Minutes of the 6th Meeting of CSC held on 20th January, 2020.

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1. The 6th Meeting of CSC held on 20th January 2020 at the Committee Room of DRAP, Islamabad under chairmanship of Dr. Abdur Rashid, Director Pharmacy Services Division.

2. The following members attended the meeting:-

Sr. No.	Name	Designation
01	Dr. Abdur Rashid.	Chairman CSC / Director Pharmacy Services.
02	Dr. Masud Ur Rehman.	Secretary CSC / Additional Director, Pharmacy Services.
03	Ms. Salwa Ahsan.	Chief of Pharmacy, Shifa International Hospital, Islamabad. Member CSC.
04	Prof. Nadeem Irfan Bukhari.	Professor of Bio-Pharmaceutics & Pharmacokinetics, University of Punjab, Lahore. Member CSC.
05	Dr. Farhana Badar.	Biostatistician & Epidemiologist, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore. Member CSC.
06	Prof. Dr. Sheikh Riaz-ud-Din	Director of Center for Excellence in Molecular Biology (CEMB) in Lahore. Co-opted CSC Member.
07	Dr. Tayab Husnain.	Head of CEMB / CAMB, Lahore. Co-opted CSC Member.
08	Dr. Naseem Salahuddin.	Director Infectious Diseases Indus Hospital, Karachi Co-opted CSC Member.
09	Prof. Dr. Rizwana Chaudhri	HOD Gynecologist Holy Family Hospital, Rawalpindi. Co-opted CSC Member.

3. 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.

AGENDA ITEM - I:

A) CONFIRMATION OF 5TH CSC MEETING MINUTES & APPROVAL

1. All the members confirmed the 5th CSC meeting & decision taken in the meeting. The 5th Meeting of CSC was held on 08th August, 2019 at the Committee Room of DRAP, Islamabad, Whereas Chairman and Secretary CSC was on official duty abroad (Hajj medical duty, Saudi Arab). For the fifth meeting stop gap arrangement to the position of additional director (secretary CSC) was made through the notification of DRAP but that for Director (ex-officio chairman CSC) was not made. Further the requests of applicants suffering due to non-functional of CSC for the time being because of above said reason was creating factor of urgency on DRAP to conduct the CSC meeting.

2. The Chairman & Secretary confirmed the minutes of the 5th CSC meeting conducted during their official duty abroad.

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

4. Chairman CSC discussed regarding Inspection checklist and pointed out that there are following three options for recommendations in the inspection checklists:

i. **Recommended for Approval**
ii. **Recommended for Rejection**
iii. **Recommended for Provisional approval for improvements**

5. Chairman CSC also highlighted that inspection panel report of Center for Biological Scientific & Chemical Research (ICCBS) (BA/BE Studies Center) was included in the 4th CSC meeting and in minutes 3rd option "**Recommended for Provisional approval for improvements**" marked by the panel so the same was finalized for the minutes, but two of the panel members (Dr Javed Akram & Dr. Farhana Badar), changed the decision and added addendum as "**Deferred for reinspection of BA/BE Studies Site**"

6. As per decision of 4th CSC meeting for "Center for Biological Scientific & Chemical Research (ICCBS)" (BA/BE Studies Center), Chairman CSC proposed correction in the inspection checklists, as 3rd option, "**Recommended for Provisional approval for improvements",** creates confusion & may be replaced with **"Deferred for improvements".**

7. Dr. Rizwana Chaudhry suggested that the term "**Deferred for ratification of deficiencies**" is most suitable for replacement.

8. **Decision of the 6th CSC meeting:**

All members of Clinical Studies Committee agreed on the proposal & approved substitution of 3rd option "Recommended for Provisional approval for improvements" with "Deferred for ratification of deficiencies", and approved following three options for inspection checklist, which could be marked by panel experts:

i. **Recommended for Approval.**
ii. **Recommended for Rejection.**
iii. **Deferred for ratification of deficiencies.**

9. Dr. Farhana Badar discussed regarding SOP for BA/BE Studies Center inspection checklists, as assigned by CSC in its 5th meeting, and said that she will also submit her prepared checklists.

10 Secretary CSC, Dr. Masud Ur Rehman added that BA/BE Studies are very sensitive & Scientific work, which required sophisticated equipment, so DRAP & inspection penal should ensure the ability & availability of required all equipment for BA/BE Studies.

11. **Decision of the 6th CSC meeting**

Clinical Studies Committee assign the task to following members:

i. Dr. Masud Ur Rehman (Coordinator)
ii. Prof. Dr. Nadeem Irfan
iii. Dr. Farhana Badar

12 Nominated CSC members will work on the task of BA/BE Studies Centers prerequisites & present their report in the next CSC meeting.

13. During discussion regarding inspection, conducted in bits & pieces, members of CSC discussed the matter & decided that inspection report may acceptable even if inspection conducted in two different dates with different panel of experts if all members sign for same recommendations.

14. It is also discussed that availability of all panel members on the stipulated date & time is some time not possible, even after replacement of members from inspection pool, member's availability on same date & time is a problematic task.

15. CSC members discussed & suggested that, it is not always necessary that a panel consist of five members. If members are not available and 3 out of five 5 members

conduct inspection on same date and agreed on a recommendation, so the recommendations will be placed before the CSC for decision.

16. It is also discussed by the CSC members that all the responsibility of the trial should be on trial initiator (Principle Investigator), and major or Principle Investigator's trial site should be inspected rather than all trial sites/decided by the CSC, whereas responsibility of all trial sites should be on National Principle Investigator.

AGENDA ITEM II: AMMENDMENT IN RULE 13 OF THE BIO-STUDY RULES 2017 & CO-OPTING THE EXPERT MEMBERS

2.1.1 The Honorable Minister & Secretary M/o National Health Services Regulation & Coordination has desired to augment and enhance the scope of Clinical Research in Pakistan. The authorities has desired to add names of following experts as member of Clinical Studies Committee (CSC), which is a legal Statutory forum for Registration of Clinical Studies and licensing of CRO, Clinical Trial Sites, Bio-Analytical Laboratories & BA/ BE Studies Centers. For which draft notification has been forwarded for approval from Authority and for further legal process, As for amendments in existing rules is a lengthy legal process, the Drug Regulatory Authority of Pakistan (DRAP) may utilize their experties by co-opting them:

- **i.** Vice Chancellor, University of Health Sciences or their nominee.
- **ii.** Vice Chancellor, University of the Punjab or their nominee.
- **iii.** Head of CEMB/CAMB Lahore.
- **iv.** Dr. Naseem Salahuddin, Director Infectious Diseases Indus Hospital, Karachi, Sindh;
- **v.** Dr. Aamir Jaffary, Sindh Institute of Urology & Transplantation (SIUT), Karachi, Sindh;
- **vi.** Dr. Rizwana Chaudhry, HOD Gynecologist Holy Family Hospital, Rawalpindi, The Punjab; and
- **vii.** Prof: Dr. Mushtaq Ahmed, Professor of Cardiology, Bacha Khan Medical College Mardan, Khyber Pakhtoonkhwa.

2.1.2. CVs of Dr. Naseem Salahuddin, Dr. Aamir Jafarey & Prof. Dr. Tayyab Husnain has been received.

2.1.3 All the newly opted members are requested to give certificate for Non-Conflict of interest.

2.1.4 Dr. Masud Ur Rehman, Secretary CSC presented & described the background regarding Honorable Supreme Court order dated 15-01-2019 in C.P. No.73 of 2018 & proposal of Honorable Minister & Secretary of the M/o National Health Services Regulation & Coordination.

2.1.5 Dr. Sheikh Riaz Ud Din added that CEMB/ CAMB are previously same but now these are two separate & independent facilities.

2.1.6 *Dr. Tayab Husnain, Head of Center of Excellence for Molecular Biology (CEMB), Lahore, Dr. Naseem Salahuddin, Director Infectious Diseases Indus Hospital, Karachi &*

Prof. Dr. Rizwana Chaudhri, HOD Gynecologist Holy Family Hospital, Rawalpindi attended the 6th CSC meeting, all proposed members were co-opted by the Clinical Studies Committee.

2.1.7. **Decision of 6th CSC meeting:**

All proposed names already approved by the CEO-DRAP are approved by CSC as Co-Opted members.

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

3.1) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, "JINNAH POST GRADUATE MEDICAL CENTER (JPMC)" FOR CLINICAL TRIAL "PREVENTION OF MATERNAL AND 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. 15-33/2019-DD (PS))

3.1.1. Application on Form-I of the Bio-Study Rule 2017 is from Prof. Dr. Khadija Bano, of Department of Obstetrics & Gynecology, Jinnah Postgraduate Medical Center, Karachi, and request has been submitted by Dr. Sarah Saleem, (Principal Investigator of the trial), Professor & Head, Population and Reproductive Health Section, Director, Continuing Education Program, Department of Community Health Sciences, Aga Khan University, Karachi, dated 24th October, 2019, along with fee of Rs.100,000/-, deposited vide challan number 1915788, dated 23rd October, 2019.

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

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached,
2	Prescribed fee	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, whereas applied site is a tertiary care government hospital.
4	Details of premises including layout plan of the site.	A general map and brief details are provided.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	A brief detail is provided regarding equipment & facilities available at Gynae Ward 08 & 09

		of JPMC, Karachi.
6	Names and qualifications of the above sections along with their staff.	A brief detail is provided regarding officers & staff serving in the Gynae Ward 08 & 09 of JPMC, Karachi.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached. Applied site is a tertiary care government hospital
8	Undertaking on stamp paper	Attached.

3.1.3. Submitted for perusal, discussion and consideration & constitution of panel by the CSC.

3.1.4 **Decision of 6th CSC Meeting:-**

The 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 "Azithromycin-Prevention in Labor Use Study (A-PLUS)" Clinical Studies, at Gynae Department of Jinnah Post Graduate Medical Center (JPMC).

3.2) REQUEST FOR APPROVAL OF ACTION TRIAL, CARRIED OUT AT LIAQUAT UNIVERSITY HOSPITAL, JAMSHORO / HYDERABAD. (F.No. 15-30/2019-DD (PS))

3.2.1. Application is from Dr. Mubeen Ahmed Memon, Liaquat University Hospital, Jamshoro / Hyderabad, submitted by Dr. Shabina Ariff (P.I of Action Trial), Assistant Professor, Department of Pediatrics, Aga Khan University, Karachi, dated 10th July, 2019, wherein the application is in reply of this division letter number F.No.3-1/2018-DD (PS), for licensing of their Clinical Trial Site, to conduct Action Trial.

3.2.2. The application is on Form-I of the Bio-Study Rules 2017 without fee.

3.2.3. 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	Remarks

1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached
2	Fee	Processing fee of Rs.100000/- deposited vide deposit slip number 0801286, dated 18th November, 2019.
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, Applied Site is a tertiary care Government Hospital.
4	Details of premises including layout plan of the site.	Layout not provided. Whereas applied Site is a tertiary care Government Hospital.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached. Applied Site is a Government Hospital.
6	Names and qualifications of the above sections along with their staff.	Not provided. Whereas applicant is a Provincial Government Employee.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached. Applied Site is a tertiary care Government Hospital.
8	Undertaking on stamp paper	Attached.

3.2.4. Submitted for perusal, discussion and consideration & constitution of panel by the CSC.

3.2.5. **Decision of 6th CSC Meeting:-**

The 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 "Action Trial" Clinical Studies.

3.3) REQUEST FOR APPROVAL OF ACTION TRIAL, CARRIED OUT AT SHEIKH ZAYED HOSPITAL, RAHIM YAR KHAN. (F.No. 15-31/2019-DD (PS))

3.3.1. Application is from Dr. Ghullam, Sheikh Zayad Hospital, Rahim Yar Khan, submitted by Dr. Shabina Ariff (P.I of Action Trial), Assistant Professor, Department of Pediatrics, Aga Khan University, Karachi, dated 10th July, 2019, wherein the application is in reply of this division letter number F.No.3-1/2018-DD (PS), for licensing of their Clinical Trial Site, to conduct Action Trial.

3.3.2. The application is on Form-I of the Bio-Study Rules 2017 without fee.

3.3.3. 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	Processing fee of Rs.100000/- deposited vide deposit slip number 0801285, dated 18th November, 2019.
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).	Applied Site is a tertiary care hospital & applicant is Provincial Government Servant & M.S. of Government Hospital.

4	Details of premises including layout plan of the site.	Layout of the Sheikh Zayad Hospital is not provided, details are attached. Applied Site is a Government Hospital.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached. Applied Site is a tertiary care Government 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.	Not provided. Applied Site is a tertiary care Government Hospital.
8	Undertaking on stamp paper	Attached.

3.3.4. Submitted for perusal, discussion and consideration & constitution of panel by the CSC.

3.3.5 **Decision of 6th CSC Meeting:-**

The 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 "Action Trial" Clinical Studies.

3.4) APPLICATION FOR LICENSE TO ACT AS BA/BE STUDIES CENTER, AT M/S OLIVE WORLDWIDE (SMC-PVT) LTD. (F.No. 15-32/2019-DD (PS))

3.4.1. 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 BA/BE studies lab at 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 vide challan no.0846242, dated 29th August 2019.

3.4.2. Application evaluated according pre-requisites as mentioned in Form-I of the Bio-Study Rules 2017, and status of application is as follows:

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.	Only layout Attached, details not provided.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	List attached, Only name & number of equipment described. Detailed list is asked from applicant.
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.	List of available services at Wilcare Hospital is attached.
8	Undertaking on stamp paper	Not provided.

3.4.3. Applicant asked to submit required details regarding equipment through letter number F.No. 15-32/2019-DD (PS), dated 11th November 2019, but still response is awaited.

3.4.4. Submitted for perusal, discussion and consideration & constitution of panel by the CSC.

3.4.5 Decision of 6th CSC Meeting:-

The CSC after deliberations decided to conduct the inspection of BA/BE Studies Center 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 expertise from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly.-

i.	Dr. Abdur Rashid
ii.	Prof. Dr. Javaid Akram
iii.	Dr. Masud Ur Rehman
Iv	Prof. Dr. Nadeem Irfan
v	Dr. Farhana Badar

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) 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.

4.1.1. 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.

4.1.2. 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.

4.1.3. 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.

4.1.4. 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.

4.1.5. Application was discussed in the 4th CSC meeting & the CSC decided as follows:

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

4.1.6. Application for "Observational Study Program Assessing Effectiveness And Tolerability Of Gliclazide 60 Mg Modified Release Tablet In Patients With Type-II Diabetes Fasting During Ramadan", discussed in the 5th CSC meeting vide file number (F. No. 03-01/2019) and CSC decided as follows:

Decision of 5thCSC Meeting: -

"The CSC after deliberations deferred the case till inspection of all clinical trial sites & constituted the panel for inspection of remaining two Clinical Trial Sites.

CSC nominated following inspection panel to conduct the inspection of Clinical Trial Sites."

i) Hayatabad Medical Complex (Medical Teaching Institute), Peshawar, will be inspected by following panel:

i.	Muhammad Adnan Faisal Saim
ii.	Dr. Salwa Ahsan
iii.	Dr. Faiza Bashir

ii) Baqai Institute of Diabetes and Endocrinology, Karachi, will be inspected by following panel:-

i.	Prof. Dr. Javed Akram.
ii.	Dr. Najam Us Saqib Additional Director DRAP-Karachi.

4.1.7. Inspection panel constituted in the 5th CSC meeting conducted inspection of the Clinical Trial Site and submitted report with following remarks:

"*The Panel unanimously recommended the site for conducting DiaRamadan study, by keeping in view the potential and tertiary care hospital facilities of the site, as informed & observed during the visit."*

4.1.8. **Concluding status / remarks of inspection panel:**

Recommended for approval

4.1.9. Submitted for perusal discussion and decision of CSC.

4.1.10. **Decision of 6th CSC Meeting:-**

The CSC after deliberations & upon recommendation of inspection panel, decided to approve the Clinical Trial Site, to conduct "Dia-Ramadan Observational Studies", Phase-IV Clinical Trial.

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

4.2.1. 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.

4.2.2. 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	Fee of Rs.100000/- deposited vide challan number 1960636, dated 9th July 2019.
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

	name and address of the company and its directors).	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.

4.2.3. Application was discussed in the 4th CSC meeting & the CSC decided as follows:

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.	Mr. Sajjad Ahmed Abbasi, Area F.I.D

4.2.4. Due to unavailability of area F.I.D, following inspection panel conducted inspection on 1st & 2nd November 2019, which was approved later on by Chairman CSC:

i.	Muhammad Adnan Faisal Saim Deputy Director, Pharmacy Services Division, DRAP-Islamabad.
ii.	Fahad Nadeem, Area ADC

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

The Unit I & II works alternate days. The unit visited, exist in tertiary care Govt: governed public hospital. The training provided by sponsor / P.I. and facility given by hospital as informed & observed during the visit suggest the panel to recommend unanimously, the site for Women trial II only.

4.2.5. **Concluding status / remarks of inspection panel:**

Recommended for approval

4.2.6. Submitted for perusal discussion and decision of CSC.

4.2.7. Decision of 6th CSC Meeting:-

The CSC after deliberations & upon recommendation of inspection panel decided that, as the applied site is a tertiary care Government Hospital, hence decided to approve Unit I & II of the Gynae Unit of the Bolan Medical Complex, Quetta, as Clinical Trial Site, to conduct Women-II Clinical Studies.

4.3) APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE, AT SANDEMAN PROVINCIAL HOSPITAL, QUETTA. F. No.15-35/2019 DD (PS)

4.3.1. Application 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.

4.3.2. 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	Fee of Rs.100000/- deposited vide challan number 1960627, dated 9th July 2019.
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.

4.3.3. Application was discussed in the 4th CSC meeting & the CSC decided as follows:

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.	Mr. Sajjad Ahmed Abbasi, Area F.I.D

4.3.4. Due to unavailability of area F.I.D, following inspection panel conducted inspection on 1st & 2nd November 2019, which was approved later on by Chairman CSC:

i.	Muhammad Adnan Faisal Saim Deputy Director, Pharmacy Services Division, DRAP-Islamabad.
ii.	Fahad Nadeem, Area ADC

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

"Tertiary Care Public Hospital with teaching facilities. Based on the information provided & visited the panel unanimously recommends the Gynae Unit for Women trial II only."

4.3.5. **Concluding status / remarks of inspection panel:**

Recommended for approval

4.3.6. Submitted for perusal discussion and decision of CSC.

4.3.7. **Decision of 6th CSC Meeting:-**

The CSC after deliberations & upon recommendation of inspection panel, decided that as the applied site is a tertiary care Government Hospital, hence decided to approve Unit I & II of the Gynae Unit of the Sandeman Provincial Hospital, Quetta, as Clinical Trial Site, to conduct Women-II Clinical Studies.

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

4.4.1. Application 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, dated 9th July 2019.

4.4.2. 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).	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.

4.4.3. Application was discussed in the 4th CSC meeting & the CSC decided as follows:

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 / replace 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.	Mr. Ziaullah, Area F.I.D

4.4.4. Inspection panel constituted in the 4th CSC meeting conducted inspection of the Clinical Trial Site on 6th December 2019, and submitted report with following remarks:

The team of inspectors, as approved by CSC visited the Gynae Unit (A, B, C) of Ayub Teaching Hospital, a tertiary care facility, was inspected as per protocols of study and ICH guidelines. The team found all systems, protocols up to marks. Human resource, clinicians well trained, storage, distribution of trial medicine were as per ICH-Guidelines. They already had conducted women trial I. Team was satisfied all levels.

4.4.5. **Concluding status / remarks of inspection panel:**

Recommended for approval

4.4.6. Submitted for perusal discussion and decision of CSC.

4.4.7. **Decision of 6th CSC Meeting:-**

The CSC after deliberations & upon recommendation of inspection panel decided that as the applied site is a tertiary care Government Hospital, hence decided

to approve Gynae Unit (A, B, C) of Ayub Teaching Hospital, as Clinical Trial Site, to conduct Women-II Clinical Studies.

4.5) APPLICATION FOR THE LICENSE OF M/S METRICS RESEARCH (PVT) LTD, TO ACT AS CRO, F.NO.03-07/2018-DD (PS).

4.5.1. Application is from Sayed 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).

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

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached
2	Prescribed Fee	Fee of Rs.300000/- paid vide challan number 0843485.
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.	Not provided Applied for CRO.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not provided Applied for CRO.
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 Applied for CRO.

8	Undertaking on Stamp Paper	Attached

4.5.3. Application was discussed in the 3rd CSC meeting & the CSC decided as follows:

Decision of 3rd CSC Meeting:-

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. Ali Jawa
ii.	Prof. Dr. Nadeem Afzal
iii.	Mr. Waqas Latif from UHS as Biostatistician
iv.	Dr. Faiza Bashir
v.	Dr. Masud Ur Rehman (Coordinator)

4.5.5. Letter for inspection issued on 21st June, 2019 to panel members & applicant, but any report regarding inspection not received. So the case was again placed in the 4th CSC meeting and the CSC decided as follows:

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."

4.5.6. Letter for inspection issued on 3rd October, 2019, due to unavailability of nominated panel members, panel coordinator Dr. Masud Ur Rehman, Secretary CSC / Additional Director Pharmacy Services communicated telephonically with Dr. Abdur Rashid, Chairman CSC / Director Pharmacy Services.

4.5.7. Dr. Abdur Rashid, Chairman CSC / Director Pharmacy Services, exercising powers delegated by the CSC nominated following panel members due to unavailability of CSC nominated panel members:

i.	Prof. Dr. Ali Jawa
ii.	Dr. Saif Ur Rehman Khattak, CDL-Karachi

iii.	Dr. Kirshan DRAP, Karachi.
iv.	Dr. Fareeha (PHRC, Karachi)
v.	Dr. Masud Ur Rehman (Coordinator)

4.5.8. Above iinspection panel conducted inspection of the M/s Matrics Research Pvt Ltd, Karachi for CRO on 21/10/2019, and submitted report with following remarks:

"Fair enough to contact, record, maintain data and protect the data. Has experts Human Resource, who had been in Clinical Trials. To augment & bring Clinical Research in Pakistan, CRO will play a significant role. Material, Protocols, SOPs up to qualifying position as CRO under Bio-Study Rules 2017."

4.5.9. **Concluding status / remarks of inspection panel:**

Recommended for approval

4.5.10. Submitted for perusal discussion and decision of CSC.

4.5.11. **Decision of 6th CSC Meeting:-**

The CSC after deliberations & upon recommendation of inspection panel unanimously approved the M/s Metrics Research (Private) Ltd., Plot No. 23-C, 3rd Floor, Old Sunset Boulevard, DHA Phase-II, Karachi, to act as a Contract Research Organization (CRO), under the Bio Study Rules 2017.

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

4.6.1 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.

4.6.2. 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:

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Not Provided
2	Prescribed 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).	Attached
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.
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.	Not provided.
8	Undertaking on Stamp Paper	Not provided.

4.6.3. **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.

4.6.4. The firm repeatedly informed regarding shortcomings, last reminder issued on 13th November, 2019, but still response is awaited.

4.6.5. 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.

4.6.6. The case was discussed in the 4th CSC meeting & the CSC decided as follows:

Decision of 4th CSC Meeting:-

The CSC after deliberations deferred the case.

4.6.7. Submitted for perusal discussion and decision for rejection by the CSC.

4.6.8. **Decision of 6th CSC Meeting:-**

The CSC after deliberations based on mentioned shortcomings & lack of response from the firm, despite many reminders decided to reject the application.

4.7) APPLICATION FROM M/S DIMENSION RESEARCH FOR GRANT OF LICENSE TO ACT AS CRO. F. No.11-2/2018 DD (PS)

4.7.1. Application 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 licensing of their company with DRAP to work as Clinical Research Organization (CRO) and for management service provider for Clinical Trial Sites, Fee amount of Rs. 100000/- is provided vide Challan No.0781309 dated 03.08.2018, & remaining amount of Rs.200000/- deposited vide challan no. 1945214 dated 08.07.2019

4.7.2. Application evaluated according pre-requisites as mentioned in Form-I of the Bio-Study Rules 2017, and following shortcoming observed:

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached
2	Fee	Attached
3	Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).	Attached
4	Details of premises including layout plan of the site.	Not Provided. As per reply Not applicable for the services they are

		offering.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not Provided. As per reply Not applicable for the services they are offering.
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. As per reply Not applicable for the services they are offering.
8	Undertaking on stamp paper	Attached

4.7.3. Application was discussed in the 4th CSC meeting & the CSC decided as follows:

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 / replace 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

4.7.4. Inspection panel constituted in the 4th CSC meeting conducted inspection of the Clinical Trial Site on 9th October 2019, Dr. Ali Jawa informed that Prof. Nisar Hussain was with him on the inspection site at the same time, whereas Dr. Najam Us Saquib was not present there when they inspected the site and due to their flight they returned from the site at about 2:00 PM.

4.7.5. Dr. Najam Us Saquib informed that when he reached the inspection site Dr. Ali Jawa & Prof. Nisar Hussain leave the site after inspection due to their flight, afterwards he inspected the site and forwarded signed report for signature of other members.

4.7.6. Dr. Ali Jawa sent his separate signed inspection report by courier, Prof. Nisar Hussain submitted his separate signed inspection report by courier.

4.7.7. Dr. Najam Us Saquib sent inspection report duly signed by Prof. Nisar Hussain Shah, Dr. Ali Jawa & Dr. Najam Us Saqib on 7th November 2019.

4.7.8. **Concluding status / remarks of inspection panel:**

Recommended for approval

4.7.9. Submitted for perusal discussion and decision of CSC.

4.7.10. **Decision of 6th CSC Meeting:-**

The CSC after deliberations & upon recommendation of inspection panel unanimously approved the M/s M/s Dimension Research CRO & SMO, Gulistan-e-Jauhar, Scheme-36, Karachi, to act as a Contract Research Organization (CRO), under the Bio Study Rules 2017.

4.8) APPLICATION FROM M/S PHARMA PROFESSIONAL SERVICES (PVT) LTD, FOR THE LICENCE TO ACT AS CLINICAL TRIAL SITE. (F.No.15-4/2019 DD (PS)).

4.8.1 Application is from Prof. Dr. Tasneem Ahmed, CEO, Pharma Professional Services (Pvt.) Ltd, A-93 Ettawah society, Ahsanabad, [near Gulshan-e-Maymar], Gadap Town, Karachi, wherein the request has been made to register their site with DRAP as clinical trial site dated l5d, January,2019.

4.8.2. Application evaluated according pre-requisites as mentioned in 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	Attached

	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.	Attached
4	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached
5	Names and qualifications of the above sections along with their staff.	Attached
6	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached
7	Affidavit on Stamp paper	Attached
8	Prescribed Fee	Only Rs.20000/- submitted for both Clinical Trial Site & BA/BE Studies Center.

4.8.3. After evaluation observations were communicated as per prerequisites of prescribed Form-I of the Bio-study Rules 2017 on 23-01-2019. The firm accordingly on 26th January, 2019 has submitted the application on Form-I, duly stamped and signed along with undertaking and fee.

4.8.4. Application was discussed in the 3rd CSC meeting & the CSC decided as follows:

Decision of 3rd CSC Meeting:-

The CSC after deliberations decided to conduct the inspection of Site 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 relevant 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:-

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

4.8.5. Letter for inspection issued on 8th July, 2019 to panel members & applicant, but any report regarding inspection not yet received.

4.8.6. Applicant vide letter number nil, dated 6th August 2019, requested for withdrawal of Application for license of Clinical Trial Center.

4.8.7. Submitted for perusal discussion and decision for rejection by the CSC.

4.8.8. **Decision of 6th CSC Meeting:-**

The CSC after deliberations based on mentioned shortcomings & upon request of applicant/firm decided to approve withdrawal of application.

4.9) APPLICATION FROM SHIFA CLINICAL RESEARCH CENTER (SCRC), SHIFA INTERNATIONAL HOSPITAL LTD, ISLAMABAD FOR GRANT OF NEW LICENSE FOR CLINICAL TRIAL SITE. (F.No.15-14/2019 DD (PS))

4.9.1. 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.

4.9.2. Application evaluated according pre-requisites as mentioned in 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).	Attached
3	Details of premises including layout plan of the site.	Layout plan 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 for only Obstetrics & Gynecology section.
6	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Not provided. Applied site is a Tertiary Care Private Hospital.
7	Affidavit on Stamp paper	Attached
8	Fee	Fee of Rs.100000/- submitted vide Challan Number 1943309, dated 15 May 2019.

4.9.3. Application was discussed in the 4th CSC meeting & the CSC decided as follows:

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

4.9.5. Dr. Abdur Rashid, Chairman CSC / Director Pharmacy Services and panel coordinator has been decided to conduct inspection on 23rd September, 2019 and directed Shafqat Hussain Danish, Assistant Director, Pharmacy Services to assist him in this inspection, afterward Chairman CSC, exercising powers delegated by the CSC included Shafqat Hussain Danish in the panel for inspection, and following panel inspected M/s Shifa International Hospital, Islamabad and submitted duly signed inspection report with following remarks:

i.	Dr. Abdur Rashid
ii.	Dr. Farhana Badar
iii.	Dr. Gul Majeed
iv.	Dr. Rizwana Choudhry
v.	Shafqat Hussain Danish

"Keeping in the view the human resource, technical expertise, documentation, safety measures, record archive, training of working personnel and other related space / facilities, panel recommends the Shifa International Hospital as Clinical Trial Site."

4.9.6. **Concluding status / remarks of inspection panel:**

Recommended for approval

4.9.7. Submitted for perusal discussion and decision of CSC.

4.9.8. **Decision of 6th CSC Meeting:-**

The CSC after deliberations & upon recommendation of inspection panel decided that, as the applied site is a tertiary care Private Hospital, hence decided to approve Shifa Clinical Research Center (SCRC), Shifa International Hospital Ltd, Islamabad, as Clinical Trial Site, to conduct* "Perioperative Ischemic Evaluation-3" (Poise-3) *Clinical Studies.

4.10) **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.**

4.10.1. 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.

4.10.2. 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.

4.10.3. 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	Not provided.

	along with their staff.	
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.

4.10.4. 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.

4.10.5. Application was discussed in the 4th CSC meeting & the CSC decided as follows:

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.	Najam Us Saqib
ii.	Dr. Mehboob Rabbani
iii.	Dr. Saif Ur Rehman Khattak

4.10.6. Application for "Observational Study Program Assessing Effectiveness And Tolerability Of Gliclazide 60 Mg Modified Release Tablet In Patients With Type-II Diabetes Fasting During Ramadan", discussed in the 5th CSC meeting vide file number (F. No. 03-01/2019) and CSC decided as follows:

Decision of 5thCSC Meeting: -

"The CSC after deliberations deferred the case till inspection of all clinical trial sites & constituted the panel for inspection of remaining two Clinical Trial Sites.

CSC nominated following inspection panel to conduct the inspection of Clinical Trial Sites."

i) Hayatabad Medical Complex (Medical Teaching Institute), Peshawar, will be inspected by following panel:

i.	Muhammad Adnan Faisal Saim
ii.	Dr. Salwa Ahsan
iii.	Dr. Faiza Bashir

ii) Baqai Institute of Diabetes and Endocrinology, Karachi, will be inspected by following panel:-

iii.	Prof. Dr. Javed Akram.
iv.	Dr. Najam Us Saqib Additional Director DRAP-Karachi.

4.10.7. Accordingly inspection of Baqai Institute of Diabetes and Endocrinology, Karachi conducted on 24th September, 2019 and panel inspection report with following remarks & recommendations:

i. -80°C freezer was out of order and undertaking has been taken from HOD Laboratory Dr. Rubina Sabir.
ii. Janitorial services was compromised. It was communicated to staff to improve the condition immediately.
iii. Infrastructure interior is compromised with overcrowding, unsafe electrical conduits and deficient in greenery/open spaces. The management is advised to improve the situation within 3 months.
iv. Equipment calibration record of laboratory to be made digital and updated.

"In view of patient load in outpatient and in-patient and available human resource along with the experience of the conducting clinical studies it is recommended that the study site under consideration be approved for observational/phase 3 and phase 4 clinical; trials pertaining to diabetes and endocrinology after obtaining an undertaking from BIDE Director that the observations mentioned above shall be addressed within the stipulated time"

4.10.8. **Concluding status / remarks of inspection panel:**

Recommended for approval

4.10.9. Submitted for perusal discussion and decision of CSC.

4.10.10. **Decision of 6th CSC Meeting:-**

The CSC after deliberations & upon recommendation of inspection panel decided to approve the Clinical Trial Site, to conduct "Dia-Ramadan Observational Studies", Phase-IV Clinical Trial.

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

4.11.1. Application 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.

4.11.2. 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).	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.

4.11.3. Application was discussed in the 4th CSC meeting & the CSC decided as follows:

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. Additional Director, DRAP- Karachi
ii.	Area F.I.D

4.11.4. Nominated inspection panel conducted inspection of the Koohi Goth Women Hospital, Karachi, on 5th December 2019 and submitted report with following remarks:

"M/s Koohi Goth Women Hospital, Karachi was inspected on 05th December 2019 by the panel constituted as per DRAP letter No. F.15-28/2019-DD (PS) dated 13th October 2019 for the license to act as Clinical Trial Site for Women-II trial.

The premises of above mentioned area was visited and related documents were reviewed. ***The Panel is of opinion to recommend the facility as clinical trial site for Women-II Trial only.***

During inspection management of M/s Koohi Goth Women Hospital exhibited their interest towards further establishment of Clinical Trial Site. The hospital was established in 2006, located in the Deh Landhi area on a piece of land owned by Atia and Zafar Foundation Charitable Trust, a non-profit organization. Today, the hospital serves as a sole provider of

health care facilities to millions of unprivileged patients coming from Balochistan, Khyber Pakhtunkhwa, Punjab and interior Sindh.

The hospital is actively working towards elimination of gynaecological complications especially Retrovaginal fistula and vesicovaginal fistula. Furthermore, nursing and mid-wife education and trainings are also provided to the people who haven't any access to attain quality education due to financial constraints."

4.11.5. **Concluding status / remarks of inspection panel:**

Recommended for approval

4.11.6. Submitted for perusal discussion and decision of CSC.

4.11.7. **Decision of 6th CSC Meeting:-**

The CSC after deliberations & upon recommendation of inspection panel decided to approve the Clinical Trial Site, to conduct Women-II Clinical Studies.

4.12) APPLICATION FOR THE LICENSE OF THE CENTER FOR BIOEQUVALANCE STUDIES AND CLINICAL RESEARCH (CBSCR) FOR BA/BE SITE, AT INTERNATIONAL CENTER FOR CHEMICAL AND BIOLOGICAL SCIENCES (ICCBS), UNIVERSITY OF KARACHI. F. No.15-7/2019 DD (PS)

4.12.1. 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 along without fee, which may be paid/ asked after notification.

4.12.2. Application evaluated according pre-requisites as mentioned in Form-I of the Bio-Study Rules 2017, and following shortcoming observed:

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached
2	Prescribed 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 Provincial Government organization working under the University of Karachi, No evidence provided for its legal status.

4	Details of premises including layout plan of the site.	Layout of ground & 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
8	Undertaking on stamp paper	Attached

4.12.3. Application was discussed in the 3rd CSC meeting & the CSC decided as follows:

Decision of 3rd CSC Meeting:-

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 Ahsan
iii.	Prof. Dr. Nadeem Afzal
iv.	Dr. Farhana Badar
v.	Dr. Abdur Rashid (Coordinator)

4.12.4. Inspection panel conducted the inspection & inspection report placed before CSC in its 4th meeting, with recommendations **"Recommended for provisional approval for improvements**", after discussion CSC in its 4th meeting decided as follows:

Decision of 4th CSC Meeting:-

Deferred for re-inspection of BA/BE Site.

4.12.5. Inspection letter issued on 8th October 2019, due to unavailability of nominated panel members Chairman CSC / Director Pharmacy Services exercising powers delegated by the CSC substituted & nominated following panel members for inspection:

i.	Prof. Dr. Javed Akram
ii.	Mr. Waqas Latif
iii.	Prof. Dr. Nadeem Afzal
iv.	Dr. Saif Ur Rehman
v.	Dr. Abdur Rashid (Coordinator)

4.12.6. Due to unavailability of nominated panel members Chairman CSC / Director Pharmacy Services exercising powers delegated by the CSC added following panel members for inspection & letter issued on 3rd December 2019:

i.	Dr. Najam Us Saquib, Additional Director DRAP-Karachi.
ii.	Prof Nisar Ahmed, Bahauddin Zakariya University, Multan.

4.12.7. Following inspection panel reconstituted by the Chairman CSC, due to unavailability of nominated panel members:

i.	Prof. Dr. Javed Akram
ii.	Prof Nisar Ahmed, Bahauddin Zakariya University, Multan.
iii.	Dr. Najam Us Saquib, Additional Director DRAP-Karachi.
iv.	Dr. Saif Ur Rehman
v.	Dr. Abdur Rashid **(Coordinator)**

4.12.8. The panel conducted inspection of CRO on 15th, 16th & 22nd November 2019 and submitted its report with following remarks:

"Keeping in view the premises technical personnel expertize, documentations, SOPs and other facilities, recommends for BA/BE"

4.12.9. **Concluding status / remarks of inspection panel:**

Recommended for approval

4.12.10. Submitted for perusal discussion and decision of CSC.

4.12.11. **Decision of 6th CSC Meeting:-**

i. The CSC after deliberations & upon recommendation of inspection panel decided to approve the M/s Center for Bioequivalence Studies and Clinical Research (CBSCR), At International Center for Chemical and Biological Sciences (ICCBS), University Of Karachi, Karachi as BA/BE Studies Center, under the Bio Study Rules 2017.

ii. During discussing the cases regarding BA/BE Studies Centres, Chainman CSC informed that DRAP hired a consultant Mr Sultan Ghani, who is working on international standards of BA/BE Studies Centres, after formulation, submission & implementation of the new guidelines for BA/BE Studies Centres than all BA/BE Studies Centres will be reviewed according to new guidelines by Mr Sultan Ghani.

4.13) APPLICATION FOR THE LICENSE OF THE CENTER FOR BIOEQUVALANCE STUDIES AND CLINICAL RESEARCH (CBSCR) FOR CRO AT INTERNATIONAL CENTER FOR CHEMICAL AND BIOLOGICAL SCIENCES (ICCBS), UNIVERSITY OF KARACHI. F. No.15-06/2019 DD (PS).

4.13.1. 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 Contract Research Organization (CRO), the application is on prescribed Form-I of the Bio-Study Rules 2017 along without fee, which may be paid/ asked after notification.

4.13.2. Application evaluated according pre-requisites as mentioned in Form-I of the Bio-Study Rules 2017, and following shortcoming observed:

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached
2	Prescribed 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	It's a Government organization working under the University

	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).	of Karachi, No evidence provided for its legal status.
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.	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 Provided

4.13.3. The firm informed regarding following shortcomings through letter no.F.No.15-06/2019 DD (PS), dated 8th July, 2019.

4.13.4. Application was discussed in the 3rd CSC meeting & the CSC decided as follows:

Decision of 3rd CSC Meeting:-

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. Salva Ahsan
iii.	Prof. Dr. Nadeem Afzal
iv.	Dr. Farhana Badar

v.	Dr. Abdur Rashid (Coordinator)

4.13.5. Letter for inspection issued on 21st June, 2019 to panel members & applicant, but any report regarding inspection not yet received, reminder letter for inspection issued on 14th November, 2019 but still inspection report awaited.

4.13.6. Following inspection panel reconstituted by the Chairman CSC, due to unavailability of nominated panel members:

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

4.13.7. The panel conducted inspection of CRO on 15th, 16th & 22nd November 2019 and submitted its report with following remarks:

"Keeping in view the premises, human resource, integrity, IT System, expertize, SOPs and other facilities, panel recommends the approval of CRO, HEJ Karachi."

4.13.8. **Concluding status / remarks of inspection panel:**

Recommended for approval

4.13.9. Submitted for perusal discussion and decision of CSC.

4.13.10. **Decision of 6th CSC Meeting:-**

The CSC after deliberations & upon recommendation of inspection panel decided to approve the M/s Center for Bioequivalence Studies and Clinical Research (CBSCR), At International Center for Chemical and Biological Sciences (ICCBS), University Of Karachi, Karachi as Contract Research Organization (CRO), under the Bio Study Rules 2017.

AGENDA ITEM - V: **REGISTRATION OF CLINICAL TRIAL & BA/BE STUDIES UNDER THE BIO STUDY RULES, 2017. (Ongoing cases)**

5.1) **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).**

5.1.1. 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 Centre (DMC) and Jinnah Post Graduate Medical Centre (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.

5.1.2. 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.

5.1.3. 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-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	Attached

	material.	
9	Site of the trial	The Indus Hospital. 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 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 centre.	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

5.1.4. 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:

S. No	International Nonproprietary Names (INN) for Pharmaceutical Products	Manufacturer	Country of origin	Shelf life (months)	Total Quantity
	Investigational Medicinal Products (IP) TB Drugs				
1	AMIKACIN sulfate, eq. 250 mg/ml base, 2 ml, amp.	**MEDOCHEMIE**	CYPRUS	48	1200
2	BEDAQUILINE, 100 mg, tab.	**JANSSEN**	BELGIUM	36	27833
3	CLOFAZIMINE, 100 mg, soft caps.	**NOVARTIS**	SWITZERLAND /FRANCE	60	28350
4	CYCLOSERINE 250 mg caps.	**MACLEODS**	INDIA	36	23100
5	DELAMANID, 50mg, tab., blister	**OTSUKA**	GERMANY	60	71971
6	ETHIONAMIDE, 250 mg, tab., blister	**MACLEODS**	INDIA	48	10290
7	LEVOFLOXACIN hemihydrates, eq. 250 mg base, tab.	**HETERO**	SPAIN	36	8400
8	LEVOFLOXACIN hemihydrates, eq. 500 mg base, tab.	**MACLEODS**	INDIA	48	38115
9	LINEZOLID, 600 mg, coated tab.	**HETERO**	INDIA	36	28245
10	MOXIFLOXACIN hydrochloride eq. to 400 mg base , tab.	**HETERO**	INDIA	36	12322
11	PARA-AMINOSALICYLIC acid (PAS),del.rel.gran, 4g, sach.(25°C)	**JACOBUS**	US	24	2583
12	ETHAMBUTOL hydrochloride (E), eq. 400	**MACLEODS**	INDIA	36	11550

	mg base, tab. blister				
13	ISONIAZID (H), 300 mg, tab., blister	**MACLEODS**	INDIA	36	3150
14	PYRAZINAMIDE (PZA), 400 mg, tab., blister	**MACLEODS**	INDIA	48	132653
	Ancillary medicines				
1	AMITRIPTYLINE hydrochloride, 25 mg, tab.	**REMEDICA LTD**	CYPRUS	60	4000
2	BECLOMETASONE dipropionate, 0.10mg/puff, 200 puffs,aerosol	**LABORATORIO ALDO-UNION S.L.**	SPAIN	36	8
3	TRIHEXYPHENIDYL hydrochloride, 2 mg, tab.	**REMEDICA LTD**	CYPRUS	60	100
4	CARBAMAZEPINE, 200 mg, tab.	**MEDOCHEMIE**	CYPRUS	60	1000
5	CHLORPHENAMINE maleate, 4 mg, tab.	**CADILA**	INDIA	48	2000
6	FLUOXETINE, 20mg, caps.	**MYLAN**	FRANCE	48	900
7	HALOPERIDOL, 5 mg, tab.	**REMEDICA LTD**	CYPRUS	60	1500
8	IBUPROFEN, 400 mg, tab.	**REMEDICA LTD**	CYPRUS	60	16000
9	LEVOTHYROXINE SODIUM, 0.025 mg, tab.	**MERCURY PHARMACEUTICALS LTD**	UK	24	5376
10	LOPERAMIDE hydrochloride, 2 mg, tab.	**REMEDICA LTD**	CYPRUS	60	1000
11	MAGNESIUM OXIDE 270 mg, eq. to 150 mg Magnesium, efferv. tab	**ARROW GENERIQUE**	FRANCE	36	8940
12	METOCLOPRAMIDE hydrochloride anhydrous,	**REMEDICA LTD**	CYPRUS	60	1000

	10 mg, tab.				
13	OMEPRAZOLE 20 mg, enteric caps.	**MEDOCHEMIE**	CYPRUS	36	3752
14	ONDANSETRON hydrochloride, eq. 8 mg base, tab.	**PLIVA**	UK	60	60
15	PARACETAMOL (acetaminophen), 500 mg, tab.	**REMEDICA LTD**	CYPRUS	60	16000
16	POTASSIUM chloride, 600 mg, sustained release tab.	**LABORATOIRE LEO**	FRANCE	60	44700
17	PREDNISOLONE, 5mg, tab.	**REMEDICA LTD**	CYPRUS	36	1000
18	PROMETHAZINE hydrochloride, eq. 25 mg base, tab.	**REMEDICA LTD (CY)**	CYPRUS	60	1000
19	PYRIDOXINE hydrochloride (vitamin B6), 50 mg tab.	**MACLEODS**	INDIA	24	268000
20	RISPERIDONE, 1 mg, tab.	**REMEDICA LTD**	CYPRUS	36	540
21	SULBUTAMOL sulfate, eq.0.1mg base/puff, 200 puffs, inhaler	**LABORATORIO ALDO-UNION S.L.**	SPAIN	36	108
22	CLOTRIMAZOLE, 500 mg, vaginal tab. + applicator	**REMEDICA LTD**	CYPRUS	36	45
23	MICONAZOL nitrate, 2%, cream, 30 g, tube	**MEDOCHYME**	CYPRUS	36	10
24	EPOETIN ALFA 10000 IU/ml, 1ml, syringe	**JANSEEN**	FRANCE	18	144
25	MEGNESIUM sulfate, 0.5 g/ml, 10ml, vial.	**AURUM PHARMACEUTI**	UK	36	420

		CALS			
26	POTASSIUM chloride 100 mg/ml, 10 ml amp.	**AGUETTANT LABORATOIRE**	FRANCE	36	850
27	SODIUM chloride, 0.9%, 250 ml, plastic pouch.	**BAXTER S.L.**	SPAIN	24	750
28	VALPROATE SODIUM, 500 mg, enteric coated tab.	**SANOFI**	UK	36	600
29	WATER for injection, 10ml, plastic amp	**B.BRAUN**	GERMANY	36	10700

5.1.5. The case was discussed in the 4th CSC meeting, where Dr. Mehrun Nisa Hameed, representative from The Indus Hospital, delivered the presentation of the endTB Clinical Studies before CSC in the 4th CSC meeting. 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. After discussion

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

The CSC after deliberations 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.

5.1.7. Applicant provided the required data, and Secretary CSC sent it to Prof. Brig. (R), Muzammil Hassan Najmi, expert member of the CSC.

5.1.8. Prof. Brig. (R), Muzammil Hassan Najmi, expert member of the CSC submitted his reply through letter number FF/FUMC/PF/501, dated 05th August, 2019, as follows:

EXPERT OPINION

i) Evaluation of data of phase-2 and phase-3 clinical trials provided by the Indus Hospital reveals that the newer anti tuberculosis drugs i.e. delamanid and bedaquiline have been used in these trials with reasonable degree of safety.

ii) However, WHO has advised the national TB programmes and other stakeholders to only add delamanid to a longer MDR-TB regimen when it cannot be composed according to WHO recommendations. When an effective and well tolerated longer MDR-TB regimen can be otherwise composed, the addition of delamanid may not be warranted. Use of delamanid may not be warranted. Use of delamanid in the shorter MDR-TB regimen under programmatic conditions is not recommended by WHO given the lack of data.

iii) Bedaquiline was approved for medical use in the United States in 2012. It is on the World Health Organization's List of Essential Medicines, the most effective and safe medicines needed in a health system. However, there is considerable controversy over the approval for the drug, as one of the largest studies to date had more deaths in the group receiving bedaquiline than those receiving placebo. Serious side effects include QT prolongation, liver dysfunction, and an increased risk of death. While harm during pregnancy has not been well studied in this population.

iv) In view of above, it is recommended that the Phase-3 trial may be conducted according to the above recommendations and after explaining the facts elaborately to the participants before taking the consent.

5.1.9. Application along with report of expert member discussed in the 5th CSC meeting, CSC discussed in the 5th CSC Meeting that the drugs used in this trial are Category C drugs and data regarding medicines safety profile asked, if any data available on animal / human. The use of these drugs in women of child-bearing age will require the investigators to ensure compliance of contraception, and even after contraception if pregnancy sustains, pregnant women and lactating mothers excluded from the study.

5.1.10. Decision of 5thCSC Meeting: -

"The CSC after deliberations approved the endTB Clinical Studies subject to following conditions:

i) Females recruited in the study will be briefed to use contraception and have consultation to avoid pregnancy during the duration of the trial.

ii) Even after contraception if the pregnancy sustains the subject will be considered as dropout or excluded from the study.

5.1.11. Decision of the 5th CSC meeting communicated to the applicant vide letter number F.No.03-04/2019 DD (PS), dated 20th August 2019.

5.1.12 Applicant submitted their reply vide letter number nil, dated 21st August 2019 and explained their reservations about CSC decision and conditions applied by CSC on their clinical trial, and requested for personal hearing.

5.1.13. Secretary CSC / Chairman CSC approved the request of applicant and invitation letter for personal hearing communicated vide letter number F.No.03-04/2019 DD (PS), dated 3rd January 2020.

5.1.14. Dr. Uzma Khan, Co-Principal Investigator & Director IRD, present before CSC for personal hearing and described the Clinical Studies.

5.1.15. Submitted for perusal discussion and decision of CSC.

5.1.16. **Decision of 6thCSC Meeting:** -

"The CSC after deliberations approved the endTB Clinical Studies, to be conducted at Ghauri Clinic of the Indus Hospital, Karachi, subject to following conditions:

i) Females recruited in the study will be briefed to use contraception and strong measure for contraception will be arranged.

ii) Even after contraception if the pregnancy sustains the subject will be asked again for their consent.

5.2) 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.

5.2.1. 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.

5.2.2. 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.

5.2.3. 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

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

5.2.5. After initial evaluation details of the submitted documents is 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 &	Locally manufactured & registered product will be used in the trial.

	Export) Rules, 1976 and application for import of trial material.	
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)	Attached.
12	CV's of the Investigators	i- Prof. Dr. Mohammad Aamir (PI), Shifa Int. Hospital Ltd, Islamabad.(Site#520) ii- 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.	Attached.
23	Duration of trial	48 Months
24	Undertaking on stamp paper	Attached.

5.2.6. 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.

5.2.7. Application discussed in the 4th CSC meeting, and the CSC decided as follows:

Decision of 4th CSC Meeting:-

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

5.2.8. It is pertinent to mention here that this is a multicounty trail, whereas Investigational Medicinal Product of different origins, as informed by the sponsor.

5.2.9. Prof. Dr. Muhammad Aamir, Consultant General Surgery, Shifa International Hospital, present before CSC & described the Clinical Studies.

5.2.10. Submitted for perusal discussion and decision of CSC.

5.2.11. **Decision of 6thCSC Meeting: -**

"The CSC after deliberations approved the Clinical Studies Perioperative Ischemic Evaluation-3 (POISE-3), to be conducted at Shifa Clinical Research Center (SCRC) of Shifa International Hospital, Islamabad & Clinical Trial Unit of Aga Khan University Hospital, Karachi.

5.3) <u>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).</u>

5.3.1 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.

5.3.2. 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

5.3.3. 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

5.3.4. 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.

5.3.5. Application discussed in the 4th CSC meeting, and the CSC decided as follows:

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.

5.3.6. The firm replied vide letter number nil dated 05th July 2019 & informed that they want to withdraw their application.

5.3.7. Submitted for perusal discussion and decision for rejection by the CSC.

5.3.8. **Decision of 6th CSC Meeting:-**

The CSC after deliberations based on mentioned shortcomings & upon request of applicant/firm, decided to approve withdrawal application.

5.4) 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))

5.4.1 Application is from Prof. Dr. Sarah Saleem, Principle Investigator of subject (A-PLUS) clinical 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 dated 24th May 2019 & Rs.150000/- deposited vide challan no.1915787 dated 28th October 2019.

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

5.4.3. 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.

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached
2	Fee	Rs.50000/- deposited vide challan no.1943654 dated 24th May 2019 & Rs.150000/- deposited vide challan no.1915787 dated 28th October 2019.
3	Investigator Brochure (s)	Attached
4	Final protocol	Attached
5	Informed consent and participant	Attached

	information sheet (Urdu to English)	
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 received but not approved yet. *Application is included in agenda for constitution for panel inspection.
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.	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 enrolled in each center.	4250
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	Attached.

	investigational product / drug.	
22	Duration of trial	36 Months
23	Undertaking on Stamp paper	Attached.

5.4.5. Application discussed in the 4th CSC meeting, Dr. Saleem Jessani on behalf of the P.I presented the Studies before the CSC and the CSC decided as follows:

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.

5.4.8. Dr. Sarah Saleem & Dr. Saleem Jessani of Aga Khan University Hospital Karachi, (Principle Investigator & Co- Principle Investigator of the subject clinical studies), present before CSC, and answered the questions asked by the CSC members regarding the trial and briefed regarding the trial.

5.4.9. Submitted for perusal discussion and decision of CSC.

5.4.10. **Decision of 6thCSC Meeting: -**

"The CSC after deliberations approved the Clinical Studies "Prevention of Maternal & Neonatal Death/Infections with a Single Oral Dose of 2gms Azithromycin in Women in Labor (In Low & Middle Income Countries) (A-PLUS Clinical Studies), to be conducted at Gynae Department of Jinnah Post Graduate Medical Center (JPMC), Karachi, subject to following conditions:

i) Principal Investigator requested to provide data regarding "Maximum Toxic Concentration"

ii) Strong system for Pharmacovigilance & Activities regarding Antimicrobial Resistance (AMR) will be developed before starting the trial

iii) Activities regarding Antimicrobial Resistance (AMR) & ADR data will be managed carefully & shared periodically with Division of Pharmacy Services DRAP.

5.5) **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).**

5.5.1. 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 Hospital and Medical Center, Lahore.

iii) Akram Medical Complex, Lahore.

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

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

5.5.2. 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	Fee of Rs.200000/- deposited vide challan number 0550704, dated 23rd May 2019.
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 Hospital& Medical Centre, Lahore. 3. Akram Medical Complex, 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 yr Exten+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 centre	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	Attached.

5.5.3. 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)

5.5.4. Application discussed in the 4th & 5th CSC meeting and the CSC decided as follows:

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.

5.5.5. Dr. Aatif Mirza, President Clinical Operations, M/s DRK Pharma Solutions, Lahore, presented the case before CSC in its 5th meeting on behalf of applicant, and the CSC decided as follows:

Decision of 5thCSC Meeting: -

"The CSC after deliberations deferred the case till inspection of all clinical trial sites & constituted the panel for inspection of remaining two Clinical Trial Sites.

CSC nominated following inspection panel to conduct the inspection of Clinical Trial Sites."

***i) Hayatabad Medical Complex** (Medical Teaching Institute), Peshawar, will be inspected by following panel:*

i.	Muhammad Adnan Faisal Saim
ii.	Dr. Salwa Ahsan
iii.	Dr. Faiza Bashir

***ii) Baqai Institute of Diabetes and Endocrinology, Karachi,** will be inspected by following panel:-*

v.	Prof. Dr. Javed Akram.
vi.	Dr. Najam Us Saqib Additional Director DRAP-Karachi.

5.5.6. Letter from Dr. Ahmed Atif Mirza, President Clinical Operations, M/s DRK Pharma Solutions (Pvt) Ltd, Lahore, received in which "Closeout Report for OBSERVATIONAL STUDY PROGRAMME ASSESSING EFFECTIVENESS AND TOLERABILITY OF GLICLAZIDE 60mg MODIFIED RELEASE TABLET IN PATIENTS WITH TYPE-II DIABETES FASTING DURING RAMADAN" is attached, and trial closeout summery is also provided.

5.5.7. It is submitted that the application was discussed in 2nd, 3rd, 4th, & 5th CSC meeting but not approved yet. Whereas applicant conducted the trial without prior approval from DRAP, that is violation of rule 14 (1) & (2) of the Bio-Study rules 2017.

5.5.8. Submitted for perusal discussion and decision of CSC.

5.5.9. **Decision of 6thCSC Meeting: -**

"The CSC after deliberations approved the "Observational Study Program Assessing Effectiveness And Tolerability Of Gliclazide 60 Mg Modified Release Tablet In Patients With Type-Ii Diabetes Fasting During Ramadan", to be conducted at following Clinical Trial Sites:

i) **Baqai Institute of Diabetes and Endocrinology, Karachi.**

ii) **National Hospital and Medical Center, Lahore.**

iii) **Akram Medical Complex, Lahore.**

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

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

5.6) 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).

5.6.1. 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).

5.6.2. 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	Not provided & claimed

	associate	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

5.6.3. **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.

5.6.4. Application discussed in the 3rd CSC meeting and the CSC decided as follows:

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.

5.6.5. 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.

5.6.6. Application again discussed in the 4th CSC meeting and the CSC decided as follows:

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.

5.6.7. The firm informed 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 terminating the project and will not conduct the said studies & want to withdraw their application.

5.6.8. Submitted for perusal discussion and decision for rejection by the CSC.

5.6.9. **Decision of 6th CSC Meeting:-**

The CSC after deliberations based on mentioned shortcomings & upon request of applicant/firm, decided to approve the withdrawal application.

5.7) REGULATORY APPROVAL FOR SCYNEXIS PROTOCOL NUMBER SCY-078-305, OPEN-LABEL STUDY TO EVALUATE THE EFFICACY, SAFETY, TOLERABILITY AND PHARMACOKINETICS OF SCY 078 (IBREXAFUNGERP) IN PATIENTS WITH CANDIDIASIS INCLUDING CANDIDEMIA, CAUSED BY CANDIDA AURIS. F. No.03-15/2019-DD (PS)

5.7.1 Application is from Dr. Faisal Mahmood, Associate Professor and Sec: Head Medicine, Aga Khan University, Karachi dated 08th October, 2019, wherein request has been made for registration & approval of subject clinical trial, which will be carried out at Aga Khan University Hospital, Karachi. Application is on prescribed Form-II, along with a fee of Rs.200,000/- deposited vide challan no.1963578.

5.7.2. This is a multicenter, open-label, non-comparator, single-arm study to evaluate the efficacy, safety, tolerability and PK (pharmacokinetics) of oral SCY-078 as an emergency use treatment for patients with a documented Candida Auris infection as per available record on U.S National Trial Registry with identification number **NCT03363841** (Page 328-334/corr.)**,** and as per the registry there are 5 locations globally, details of location is as follows:

United States, New Jersey

I. Scynexis, Inc. **Recruiting**
Jersey City, New Jersey, United States, 07302
Contact: David Angulo, MD 201-884-5471 david.angulo@scynexis.com

India

II. St John's Medical College and Hospital **Recruiting**
Bangalore, Karnataka, India, 560034
Contact: Alekya Vemula 8897752905 hemtrials.stjohns@sjri.res.in
Principal Investigator: Ross C Reuben, MD

III. Amrita Institute of Medical Sciences (AIMS) **Recruiting**
Kanayannur, Kochi, India, 682041
Contact: Puneet Dhar, MD 484-9447736769 pdhar@aims.amrita.cdu
Contact: Deepa Gijesh 484-9995184399 deepagijesh@aims.amrita.edu

IV. Institute of Critical Care Medicine Max Super Specialty Hospital **Recruiting**
Saket, New Delhi, India, 110017
Contact: Komal Handa 7888600688 Komal2@maxhealthcare.com
Principal Investigator: Deven Juneja, MD

V. Postgraduate Institute of Medical Education and Research, Department of Anaesthesia and special care **Recruiting**
Chandigarh, India, 160012
Contact: Narayana Yaddanapudi,
MD 9815836656 narayana.yaddanapudi@gmail.com
Principal Investigator: Narayana Yaddanapudi, MD

5.7.3. The study carried out under the supervision of Dr. Faisal Mahmood (PI), along with Dr. Joveria Farooqi (Co-PI).

5.7.4. The trial comprises of following primary objective;

i. Efficacy as measured by the percentage of subjects with global success at end of treatment [Time Frame: Up to 90 days of study treatment]
Efficacy as measured by the percentage of subjects with global success (complete or partial global response) at EoT as determined by the Data Monitoring Committee

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached
2	Fee	Rs.200000/- deposited vide challan number: 1963578, dated 08th October, 2019.
3	Investigator Brochure (s)	Attached
4	Final protocol	Attached
5	Informed consent and	Attached

	participant information sheet (Urdu to English)	
6	List of participating countries	USA, India, Kenya, South Africa & Pakistan.(As per application) Only USA & India as per US National Trial Registry.
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.	162 Bottles (30 Tablets / Bottle).
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.	Inspection Exit Notice & Notice for compliant rated inspection for M/s Corealis Pharma Inc. issued from Department of Health Canada is 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.	Total 30 subjects globally. 15 subjects will enrolled in Pakistan.
19	Name of Monitors & Clinical Research Associate	Dr. Abdul Qaseem Khan (Pakistan) Dr. Nazish Urooj Metrics Research (Pvt) Ltd is

		appointed as CRO. (Inspection of the CRO is carried out by Panel constituted by the CSC, and case included in the meeting)
20	Evidence of registration in country of origin.	Not provided.
21	Copy of registration letter (if registered in Pakistan)	N/A
22	Sample of label of the investigational product / drug.	Attached.
22	Duration of trial	Approximately 132 days.
23	Undertaking on Stamp paper	Attached.

5.7.6. Shortcoming & clarifications required

I. Kindly provide Sponsor's approval for nomination of M/s Metrics Research (Pvt) Ltd as CRO & following monitors for the trial:

i. Dr. Abdul Qaseem Khan, Sr. CRA. (Qaseem.khan@marco.com)
ii. Dr. Nazish Urooj, Sr. Manager. (drnazishi@marco.com)

II. Further as per trial application form & submitted protocol, it is stated that the trail is a Phase-III study, whereas study subject & sample size is not supporting the claim, so clarification is required.

5.7.7. Shortcomings were communicated through letter no. F.No.03-14/2019 DD (PS), dated 12th December 2019, but still response is awaited.

5.7.8. Submitted for perusal discussion and decision of CSC.

5.7.9. Dr. Sayed Faisal Mahmood, Associate Professor, Infectious Diseases, Aga Khan University Hospital, Karachi present before CSC & briefed regarding the trial.

5.7.10. **Decision of 6th CSC Meeting: -**

"The CSC after deliberations deferred the case & decided to get experts opinion, because investigational drug is a new drug.

Applicant will be asked for trial data to be sent to the following experts for their opinion regarding the trail:

i) Dr. Faisal Sultan, Shaukat Khanum Memorial Hospital & Research Center

ii) Dr. Javaid Bhutta, Shifa International Hospital, Islamabad.

iii) Dr. Sobia Qazi, Services Hospital, Lahore.

iv) Head of Department of Infectious Diseases, Combined Military Hospital, (CMH), Rawalpindi.

Expert's opinion & recommendations will be presented before CSC in its next meeting."

5.8) APPLICATION FOR THE USE OF GRANULOCYTE COLONY STIMULATING FACTOR (GCSF) FOR BILIARY ATRESIA AS PART OF A PHASE-II CLINICAL TRIAL. F. No.03-10/2019-DD (PS)

5.8.1. 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 16th May, 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.

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

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached.
2	Fee	Differential fee of Rs.100000/- is provided instead of approved fee of Rs.200000/-.
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, Vietnam and 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 and designation of members.	Attached.
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	Not provided.

	investigational product / drug.	
22	Duration of trial	48 Months
23	Undertaking on Stamp paper	Not provided.

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

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

5.8.5. Shortcomings were communicated through letter no. F.No.03-10/2019 DD (PS), dated 11th April, 2019, but still response is awaited.

5.8.6. Reply of this division letter even number dated 08th July, 2019, 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, received on 2nd October, 2019. After evaluation of reply as per prerequisites of Form-II of the Bio-Study Rules 2017, following shortcoming observed;

i) Proof of authorization from Sponsor for the subject trial is not provided.

ii) Name & Contact details of Global Trial Lead & Sponsor of the subject trial.

iii) As per US Trial Registry the said trial is in early Phase-I and not completed yet, so how you can start Phase-II trial when Phase-I is in progress.
iv) Phase-I trial results are not provided.
v) Processing fee of Rs.100000/- is submitted whereas approved fee for Clinical Trial is Rs.200000/- as per S.R.O. 1047(I)/2019.
vi) As it is a multicounty trial so the source of medicine should be same for uniform results.
vii) Provided Investigator's Brochure is not as defined in ICH-GCP Guidelines.
viii) Study Protocol is not as defined in ICH-GCP Guidelines.
ix) Quantity of drug / trial material to be imported is not described.
v) GMP certificate along with COPP & free sale certificate of the investigational product to be imported are not provided.
vii) Summary of Protocol & Summary of Investigator Brochure are not provided.

5.8.7. Shortcomings were communicated through letter no. F.No.03-104/2019 DD (PS), dated 11th September, 2019, but still response is awaited.

5.8.8. It is pertinent to mention here that as per applicant claim when trial researched & verified from U.S. National Trial Registry it is found that the trial is in early Phase-I stage and they are not recruiting yet, whereas applicant claiming the trial Phase-II studies.

5.8.8. Submitted for perusal discussion and decision of CSC.

5.8.9. Dr. Jai K. Das, Assistant Professor, Aga Khan University Hospital, Karachi, present before CSC & briefed regarding the trial.

5.8.10. **Decision of 6thCSC Meeting: -**

"The CSC after deliberations deferred the case & decided to get experts opinion, because investigational drug is a chemotherapeutic drug and utilized & tested in the trial for it's off label use.

Applicant will be asked for trial data to be sent to the following experts for their opinion regarding the trail:

i) Maj. Gen. Dr. Salma, Fazaia Medical College, Rawalpindi.

ii) Dr. Yasir, Oncologist, Shifa International Hospital, Islamabad.

iii) Dr. Samiya, ex-Head of Paediatrics Department, PIMS Hospital, Islamabad.

Expert's opinion & recommendations will be presented before CSC in its next meeting."

5.9) 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).

5.9.1. 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"*

5.9.2. 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	Unverified Challan of Rs.50000/- submitted. Rs. 200000/- deposited vide challan number 1915740, dated 26th August 2019.
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	Attached

5.9.3. Description of shortcomings:

i) Rs.50000/- deposited vide challan number 0600476 dated 16th March 2017, which is not verified by division of Budget & Accounts, whereas Rs.150000/- 1915740, dated 26th August 2019, Rs. 50000/- is still due

5.9.4. Applicant informed regarding shortcomings through letter number F.No.3-2/2017 DD (PS), dated 13th December 2019, but still response is awaited.

5.9.5. Application placed before CSC in its 4th meeting, Dr. Laila on behalf of P.I presented the Clinical Studies before the CSC experts. CSC decided as follows:

Decision of 4th CSC Meeting:-

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.

5.9.6. It is pertinent to mention here that as per 4th CSC meeting decision when application reevaluated for pre-requisites as per the Bio-Study Rules 2017, and sponsor contacted for details, it was found that Phase I or II studies for the said combination of Investigational Medicinal Products (IMP) were not carried out, sponsor informed that they relied on other studies and designed their Phase-III trial.

5.9.7. Dr. Jai K. Das, Assistant Professor, Aga Khan University Hospital, Karachi, present before CSC & briefed regarding the trial.

5.9.8. Submitted for perusal discussion and decision of CSC.

5.9.9. **Decision of 6thCSC Meeting: -**

"The CSC after deliberations approved the Clinical Studies "Lactoferrin Evaluation in Anemia in Pregnancy (LEAP-1), to be conducted at Clinical Trial Unit, Aga Khan University Hospital, Karachi. As the Investigational Medicinal Product (IMP) is a protein extracted from Cow's milk".

5.10) 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)).

5.10.1. 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.

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

5.10.3. 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; i) The Aga Khan University Hospital, Karachi. ii) 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

5.10.4. Application was placed before CSC in its 4th meeting, Dr. Summaeya on the behalf of P.I. attended the 4th CSC meeting and presented the Clinical Studies before CSC, after discussion CSC decided as follows:

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.

5.10.**5.** It is pertinent to mention here that as per 4th CSC meeting decision when application reevaluated for pre-requisites as per the Bio-Study Rules 2017, before issuance of registration certificate, sponsor contacted for details, it was found that they have decided to change the source of Investigational Medicinal Products (IMP). In application it is described that Investigational Medicinal Products (IMP) will be imported from M/s Macleods India, whereas as informed by the Global Principal Investigator now they will arrange IMPs from M/s Pacific Pharmaceutical, Lahore Pakistan, but still officially not informed.

5.10.6. Shortcomings were communicated through letter no. F.No.03-11/2019 DD (PS), dated 11th April, 2019, in response of this division letter, Dr. Bushra Jamil, Co-P.I. RIFA-SHORT Trial, Aga Khan University, Karachi, provided following documents:

i. Product Registration letter (Rifadin 150 & 300mg Capsule, Rifadin 450 & 600mg Tablet, Rifadin 2% w/v Syrup, Rifinah Tablet, Rifin Forte Tablet).
ii. GMP Certificate (Issued by DRAP).
iii. Certificate of analysis.
iv. GMP Certificate (Issued by Eudra).
v. MHRA Certificate 2017.
vi. Pacific Pharmaceutical Brochure.
vii. Pacific Pharma Profile.

5.10.7. Dr. Bushra Jamil, Co-P.I. RIFA-SHORT Trial, Aga Khan University, Karachi, present before CSC & briefed regarding the trial.

5.10.8. Submitted for perusal discussion and decision of CSC.

5.10.9. **Decision of 6th CSC Meeting:** -

The CSC after deliberations approved the Clinical Studies/ 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 (RIFA-SHOT)", to be conducted at Clinical Trial Unit, Aga Khan University Hospital, Karachi & Shaukat Khanum Memorial Cancer Hospital, Lahore.

CSC also approved that locally manufactured IMP can be replaced with imported medicine, as requested & informed by the applicant".

Additional Agenda Items of 6th CSC Meeting to be held on 20th January 2020

1.1A) APPLICATION FOR APPROVAL AND REGISTRATION OF CLINICAL TRIAL FOR THE EVALUATING NEWLY APPROVED DRUGS IN COMBINATION REGIMENS FOR MULTI DRUG-RESISTANT TB WITH FLOUROQUINOLONE RESISTANCE (Q) (endTB-Q) PHASE-III CLINICAL TRIAL F. No.03-17/2019-DD (PS).

1.1.1A) Application from Dr. Abdul Bari Khan, CEO, Indus Hospital, Karachi, dated 25th November, 2019, wherein request has been made for registration & approval of subject clinical trial, which will be carried out at The Indus Hospital, Karachi, under the supervision of Dr. Naseem Salahuddin M.D (PI), Professor & Head, Department of Medicine &Division of Infectious Diseases (ID)

1.1.2A) The study conducted in partnership between Partners In Health (PIH), Médecins sans Frontières (MSF), and Interactive Research & Development (IRD) and has a financial partner UNITAD. The trial will be implemented in India, Lesotho, Kazakhstan, Peru, South Africa & Pakistan. Details are also available on www.ClinicalTrials.gov, uploaded with identification number NCT03896685.

1.1.3A) Moreover it is informed by the applicant that mainly trial will be carried out at the Indus Hospital, whereas Delhi Medical Center (DMC) and Jinnah Post Graduate Medical Center (JPMC), will involve partially in the trial activities. (Page 1530/corr.)

1.1.4A) Detailed description of trial is as follows:

This is a Phase III, randomized, controlled, open-label, multi-country trial evaluating the efficacy of new combination regimens for treatment of fluoroquinolone-resistant MDR-TB. Regimens examined combine newly approved drugs bedaquiline and delamanid with existing drugs known to be active against Mycobacterium tuberculosis (linezolid and clofazimine). The study will enroll in parallel across 1 experimental and 1 standard-of-care control arms, in a 2:1 ratio. Randomization will be stratified by extent-of-TB-disease phenotype. In the experimental arm, treatment will be for 24 or 39 weeks; duration will be assigned according to extent-of-TB-disease phenotype. In the control arm, treatment will be delivered according to WHO guidelines (and local practice); duration will be variable. Trial participation in both arms will last at least until Week 73, and up to Week 104. Non-inferiority will be established for the experimental arm if the lower bound of the one-sided 97.5% confidence interval around the difference in favorable outcome between the control and experimental arms is greater than or equal to -12%.

1.1.5A) The trial comprises of following Primary objective;

i. To assess whether the efficacy of experimental regimens at Week 73 is inferior to that of the control.

1.1.6A) The details of the submitted documents are as under;

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached.
	Prescribed Fee	Prescribed fee of Rs.200000/- deposited vide challan number 2018801, dated 5th December 2019.
2	Investigator Brochure (s)	Provided for Bedaquiline & Delamanid only and reason explained that except Bedaquiline & Delamanid all medicinal products in the trial are not in any development phase.
3	Final protocol	Attached. (Version 2.2)
4	Informed consent and participant information sheet (Urdu to English)	Attached.
5	List of participating countries	India, Lesotho, Kazakhstan, Peru, South Africa and Pakistan
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.	Quantities of Investigational & Ancillary medicines used in the trial / studies to be imported are mentioned. Attached
8	Site of the trial	It is informed that Trial will be carried out mainly at the Indus Hospital, whereas Delhi Medical Center (DMC) and Jinnah Post Graduate Medical Center (JPMC) will also partially involved in the studies. Ghouri Clinic of the Indus Hospital is licensed with DRAP. Licence number CTS-0002 granted for the site.

		Primarily site is inspected in reference to endTB clinical studies.
9	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	IRB / IRD approval from Harvard Faculty of Medicine, Boston, Ethics Review Board of Médecins Sans Frontières and WHO-ERC are attached. Approval from IRB or Ethics Review Committee of The Indus Hospital is not provided.
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.	Copy of COA, COPP & GMP certificate attached.
13	Pre-clinical/clinical safety studies	Not provided.
14	Summary of Protocol	Attached
15	Summary of Investigator Brochure	Attached
16	Adverse Event Reporting Form	Attached.
17	No of patients to be enrolled in each center.	Total Participating Subjects 500. Approx. 72 subjects in Pakistan.
18	Name of Monitors & Clinical Research Associate	Dr. Naseem Salahuddin M.D (PI) & M/s Dimension Research Pvt Ltd.(Not approved yet by DRAP) Miss Sadaf, Project Manager
19	Evidence of registration in country of origin.	Copy of COA, COPP & GMP certificate attached.
20	Copy of registration letter (if registered in Pakistan)	N/A All trial IMPs will be provided by MSF, and exported to Pakistan.
21	Sample of label of the	Attached

	investigational product / drug.	
22	Duration of trial	48 Months
23	Undertaking on Stamp Paper	Attached

1.1.7A) Applicant provided following list of investigational products and ancillary drugs to be used in the trial and will be provided by the sponsor:

Investigational Medicinal Products (IP)					
S. No.	**Generic Name**	**Trade Name**	**Manufacturer**		**Total Quantities (Unit (Tab, Cap, Amp.))**
1	AMIKACIN sulfate, eq. 250 mg/ml base, 2 ml, amp.	SELEMYCIN ® 500mg/2ml	M/s Medochemie Ltd, Cyprus.	COPP, GMP+COA	1700
2	AMOXICILLIN 500 mg / CLAVULANIC acid 125 mg Tab.	CLAVOMID® 500mg/125mg	M/s Remedica Ltd, Cyprus.	COPP, GMP+COA	4100
3	BEDAQUILINE, 100 mg, tab.	SIRTURO® 100mg Tablets	M/s Recipharm Pharma Services Pvt. Ltd. India	COPP, GMP+COA	42676
4	CLOFAZIMINE, 100 mg, soft caps.	Lamprene Capsule 100mg	M/s Sandoz Private Ltd. India	COPP, GMP+COA	47400
5	CYCLOSERINE 250 mg caps.	CYCLOSERINE Capsules 250mg	M/s Macleods Pharmaceuticals India.	COPP, GMP+COA	66900
6	DELAMANID, 50mg, tab., blister	Deltyba ™ 50mg	M/s Otsuka Pharmaceutical Co., Ltd,	COPP, GMP+COA	145152

			Japan.		
7	ETHAMBUTOL hydrochloride (E), eq. 400 mg base, tab. blister	ETHAMBUTOL Tablets 400mg	M/s Macleods Pharmaceuticals India.	COPP, GMP+COA	7800
8	ETHIONAMIDE, 250 mg, tab., blister	ETHIONAMIDE Tablets 250mg	M/s Macleods Pharmaceuticals India.	COPP, GMP+COA	18300
9	ISONIAZID, 300, breakable tab, blister	ISONIAZID Tablets 300mg	M/s Oxalis Labs, India	COPP, GMP+COA	6720
10	IMIPENEM-CILASTATIN 500+500mg Powder for solution for infusion	IMIPENEM-CILASTATIN 500+500mg Powder for solution for infusion	M/s Panpharma, France.	COPP, GMP+COA	7970
11	LEVOFLOXACIN hemihydrate, eq. 250 mg base, tab.	LEVOFLOXACIN Hetero 250mg Tablet	M/s Hetero Labs Limited, India.	COPP, GMP+COA	1000
12	LEVOFLOXACIN hemihydrate, eq. 500 mg base, tab.	LEVOFLOXACIN 500mg Tablets	M/s Macleods Pharmaceuticals India.		2700
13	LINEZOLID, 600 mg, coated tab.	Linezolid Tablets 600mg	M/s Hetero Labs Limited, India.	COPP, GMP+COA	30400
14	MOXIFLOXACIN hydrochloride eq. to 400 mg base , tab.	MOXIFLOXACIN Hetero 400 mg Tablets	M/s Hetero Labs Limited, India.	COPP, GMP+COA	7100
15	PARA-AMINOSALICYLIC acid (PAS),del.rel.gran, 4g, sachets.(25°C)	Paser ® Granules	M/s Jacobus Pharmaceutical Company Inc. New Jersey, USA.	COPP, GMP+COA	5160
16	PYRAZINAMIDE (PZA), 400 mg, tab.,	PYRAZINAMIDE Tablet 400	M/s Macleods Pharmaceutic	COPP, GMP+COA	73920

	blister	mg	als India.		
Ancillary Drugs					
S. No.	**Generic Name**	**Trade Name**	**Manufacturer**		**Total Quantities (Unit (Tab, Cap, Amp.))**
01	AMITRIPTYLINE hydrochloride, 25 mg, tab.	Amirol 25 Tablet	M/s Remedica Ltd, Cyprus.	COPP, GMP+COA	4000
02	BECLOMETASONE dipropionate, 100 mcg/puff, 200 puffs, aerosol	Baclo-Asma 100 Micrograms	M/s Laboratorio Aldo-Union SL, Barcelona.	COPP, GMP+COA	6
03	CHLORPHENIRAMINE Maleate	Cadiphen Tablet	M/s Cadila Pharmaceuticals Limited, India.	COPP, GMP+COA	2000
04	CARBAMAZEPINE, 200 mg, tab.	Taver 200mg Tablets	M/s Medochemie Ltd, Cyprus	COPP, GMP+COA	1000
05	Clotrimazol 500 mg vaginal Tablets	Mycoril 500 vaginal Tablets	M/s Remedica Ltd, Cyprus.	COPP, GMP+COA	35
06	Epoetinum alfa, prefilled Syringes.	Eprex 10000 IU/ml (1 ml Syringe)	M/s Janseen Biologics B.V. , Netherlands	COPP, GMP+COA	96
07	FLUOXETINE, 20mg, caps.	FLUOXETINE Mylan 20mg Tablet.	M/s Mylan SAS, France.	COPP, GMP+COA	700
08	HALOPERIDOL, 5 mg, tab.	Haloxen 5 Tablets	M/s Remedica Ltd., Cyprus.	COPP, GMP+COA	13000

09	IBUPROFEN, 400 mg, tab.	Perofen 400mg Tablet	M/s Remedica Ltd., Cyprus.	COPP, GMP+COA	13000
10	LEVOTHYROXINE SODIUM, 0.025 mg, tab.	LEVOTHYROXIN 0.025 mg Tablets.	M/s Mercury Pharmaceuticals Ltd., UK.	COPP, GMP+COA	4172
11	LOPERAMIDE hydrochloride, 2 mg, tab.	Loperium 2 Tablets	M/s Remedica Ltd., Cyprus.	COPP, GMP+COA	1000
12	MAGNESIUM OXIDE 150 mg Magnesium, effervescent. tab	Magnesium Arrow 150mg	M/s Hermes Arzneimittel GmbH,Germany	COPP, GMP+COA	8940
13	MAGNESIUM Sulphate Injection 50% w/v, Solotion for injection.	MAGNESIUM Sulfate Injection 50% w/v (5gm / 10ml)	M/s Macarthys Laboratories Ltd T/A Martindale Pharma, UK.	COPP, GMP+COA	330
14	METOCLOPRAMIDE hydrochloride anhydrous, 10 mg, tab.	Cloperan 10 Tablets	M/s Remedica Ltd., Cyprus.	COPP, GMP+COA	1000
15	MICONAZOL nitrate, 2%, cream, 30 g, tube	Candiplas Cream 2% w/w	M/s Medochemie Ltd, Cyprus.	COPP, GMP+COA	10
16	OMEPRAZOLE 20 mg, enteric caps.	Medoprazole 20 mg Capsule	M/s Medochemie Ltd, Cyprus.	COPP, GMP+COA	2912
17	ONDANSETRON hydrochloride, eq. 4 mg base, tab.	ONDANSETRON 4mg film coated tablets	M/s Medochemie Ltd, Cyprus.	COPP, GMP+COA	60
18	PARACETAMOL (acetaminophen), 500 mg, tab.	PARACETAMOL-Remedica 500mg Tablet	M/s Remedica Ltd., Cyprus.	COPP, GMP+COA	13000
19	POTASSIUM chloride, 0.10gm/ml, conc. For solution	POTASSIUM chloride Proamp	M/s Laboratoire Aguettant	COPP, GMP+COA	650

	for infusion.	0.10gm/ml	Champane, France		
20	POTASSIUM chloride, 600 mg, sustained release tab.	Kaleorid Tab 600mg Sust. / Controlled Release Tablets	M/s Leo Pharma A/S, Denmark.	COPP, GMP+COA	34800
21	PREDNISOLONE, 5mg, tab.	Corotrope 5mg Tablet	M/s Remedica Ltd., Cyprus.	COPP, GMP+COA	1000
22	PROMETHAZINE hydrochloride, eq. 25 mg base, tab.	PROMETHAZINE 25mg Tablets	M/s Remedica Ltd., Cyprus.	COPP, GMP+COA	1000
23	PYRIDOXINE hydrochloride (vitamin B6), 50 mg tab.	PYRIDOXINE 50mg Tablets	M/s Macleods Pharmaceuticals, India	COPP, GMP+COA	76000
24	RISPERIDONE, 1 mg, tab.	RISPERIDONE-Remedica 1mg Tablet	M/s Remedica Ltd., Cyprus.	COPP, GMP+COA	420
25	SULBUTAMOL sulfate, eq.0.1mg base/puff, 200 puffs, inhaler	BUTO-ASMA Aerosol (Salbutamol Inhaler 100 mcg)	M/s Laboratoria Aldo-Union, S.L., Barcelona Spain.	COPP, GMP+COA	83
26	SODIUM chloride, 0.9%, 250 ml, plastic pouch.	SODIUM chloride 0.9% w/v, 30ml.	M/s Bieffe Medital, S.A., Spain.	COPP, GMP+COA	4080
27	SODIUM VALPROATE, 500 mg, enteric coated 500mg tab.	Epilim 500 Gastro-Resistant Tablets	M/s Sanofi Aventis, S.A., Spain.	COPP, GMP+COA	600
28	WATER for injection, 20*10ml, plastic amp	WATER for injection 20*10ml	M/s B.Braun Melsungen AG,	COPP, GMP+COA	8300

			Germany.		
29	Trihexyphenidyl Hydrochloride/BENZHEXOL Hydrochloride 2mg Tablet.	BENZHEXOL 2mg, Tablets	M/s Remedica Ltd., Cyprus.	COPP, GMP+COA	100

1.1.8A) After evaluation following shortcomings observed:

i. Clinical trial site of Delhi Medical Center (DMC) and Jinnah Post Graduate Medical Center (JPMC) is not approved.
ii. Institutional Review Board (IRB) / Ethics Review Committee approval from Delhi Medical Center, Karachi & Jinnah Post Graduate Medical Center, Karachi (JPMC) is not provided.
iii. Phase I & II studies results are not provided.

1.1.9A) Shortcomings were communicated through letter no. F.No.03-17/2019 DD (PS), dated 31st December, 2019, but still response is awaited.

1.1.10A) Submitted for perusal discussion and decision of CSC.

1.1.11A) **Decision of 6thCSC Meeting: -**

"The CSC after deliberations approved the endTB-Q Clinical Studies, to be conducted at Ghauri Clinic of the Indus Hospital, Karachi, subject to following conditions:

i) Females recruited in the study will be briefed to use contraception and strong measure for contraception will be arranged.

ii) Even after contraception if the pregnancy sustains the subject will be asked again for their consent.

1.2.A) APPLICATION FOR LICENSE TO ACT AS CRO AND CLINICAL TRIAL MONITORING SERVICES-IQVIA SOLUTIONS PAKISTAN (PRIVATE) LIMITED. F. No.15-09/2019 DD (PS)

1.2.1.A) Application 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 along without fee, which may be paid/ asked after notification.

1.2.2.A) 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	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.	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.	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.	Not provided. 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 within the approved hospital / clinical site by DRAP under the supervision on local EC and NBC with qualified investigators as per ICH-GCP guidelines and Patient Wellbeing.
8	Undertaking	Attached

1.2.3.A) Application was discussed in the 3rd CSC meeting & the CSC decided as follows:

Decision of 3rd CSC Meeting:-

The CSC afire 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. Salva Ahsan
iii.	Prof. Dr. Nadeem Afzal
iv.	Dr. Farhana Badar
v.	Dr. Abdur Rashid (Coordinator)

1.2.4.A) Inspection panel conducted the inspection & inspection report placed before CSC in its 4th meeting, with recommendations **"Recommended for provisional approval for improvements**", after discussion CSC in its 4th meeting decided as follows:

Decision of 4th CSC 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.

1.2.5.A) Due to unavailability of Dr. Salwa Ahsan & Dr. Farhana Badar in scheduled dates, Chairman CSC / Director Pharmacy Services exercising powers delegated by the CSC substituted Dr. Salwa Ahsan & Dr. Farhana Badar with Mr. Waqas Latif, UHS, Lahore & Dr. Saif Ur Rehman, Additional Director, CDL-Karachi. And letter for inspection issued on 13th November 2019.

1.2.6.A) Prof. Dr. Javed Akram, Dr. Saif Ur Rehman Khattak & Dr. Abdur Rashid (Coordinator) conducted inspection of the M/s IQVIA Solutions Pakistan (Pvt) Ltd, on 16th November 2019 & due to unavailability of Mr. Waqas Latif, UHS, Lahore & Prof. Dr. Nadeem Afzal, Chairman CSC / Director Pharmacy Services nominated following members for inspetion:

i.	Prof. Dr. Nisar Hussain Shah.
ii.	Dr. Najam Us Saquib.

1.2.7.A) Nominated members conducted inspection of the M/s IQVIA Solutions Pakistan (Pvt) Ltd, on 31st December 2019.

1.2.8.A) **The report submitted by Dr. Najam Us Saqib (Additional director DRAP Karachi) to the division of pharmacy Services for the Inspection of the M/s IQVIA Solutions Pakistan (Pvt) Ltd, on 16th November 2019 & 31st December 2019 concluded the following remarks:**

"All necessary / relevant documents were thoroughly reviewed by the team and found satisfactory. The team especially reviewed the subsidiary certificate issued in favour of IQVIA Solution Pakistan (Pvt) Ltd, by IQVIA Inc. NJ, and SECP Company Reg: Certificate presented by the management which are also attached with the report"

1.2.9.A) **Concluding status / remarks of inspection panel:**

Recommended for approval

The inspection was done in bit and pieces and not compositely. Further that the active composition of CRO has been changed, and is only two member from actual composition i.e. Dr. Abdur Rashid & Dr. Javed Akram had conducted the inspection. The report submitted has not the signature of Dr. Javed Akram (member of panel).

1.2.10.A) Submitted for perusal discussion and decision of CSC.

1.2.11.A) **Decision of 6th CSC Meeting:-**

The CSC after deliberations & upon recommendation of inspection panel, decided to approve the M/s IQUVIA Solutions Pakistan (Pvt) Ltd., Karachi to act as Contract Research Organization (CRO), under the Bio Study Rules 2017.

1.3.A) DELEGATION OF POWER TO CHAIRMAN CSC FOR CONSTITUTION OF INSPECTION PANEL FOR APPLICATIONS RECEIVED ON FORM-I OF THE BIO-STUDY RULES.

1.3.1A) Many applications for approval to act as CROs, Clinical Trial Sites, Bio-Analytical Laboratories & BA/BE Studies Centers are processed by the division of Pharmacy Services and placed before CSC for constitution of panel. On inspection date, if any member of panel is not available, addition of another member of relevant expertise to replace the non-available member become time consuming and bothers the ongoing inspection as scheduled. .

1.3.2A) The CSC may release its burden and for speedy disposal by authorizing Chairman CSC for addition of another relevant member to already constituted panel by CSC. The panel shall consist of four members who has been trained for such inspections at UHS or other institution for such relevant purpose, having relevant experience. The panel shall have composition of a clinician having experience of epidemiology, a biostatistician, a pharmacist having clinical experience of clinical pharmacy and an IT relevant person. The panel shall inspect the site at one time compositely, and not in bit and pieces. This initiative is not from driven from section but has added by the initiative of Director / Chairman CSC.

1.3.3A) Submitted for perusal, discussion and decision of CSC.

i. After discussion CSC authorize / delegated its power to Chairman CSC / Director Pharmacy Services for constitution of panel for inspection regarding Contract Research Organization (CROs),Clinical Trial Sites (CTS), BA/BE Studies Center & Bio-Analytical Laboratories.

ii. Summary / status of application (Softcopy) will also forwarded to all members of the committee regarding application documentation.
