Minutes of 2nd Meeting of CSC scheduled on 9th May, 2019.

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1. The 2nd Meeting of CSC was held on 09.05.2019 at the Senate Hall of University of Health Sciences, Lahore.

2. The Meeting started with the Holy Verses of Quran. The following cases was taken one by one. The decision of the CSC is written at the end of each agenda item.

3. In principle it was decided that priorities shall be given to government insititution or non profit earning charity insititution in the initial licencing of CROs, Clinical Trials, Clinical Sites & BA /BE studies and rest of the cases shall follow.

AGENDA ITEM - I: CONFIRMATION OF THE MINUTES OF THE 1ST CLINICAL STUDIES COMMITTEE MEETING.

The CSC confirmed the minutes of 1st Meeting of Clinical Studies Committee (CSC) held on 07th February, 2019.

AGENDA ITEM - II: CONSTITUTION OF NATIONAL POOL FOR INSPECTION OF CROS, CLINICAL TRIAL SITES, BE/BA STUDIES CENTRES AND CLINICAL RESEARCH LABORATORIES.

It was decided in the first CSC meeting held on 7th February, 2019, at University of Health Sciences, Lahore, that a National Inspection Pool of experts in the Clinical Studies may be constituted to conduct inspection of CROs, Clinical Trial Sites, BA/BE studies centres and Clinical Research Laboratories.

The CSC approved the following inspection pool:-

S.No.	Name	Designation
1.	Prof. Dr. Javed Akram	VC, UHS, Lahore
2.	Prof. Dr. Nawaz	Ex-VC, UVAAS, Lhr
3.	Dr. Addur Rashid	Director, Pharmacy Services, DRAP
4.	Dr. Masud ur Rehman	Additional Director, Pharmacy Services, DRAP
5.	Dr. Farzana Chaudhary	Ex-Drug Controller, Lahore
6.	Prof. Dr. Ali Jawa	Adj. Professor, UHS Lahore
7.	Prof. Dr. Nadeem Irfan Bukhari	Professor, University of Punjab, Lahore
8.	Prof. Dr. Nadeem Afzal	Prof. of Immuonology, UHS Lahore
9.	Prof. Dr. Mahboob Rabbani	Ex-Dean Faculty of Pharmacy, BZU, Multan
10.	Dr. Nazli Hameed	Gyanaecologist & Obstetrician, Shalimar Medical and Dental College, Lahore
11.	Prof. Dr. Gul Majeed	Chairman Department of Pharmacy, Quaid-e-Azam University, Islamabad
12.	Prof. Rizwana Chaudhary	Department of Gynaecology, Holy Family Hospital, Rwp
13.	Muhammad `Adnan Faisal Saim	Deputy Director, Division of Pharmacy Services, DRAP
14.	Dr. Jamshed Iqbal	Director Research Center, COMSAT Abbottabad
15.	Dr. M. Sami Mumtaz	Principal Gujranwala Medical Center
16.	Uzma Malik	Asstt. Prof., Kind Edward University, Lahore
17.	Dr. Farhana Badar	Biostatistician & Epediomologist, SKM Cancer Hospital and Research Center, Lahore
18.	Prof. Munir Ahmed Malik	Department of Peads, Shifa International Hospial, Islamabad
19.	Prof. Nisar Ahmed Shah	Dean, BZU Multan
20.	Beenish Pervaiz	Pharmacist , Pharm-D

It was also decided to give a training of two days for the above pool of experts to synchronise their experties and harmonize the working of pool at tendam with International practices. UHS shall arrange such training module at an earliest to expedite the process. Certificate of such training of 6 credit hours shall also be given by UHS.

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

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

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

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

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

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Sign and stamp are missing on Form-I and applied to act as CRO, and to conduct and monitor Clinical Trials and BA/BE Studies.
2	Fee	Not Provided
3	Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).	Attached
4	Details of premises including layout plan of the site.	Layout of ground & first floor attached, same premises will be also be utilized for BA/BE Site & Clinical Trial Site.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Not Provided
6	Names and qualifications of the above sections along with their staff.	Attached
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	No details provided
8	Undertaking	Attached

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

i) Aga Khan University Hospital (Karachi).

ii) Shifa International Hospital (Islamabad).

iii) ShaukatKhanum Memorial Cancer Hospital and Research Centre (Lahore).

Description of shortcomings:

i) Fee not provided.
ii) Sign and stamp are missing on prescribed Form-I.
iii) Applied for CRO, Clinical Trial Site, BA/BE Studies on same application form.
iv) Details regarding ambulatory services are not provided.

The firm informed regarding shortcomings through letter no. F.No.15-09/2019 DD (PS), dated 07th March, 2019, firm repied as follows:

S.No.	Shortcomings	Reply
01	Fee not provided.	While we understand that no formal approval has been made in term of the applicable fee for the CRO license, we understand that previously PKR 50,000 was proposed as the fee for application. In this regard, we have submitted PKR 50,000 as the applicable fee. In the event that a revised applicable fee is notified, we will submit the remainder amount once it is notified. Please find the challan evidencing the submission of the above mentioned fee attached herewith.
02	Sign and stamp are missing on prescribed Form-I.	Please find attached herewith a revised Form-I as per SRO format.
03	Applied for CRO, Clinical Trial Site, BA/BE Studies on same application.	This is to confirm that the application is only about CRO (Contract Research Organization) license.
04	Details regarding ambulatory services are not provided.	Please note that the ambulatory services are not required in relation to Contract Research Organization license application, hence we understand that such information is not required along with the application. IQVIA will manage study with in the approved hospital/clinical site by DRAP under the supervision on local EC and NBC with qualifies investigators as per ICH-GCP guidelines and Patient Wellbeing...(Appendix-4)

Description of shortcomings

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

- Submitted for the consideration of CSC.

Decision:-

The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

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

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

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

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

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached
2	Fee	Attached
3	Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).	Attached
4	Details of premises including layout plan of the site.	Only Layout is attached no details provided.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached
6	Names and qualifications of the above sections along with their staff.	Attached
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Applied site is a private hospital. Details of its facilities are attached.
8	Undertaking on stamp paper	Attached

Description of shortcomings

i) Applied for the Indus Hospital & Delhi Medical Center, application for Delhi Medical Center is not submitted.

The firm informed regarding shortcomings through letter no. F.No.15-05/2019 DD (PS), dated 29th April, 2019, response is awaited.

- Submitted for the consideration of CSC.

Decision:-

The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

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

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

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

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

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached
2	Fee	Attached
3	Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).	It's a Government organization working under the University of Karachi. No evidence provided for its legal status.
4	Details of premises including layout plan of 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.	Attached (Copy)
8	Undertaking on stamp paper	Not provided

Description of shortcomings

i) Undertaking on stamp paper is not provided.

- Submitted for the consideration of CSC.

Decision:-

The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

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

Application is from Prof.Dr. M. Iqbal Choudhary, Director, CenterFor 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.

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

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

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached
2	Fee	Attached
3	Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).	It's a Government organization working under the University of Karachi, No evidence provided for its legal status.
4	Details of premises including layout plan of 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	Attached

	machinery required for the analytical or bio-analytical and clinical studies.	
6	Names and qualifications of the above sections along with their staff.	Attached
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached (Copy)
8	Undertaking on stamp paper	Not provided

Description of shortcomings

i) Undertaking on stamp paper is not provided

- Submitted for the consideration of CSC.

Decision:-

The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

5) APPLICATION FOR THE LICENSE OF THE CENTER FOR BIOEQUVALANCE STUDIES AND CLINICAL RESEARCH (CBSCR) FOR BA/BE SITE, CRO AND CLINICAL TRIAL SITE AT INTERNATIONAL CENTER FOR CHEMICAL AND BIOLOGICAL SCIENCES (ICCBS), UNIVERSITY OF KARACHI, (F. No.15-08/2019).

Application is from Prof.Dr. M. Iqbal Choudhary, Director, CenterFor 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 Clinical Trial Site, the application is on prescribed Form-I of the Bio-Study Rules 2017.

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

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

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached
2	Fee	Attached
3	Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).	It's a Government organization working under the University of Karachi, No evidence provided for its legal status.
4	Details of premises including layout plan of the site.	Layout of ground & first floor attached,

		same premises will be also be utilized for BA/BE Site & CRO.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached
6	Names and qualifications of the above sections along with their staff.	Attached
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached (Copy)
8	Undertaking on stamp paper	Not provided

Description of shortcomings

i) Fee of Rs.50000 submitted vide challan number 0813984, which is verified for Rs.49970, from Budget & Accounts Division. Whereas fee challan of Rs.50000, which was previously submitted vide deposit slip number 0790762 was for renewal of license, and has been not verified from Budget & Accounts Division and can't be used with a new application.

ii) Applicant directed to submit differential amount of fee (i.e. Rs.50030/-) for further perusal.

The firm informed regarding shortcomings through letter no. F.No.15-08/2019 DD (PS), dated 29th April, 2019, but still response is awaited.

- Submitted for the consideration of CSC.

Decision:- The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

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

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

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

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

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached, But applied for Contract Research Organization (CRO), BA/BE Studies Center and Bio-Laboratory, on same application form.
2	Fee	Not provided
3	Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).	Not Provided.
4	Details of premises including layout plan of the site.	Layout of ground & first floor attached.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached
6	Names and qualifications of the above sections along with their staff.	Attached
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	No details provided
8	Undertaking on stamp paper	Not on Stamp paper

Description of shortcomings

i) Applied for Contract Research Organization (CRO), BA/BE Studies Center and Bio-Laboratory, on same application form.

ii) Particulars regarding the legal status of the applicant are not provided.

iii) Details of the allied facilities associated with center are not provided.

iv) Fee not submitted.

v) Undertaking is not on stamp paper.

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

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting

The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

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

Application is from Dr. Saeed Hamid, Director, Clinical Trail Unit, Professor and Consultant Gastroenterologist, Department of Medicine, Aga Khan University, Karachi, dated 7th March, 2019, wherein the request has been made to license their firm with DRAP to act as a Clinical Trial Site, the application is not on prescribed Form-I of the Bio-Study Rules 2017 along with fee of Rs.50000/-, where a copy of challan also attached and claimed that another application was previously submitted with a fee of Rs.50000/-, so now they are submitting remaining amount, Also provided previously submitted application.

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

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

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Not on prescribed Form-I.
2	Fee	Not Provided
3	Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).	Applicant claimed that Aga Khan University is Chartered through President Order, but evidence (Gazzette Notification) is not provided
4	Details of premises including layout plan of the site.	Attached.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Not Provided

Description of shortcomings

i) Application is not on prescribed Form-I

ii) Layout plan of the place, where Clinical Studies shall be conducted is not provided.

iii) Evidence regarding legal status of the firm is not provided.

The firm informed regarding shortcomings through letter no.F.No.15-08/2019 DD (PS), dated 29th April, 2019, but still response is awaited.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting

The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

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

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

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

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

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached.
2	Fee	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.	Attached.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached.
6	Names and qualifications of the above sections along with their staff.	Attached.
7	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Attached.
8	Undertaking on stamp paper	Not Provided.

Description of shortcomings

i) Processing fee not provided.

ii) Undertaking on stamp paer is not provided.

The firm informed regarding shortcomings through letter no.F.No.15-08/2019 DD (PS), dated 29thApril, 2019, but still response is awaited.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting

The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

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

Application is from Dr. Nasir Mahmood, Medical Superintendent, Holy Family Hospital, Rawalpindi, dated 4thApril, 2019, wherein the request has been made to license their firm with DRAP to act as a Clinical Trial Site, the application is on prescribed Form-I of the Bio-Study Rules 2017 without fee.

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

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

S. No.	Required Documents / Information	Remarks
1	Application on prescribed Form-I of The Bio-Study Rules 2017.	Attached.
2	Fee	Not provided.
3	Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors).	Not provided. The firm is a Tertiary care Provincial Government Hospital, and applicant is Medical Superintendent.
4	Details of premises including layout plan of the site.	Only Layout is attached no details provided.
5	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Attached.
6	Names and qualifications of the above sections along with their staff.	Attached for only Obstetrics & Gynecology section..
7	Details of the allied facilities associated with the trial center	Not provided.

	including ambulatory services, emergency handling etc.	Applied site is a Tertiary care Provincial Government Hospital.
8	Undertaking on stamp paper	Attached.

Description of shortcomings

i) Details regarding premesis is not provided.
ii) Processing fee not provided.

The firm informed regarding shortcomings through letter no.F.No.15-13/2019 DD (PS), dated 29th April, 2019, but still response is awaited.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

Agenda Item - IV: LICENSING OF CRO, CLINICAL TRIAL SITE AND BA/BE CENTRE UNDER THE BIO STUDY RULES, 2017. (Old Cases, Discussed in first CSC Meeting)

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

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

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

Summary of reply against observations are as follow:

S.No.	Observations	Comments / Reply
1	The firm is applying for license of both CRO and Clinical Trial Site, However, for each category a separate application is required.	We as the subject specifies have applied only for CRO. As given above in the "*Independent ethics committee (IEC)"* definition and explanation IEC is responsible to ensure the protection of the rights, safety and well-being of human subjects involved in a trial protocol and to provide public assurance of that protection by among other thing, reviewing and approving or providing favorable opinion on the trial protocol, the suitability of the investigators, facilities, methods and material to be used in obtaining and documenting informed consent of the trial subjects.
2	Details of premises including layout plan not provided.	The layout plan of our office has been attached as Annex 3.

3	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies is not provided.	We shall not be required to do these as sponsor of clinical trial Phase II, III and IV. These are required by Bioequivalence centers and for Phase-I trials. As per our application on Form-I (attached) we have applied for organizing and monitoring Phase II, III and IV.
4	Names and qualifications of the section wise staff not provided.	The document attached as Annexure 2, contains the CVs of the employees required for conduct of clinical trial and monitoring.
5	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling not provided.	The trial sites to be monitored by us are hospitals which has all the facilities required for any emergency and is reviewed and approved by IEC.
6	Deposited fee will be adjusted after notification by the Authority.	Shall be done as required.

After submission of reply and clarification regarding observations, it is clear that the applicant firm only work as CRO and provide services to conduct clinical trial, and not conduct clinical trial itself.

After scrutiny status of application is as follows:

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

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

7	Names and qualifications of the above sections along with their staff.	Yes	--
8	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	As per reply Not applicable as they will not conduct any studies.	--
9	Undertaking	Provided on stamp paper.	--
10	Prescribed Fee	Rs.50000 submitted.	--

Following deficiencies were identified:

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

Decision in 1st CSC Meeting: *The Committee decided that the applicant be asked to submit fee which has been approved by the Authority. The CSC also decided to inspect the CRO, through a panel of relevant experts approved by CEO, DRAP, after formation of National Inspection Pool.*

- Submitted for further perusal please.

Decision in 2nd CSC Meeting The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

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

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

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.

After scrutiny status of application is as follows

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

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

Description of shortcomings:

Following deficiencies were identified:

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.

Decision in 1st CSC Meeting: The Committee decided that the applicant be asked to submit fee which has been approved by the Authority and to complete all the deficiencies in the application. The CSC also decided to inspect the CRO, through a panel of relevant experts approved by CEO, DRAP, after formation of National Inspection Pool.

Decision in 2nd CSC Meeting The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

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

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

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

After scrutiny the status of application is as follows:

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

S.No.	Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017	Provided	Not Provided
1	Application on prescribed Form-I	Yes	--
2	Description regarding applicant and the firm	Yes	--
3	Type of the site meant for (whichever is applicable) (i) Bio-equivalence and Bio-availability studies (ii) CRO (iii) Laboratory (iv) Clinical trials- (a) Phase I	As per the most recent submission, application is submitted on Form-I for BA/BE Centre	--

	(b) Phase II (c) Phase III (d) Phase IV		
4	Particulars regarding the legal status of the applicant	Yes	--
5	Details of premises including layout plan of the site	Yes	--
6	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Yes	--
7	Names and qualifications of the above sections along with their staff.	Yes	--
8	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Yes	--
9	Undertaking	Yes	--
10	Prescribed Fee	*Fee of 20,000 has been submitted on one challan for both Clinical trial site and BE/BA Centre.	

Description of shortcomings:

Following deficiencies were identified:

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

Decision in 1st CSC Meeting: The Committee decided that the applicant be asked to submit fee which has been approved by the Authority. The CSC also decided to inspect the BA/BE Centre, through a panel of relevant experts approved by CEO, DRAP, after formation of National Inspection Pool.

Decision in 2nd CSC Meeting The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

4) M/s Pharma Professional Services (Pvt) Ltd, For the License of Clinical Trials Site F.No. 15-4/2019 DD (PS)

Application is from Prof. Dr. Tasneem Ahmed, CEO, Pharma Professional Services (Pvt.) Ltd, A-93 Ettawah society, Ahsanabad, [near Gulshan-e-Maimar], Gadap Town, Karachi, wherein the request has been made to register their site with DRAP as Clinical trial site dated 15th January, 2019.

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.

After scrutiny the status of application is as follows:

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

S. No.	Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017	Provided	Not Provided
1	Application on prescribed Form-I	Yes	--
2	Description regarding applicant and the firm	Yes	--
3	Type of the site meant for (whichever is applicable) (i) Bio-equivalence and Bio-availability studies (ii) CRO (iii) Laboratory (iv) Clinical trials- (a) Phase I (b) Phase II (c) Phase III (d) Phase IV	Applied on Form-I.	--
4	Particulars regarding the legal status of the applicant	Yes	--
5	Details of premises including layout plan of the site	Yes	--
6	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Yes	--
7	Names and qualifications of the above sections along with their staff.	Yes	--
8	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Yes	--
9	Undertaking	Provided	
10	Prescribed Fee	*Fee of 20,000 has been submitted on one challan for both Clinical trial site and BE/BA Centre.	

Description of shortcomings:

Following deficiencies were identified:

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

Decision in 1st CSC Meeting: The Committee decided that the applicant be asked to submit fee which has been approved by the Authority. The CSC also decided to inspect the Clinical Trial Site, through a panel of relevant experts approved by CEO, DRAP, after formation of National Inspection Pool.

Decision in 2nd CSC Meeting The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

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

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

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

After scrutiny the status of application is as follows:

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

S.No.	Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017	Provided	Not Provided
1	Application on prescribed Form-I	Yes	--
2	Description regarding applicant and the firm	Yes	--
3	Type of the site meant for (whichever is applicable) (i) Bio-equivalence and Bio-availability studies (ii) CRO (iii) Laboratory (iv) Clinical trials- (a) Phase I (b) Phase II (c) Phase III (d) Phase IV	Nothing ticked on Form-I.	--
4	Particulars regarding the legal status of the applicant	Yes	--
5	Details of premises including layout plan of the site	--	Not Provided
6	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	--	Not Provided

7	Names and qualifications of the above sections along with their staff.	Provided	
8	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	--	Not Provided
9	Undertaking	--	Not on stamp paper
10	Prescribed Fee	--	Not provided

Description of shortcomings:

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

Decision in 1st CSC Meeting: The Committee decided that the applicant be asked to submit fee which has been approved by the Authority and to complete all the deficiencies in the application. The CSC also decided to inspect the CRO, through a panel of relevant experts approved by CEO, DRAP, after formation of National Inspection Pool.

Decision in 2nd CSC Meeting:- The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

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

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

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

After scrutiny status of application is as follows:

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

S.No.	Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017	Provided	Not Provided
1	Application on prescribed Form-I	Yes	--
2	Description regarding applicant and the firm	Yes	--
3	Type of the site meant for (whichever is applicable) (i) Bio-equivalence and Bio-availability studies (ii) CRO (iii) Laboratory (iv) Clinical trials- (a) Phase I (b) Phase II (c) Phase III (d) Phase IV	Both CRO and Clinical Trial Center are Ticked. But the Firm in response letter confirmed it is a "CRO".	--
4	Particulars regarding the legal status of the applicant	Yes	--
5	Details of premises including layout plan of the site	As per reply Not applicable for the services they are offering.	Not Provided
6	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	As per reply Not applicable for the services they are offering.	Not Provided
7	Names and qualifications of the above sections along with their staff.	Yes	--
8	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	As per reply Not applicable for the services they are offering.	Not Provided
9	Undertaking	Yes	--
10	Prescribed Fee	Rs.100000 Deposited.	--

Description of shortcomings:

Following deficiencies were identified:

i) Application to issue license for CRO and Clinical Trial Site on one application. However, in letter they confirm that it will be a CRO.

ii) Details of premises including layout plan of the clinical trial site is not provided.

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

iv) Details of the allied facilities associated with the trial center/CRO including ambulatory services, emergency handling not mentioned.

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

Decision in 1st CSC Meeting: The Committee decided that the applicant be asked to submit fee which has been approved by the Authority and to complete all the deficiencies in the application. The CSC also decided to inspect the CRO, through a panel of relevant experts approved by CEO, DRAP, after formation of National Inspection Pool.

Decision in 2nd CSC Meeting:- The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

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

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

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

After scrutiny the status of application is as follows:

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

S.No.	Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017	Provided	Not Provided
1	Application on prescribed Form-I	Yes	--
2	Description regarding applicant and the firm	Yes	--
3	Type of the site meant for (whichever is applicable) (i) Bio-equivalence and Bio-availability studies (ii) CRO (iii) Laboratory (iv) Clinical trials- (a) Phase I (b) Phase II (c) Phase III (d) Phase IV	Laboratory	--
4	Particulars regarding the legal status of the applicant	Yes	--
5	Details of premises including layout plan of the site	Yes	--
6	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Yes	--
7	Names and qualifications of the above sections along with their staff.	Yes	--

8	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	As per reply Not applicable.	Not Provided
9	Undertaking	--	Not Provided
10	Prescribed Fee	--	Not Provided

Description of shortcomings:

Following deficiencies were identified:

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

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

iii) Fee is not submitted.

iv) Undertaking on stamp paper is not provided.

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

Decision in 1st CSC Meeting: The Committee decided that the applicant be asked to submit fee which has been approved by the Authority and to complete all the deficiencies in the application. The CSC also decided to inspect the Bio-Lab, through a panel of relevant experts approved by CEO, DRAP, after formation of National Inspection Pool.

Decision in 2nd CSC Meeting:- The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

8) M/s Center for Bioequivalence Studies and Clinical Research (CBSCR), International Center for Chemical and Biological Sciences (ICCBS), University of Karachi, For CRO, Clinical Trial Site and BA/BE Studies Center. F.1-11/2010

Application is from Prof Dr. Muhammad Iqbal Choudary, Director, CBSCR-International Centre for Chemical and Biological Sciences, University of Karachi, dated 19th September, 2018, wherein the request has been made for license of their Centre with DRAP to work as Clinical Research Organization (CRO), Clinical Trial Site and BA/BE studies Centre.

After evaluation following observations were communicated as per prerequisites of prescribed **Form-I** of the **Bio-Study Rules 2017** on **12th December, 2018 and a reminder also send on 28th January, 2019** to submit separate application for each facility on form-I under the Bio-study rules, 2017 for CRO, Clinical Trial site and BA/BE Centre. However, no reply has been received so far.

After scrutiny status of application is as follows

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

S.No.	Prerequisites as per prescribed Form-I of the Bio-Study Rules 2017	Provided	Not Provided
1	Application on prescribed Form-I	Yes	--
2	Description regarding applicant and the firm	Yes	--
3	Type of the site meant for (whichever is applicable) (i) Bio-equivalence and Bio-availability studies (ii) CRO (iii) Laboratory (iv) Clinical trials- (a) Phase I (b) Phase II (c) Phase III (d) Phase IV	Firm has applied for CRO, Clinical Trial site and BA/BE studies Centre on the same application	--
4	Particulars regarding the legal status of the applicant	Yes	--
5	Details of premises including layout plan of the site	Yes	--
6	Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies.	Yes	--
7	Names and qualifications of the above sections along with their staff.	Yes	--
8	Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc.	Details of Facilities for first aid and emergency treatment for the staff and subjects are mentioned on one page and about the diagnostic lab, information technology and ambulatory services are mentioned on another page.	
9	Undertaking	--	Not Provided
10	Prescribed Fee	50,000PKRs submitted.	

Description of shortcomings:

Following deficiencies were identified:

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

ii) Undertaking on stamp paper is not provided.

Decision in 1st CSC Meeting: The Committee decided that the applicant be asked to submit fee which has been approved by the Authority and to complete all the deficiencies in the application. The CSC also decided to inspect the CRO, Clinical Trial Site and BE/BA Centre, through a panel of relevant experts approved by CEO, DRAP, after formation of National Inspection Pool.

Decision in 2nd CSC Meeting:- The CSC after deliberation and considering the facts of the case decided to conduct panel inspection from the members of inspection pool and advised the applicant to remove the shortcomings meanwhile before the inspection.

AGENDA ITEM NO. V: CLINICAL TRIALS/STUDIES REGISTRATION.

All the following cases for registration of Clinical Studies under agenda item no. V were discussed in the first CSC meeting and are still incomplete, as the applicants required licensefor their Clinical Trial Sites. CSC decided in its first meeting, that applicant were asked for 7-8 minutes presentation, CSC decision alongwith application defeciencies were communicated to all applicants, now again placed before CSC for disposal:

1) M/s ATCO Laboratories (Pvt) Ltd, For Clinical Trial on Aspirin, F.3-11/2018-DD (PS)

Application is from Maj. Amjad Farooq Butt (R) Manager Regulatory Affairs, ATCO Laboratories Limited Karachi, wherein request has been made for approval of Aspirin clinical trial, which will be carried out by Principal Investigator Prof.JavedAkram Vice Chancellor University of Health Sciences, Lahore and Dr. Muhammad Zaman Khan Co-Principal Investigator.

Application is containing only two pages, one letter is from Pakistan Aspirin Foundation in the name of Chairman ATCO Laboratories Karachi for provision of Enteric Coated Aspirin 75mg (Ascard 75mg) and Placebo Tablets, and another is an application on ATCO's Letter head in the name of Director Pharmacy Services for approval of said clinical trial.

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

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Not provided
2	Fee	Not provided

3	Investigator Brochure (s)	Not provided
4	Final protocol	Not provided
5	Informed consent and participant information sheet (Urdu to English)	Not provided
6	List of participating countries	Not provided
7	Phase of trial.	Not provided
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for import of trial material.	Not provided
9	Site approval of the trial and sites	Not provided
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Not provided
11	Approval of National Bio-ethics Committee (NBC)	Not provided
12	CV's of the Investigators	Not provided
13	GMP certificate along with COPP & free sale certificate of the investigational product.	Not provided
14	Pre-clinical/clinical safety studies	N/A
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.	49000 Patients, Details not provided
19	Name of Monitors & Clinical Research Associate	Prof.JavedAkram (P.I) Dr.Zaman Khan (Co-P.I)
20	Evidence of registration in country of origin.	Not provided
21	Evidence of registration in Pakistan.	Not provided
22	Sample of label of the investigational product / drug.	Not provided
23	Duration of trial	66 Months

The deficiencies observed in the application was communicated to the applicant on 9th January, 2019 and subsequent reminder was also sent on 30th January, 2019, to fulfill all prerequisites according to the Bio-Study Rules 2017, butno reply received.

Afterwards case was discussed in the 1st CSC meeting and CSC decided as Follows:

> ***Decision:*** *"The CSC decided to call the applicant/Principal Investigator to give a 7 to 8 minutes presentation on their clinical study before the CSC in the next meeting. The committee also decided, that the applicant be conveyed to fulfill the shortcomings for completion of application and submit fee which has been approved by the Authority."*

The decision of CSC along with deficiencies and invitation for presentation on their application in the 2nd CSC meeting was communicated to the firm on5th March, 2019, but still response in reference to shortcomings is awaited.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- No one representative of the firm / institution appeared before the CSC. The case was so deferred for panel inspection of the trial site and proper presentation of the clinical trial.

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

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

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

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Not provided
2	Fee	Not provided
3	Investigator Brochure (s)	Not provided
4	Final protocol	Not provided

5	Informed consent and participant information sheet (Urdu to English)	Not provided
6	List of participating countries	Not provided
7	Phase of trial.	Phase-III (Details not provided)
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for import of trial material.	10*2000 Boxes
9	Site approval of the trial and sites	Anwar Riyaz-I-Qadeer Diabetes Institute Lahore. (Not approved yet by the DRAP)
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Not provided
11	Approval of National Bio-ethics Committee (NBC)	Not provided
12	CV's of the Investigators	Not provided
13	GMP certificate along with COPP & free sale certificate of the investigational product.	Not provided
14	Pre-clinical/clinical safety studies	Not provided
15	Summary of the Protocol	Not provided
16	Summary of the Investigator Brochure	Not provided
17	Adverse Event Reporting Form	Not provided
18	No of patients to be enrolled in each center.	200 Patients, Details not provided
19	Name of Monitors & Clinical Research Associate	Principal Investigator: Dr. Arif Riaz Qader
20	Evidence of registration in country of origin.	Not provided
21	Evidence of registration in Pakistan.	Not provided
22	Sample of label of the investigational product / drug.	Not provided
23	Duration of trial	66 Months

Description of shortcomings:

i) Application is for import of the drug for clinical trial, where clinical trial site and clinical trial is not approved from the DRAP.

ii) Application for clinical trial approval is not on prescribed form-II of the Bio-Study Rules 2017.

iii) Fee deposit slip is not attached.

iv) Prerequisite information as per form-II of the bio-Study rules 2017 are not provided

v) The firm was advised to apply on prescribed form-I of the Bio-Study Rules 2017 for approval of Clinical Trial Site before applying for clinical trial approval

The deficiencies observed in the application was communicated to the applicant on 7th January, 2019 and subsequent reminder was also sent on 11th& 30th January, 2019, to fulfill all prerequisites according to the Bio-Study Rules 2017, but no reply received.

Afterwards case was discussed in the 1st CSC meeting and CSC decided as Follows:

> ***Decision:*** *"The CSC decided to call the applicant/Principal Investigator to give a 7 to 8 minutes presentation on their clinical study before the CSC in the next meeting. The committee also decided, that the applicant be conveyed to fulfill the shortcomings for completion of application and submit fee which has been approved by the Authority."*

The decision of CSC along with deficiencies and invitation for presentation on their application in the 2nd CSC meeting was communicated to the firm on 5th March, 2019, but still response in reference to shortcomings is awaited.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- No one representative of the firm / institution appeared before the CSC. The case was so deferred for panel inspection of the trial site and proper presentation of the clinical trial.

3) A Randomized Double-Blind, Clinical Trial on The Efficacy and Safety of "YinhuangQinfei Capsule" in The Treatment of Acute Exacerbation of Chronic Simple Bronchitis,F.No.03-05/2018-DD (PS).

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

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

Following deficiencies were identified:

S. No.	Document	Remarks
1	Application on prescribed Form-II	Not provided
2	Fee	Rs.50000/- provided only.

3	Investigator Brochure (s)	Attached
4	Final protocol	Attached
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries	Pakistan and China.
7	Phase of trial.	Phase – II
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for import of trial material.	Not provided
9	Site approval of the trial and sites	Not provided
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Not provided
11	Approval of National Bio-ethics Committee (NBC)	Not provided
12	CV's of the Investigators	Attached
13	GMP certificate along with COPP & free sale certificate of the investigational product.	Valid GMP Certificate of M/s Hunan Anbang Pharmaceutical Co. Ltd., has been furnished.
14	Pre-clinical/clinical safety studies	Reports of animal studies are attached. However, no data regarding the Phase – I studies has been provided.
15	Summary of the Protocol	Attached
16	Summary of the Investigator Brochure	Attached
17	Adverse Event Reporting Form	Attached
18	No of patients to be enrolled in each center.	Attached. 212 patients. (106 in each group)
19	Name of Monitors & Clinical Research Associate	Attached
20	Evidence of registration in country of origin.	Attached
21	Evidence of registration in Pakistan.	Not registered in Pakistan.
22	Sample of label of the investigational product / drug.	Attached
23	Duration of trial	12 Months

The deficiencies observed in the application was communicated to the applicant and advised to apply on prescribed Form-I for Clinical trial site approval and for Clinical Trial Studies on prescribed Form-II of the Bio-Study Rule 2017 along with all prerequisites, but no reply received.

Afterwards case was discussed in the 1st CSC meeting and CSC decided as Follows:

Decision: *"The CSC decided to call the applicant/Principal Investigator to give a 7 to 8 minutes presentation on their clinical study before the CSC in the next meeting. The committee also decided, that the applicant be conveyed to fulfill the shortcomings for completion of application and submit fee which has been approved by the Authority."*

The decision of CSC along with deficiencies and invitation for presentation on their application in the 2nd CSC meeting was communicated to the firm on 5thMarch, 2019, but still response is awaited.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- The case was deferred and the applicant will be called for presentation.

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

Application is from Prof.Dr. Syed Muhammad Zahid Azam, Dow University Hospital, Karachi, for approval of "Open Label, Non-Randomized, Multi-Center Investigator Initiated Study to Evaluate Effectiveness of Generic Velpatasvir and Sofosbuvir in Hepatitis-C with or without Ribavirin among Pakistani Population", Phase-IV clinical trial.

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

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

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

	Drugs (Import & Export) Rules, 1976 and application for import of trial material.	Applicant has informed that the study drug will be provided by the M/s CCL Pharma, Lahore which has submitted that their product is pending for approval in Registration Division, DRAP. Whereas they have the registration of the same product for export purpose only and they can supply the same for study purpose. **Information regarding quantities and source of other trial material i.e Ribavirin has not been disclosed.**
9	Site approval of the trial and sites	Anwar Riyaz-I-Qadeer Diabetes Institute Lahore. Not approved yet.
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Applicant has provided the approval of Institutional Review Committee, Dow University, Karachi.
11	Approval of National Bio-ethics Committee (NBC)	Not provided
12	CV's of the Investigators	Attached.
13	GMP certificate along with COPP & free sale certificate of the investigational product.	In-valid GMP Certificate of M/s CCL Pharmaceuticals (Pvt.) Ltd., has been furnished which has expired on 30-03-2018
14	Pre-clinical/clinical safety studies	Not provided
15	Summary of the Protocol	Attached.
16	Summary of the Investigator Brochure	Attached
17	Adverse Event Reporting Form	Attached
18	No of patients to be enrolled in each center.	Attached. 30 to 40 patients at each site. Total 300 Patients approximately.
19	Name of Monitors & Clinical Research Associate	Attached
20	Evidence of registration in country of origin.	Not provided.
21	Evidence of registration in Pakistan.	Registration letter of Abriva Forte Tablet (Velpatasvir/Sofosbuvir 100mg/400mg) for Export Purpose, is attached.
22	Sample of label of the investigational product / drug.	Attached
23	Duration of trial	12 Months

Following deficiencies were identified:

i) Application for Clinical Trial Site approval on prescribed Form-I of the said rules and for approval of Clinical Studies to apply on prescribed Form-II.

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

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

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

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

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

The firm was communicated through letter no. F.No.3-3/2018 DD (PS), dated 06th June, 2018, after scrutiny of the reply another letter sent on 11th January, 2019, that apply on prescribed Form-I for Clinical trial site approval and for Clinical Trial Studies on prescribed Form-II of the Bio-Study Rule 2017 along with all prerequisites, But still response is awaited.

The deficiencies observed in the application was communicated to the applicant on 7th January, 2019 and subsequent reminder was also sent on 11th& 30th January, 2019, to fulfill all prerequisites according to the Bio-Study Rules 2017, but no reply received.

Afterwards case was discussed in the 1st CSC meeting and CSC decided as Follows:

> ***Decision:*** *"The CSC decided to call the applicant/Principal Investigator to give a 7 to 8 minutes presentation on their clinical study before the CSC in the next meeting. The committee also decided, that the applicant be conveyed to fulfill the shortcomings for completion of application and submit fee which has been approved by the Authority."*

The decision of CSC along with deficiencies and invitation for presentation on their application in the 2nd CSC meeting was communicated to the firm on 5th March, 2019, but still response is awaited.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- No one representative of the firm / institution appeared before the CSC. The case was so deferred for panel inspection of the trial site and proper presentation of the clinical trial.

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

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

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

The short summary of the proposed study is as under;

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	Rs.50000/- deposited instead of Rs.200000 as approved by the Authority.
3.	Investigator Brochure	Attached
4.	Final Protocol	Protocol Version 6.0 dated 15th June, 2017, has been provided.
5.	Informed consent form (English & Urdu)	Attached
6.	List of participating countries (If applicable)	07 countries including Botswana, Peru, Uganda, Nepal, Mexico, Republic of Guinea and Pakistan.
7.	Phase of trial	Phase – III
8.	Quantity of Drug(s) to be imported/procured/manufactured for the trial	Attached
9.	Site(s) of the trial	Trial will be conducted at following two sites in Pakistan; The Aga Khan University Hospital, Karachi. ShaukatKhanum 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. However, no CoPP or Free Sale Certificates of the investigational products, have been furnished.
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	

Following deficiencies were identified:

i) The evidence of registration/marketing authorization of all investigational products in the country of origin along with their CoPPs and Free Sale Certificates not provided.

ii) Authorization of the sponsor to conduct the subject trial in Pakistan.

iii) The proposed clinical trial sites i.e. Aga Khan University Hospital, Karachi and ShaukatKhanum Memorial Cancer Hospital, Lahore, are required to be licensed as Clinical Trial Sites, under the Bio-study Rules, 2017.

iv) Apart from the proposed clinical trial site, the role of Aga Khan University, Karachi, in the subject clinical trial, is not well defined.

v) The mechanism for monitoring and oversight of the subject clinical trial in Pakistan and responsible person/firm for the said purpose, needs to be defined.

The deficiencies observed in the application was communicated to the applicant on 12th January, 2018, to fulfill all prerequisites according to the Bio-Study Rules 2017, but no reply received.

Afterwards case was discussed in the 1st CSC meeting and CSC decided as Follows:

> ***Decision of 1st CSC Meeting:*** *"The CSC decided to call the applicant/Principal Investigator to give a 7 to 8 minutes presentation on their clinical study before the CSC in the next meeting. The committee also decided, that the applicant be conveyed to fulfill the shortcomings for completion of application and submit fee which has been approved by the Authority."*

The decision of CSC along with deficiencies and invitation for presentation on their application in the 2nd CSC meeting was communicated to the firm on 5th March, 2019, but still response is awaited.

- Submitted for the consideration of CSC.

Decision of 2nd CSC Meeting

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

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

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

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

All the following cases are for registration of Clinical Studies and were not discussed in the first CSC meeting, as per decision for clinical studies taken in the first meeting, new applicants are also invited to present their application in form of presentation (7-8 minute) before CSC.

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).

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

The study carried out under the supervision of Dr.NaseemSalahuddin 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.

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

S. No.	Document	Remarks
1	Application on prescribed Form-I	Attached
2	Fee	Attached
3	Investigator Brochure (s)	Attached
4	Final protocol	Attached
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries	Georgia, Lesotho, Kazakhstan, Kyrgyzstan, Peru, South Africa and Pakistan
7	Phase of trial.	Phase – III
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for import of trial material.	Attached
9	Site of the trial	The Indus Hospital. Application for Site approval, applied but not approved yet.
10	Institutional Review Board (IRB) approval 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 center.	108
19	Name of Monitors & Clinical Research Associate	Attached
20	Evidence of registration in country of origin.	Attached. Explanatory note regarding two ancillary medicine attached regarding their GMP status
21	Copy of registration letter (if registered in Pakistan)	Not registered in Pakistan

22	Sample of label of the investigational product / drug.	Attached
22	Duration of trial	48 Months
23	Undertaking on stamp	Attached

It is pertanient 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 shelflife** intended to be used in this clinical trial only and NOT FOR SALE, details are as follows:

International Nonproprietary Names (INN) for Pharmaceutical Products	**Manufacturer**	**Country of origin**	**Shelf life (months)**
Investigational Medicinal Products (IP) TB Drugs			
AMIKACIN sulfate, eq. 250 mg/ml base, 2 ml, amp.	**MEDOCHEMIE**	CYPRUS	48
BEDAQUILINE, 100 mg, tab.	**JANSSEN**	BELGIUM	36
CLOFAZIMINE, 100 mg, soft caps.	**NOVARTIS**	SWITZERLAND/FRANCE	60
CYCLOSERINE 250 mg caps.	**MACLEODS**	INDIA	36
DELAMANID, 50mg, tab., blister	**OTSUKA**	GERMANY	60
ETHIONAMIDE, 250 mg, tab., blister	**MACLEODS**	INDIA	48
LEVOFLOXACIN hemihydrate, eq. 250 mg base, tab.	**HETERO**	SPAIN	36
LEVOFLOXACIN hemihydrate, eq. 500 mg base, tab.	**MACLEODS**	INDIA	48
LINEZOLID, 600 mg, coated tab.	**HETERO**	INDIA	36
MOXIFLOXACIN hydrochloride eq. to 400 mg base , tab.	**HETERO**	INDIA	36
PARA-AMINOSALICYLIC acid (PAS),del.rel.gran, 4g, sach.(25°C)	**JACOBUS**	US	24
ETHAMBUTOL hydrochloride (E), eq. 400 mg base, tab. blister	**MACLEODS**	INDIA	36
ISONIAZID (H), 300 mg, tab., blister	**MACLEODS**	INDIA	36
PYRAZINAMIDE (PZA), 400 mg, tab., blister	**MACLEODS**	INDIA	48
Ancillary medicines			
AMITRIPTYLINE hydrochloride, 25 mg, tab.	**REMEDICA LTD**	CYPRUS	60
BECLOMETASONE dipropionate, 0.10mg/puff, 200 puffs,aerosol	**LABORATORIO ALDO-UNION S.L.**	SPAIN	36
TRIHEXYPHENIDYL hydrochloride, 2 mg, tab.	**REMEDICA LTD**	CYPRUS	60
CARBAMAZEPINE, 200 mg, tab.	**MEDOCHEMIE**	CYPRUS	60
CHLORPHENAMINE maleate, 4 mg, tab.	**CADILA**	INDIA	48
FLUOXETINE, 20mg, caps.	**MYLAN**	FRANCE	48
HALOPERIDOL, 5 mg, tab.	**REMEDICA LTD**	CYPRUS	60

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

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- The Indus Hospital was advised to pay requisite fee for Dehli Medical Center also for the the approval of clinical site beside Indus Hospital. The case was deferred for inspection.

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

Application is from 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 centers:

i) Baqai Institute of Diabetes and Endocrinology, Karachi.

ii) National Defence Hospital, Lahore.

iii) University of Health Sciences, Lahore.

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

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

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

S. No.	Required Documents	Remarks
1.	Application on prescribed Form-II	Attached
2.	Fee	Not provided

3.	Investigator Brochure	Not provided & claimed that it's an observational study.
4.	Final Protocol	Protocol Version 1.1.0 dated 20th November, 2017.
5.	Informed consent form (English & Urdu)	Attached
6.	List of participating countries (If applicable)	09 countries including Bangladesh, India, Indonesia, Malaysia, Saudi Arab, United Arab Emirates, Kuwait, Egypt and Pakistan.
7.	Phase of trial	Phase-IV
8.	Quantity of Drug(s) to be imported/procured/manufactured for the trial	Details not provided. Applicant claimed as it is an observational study, there is no need to import medicines.
9.	Site(s) of the trial	Trial will be conducted at following five sites in Pakistan; 1. Baqai Institute of Diabetes and Endocrinology, Karachi. 2. National Defence Hospital, Lahore. 3. University of Health Sciences, Lahore. 4. Diabetes Institute of Pakistan, Jail Road, Lahore. 5. Hayatabad Medical Complex (Medical Teaching Institute), Peshawar.
10.	C.Vs of investigator(s)	Attached.
11.	Ethical committee approval with complete composition of committee i.e. Name and designations of the members	Ethical Committee Composition and approval from each Clinical trial Site is not provided.
12.	Approval from National Bio-ethics Committee (PHRC)	NBC Approval vide letter No.4-87/NBC-302(2ndyrExten+Amed/19/360) Dated 4th January, 2019, is attached.
13.	GMP certificate along with Free Sale Certificate/Certificate of Pharmaceutical Product (Note: For locally manufactured product GMP Cert., COA of the Product and Registration Letter will be required)	Not Provided.
14.	Pre-clinical, clinical data and safety studies.	Not provided & claimed that it's an observational Study.
15.	Summary of the protocol	Attached
16.	Summary of the Investigator Brochure	Not provided.
17.	Adverse Event Reporting form	Attached
18.	No. of Patients to be enrolled in each center	20 patients at each site.
19.	Name of monitors/clinical research associate	Mr.FaheemShehzad.
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.	Underaking on stamp paper	Not provided

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)

Description of shortcomings:

i) None of the Clinical Trial Site is licensed from the DRAP.
ii) Fee not provided.
iii) Undertaking on Stamp Paper is not provided.

The firm was communicated through letter no. F.No.03-04/2019 DD (PS), dated 02nd April, 2019, But still response is awaited.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- The case was deffered for presentation and for panel inspection if required. The case was presented before the committee wherein the committee decided to direct the firm to submit requisite fee for each site

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

Application is from Dr. Farah Qamar, Associate Professor Department of Pediatrics and Child Health, Aga Khan University, Karachi, wherein request has been made for approval for import of study medicine for subject clinical trial, which was being carried out bythe 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.

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 isnot 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 thatit's a clinical Trial ofalready 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

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

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

Aftere evaluation of the reply following shortcomings were recorded:

i) Applicant is not properly applying for approval of Clinical Studies.

ii) Applicant continuously insisting to grant approval for impot of trial medication.

iii) No evidence is provided for exemption, granted by Ministary of Foreign Affairs.

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

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- After presentation from Principal Investigator (PI) it was decided that the import of unregistered drug has taken place inadvertantly. The PI shall write to CEO DRAP for not following the procedures of import and giving declarations that import shall be carried out as per import laws of investigational drugs for clinical studies and requested to condone. The inspection will be conducted if required.

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

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

2. The trial comprises of two primary objectives;

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

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

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached
2	Fee	Rs.50000/- deposited instead of Rs.200000/-
3	Investigator Brochure (s)	Attached
4	Final protocol	Attached Action – I (Version 1.9.2) Action – II (Version 1.5)
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries	Bangladesh, India, Kenya, Nigeria and Pakistan
7	Phase of trial.	Phase – IV
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for import of trial material.	**ACTION – I Trial** Dexamethasone Injection 4mg/ml = 5760 ampoules Placebo (Sodium chloride 0.9%) = 5,760 ampoules **ACTION – II Trial** Dexamethasone Injection 4mg/ml = 10,800 ampoules Placebo (Sodium chloride 0.9%) = 10,800 ampoules
9	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Approval from Ethics Review Committee of Aga Khan University is attached
10	Approval of National Bio-ethics Committee (NBC)	Attached
11	CV's of the Investigators	Attached
12	GMP certificate along with COPP & free sale certificate of the investigational product.	GMP Certificate of the manufacturer i.e M/s Fresenius Kabi Manufacturing SA (Pty) Ltd., South Africa and Registration Certificate of Dexamethasone Injection 4mg/ml is attached.
13	Pre-clinical/clinical safety studies	Attached
14	Summary of Protocol and Investigator Brochure	Attached
15	Adverse Event Reporting Form	Attached
16	No of patients to be enrolled in each center.	**Liaquat University Hospital, Hyderabad** ACTION – I Trial = 120 ACTION – II Trial = 480 **Sheikh Zaid Hospital, RYK** ACTION – I Trial = 600 ACTION – II Trial = 2220 **Total:** **ACTION – I Trial = 720**

		ACTION – II Trial = 2700
17	Name of Monitors & Clinical Research Associate	Attached
18	Evidence of registration in country of origin.	Registration Certificate of Dexamethasone Injection 4mg/ml is attached.
19	Evidence of registration in Pakistan.	N/A
20	Sample of label of the investigational product / drug.	Attached
21	Duration of trial	24 Months
22	Undertaking on stamp paper	Not provided

Description of shortcomings:

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

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

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- No one representative of the firm / institution appeared before the CSC. The case was so deferred for panel inspection of the trial site and proper presentation of the clinical trial.

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

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

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

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Attached

2	Fee	Rs.50000/- deposited instead of Rs.200000/- Approved amount of fee by the Authority
3	Investigator Brochure (s)	Attached
4	Final protocol	Attached
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries	The study is Pakistan specific only
7	Phase of trial.	Phase – III
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for import of trial material.	Bovine Lactoferrin (150mg)=3150 Bovine Lactoferrin (300mg)=3150 Placebo D-Glucose=3150 Sachets
9	Institutional Review Board (IRB) approval with complete composition of committee i.e. names and designation of members.	Attached
10	National Bioethics Committee approval	Attached
11	CV's of the Investigators	Attached.
12	GMP certificate along with COPP & free sale certificate of the investigational product.	Attached.
13	Pre-clinical/clinical safety studies	Attached.
14	Summary of Protocol	Not provided.
15	Safety and progress report	Not provided.
16	Adverse Event Reporting Form	Attached
17	No of patients to be enrolled in each center.	Attached. Three Arms: 100 patients in each. **Total 300 Patients.**
18	Name of Monitors & Clinical Research Associate	Attached
19	Evidence of registration in country of origin.	Registration certificate for Glucose – D is not provided.
20	Evidence of registration in Pakistan.	Not registered in Pakistan
21	Sample of label of the investigational product / drug.	Attached
22	Duration of trial	24 Months

Description of shortcomings:

i) Application for Clinical Trial Site approval on prescribed Form-I submitted but not approved yet, from DRAP.

ii) Fee not deposited.
iii) Undertaking on stamp paper is not provided.
iv) CoPP and free sale certificates for the investigational product are not provided.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- As the Bovine Lactoferin (BLT) is not a registered drug but is a food supplement, the material cannot be allowed to be imported as drug. The studies can be carried out at approved clinical sties of DRAP, on their own of principal investigator and panel inspection will be conducted.

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).

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).

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

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

12.	Approval from National Bio-ethics Committee (PHRC)	Not provided.
13.	GMP certificate along with Free Sale Certificate/Certificate of Pharmaceutical Product (Note: For locally manufactured product GMP Cert., COA of the Product and Registration Letter will be required)	Not provided.
14.	Pre-clinical, clinical data and safety studies.	Not provided.
15.	Summary of the protocol	Not provided.
16.	Summary of the Investigator Brochure	Not provided.
17.	Adverse Event Reporting form	Not provided.
18.	No. of Patients to be enrolled in each center	150 patients.
19.	Name of monitors/clinical research associate	Not provided & claimed that it's an already registered & marketed.
20.	Evidence of registration of study drug in country of origin	Not provided.
21.	Copy of registration letter (if drug is registered in Pakistan)	Not provided.
22.	Sample of label of drug	Attached
23.	Duration of trial	Not provided.
24.	Undertaking on Stamp Paper	Not provided

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.

The firm was communicated through letter no. F.No.03-05/2019 DD (PS), dated 11th April, 2019, But still response is awaited.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- No one representative of the firm / institution appeared before the CSC. The case was so deferred for panel inspection of the trial site and proper presentation of the clinical trial.

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

Application is from Dr.Sajid Soofi, Associate Professor, Department of Paediatrics & 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, Registraion 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"

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

S. No.	Document	Remarks
1.	Application on prescribed Form-II	Attached
2.	Fee	Rs.50000/- submitted instead of Rs.200000.
3.	Investigator Brochure (s)	Not provided
4.	Final protocol	Attached
5.	Informed consent and participant information sheet (Urdu to English)	Attached
6.	List of participating countries	Pakistan, Australia and New Zealand
7.	Phase of trial.	Phase – II trial
8.	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and	Lactoferrin Capsules 200mg: 840 bottles x 30 Capsules = 25,200 Capsules

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

Description of shortcomings:

i) Application for Clinical Trial Site approval on prescribed Form-I submitted but not approved yet, from DRAP.
ii) Rs.50000/- deposited instead of Rs.200000/-.
iii) Undertaking on stamp paper is not provided.
iv) Evidence of registration in country of origin is not provided.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- No one representative of the firm / institution appeared before the CSC. The case was so deferred for panel inspection of the trial site and proper presentation of the clinical trial.

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

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

S.No.	Site Name	Investigators
01	Ayub Teaching Hospital, Abbottabad (Units A,B,C,D)	Prof. AzizunisaAbbasi Dr. Ruqia Sultana Dr. Sadia Habib Dr. Shehla Noor
02	Azad Jammu Kashmir Medical College, Muzaffarabad	Dr. Nosheen Akhter Shabbir
03	Aziz Bhatti Teaching Hospital, Gujrat	Dr. Shazia Saeed
04	Bahawalpur Victoria Hospital (Unit I, II)	Prof. Naheed Fatima Prof. BushraSherZaman
05	Baqai Medical University, Karachi	Prof. FarrukhNaheed
06	Benazir Bhutto Shaheed Hospital, Rawalpindi	Prof ShuguftaSial
07	Bolan Medical Complex Unit, Quetta (Unit I, II, III, IV)	Prof. NailaEhsan Prof. AyshaSiddiqa Prof. UzmaSohail Prof. NajmaGhaffar
08	Chandka Medical College, ShaheedMohtarma Benazir Bhutto Medical University, Larkana (Unit I, II, III)	Prof. RafiaBaloch Prof. Shahida Sheikh Prof. FoziaKashif
09	Civil Hospital Bahawalpur	Prof. Sohail Chaudhry
10	Civil Hospital Karachi (Unit I, II, III)	Prof. FauziaParveen Prof. Nazli Hossain Prof. Nusrat Shah
11	DHQ Rawalpindi	Dr. Attiya Begum
12	Federal Government Polyclinic Hospital, Islamabad	Dr. NailaIsrar
13	Holy Family Hospital Unit, Rawalpindi (Unit I, II)	Prof. Rizwana Chaudhri
14	Junnah Hospital Lahore (Unit I, II)	Prof. Tayyab Prof. ArifTajamal
15	Jinnah Post Graduate Medical Centre, Karachi (Wards 8 & 9)	Prof. HaleemaYaseen Prof. Khadija Bano
16	KEMC, Lady Willington Hospital, Lahore (Units I, II, V)	Prof. Arshad Chohan Prof. Aysha Malik Prof. AbidaSajid

17	KoohiGoath Women's Hospital, Karachi	Dr. MubasshraSamina
18	Lady Reading Hospital, Peshawar Gynecolgy A	Prof. SadaqatJabeen
19	Liaquat University of Medical & Health Sciences Hyderabad (Units I, II, III)	Prof. SajidaYousfani Prof. RaheelSikander Prof. SeemaBibi Qureshi
20	MCH Centre PIMS, Islamabad (Units I, II)	Prof. SayyedaBatoolMazhar Prof. NasiraTasneem
21	Military Hospital Rawalpindi	Prof. Shehla Baqai
22	Murshid Hospital Larkana	Dr. TayyabaNaseer
23	Nishtar Hospital, Multan (Units I, II, III)	Prof. HumaQuddusi Prof. MehnazKhakwani Dr. Shahid Irshad Rao
24	Services Hospital Lahore (Units I, II)	Prof. RubinaSohail Prof. TayyibaWasim
25	Sir Ganga Ram Hospital Lahore (Units I, II, III, IV)	Prof. ShamsaHumayun Prof. Zohra Khanum Prof. Noreen Akmal Prof. ShamilaIjaz
26	Ziauddin University Hospital, Karachi	Prof. Rubina Hussain

2. The trial comprises of primary objective;

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

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

S. No.	Document	Remarks
1	Application on prescribed form along with Fee	Attached but sign and stamp missing.
2	Fee	Deposited Rs.200000/-
3	Investigator Brochure (s)	Attached
4	Final protocol	Attached
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries	Uganda, Nigeria and Pakistan
7	Phase of trial.	Phase – III
8	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and	Not Provided

	application for import of trial material.	
9	Site of the trial	26 Clinical Trial Sites, in Pakistan, applications for Clinical Trial Sites not yetrecieved.
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Approval from Ethics Review Committees of Clinical Trial Sites with Composition not provided.
11	Approval of National Bio-ethics Committee (NBC)	Attached, dated 27th November, 2018
12	CV's of the Investigators	Attached
13	GMP certificate along with COPP & free sale certificate of the investigational product.	GMP for the Manufacturer is Attached. COPP & Free Sale Certificate are not provided.
14	Pre-clinical/clinical safety studies	Not provided. Claimed that as the product is alredy a registered product, its safety profile is well established.
15	Summary of Protocol	Attached
16	Summary of Investigator Brochure	Attached
17	Adverse Event Reporting Form	Attached
18	No of patients to be enrolled in each center.	Not Described
19	Name of Monitors & Clinical Research Associate	Dr. AasiaKayani, RMU-LSHTM Research Collaboration Centre, Holy Family Hospital, Rawalpindi, Pakistan. Dr. Kiran Javaid Research Collaboration Centre, Holy Family Hospital, Rawalpindi, Pakistan.
20	Evidence of registration in country of origin.	Not Provided
21	Copy of registration letter (if registered in Pakistan)	Not registered in Pakistan
22	Sample of label of the investigational product / drug.	Attached.
23	Duration of trial	38 Months
24	Undertaking	Undertaking is not provided.

Description of shortcomings:

After evaluation following shortcoming observed:

i) In place of CoPP / Free Sale Certificate and Evidence of registration in country of origin, for investigational product, applicant provided GMP certificate issued by MHRA, If CSC doesnot satisfied, then all documents will be required.

ii) Clinical Trial Sites described in the application are not licensed from DRAP.

The firm was communicated through letter no. F.No.03-04/2019 DD (PS), dated 03rd May, 2019, But still response is awaited.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- Prof. Rizwana given the presentation the committee in principle and the committee decided to conduct the panel inspection.

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

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

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

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

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

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

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

6	Phase of trial.	Phase – III
7	Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for import of trial material.	5000 boxes containing 40 tablets each.
8	Independent Ethics Committee (IEC)/National Bioethics Committee/Institutional Review Board (IRB) approval with complete composition of committee i.e. names and designation of members.	Not provided.
9	Trial Site	Applied Clinical Trial Site is not licensed from DRAP, and also not applied yet.
10	CV's of the Investigators	Attached.
11	GMP certificate along with COPP & free sale certificate of the investigational product.	Two GMP certificates have been provided. One issued by MoH Russia dated 10-12-2007 which was valid for 03 years and expired in 2010. Other GMP certificate is issued by Govt of Ukraine dated 21-10-2012 which expired on 21-10-2015
12	Pre-clinical/clinical safety studies	Data of a safety and efficacy study has been provided but the applicant has not furnished any comprehensive information about pre-clinical / animal studies and Phase – I and Phase – II studies.
13	Summary of Protocol	Not provided.
14	Safety and progress report	Not provided.
15	Adverse Event Reporting Form	Not provided
16	No of patients to be enrolled at each center.	5000 patients.
17	Name of Monitors & Clinical Research Associate	Not provided.
18	Evidence of registration in country of origin.	The provided document is in Russian language and therefore not readable.
19	Evidence of registration in Pakistan.	Not provided.
20	Sample of label of the investigational product / drug.	Outer label of commercial pack has been submitted.
21	Duration of trial	01 year.
22	Undertaking on stamp paper	Not provided.

Description of shortcomings:

i) Protocol of the trial is not attached with the application, which should be provided in a format as defined under Good Clinical Practice (GCP) Guidelines of International Council for Harmonization (ICH).

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

Dficiencies observed in the application was communicated to the applicant on 2nd July, 2019 and subsequent reminder was also sent on 3rd May, 2019, to fulfill all prerequisites according to the Bio-Study Rules 2017, but no reply received yet.

Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- No one representative of the firm / institution appeared before the CSC. The case was so deferred for panel inspection to see the facility at the clinical trial site.

AGENDA ITEM - VII: BA/BE Studies Registration

All the following cases for registration of BA/BE studies under agenda item-VII were discussed in the first CSC meeting. All the applicants required licensing of their BA/BE Centre from DRAP, CSC decided in its first meeting, that applicant were asked for 7-8 minutes presentation, CSC decision alongwith application defeciencies were communicated to all applicants, now again placed before CSC for disposal:

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

Application is from Professor Dr.Tasneem Ahmed, CEO M/s Pharma Professional Services Pvt Ltd, PPS House A-93, Ettawah Cooperative Housing Society, Gadap Town, Near Gulshan-e-Maymar, Karachi, wherein request has been made to register a comparative

clinical study to determine the efficacy and tolerability of combination tablets of Iron Polymaltose and Folic Acid of test product **Irpo-FA ® tablets** manufactured by M/s Nabiqasim Industries (PVT) Ltd, Karachi compared with reference product **MaltoferFol® tablets,** manufactured under license of M/s (Vifor International) Inc, in woman with Iron deficiency Anaemia(IDA) including pregnant woman.

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

i. **Study title:** A comparative, open labelled, multicentre, double arm, controlled, and randomized study in iron deficient anaemic women including pregnant woman to compare the efficacy and tolerability of test product Irpo-FA ® tablets manufactured by M/s Nabiqasim Industries (PVT) Ltd, Karachi with reference product MaltoferFol® tablets, manufactured under license of M/s (Vifor International) Inc.
ii. **Investigational Product:** Irpo-FA ® (Iron Polymaltose and Folic Acid) tablets manufactured by M/s Nabiqasim Industries (PVT) Ltd, Karachi.
iii. **Reference Product:** MaltoferFol® (Iron Polymaltose and Folic Acid) tablets**,** manufactured under license of M/s (Vifor International) Inc.
iv. **Sponsor & Manufacturer:** M/s Nabiqasim Industries (PVT) Ltd, Karachi
v. **CRO:** M/s Pharma Professional Services (Pvt) Ltd, Karachi.
vi. **Study Sites:**
    a. Department of Gynaecology, JPMC, Karachi;
    b. Sobhraj Maternity Hospital Karachi; and
    c. Karachi Medical Complex.
vii. **Principal Investigator:** Dr.Haleema Yasmin.
viii. **Funding Source**: The sponsor
ix. **Cost of the Project**: 4,000,000 PKRs (approximately).

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Application submitted as per Form-II of the Bio study Rules, 2017.
2	Fee	Not provided
3	Investigator Brochure (s)	Attached
4	Final protocol	Attached
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries if applicable	Conduct in Pakistan
7	Phase of trial.	Post-marketing study (Phase-IV).
8	Quantity of drug / trial material to be	Reference Product:

	imported/ procured.	*Total 19380 tablets (14400 tablets for 80 subjects and remaining to be retained as per GCP standards).* Test Product: *Total 19380 tablets (14400 tablets for 80 subjects and remaining to be retained as per GCP standards).*
9	Site (s) of the trial.	a. Department of obstetrics and Gynaecology, JPMC, Karachi; b. Sobhraj Maternity Hospital Karachi; and c. Karachi Medical Complex. (All the three sites are not licensed by the DRAP neither the firm has applied for it.)
10	CVs of the Investigators	Attached
11	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Approval of trial and composition of the IRB provided; but the approval of the site by the IRB is not attached with application.
12	Approval of National Bio-ethics Committee (NBC)	Not attached.
13	GMP certificate along with COPP & free sale certificate of the investigational product. (For Local Manufacturer GMP or Registration letter)	Attached
14	Pre-clinical/clinical safety studies	Provided as in Investigator Brochure.
15	Summary of the Protocol	Attached
16	Summary of the Investigator Brochure	Provided as in Investigator Brochure
17	Adverse Event Reporting Form	Attached
18	No of patients to be enrolled in each center.	Total of 160 IDA subject (woman patient). 80 subjects for test product and 80 for reference product.
19	Name of Monitors & Clinical Research Associate.	Provided as in Final Protocol.
20	Evidence of registration in country of origin.	Not Attached
21	Evidence of registration in Pakistan.	Attached
22	Sample of label of the investigational	Attached

	product / drug.	
23	Duration of trial	8 months for completion of clinical part of the trial; whereas, estimated one month would be required for analysis of data.
24	Undertaking on stamp paper	Not provided

Following deficiencies were identified:

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

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

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

iv. Undertaking on stamp paper is not provided.

v. Fee not provided.

After evaluation observations/shortcoming were recorded as per prerequisites of prescribed Form-II of the Bio-Study Rules 2017 and were accordingly communicated to the firm on 23rd January, 2019, response is still awaited.

The deficiencies observed in the application was communicated to the applicant on 23rd January, 2019, to fulfill all prerequisites according to the Bio-Study Rules 2017, but no reply received.

Afterwards case was discussed in the 1st CSC meeting and CSC decided as Follows:

> ***Decision:*** *"The CSC decided to call the applicant/Principal Investigator to give a 7 to 8 minutes presentation on their clinical study before the CSC in the next meeting. The committee also decided, that the applicant be conveyed to fulfill the shortcomings for completion of application and submit fee which has been approved by the Authority."*

The decision of CSC along with deficiencies and invitation for presentation on their application in the 2nd CSC meeting was communicated to the firm on 5th March, 2019, but still response is awaited.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- No one representative of the firm / institution appeared before the CSC. The case was so deferred for panel inspection to observe the facilities to conduct the BA BE Studies.

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

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

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

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

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Application submitted as per Form-II of the Bio study Rules, 2017.
2	Fee	Not provided
3	Investigator Brochure (s)	Attached
4	Final protocol	Attached
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries if applicable	Conduct in Pakistan
7	Phase of trial.	Post-marketing study (Phase-IV)

8	Quantity of drug / trial material to be imported/ procured.	Reference Product: *Total 550 ampoules (400 ampoules for 40 subjects and remaining to be retained as per GCP standards)* Test Product: *Total 550 ampoules (400 ampoules for 40 subjects and remaining to be retained as per GCP standards)*
9	Site (s) of the trial.	i. Department of Obstetrics and Gynaecology, JPMC, Karachi; and ii. Sobhraj Maternity Hospital Karachi. *Both the sites are not yet licensed by the DRAP neither the firm had applied for it.*
10	CVs of the Investigators	Attached
11	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	Approval of trial and composition of the IRB provided; but the approval of the site by the IRB is not attached with application.
12	Approval of National Bio-ethics Committee (NBC)	Not attached.
13	GMP certificate along with COPP & free sale certificate of the investigational product. (For Local Manufacturer GMP or Registration letter)	Attached
14	Pre-clinical/clinical safety studies	Provided as in Investigator Brochure.
15	Summary of the Protocol	Attached
16	Summary of the Investigator Brochure	Attached
17	Adverse Event Reporting Form	Attached
18	No of patients to be enrolled in each center.	80 woman subjects with iron deficiency anemia (40 subjects for test and 40 subject for reference product).
19	Name of Monitors & Clinical Research Associate.	Provided as in Investigator Brochure
20	Evidence of registration in country of origin.	Not Attached
21	Evidence of registration in Pakistan.	Attached
22	Sample of label of the investigational product / drug.	Attached
23	Duration of trial	Clinical part of the trail will be completed in 6 months; whereas, for the analysis of date estimated one month would be required.
24	Undertaking on stamp paper	Not provided

Following deficiencies were identified:

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

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

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

iv Undertaking on stamp paper is not provided.

v. Fee not provided.

The deficiencies observed in the application was communicated to the applicant on 23rd January, 2019, to fulfill all prerequisites according to the Bio-Study Rules 2017, but no reply received.

Afterwards case was discussed in the 1st CSC meeting and CSC decided as Follows:

> ***Decision:*** *"The CSC decided to call the applicant/Principal Investigator to give a 7 to 8 minutes presentation on their clinical study before the CSC in the next meeting. The committee also decided, that the applicant be conveyed to fulfill the shortcomings for completion of application and submit fee which has been approved by the Authority."*

The decision of CSC along with deficiencies and invitation for presentation on their application in the 2nd CSC meeting was communicated to the firm on 5th March, 2019, but still response is awaited.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- No person was appeared before the CSC. The case was deferred for panel inspection to observe the facilities to conduct the BA BE Studies.

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

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

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

i. **Study title:** An open labelled, controlled, and randomized study with 2 parallel groups to compare the efficacy and safety of test drug (Rexyl cough syrup) with reference (Hydryllin cough syrup) in adult outpatients with productive cough.

ii. **Investigational Product:**Rexyl ® cough syrup (Aminophylline, Ammonium Chloride, Diphenhydramine and menthol), manufactured by Nabiqasim Industries (Pvt) limited, Karachi.

iii. **Reference Product:** Hydryllin ® cough syrup (Aminophylline, Ammonium Chloride, Diphenhydramine and Menthol) manufactured by the Searle Company Ltd.

iv. **Sponsor & Manufacturer:** M/s Nabiqasim Industries (Pvt) Ltd, Karachi.

v. **CRO:** M/s Pharma Professional Services (Pvt) Ltd, Karachi.

vi. **Study Site:** Karachi Medical Complex, Gulshan-e- Iqbal, Karachi.

vii. **Principal Investigator:** Prof Dr. M. RafiqKhanani.

viii. **Funding Source**: The sponsor

ix. **Cost of the Project**: 20,000,00 PKRs (approximately)

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

S. No.	Document	Remarks
1	Application on prescribed Form-II	Application submitted as per Form-II of the Bio study Rules, 2017.
2	Fee	Not provided
3	Investigator Brochure (s)	Attached
4	Final protocol	Attached
5	Informed consent and participant information sheet (Urdu to English)	Attached
6	List of participating countries if applicable	Conduct in Pakistan.
7	Phase of trial.	Post-marketing study (Phase-IV)
8	Quantity of drug / trial material to be imported/ procured.	Reference Product: *Total 600 Bottles (300 for 100 subjects and 300 would be retained as per GCP standards).* Test Product: Total 600 bottles (*300 for 100 subjects and 300 would be retained as per GCP standards).*
9	Site (s) of the trial.	Karachi Medical Complex, Karachi (Not approved by the CSC)
10	CVs of the Investigators	Attached

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

Following deficiencies were identified:

i. The clinical trial site of Karachi Medical Complex is not licensed with DRAP neither the hospital had applied for its license;
ii. The approval from the National Bio Ethic committee has not been attached with the application;
iii. The clinical site is not approved by the IRB (ethics-committee); and
iv. Undertaking on stamp paper is not provided and fee is not submitted.
v. Fee not provided.

The deficiencies observed in the application were communicated to the applicant on 23rd January, 2019, to fulfill all prerequisites according to the Bio-Study Rules 2017, but no reply received.

Afterwards case was discussed in the 1st CSC meeting and CSC decided as Follows:

Decision of 1st CSC meeting: *"The CSC decided to call the applicant/Principal Investigator to give a 7 to 8 minutes presentation on their clinical study before the CSC in the next meeting. The committee also decided, that the applicant be conveyed to fulfill the shortcomings for completion of application and submit fee which has been approved by the Authority."*

The decision of CSC along with deficiencies and invitation for presentation on their application in the 2nd CSC meeting was communicated to the firm on 5th March, 2019, but still response is awaited.

- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- No one representative of the firm / institution appeared before the CSC. The case was so deferred for panel inspection to observe the facilities to conduct the BA BE Studies.

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

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

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

The short summary of the proposed study is as under;

i. **Study title:** A Single Center, Open Label, Randomized, Single Dose, Two way Cross-over Study to explore the Relative Bioavailability of **Moksi (Moxifloxacin) 400mg Tablet** of M/s Abbott Laboratories and **Avelox (Moxifloxacin) 400mg Tablet** of M/s Bayer Pharmaceuticals under the fasting conditions in Healthy Male Pakistani Subjects.

ii. **Investigational Product:**Moksi (Moxifloxacin) 400mg Tablet

iii. **Reference Product:**Avelox (Moxifloxacin) 400mg Tablet of M/s Bayer Pharma

iv. **Sponsor & Manufacturer:** M/s Abbott Laboratories (Pakistan) Ltd., Karachi.

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

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

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

viii. **Funding Source**: The sponsor

ix. **Cost of the Project**: Rs.3800,000 (approximately)

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

S. No.	Document	Remarks
1	Application	Application has been submitted on prescribed Form – IIA, under the Bio-study Rules, 2017
2	Fee	Rs.50000/- deposited instead of Rs.200000
3	Formulation of Investigational Product	Attached
4	Purpose of Study along with its cost and source of fund	Attached
5	Proposed center for study	CBSCR, ICCBS Not yet approved
6	Investigational Design and Study Plan	Attached
7	Pre-clinical or clinical data or safety studies	Not applicable
8	Final protocol	Attached
9	Detail of Investigators	Attached
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	The applicant has informed that the IRB approval is still under process.
11	Approval of National Bio-ethics Committee (NBC)	Not attached.
12	Informed consent and participant information sheet (Urdu to English)	Attached
13	Summary of Protocol and Investigator Brochure	Attached
14	Adverse Event Reporting Form	Attached
15	Name of Monitors & Clinical Research Associate	Attached
16	Proof of Registration of Investigational Product in Pakistan	Attached
17	Quantity of Investigational Product	Reference Product: 350 Tablets Test Product: 350 Tablets
24	Undertaking on stamp paper	Not provided

Description of shortcomings:

Following deficiencies were identified:

i) BA/BE centre of CBSCR, ICCBS is not yet licensed by the DRAP.

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

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

iv) Undertaking on stamp paper is not provided.

- The deficiencies observed in the application was communicated to the applicant on 09th October, 2018, after scrutiny of the reply another letter sent on 11th January, 2019, to apply on prescribed Form-I for BA/BE Studies site approval and fulfill all prerequisites according to the Bio-Study Rules 2017, Now the firm applied for BA/BE Studies Centre.
- Case was discussed in the 1st CSC meeting and CSC decided as Follows:

  Decision: *"The CSC decided to call the applicant/Principal Investigator to give a 7 to 8 minutes presentation on their BA/BE study before the CSC in the next meeting. The committee also decided, that the applicant be conveyed to fulfill the shortcomings for completion of application and submit fee which has been approved by the Authority."*
- The decision of CSC along with deficiencies and invitation for presentation on their application in the 2nd CSC meeting was communicated to the firm on 5th March, 2019, but still response is awaited.
- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- The case was deferred for presentation and then panel inspection.

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

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

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

The short summary of the proposed study is as under;

i. **Study title:** A Single Center, Open Label, Randomized, Single Dose, Two way Cross-over Study to explore the Bioequivalence of Xaroban 20mg (Rivaroxaban) tablet Manufactured by The Searle Company Limited, with reference product Xarelto 20mg (Rivaroxaban) Tablet manufactured by Bayer Healthcare Pharmaceuticals under Fed conditions in Healthy male Pakistani Subjects.

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

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

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

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

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

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

viii. **Funding Source**: The sponsor

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

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

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

14	Adverse Event Reporting Form	Attached
15	Name of Monitors & Clinical Research Associate	Attached
16	Proof of Registration of Investigational Product in Pakistan	Attached
17	Quantity of Investigational Product	Reference Product: 110 Tablets Test Product: 110 Tablets

Description of shortcomings:

Following deficiencies were identified:

i) BA/BE centre of CBSCR, ICCBS is not yet licensed by the DRAP.

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

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

iv) Undertaking on stamp paper is not provided.

- The deficiencies observed in the application was communicated to the applicant on 09th October, 2018, after scrutiny of the reply another letter sent on 11th January, 2019, to apply on prescribed Form-I for BA/BE Studies site approval and fulfill all prerequisites according to the Bio-Study Rules 2017, Now the firm also applied for BA/BE Studies Centre.
- Case was discussed in the 1st CSC meeting and CSC decided as Follows:

  Decision of 1st CSC Meeting: *"The CSC decided to call the applicant/Principal Investigator to give a 7 to 8 minutes presentation on their BA/BE study before the CSC in the next meeting. The committee also decided, that the applicant be conveyed to fulfill the shortcomings for completion of application and submit fee which has been approved by the Authority."*
- The decision of CSC along with deficiencies and invitation for presentation on their application in the 2nd CSC meeting was communicated to the firm on 5th March, 2019, but still response is awaited.
- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- The case was deferred for presentation and then panel inspection.

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

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

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

The short summary of the proposed study is as under;

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

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

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

6	Investigational Design and Study Plan	Attached
7	Pre-clinical or clinical data or safety studies	Not applicable.
8	Final protocol	Attached
9	Detail of Investigators	Attached
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	The applicant has informed that the IRB approval is still under process.
11	Approval of National Bio-ethics Committee (NBC)	Provided
12	Informed consent and participant information sheet (Urdu to English)	Attached
13	Summary of Protocol and Investigator Brochure	Attached
14	Adverse Event Reporting Form	Attached
15	Name of Monitors & Clinical Research Associate	Attached
16	Proof of Registration of Investigational Product in Pakistan	Attached
17	Quantity of Investigational Product	Reference Product: 80 Tablets Test Product: 80 Tablets

Description of shortcomings:

Following deficiencies were identified:

i) BA/BE centre of CBSCR, ICCBS is not yet licensed by the DRAP.

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

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

iv) Undertaking on stamp paper is not provided.

- The deficiencies observed in the application was communicated to the applicant on 09th October, 2018, after scrutiny of the reply another letter sent on 11th January, 2019, to apply on prescribed Form-I for BA/BE Studies site approval and fulfill all prerequisites according to the Bio-Study Rules 2017, Now the firm also applied for BA/BE Studies Centre.
- Case was discussed in the 1st CSC meeting and CSC decided as Follows:

  Decision: *"The CSC decided to call the applicant/Principal Investigator to give a 7 to 8 minutes presentation on their BA/BE study before the CSC in the next meeting. The committee also*

decided, that the applicant be conveyed to fulfill the shortcomings for completion of application and submit fee which has been approved by the Authority."

- The decision of CSC along with deficiencies and invitation for presentation on their application in the 2nd CSC meeting was communicated to the firm on 5th March, 2019, but still response is awaited.
- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- The case was deferred for presentation and then panel inspection.

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

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

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

The short summary of the proposed study is as under;

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

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

S. No.	Document	Remarks
1	Application	Application has been submitted on prescribed Form – IIA, under the Bio-study Rules, 2017

2	Fee	Rs.50000/- deposited instead of Rs.200000
3	Formulation of Investigational Product	Attached
4	Purpose of Study along with its cost and source of fund	Attached
5	Proposed center for study	CBSCR, ICCBS Not yet approved by the DRAP.
6	Investigational Design and Study Plan	Attached
7	Pre-clinical or clinical data or safety studies	Not applicable.
8	Final protocol	Attached
9	Detail of Investigators	Attached
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	The applicant has informed that the IRB approval is still under process.
11	Approval of National Bio-ethics Committee (NBC)	Provided
12	Informed consent and participant information sheet (Urdu to English)	Attached
13	Summary of Protocol and Investigator Brochure	Attached
14	Adverse Event Reporting Form	Attached
15	Name of Monitors & Clinical Research Associate	Attached
16	Proof of Registration of Investigational Product in Pakistan	Attached
17	Quantity of Investigational Product	Reference Product: 80 Tablets Test Product: 110 Tablets

Description of shortcomings:

Following deficiencies were identified:

i) BA/BE Centre of CBSCR), ICCBS is not yet licensed by the DRAP.

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

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

iv) Undertaking on stamp paper is not provided.

- The deficiencies observed in the application was communicated to the applicant on 09th October, 2018, after scrutiny of the reply another letter sent on 11th January, 2019, to apply on prescribed Form-I for BA/BE Studies site approval and fulfill all prerequisites according to the Bio-Study Rules 2017, Now the firm also applied for BA/BE Studies Centre.
- Case was discussed in the 1st CSC meeting and CSC decided as Follows:

  Decision: *"The CSC decided to call the applicant/Principal Investigator to give a 7 to 8 minutes presentation on their BA/BE study before the CSC in the next meeting. The committee also decided, that the applicant be conveyed to fulfill the shortcomings for completion of application and submit fee which has been approved by the Authority."*
- The decision of CSC along with deficiencies and invitation for presentation on their application in the 2nd CSC meeting was communicated to the firm on 5th March, 2019, but still response is awaited.
- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- The case was deferred for presentation and then panel inspection.

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

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

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

The short summary of the proposed study is as under;

i. **Study title:** A Single Center, Open Label, Randomized, Single Dose, One Period Study to explore the Pharmacokinetics of Dextop (Dexlansoprazole) 60mg Capsules under the fasting conditions in Healthy Male Pakistani Subjects.
ii. **Investigational Product:**Dextop (Dexlansoprazole) 60mg Capsules of M/s Searle Company Ltd.
iii. **Sponsor & Manufacturer:** M/s The Searle Company Limited, Karachi.
iv. **CRO and Study Site:**Center for Bioequivalence Studies and Clinical Research (CBSCR), University of Karachi.

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

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

vii. **Funding Source**: The sponsor

viii. **Cost of the Project**: Rs.15,00,000 (approximately)

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

S. No.	Document	Remarks
1	Application	Application has been submitted on prescribed Form – IIA, under the Bio-study Rules, 2017
2	Fee	Rs.50000/- deposited instead of Rs.200000
3	Formulation of Investigational Product	Attached
4	Purpose of Study along with its cost and source of fund	Attached
5	Proposed center for study	CBSCR, ICCBS Not approved yet
6	Investigational Design and Study Plan	Attached
7	Pre-clinical or clinical data or safety studies	Not applicable.
8	Final protocol	Attached
9	Detail of Investigators	Attached
10	Institutional Review Board (IRB) approval of sites with complete composition of committee i.e. names and designation of members.	The applicant has informed that the IRB approval is still under process.
11	Approval of National Bio-ethics Committee (NBC)	Provided
12	Informed consent and participant information sheet (Urdu to English)	Attached
13	Summary of Protocol and Investigator Brochure	Attached
14	Adverse Event Reporting Form	Attached
15	Name of Monitors & Clinical Research Associate	Attached
16	Proof of Registration of Investigational Product in Pakistan	Attached
17	Quantity of Investigational Product	100 Capsules

Description of shortcomings

Following deficiencies were identified:

i) BA/BE centre of CBSCR, ICCBS is not yet licensed by the DRAP.

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

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

iv) Undertaking on stamp paper is not provided.

- The deficiencies observed in the application was communicated to the applicant on 09th October, 2018, after scrutiny of the reply another letter sent on 11th January, 2019, to apply on prescribed Form-I for BA/BE Studies site approval and fulfill all prerequisites according to the Bio-Study Rules 2017, Now the firm also applied for BA/BE Studies Centre.
- Case was discussed in the 1st CSC meeting and CSC decided as Follows:

  Decision: *"The CSC decided to call the applicant/Principal Investigator to give a 7 to 8 minutes presentation on their BA/BE study before the CSC in the next meeting. The committee also decided, that the applicant be conveyed to fulfill the shortcomings for completion of application and submit fee which has been approved by the Authority."*
- The decision of CSC along with deficiencies and invitation for presentation on their application in the 2nd CSC meeting was communicated to the firm on 5th March, 2019, but still response is awaited.
- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- The case was deferred for presentation and then panel inspection.

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

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

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

The short summary of the proposed study is as under;

i. **Study title:** An open labelled Two period, Two Treatments, Two Sequences, Single Dose, Single Dose, Randomized, Crossover Bioequivalence Study Of Clarithromycin (Clarithro) 500mg Tablets in Healthy Volunteers, Compared to equivalent drug dose in reference formulation of KLARICID 500mg Tablets under fasting condition.

ii. **Investigational Product:** Clarithro® (Clarithromycin) 500mg Tablets of M/s NabiQasim (Pvt) Ltd and Klaricid® (Clarithromycin) 500mg Tablets of M/s Abbott Laboratories, Karachi

iii. **Sponsor &Manufacturer:**M/s Nabiqasim Industries (Pvt) Ltd, Karachi.

iv. **CRO and Study Site:** M/s Pharma Professional Services (Pvt) Ltd, Karachi.

v. **Principal Investigator:**Prof.Dr.Tasneem Ahmad

vi. **Funding Source**: The sponsor

vii. **Cost of the Project**: Rs.3,000,000 (approximately)

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

S. No.	Document	Remarks
1	Application	Application has been submitted on prescribed Form – IIA, under the Bio-study Rules, 2017
2	Fee	Not Provided
3	Formulation of Investigational Product	Attached
4	Pharmacodynamics and Pharmacokinetics of Investigational Product	Attached
5	Purpose of Study along with its cost and source of fund	Study Objective: To determine the Bioequivalence of Test Product Clarithro® 500mg Tablets, manufactured by M/s Nabiqasim Industries (Pvt) Ltd, Karachi, Pakistan, in healthy Adult Human Subjects, compared with Reference Product: Klaricid® 500mg Tablet, manufactured by Abbott Laboratories, Karachi, Pakistan. Study Purpose: To evaluate the bioequivalence of test product (Clarithro®) as a generic replacement for the reference product (Klaricid®) Anticipated Cost of Project PKR 3,000,000/-
6	Proposed center for study	M/s Pharma Professional Services (Pvt) Ltd, Karachi.
7	Investigational Design and Study Plan	To investigate average bioequivalence in a 2x2 Crossover design in humans. Attached
8	Investigational design and study plan	Attached
9	Pre-clinical or clinical data or safety studies	Attached
10	Final protocol	Attached
11	Detail of the investigator (Principal investigator, analysts and others along with CV)	Attached

12	IRB approval	Attached
13	Ethical committee composition (names and designations)	Attached
14	Site approval by the Ethics committee	Attached
15	Informed consent (English and Urdu)	Attached
16	Summary of the protocol or synopsis (Investigational Product)	100 Capsules
17	Adverse Event Reporting Form	Attached
18	Name of the monitor or clinical research associate	Attached
19	Evidence of registration in country of origin (GMP certificate along with CoPP or Free sale certificate)	Attached
20	Copy of registration letter if registered in Pakistan	Attached
21	Proposed label of investigational product	Attached
22	Quantity of investigational product to be used in the study along with justification (Note: All the quantities of the each of investigational product should be procured from one single source)	Reference Product: 120 Tablets Test Product: 120 Tablets

Description of shortcomings:

Following deficiencies were identified:

i) It is mandatory to get approval of the BA/BE Studies Center before approval or registration of BA/BE Studies, but the applied center is still not approved/ licensed with DRAP.

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

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

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

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

The firm was communicated through letter no. F.No.14-7/2018 DD (PS), dated 09th October, 2018, that apply on prescribed Form-I for BA/BE Studies site approval and fulfill all prerequisites for approval of BA/BE Studies approval under the Bio-Study Rule 2017, Now the firm also applied for BA/BE Studies Centre.

- Case was discussed in the 1st CSC meeting and CSC decided as Follows:

  Decision: *"The CSC decided to call the applicant/Principal Investigator to give a 7 to 8 minutes presentation on their BA/BE study before the CSC in the next meeting. The committee also decided, that the applicant be conveyed to fulfill the shortcomings for completion of application and submit fee which has been approved by the Authority."*

- The decision of CSC along with deficiencies and invitation for presentation on their application in the 2nd CSC meeting was communicated to the firm on 5th March, 2019, but still response is awaited.
- Submitted for the consideration of CSC.

Decision in 2nd CSC Meeting:- No One representative of the firm / institution appeared before the CSC. However Dr.Tasneem Ahmed informed telephonically that due to short period of time he could not manage to reach the Lahore to appear before the committee. The case was deferred for presentation and then panel inspection.

Agenda Item – VIII: Minimum Divisions or Departments required to work as a CROs

A Contract Research Organization (CRO), some times also referred as Clinical Resaearch organization, is basically a company or organization that helps to conduct research for a sponsor company. This research can be anything from pre-clinical development of new products to post marketing research activities.

As per ICH-GCP Guidelines a Cintract research organization can be defined as follows:

"A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial duties and functions."

A contract research organization (CRO) can work with a number of sponsors who can be referred to a clients. Conducting a clinical research is a complex process which requires a large team of people with different skill sets and experience to perform different functions.

The main functions required for conducting clinical research which are usually also the department in a clinical research organization are:

i) Medical Function:

People working in this area are medically qualified people who help to design a clinical study, help to develop clinical trial protocols and provide medical related input throughout the study. This includes designations such as medical monitor, clinical research phjysician, medical advisor etc.

ii) Regulatory Submission Team:

This team or department assists in submitting various documents and obtaining approvals from regulatory authorities.

iii) Clinical Operations:

This team is usually the largest in a clinical research organization. It consisit of clinical research assiciates, project managers, clinical trial assistants, etc. This is the team which selects clinical trial sites, conducts monitoring at sites, assists in study closeouts and help in over all study management.

iv) Data Management:

A data management team helps in designing various tools and databases to collect data. Again this is an important team of the contract research organization. They help to ensure that the data collected from clinical trials is clean and ready for analysis.

v) Biostatistics:

Biostatistics team help to analyze the study data as per the protocol and to figure out weather the study has yielded positive or negative results. They help to generate statistical tables, figures and graphs with their interpretation which are then passed on to the medical writers for compiling into a report.

vi) Medical Writing:

Medical writers help write study results in a way which can be understood by general public. They help writing study reports, study protocols, writing promotional materials etc.

vii) Quality Assurance:

This department conducts audits to ensure all guidelines, and standard operating procedures were followed. This department is responsible for the overall quality of the organization.

viii) IT Team:

IT supports staff is a part of all CROs. They take care of IT related needs lke purchase and maintinence of desktop laptops, servers, telephones, software's etc.

ix) Admin & Finance:

This team takes care of all administration and finance related work.

x) Human Resources:

All major CROs have a dedicated human resources team. They are ones responsible for hiring new staff and developing measures to retain talent pool in the organization.

xi) Training & Development:

This is a dedicated department in all major CROs. This department / team focuses on the professional development of its employees and conducts routine trainings to ensure hat the staff remains skilled and up to date with recent advances.

Decision in 2nd CSC Meeting:- The minimum requirement for CRO was accepted.

Agenda Item - IX: GUIDELINES FOR MINIMUM REQUIREMENTS FOR CLINICAL AND ANALYTICAL LABS FOR CLINICAL STUDIES.

MINIMUM ANALYTICAL LAB EQUIPMENT LIST FOR BA/BE CENTERS OR BIO-LAB

S.No	Equipment Name	Quantity
1.	Analytical Balance	
2.	Centrifuge	
3.	Disintegration Test Appratus	
4.	Dissolution Test Appratus	
5.	Hardness Test Appratus	
6.	Friability Test Appratus	
7.	Filtration Test Assembly	
8.	LCMS	
9.	HPLC (Complete System)	
10.	UV-Visible Spectrophotometer	
11.	Karl Fischer	
12.	Magnetic Stirrer with Hot Plate	
13.	Ultrasonic Bath	
14.	Thermo-Mixer	
15.	Refrigerator 2-8°C	
16.	Refrigerator -20°C	
17.	Vaccum Oven	
18.	Vortex Mixer	
19.	Water Distillation	
20.	Stability Chamber	
21.	Standard Weights	
22.	Stop Watch	
23.	Thermometer	
24.	pH meter	
25.	Potentiometer	
26.	Polarimeter	
27.	Refractometer	
28.	Viscometer	
29.	Melting Point Appratus	
30.	Dehumidifier	
31.	Moisture Balance	
32.	Wet Dry bulb Hygro Meter	
33.	Hygrometer	
34.	TDS Meter	
35.	Conductivity Meter	
36.	Fuming Hood	
37.	Bio Shaker	
38.	MICRO-LAB	
39.	Bio-Safety Cabnet	

40.	Colony Counter	
41.	Cool Incubator	
42.	Hot Incubator	
43.	Autoclave	
44.	Laminar Flow Hood	
45.	Top Loading Balance	
46.	Dry Heat Sterilizer	

MINIMUM CLINICAL LAB EQUIPMENT LIST FOR CLINICAL TRAIL SITE / BA/BE CENTERS

S.No	Equipment Name	Quantity
01	Stethoscope	
02	Sphygmomanometer (B.P Appratus)	
03	Height & Weight Machine	
04	ECG Machine	
05	Suction Machine	
06	Oxygen Cylinder	
07	Centrifuges	
08	Refrigerator (for Madicines)	
09	Ultra Low Freezer -70 (For Samples)	
10	Temprature Monitor	
11	Digital Thermometer	
12	Refrigerated Centrifuge Machine & Tubes	
13	Resuscitator	
14	Clinical Thermometer	
15	Blood / Samples Transfer Boxes & WHO Bag	
16	Alcohol Meter	
17	Otto Scope	
18	Nebulizing System	
19	Electric Suction Appratus	
20	Laryngo Scope	
21	Defibrillator	
22	10 beds for patients	
23	Any other Miscellaneous requirement	

Decision in 2nd CSC Meeting:- The minimum requirement for Clinical Lab for clinical trial site, BA / BE Centers was accepted.