4.3. 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).	Applicant is Professor of Medicine and working at Private Hospital
4	Details of premises including layout plan of the site.	Not provided.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not provided. Applied site is a Private Hospital.
6	Names and qualifications of the above sections along with their staff.	Applied site is a Private Hospital.
7	Details of the allied facilities associated with the trial center including ambulatory services,	Applied site is a Private Hospital.

	emergency handling etc.	
8	Undertaking on stamp paper	Attached.

2.4.4. After evaluation following shortcomings were recorded:

i) Details of premises including layout plan of the site is not provided.

ii) Details of the section wise equipment is not provided.

2.4.5 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberations decided to conduct the inspection of Clinical Trial Site (CTS) from team, comprising of the following experts. In case any member is not available the committee authorized its chairman to add another suitable member of the relevant experties from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly.-

i.	Dr. Abdur Rashid
ii.	Dr. Nadeem Irfan
iii.	Dr. Farhana Badar
iv.	Dr. Ali Jawa

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2.5) **REQUEST FOR APPROVAL OF OBSERVATIONAL STUDY PROGRAM ASSESSING EFFECTIVENESS AND TOLERABILITRY OF GLICLAZIDE 60mg MODIFIED RELEASE TABLET IN PATIENTS WITH TYPE II DIABETES FASTING DURING RAMADAN, TO BE CONDUCTED AT NATIONAL HOSPITAL & MEDICAL CENTER.**

Application is from Prof. Dr. Abbas Raza, National Hospital Medical Center, Lahore, submitted by Dr. Ahmed Atif Mirza, President Clinical Operations M/s DRK Pharma Solution, Lahore on behalf of Sponsor M/s Servier Research and Pharmaceuticals (Pvt) Ltd, dated 12th July, 2019, wherein the request is in reply of this division letter number F.No.03-01/2019-DD (PS), to license their Public Hospital with DRAP to work as Clinical Trial Site (CTS), to conduct the clinical studies mentioned in subject cited above.

2.5.2. The application is on prescribed Form-I of the Bio-Study Rules 2017 along with fee of Rs.100000/- for Clinical Trial Site vide challan no.0550723, 11th July, 2019.

2.5.3. 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).	Applicant is Professor of Medicine and working at Public Hospital
4	Details of premises including layout plan of the site.	Not provided.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not provided. Applied site is a Public Hospital.
6	Names and qualifications of the above sections along with their staff.	Not provided.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Applied site is a Public Hospital.
8	Undertaking on stamp paper	Attached.

2.5.4. After evaluation following shortcomings were recorded:

i) Details of premises including layout plan of the site is not provided.

ii) Details of the section wise equipment is not provided.

iii) Names and qualifications of the section wise staff is not provided.

2.5.5 Submitted for perusal, discussion and consideration of CSC.

- **Decision of 4th CSC Meeting:-**

The CSC after deliberations decided to conduct the inspection of Clinical Trial Site (CTS) from team, comprising of the following experts. In case any member is not available the committee authorized its chairman to add another suitable member of the relevant experties from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly.-

i.	Dr. Abdur Rashid
ii.	Dr. Nadeem Irfan
iii.	Dr. Farhana Badar
iv.	Dr. Ali Jawa