**Minutes of the 5th CSC Meeting held on 8th August, 2019.**

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1. The 5th Meeting of CSC held on 08th August, 2019 at the Committee Room of DRAP, Islamabad, to dispose of matters decided in 4th meeting and could not be implemented due to the reason that the Chairman and Secretary CSC had to join abroad (Hajj medical duty, Saudi Arab). For the fifth meeting stop gap arrangement to the position of additional director (secretary CSC) was made through the notification of DRAP but that for Director (ex-officio chairman CSC) was not made. Further the requests of applicants suffering due to non-functional of CSC for the time being because of above said reason was creating factor of urgency on DRAP to conduct the CSC meeting. The risk of reversal of foreign funding with winding up of international trials in Pakistan and disenchantment of researchers for not receiving the outcomes of 4th meeting because of non-actualization of minutes of 4th meeting; all added the need for DRAP to conduct the 5th meeting on urgent basis.

As per order the additional director (ex-officio secretary of CSC) issued the notice of 5th meeting to the members of CSC. The following respectable members joined the meeting as per schedule.

2. The following members attended the meeting:-

| **Sr. No.** | **Name** | **Designation** |
|---|---|---|
| 1. | Prof. Muzammil Hassan Najmi | Chairman CSC (elected) |
| 2. | Muhammad Adnan Faisal Saim. | Secretary CSC / Additional Director, Pharmacy Services. |
| 3. | Prof. Dr. Javed Akram | VC, University of Health Sciences, Lahore |
| 4. | Dr. Faiza Bashir | Nominee of Chairman NBC-PHRC |
| 5. | Ms. Salwa Ahsan | Chief of Pharmacy, Shifa Intl Hospital, Islamabad. |
| 6. | Dr. Farhana Badar. | Biostatistician & Epidemiologist, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore. |

Due to no availability Director Pharmacy Services (Ex-Officio Chairman of CSC), CSC elected from its members; Prof. Brig. (Rtd). Muzammil Hassan Najmi as Chairman for the meeting, and decided that in future in case of non-availability of Director Pharmacy Services, who is ex-officio Chairman, CSC will elect Chairman for that meeting to conduct its proceedings.

The Meeting started with recitation of the Holy Verses of Quran.The general discussion ensued; Prof. Dr. Javed Akram raised the issue of Payment / reimbursement of TA/DA, and out station stay for meetings and during inspection of Clinical Trial Site, CROs, Bio Analytical Labs and BA/BE Studies centres to members/panels. The CSC concluded that DRAP should consider and take the measures for redressing this issue.

In the technical discussion for disposal of cases the CSC discussed that the relevant documents (i.e. Layout plan, equipment list and staff list) of applications, will be provided to the concerned panel before inspection.

Prof. Dr. Javed Akram proposed that following details should be asked from applicants and be provided to the CSC for constitution of inspection panel with relevant expertise and same information will be used to modify the inspection checklists:

i) Phase of Clinical Trial

ii) Details regarding nature of clinical studies (Inpatient or Outpatient)

iii) Specialties or number of department involved in the study.

Prof. Dr. Javed Akram added that if an applicant desire a licence for the entire facility (Hospital), they should have facility of a separate Clinical Trial Unit with relevant staff, Ms. Salwa Ahsan proposed that there should be minimum criteria for an institution / Hospital. i.e. Resuscitation room, emergency facility, ICU, pharmacy and facilities and system for ADR reporting. The committee discussed the review mechanism for the applications which will have to be finally decided by the CSC. The secretary of the CSC told the forum that there is provision in rules for CSC to make its subcommittee for reviewing etc.

CSC members discussed that SOPs regarding inspections of CROs, BA/BE studies Centres and Clinical Trial Sites (Hospitals / institutions) may be developed for qualitative and quantitative analysis and developing mechanism of scoring during inspections. As a conclusion of the technical discussion, following tasks were distributed:

| **S.No.** | **SOP Title** | **Assigned to** |
|---|---|---|
| 1 | SOP for Clinical Trial Site Inspections | i) Prof. Dr. Javed Akram<br>ii) Dr. Atif Mirza |
| 2 | SOP for BA/BE Studies Centres inspection | i) Dr. Farhana Badar |
| 3 | SOP for CROs inspections | i) Prof. Brig. Muzammil Hassan Najmi.<br>ii) Dr. Faiza Bashir<br>iii) Ms. Salwa Ahsan |

The assigned tasks will be presented through power point in the next CSC meeting.

**AGENDA ITEM - I:** **CONFIRMATION OF THE MINUTES OF THE 4th CLINICAL STUDIES COMMITTEE MEETING.**

1.1 The CSC confirmed the minutes of 4th Meeting of Clinical Studies Committee (CSC) held on 17th July, 2019, at Committee Hall, DRAP Headquarter, TF Complex, Islamabad, and signed on the hard copy of minutes for record and implementation.

Dr. Javed Akram and Dr. Farhana Badar made addendum "Deferred for reinsertion of BA/BE Site" in the case 1.2. A"International Centre For Chemical And Biological Sciences (ICCBS), University Of Karachi, (F. No.15-07/2019).

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

**2.1)** **REQUEST FOR APPROVAL OF OBSERVATIONAL STUDY PROGRAM ASSESSING EFFECTIVENESS AND TOLERABILITRY OF GLICLAZIDE 60mg MODIFIED RELEASE TABLET IN PATIENTS WITH TYPE II DIABETES FASTING DURING RAMADAN, TO BE CONDUCTED AT AKRAM MEDICAL COMPLEX, LAHORE. (F.No.15-27/2019)**

Application is from Dr. Ayesha Nasir, Akram Medical Complex, Lahore, submitted by Dr. Ahmed Aatif Mirza, President Clinical Operations M/s DRK Pharma Solution, Lahore on behalf of Sponsor M/s Servier Research and Pharmaceuticals (Pvt) Ltd, dated 12th July, 2019, wherein the request is in reply of this division letter number F.No.03-01/2019-DD (PS), to license their Private Hospital with DRAP to work as Clinical Trial Site (CTS), to conduct the clinical studies mentioned in subject cited above.

2.1.2. The application is on prescribed Form-I of the Bio-Study Rules 2017 along with fee of Rs.100000/- for Clinical Trial Site vide challan no.0550727, 11th July, 2019.

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

| S. No. | Required Documents / Information | Remarks |
|---|---|---|
| 1 | Application on prescribed Form-I of The Bio-Study Rules 2017. | Attached |
| 2 | Fee | Attached |
| 3 | Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses | Applicant is Professor of Medicine and working at Private |

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

2.1.4. After evaluation following shortcomings were recorded:

i) Details of premises including layout plan of the site is not provided.

ii) Details of the section wise equipment is not provided.

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

2.1.5 Shortcomings were communicated to the applicant vide letter number F.No.15-27/2019 DD (PS), dated 23rd July, 2019, applicant submitted their reply vide letter number nil, dated 29th July, 2019, reply of the applicant is as follows:

| S.No. | Shortcomings | Reply |
|---|---|---|
| 1 | Details of premises including layout plan of the site is not provided. | This is required for Phase-I and BA/BE Studies where there is a requirement for in-door facilities and laboratory. This being an Observational (Phase-IV) study this is not applicable here. |
| 2 | Details of the section wise equipment is not provided. | There is no equipment required in conducting this study as can be confirmed by the protocol. |
| 3 | Names and qualifications of the section wise staff is not provided. | The only two site personal engaged in the conduct of study are the investigator and his coordinator. Their names and their CVs have been provided. |

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

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

***The CSC after deliberations decided to conduct the inspection of Clinical Trial Site (CTS) from team, comprising of the following experts. In case any***

***member is not available the committee authorized its chairman to add another suitable member of the relevant expertise from the pool of experts. The applicant shall be informed for the proposed date of inspection accordingly.-***

| | |
|---|---|
| i. | Dr. Abdur Rashid |
| ii. | Dr. Nadeem Irfan |
| iii. | Dr. Farhana Badar |
| iv. | Dr. Ali Jawa |

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

2.1.8. Due to availability of some members and non-availability of other members, Chairman CSC, exercising the power delegated by the CSC in its 3rd meeting, added the inspection pool members for the inspection, and following expert's panel inspected the facility on 24th July, 2019:

| | |
|---|---|
| i. | Dr. Abdur Rashid |
| ii. | Mr. Waqas Latif |
| iii. | Ali Asghar Jawa |
| iv. | Dr. Nadeem Irfan Bukhari |

**2.1.9. Remarks of inspection team:**

Keeping in view the clinical operations, in-door & out-door facilities, pharmacy premises, SOPs, records, documentations, safety measures, environment, lab, X-ray, ICU, operation theatres, Gynae theatre, in-house incinerator, and vast previous experience of international and national clinical trials, Akram Medical Complex Lahore is recommended for approval as Clinical Trial Site not only for Dia-Ramadan but also for Phase-II, III and Phase-IV Studies.

**2.1.10. Concluding status of inspection by inspection panel:**

***"Recommended for approval"***

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

**2.1.12 Decision of 5th CSC Meeting:-**

"***The CSC unanimously approved theAKRAM MEDICAL COMPLEX, LAHORE, as Clinical Trial Site, under the Bio Study Rules 2017, to conduct phase II, III, and IV for both OPD and Indoor patients."***

**2.2)** **REQUEST FOR APPROVAL OF OBSERVATIONAL STUDY PROGRAM ASSESSING EFFECTIVENESS AND TOLERABILITRY OF GLICLAZIDE 60mg MODIFIED RELEASE TABLET IN PATIENTS WITH TYPE II DIABETES FASTING DURING RAMADAN, TO BE CONDUCTED AT DIABETES INSTITUTE OF PAKISTAN.(F.No.15-28/2019 DD (PS))**

Application is from Dr. Muhammad Imtiaz Hassan, Diabetes Institute of Pakistan, Lahore, submitted by Dr. Ahmed Aatif Mirza, President Clinical Operations M/s DRK Pharma Solution, Lahore on behalf of Sponsor M/s Servier Research and Pharmaceuticals (Pvt) Ltd, dated 12th July, 2019, wherein the request is in reply of this division letter number F.No.03-01/2019-DD (PS), to license their Public Hospital with DRAP to work as Clinical Trial Site (CTS), to conduct the clinical studies mentioned in subject cited above.

2.2.2. The application is on prescribed Form-I of the Bio-Study Rules 2017 along with fee of Rs.100000/- for Clinical Trial Site vide challan no.0550724, 11th July, 2019.

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

| S. No. | Required Documents / Information | Remarks |
|---|---|---|
| 1 | Application on prescribed Form-I of The Bio-Study Rules 2017. | Attached |
| 2 | Fee | Attached |
| 3 | Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors). | Applicant is Professor of Medicine and working at Private Hospital |
| 4 | Details of premises including layout plan of the site. | Not provided. |
| 5 | Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies. | Not provided. Applied site is a Private Hospital. |
| 6 | Names and qualifications of the above sections along with their staff. | Applied site is a Private Hospital. |
| 7 | Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc. | Applied site is a Private Hospital. |
| 8 | Undertaking on stamp paper | Attached. |

2.2.4. After evaluation following shortcomings were recorded:

i) Details of premises including layout plan of the site is not provided.

ii) Details of the section wise equipment is not provided.

2.2.5 Shortcomings were communicated to the applicant vide letter number F.No.15-28/2019 DD (PS), dated 23rd July, 2019, applicant submitted their reply vide letter number nil, dated 29th July, 2019, reply of the applicant is as follows:

| S.No. | Shortcomings | Reply |
|---|---|---|
| 1 | Details of premises including layout plan of the site is not provided. | This is required for Phase-I and BA/BE Studies where there is a requirement for in-door facilities and laboratory. This being an Observational (Phase-IV) study this is not applicable here. |
| 2 | Details of the section wise equipment is not provided. | There is no equipment required in conducting this study as can be confirmed by the protocol. |
| 3 | Names and qualifications of the section wise staff is not provided. | The only two site personal engaged in the conduct of study are the investigator and his coordinator. Their names and their CVs have been provided. |

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

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

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

| | |
|---|---|
| i. | Dr. Abdur Rashid |
| ii. | Dr. Nadeem Irfan |
| iii. | Dr. Farhana Badar |
| iv. | Dr. Ali Jawa |

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

2.2.8. Due to availability of some members and non-availability of other members, Chairman CSC, exercising the power delegated by the CSC in its 3rd meeting, added the inspection pool members for the inspection, and following expert's panel inspected the facility on 24th July, 2019:

| | |
|---|---|
| i. | Dr. Abdur Rashid |
| ii. | Mr. Waqas Latif |
| iii. | Ali Asghar Jawa |
| iv. | Dr. Nadeem Irfan Bukhari |

**2.2.9. Remarks of inspection team:**

Keeping in view the diabetes clinical facilities, physician expertise, OPD, Pharmacy records, incineration, training on GCP, documentation etc, panel recommends for Dia-Ramadan studies and diabetes related studies as Clinical Trial Site but also for Phase-II, III and Phase-IV Studies.

**2.2.10. Concluding status of inspection by inspection panel:**

***"Recommended for approval"***

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

**2.2.12 Decision of 5th CSC Meeting:-**

*"**The CSC unanimously approved the DIABETES INSTITUTE OF PAKISTAN, Lahore as Clinical Trial Site to conduct phase II, III and IV only for outdoor & diabetes related studies."***

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**2.3) REQUEST FOR APPROVAL OF OBSERVATIONAL STUDY PROGRAM ASSESSING EFFECTIVENESS AND TOLERABILITRY OF GLICLAZIDE 60mg MODIFIED RELEASE TABLET IN PATIENTS WITH TYPE II DIABETES FASTING DURING RAMADAN, TO BE CONDUCTED AT NATIONAL HOSPITAL & MEDICAL CENTER.**

Application is from Prof. Dr. Abbas Raza, National Hospital Medical Center, Lahore, submitted by Dr. Ahmed Aatif Mirza, President Clinical Operations M/s DRK Pharma Solution, Lahore on behalf of Sponsor M/s Servier Research and Pharmaceuticals (Pvt) Ltd, dated 12th July, 2019, wherein the request is in reply of this division letter number F.No.03-01/2019-DD (PS), to license their Public Hospital with DRAP to work as Clinical Trial Site (CTS), to conduct the clinical studies mentioned in subject cited above.

2.3.2. The application is on prescribed Form-I of the Bio-Study Rules 2017 along with fee of Rs.100000/- for Clinical Trial Site vide challan no.0550723, 11th July, 2019.

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

| S. No. | Required Documents / Information | Remarks |
|---|---|---|
| 1 | Application on prescribed Form-I of The Bio-Study Rules 2017. | Attached |
| 2 | Fee | Attached |
| 3 | Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors). | Applicant is Professor of Medicine and working at Public Hospital |
| 4 | Details of premises including layout plan of the site. | Not provided. |
| 5 | Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies. | Not provided. Applied site is a Public Hospital. |
| 6 | Names and qualifications of the above sections along with their staff. | Not provided. |
| 7 | Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc. | Applied site is a Public Hospital. |
| 8 | Undertaking on stamp paper | Attached. |

2.3.4. After evaluation following shortcomings were recorded:

i) Details of premises including layout plan of the site is not provided.

ii) Details of the section wise equipment is not provided.

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

2.3.5 Shortcomings were communicated to the applicant vide letter number F.No.15-26/2019 DD (PS), dated 23rd July, 2019, applicant submitted their reply vide letter number nil, dated 24124, reply of the applicant is as follows:

| S.No. | Shortcomings | Reply |
|---|---|---|
| 1 | Details of premises including layout plan of the site is not provided. | This is required for Phase-I and BA/BE Studies where there is a requirement for in-door facilities and laboratory. This being an Observational (Phase-IV) study this is not applicable here. |
| 2 | Details of the section wise | There is no equipment required in |

| | | |
|---|---|---|
| | equipment is not provided. | conducting this study as can be confirmed by the protocol. |
| 3 | Names and qualifications of the section wise staff is not provided. | The only two site personal engaged in the conduct of study are the investigator and his coordinator. Their names and their CVs have been provided. |

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

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

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

| | |
|---|---|
| i. | Dr. Abdur Rashid |
| ii. | Dr. Nadeem Irfan |
| iii. | Dr. Farhana Badar |
| iv. | Dr. Ali Jawa |

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

2.3.8. Due to availability of some members and non-availability of other members, Chairman CSC, exercising the power delegated by the CSC in its 3rd meeting, added the inspection pool members for the inspection, and following expert's panel inspected the facility on 25th July, 2019:

| | |
|---|---|
| i. | Dr. Abdur Rashid |
| ii. | Muhammad Adnan Faisal Saim |
| iii. | Dr. Ali Jawa. |
| iv. | Dr. Farhana Badar |

**2.3.9. Remarks of inspection team:**

Keeping in view the infrastructure, Human resource, their training and expertise, IRB documents, Out-door and In-door facilities, pathology lab, X-ray, critical care bed emergency department, Pharmacy, record, IT facilities, HR, Finances, the panel recommends National Hospital & Medical Centre Lahore for Clinical Trial Site and also for DiaRamzan studies.

**2.3.10. Concluding status of inspection by inspection panel:**

**Recommended for approval**

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

**2.3.12 Decision of 5th CSC Meeting:-**

*"**The CSC unanimously approved the NATIONAL HOSPITAL & MEDICAL CENTER, Lahore as Clinical Trial Site for phase II, III and IV for both outdoor and indoor patients."***

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

Application is from Mohsin Ali Jawa CEO, M/s Olive Worldwide (SMC-PVT) Ltd, 3-4-5 M, Model Town Extension, Lahore, wherein the request has been made to license their company with DRAP to work as Clinical Research Organization (CRO) (M/s Olive Worldwide (SMC-PVT) Ltd), the application is on prescribed Form-I of the Bio-Study Rules 2017 along with fee of Rs.300000/- deposited for CRO vide challan no.0846246.After scrutiny status of application is as follows:

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

| S. No. | Required Documents / Information | Remarks |
|---|---|---|
| 1 | Application on prescribed Form-I of The Bio-Study Rules 2017. | Attached |
| 2 | Fee | Attached |
| 3 | Particulars regarding the legal status of the applicant i.e. in case of proprietorship the names of proprietors and their addresses, in the case of firm the name and names and addresses of its partners and in the case of company the name and address of the company and its directors). | Attached |
| 4 | Details of premises including layout plan of the site. | Attached. |
| 5 | Details of the section wise equipment and machinery required for the analytical or bio-analytical and clinical studies. | Attached. |
| 6 | Names and qualifications of the above sections along with their staff. | Attached. |
| 7 | Details of the allied facilities associated with the trial center including ambulatory services, emergency handling etc. | Not Provided. Applied for CRO. |

| | | |
|---|---|---|
| 8 | Undertaking on stamp paper | Attached. |

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

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

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

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

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

2.4.4. Due to availability of some members and non-availability of other members, Chairman CSC, exercising the power delegated by the CSC in its 3rd meeting, added the inspection pool members for the inspection, and inspection letter was approved for following experts:

| | |
|---|---|
| i. | Prof. Dr. Javed Akram |
| ii. | Dr. Abdur Rashid |
| iii. | Muhammad Adnan Faisal Saim |
| iv. | Dr. Farhana Badar |

2.4.5. The following panel members inspected the facility on 25th July, 2019:

| | |
|---|---|
| i. | Dr. Abdur Rashid |
| ii. | Muhammad Adnan Faisal Saim |
| iii. | Dr. Farhana Badar |

**2.4.6. Remarks of inspection team:**

The facilities integrated with information technology with advanced tools currently available. The CRO hopefully will meet all the expectations as per requirements.

Keeping in view premises, infrastructure web based data security, personnel etc, the panel recommends the CRO for approval.

**2.4.7. Concluding status of inspection by inspection panel:**

***"Recommended for approval"***

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

**2.4.9. Decision of 5th CSC Meeting:-**

"***The CSC unanimously approved the M/S OLIVE WORLDWIDE (SMC-PVT) LTD as CRO for OPD & Phase-II, III and IV studies."***

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

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

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

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

| | | |
|---|---|---|
| | emergency handling etc. | |
| 8 | Undertaking on stamp paper | Attached. |

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

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

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

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

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

2.5.4. Due to availability of some members and non-availability of other members, Chairman CSC, exercising the power delegated by the CSC in its 3rd meeting, added the inspection pool members for the inspection, and inspection letter was approved for following experts:

| | |
|---|---|
| i. | Prof. Dr. Javed Akram |
| ii. | Dr. Abdur Rashid |
| iii. | Muhammad Adnan Faisal Saim |
| iv. | Dr. Farhana Badar |

2.4.5. The following panel members inspected the facility on 25th July, 2019:

| | |
|---|---|
| i. | Dr. Abdur Rashid |
| ii. | Muhammad Adnan Faisal Saim |
| iii. | Dr. Farhana Badar |

**2.5.6. Remarks of inspection team:**

Keeping in view the premises, infrastructure, human resources, training, IT system, SOPs, records, documentation, waste management, patient reported data is stored in

web base cloud system, the panel recommends for approval of Olive Worldwide (Pvt) Ltd. 3-4-5-M Model Town extension Lahore for Clinical Trial Site.

**2.5.7. Concluding status of inspection by inspection panel:**

***"Recommended for approval"***

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

**2.4.9. Decision of 5th CSC Meeting:-**

"***The CSC unanimously approved the*** **M/S WILCARE POLY CLINIC, LAHORE as Clinical Trial Site** ***for OPD & Phase-II, III and IV studies."***

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**Note:** *Following is the matter of Institute of Biological, Biochemical & Pharmaceutical Sciences (IBBPS), At Dow University of Health Sciences, Karachi, and the matter is that, in the first application, they applied for approval of BA/BE Studies Centre, CRO and Bio analytical Laboratory on one application. Upon direction of Pharmacy Services Division they applied for CRO and Bio analytical Laboratory on separate applications according to Bio-Study Rules 2017, and were included in the 4th CSC meeting and discussed along with the inspection report of panel.*

*Applicant requested for merging of their CRO & BA/BE Studies Centre applications and fee vide letter dated 9th July, 2019. The Division of Pharmacy Services on their request proceeded for merging accordingly but some further updates / requests from the applicant received for the perusal of CSC.*

*The current status of each case of Institute of Biological, Biochemical & Pharmaceutical Sciences (IBBPS), At Dow University of Health Sciences, Karachi is as under, according to separate application.*

**2.6) APPLICATION FOR LICENSE TO ACT AS BA/BE STUDIES SITE, AT INSTITUTE OF BIOLOGICAL BIOCHEMICAL & PHARMACEUTICAL SCIENCES (IBBPS), AT DOW UNIVERSITY OF HEALTH SCIENCES, KARACHI. (F.No.15-10/2019).**

Application is from Mr.Munawar Ali, Additional Director, Institute of Biological, Biochemical & Pharmaceutical Sciences (IBBPS), At Dow University of Health Sciences, Karachi, dated 28th September, 2018, wherein the request has been made to

license their firm with DRAP to act as a Contract Research Organization (CRO), BA/BE Studies Centre and Bio Analytical Laboratory, on prescribed Form-I of the Bio-Study Rules 2017 without fee.

2.6.2. 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 Centre 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 centre including ambulatory services, emergency handling etc. | No details provided |
| 8 | Undertaking on stamp paper | Not on Stamp paper |

**2.6.3. Description of shortcomings**

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

2.6.4. Application was discussed in the 4th CSC meeting after inspection and CSC decided as follows:

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

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

2.6.5. Applicant submitted their reply regarding shortcomings, dates 09th July, 2019, as follows:

| S.No. | Shortcomings | Reply / Status |
|---|---|---|
| 1 | Particulars regarding the legal status of the applicant/firm are not provided. | Public Sector University. |
| 2 | Details of premises including layout plan is not provided. | Attached. |
| 3 | Details of the allied facilities associated with centre are not provided. | Tertiary care hospital facilities are available at Dow Hospital. |
| 4 | Fee not submitted. | Not Addressed. |
| 5 | Undertaking is not on stamp paper. | Not provided. |

2.6.6. Vide their reply on 9th July, 2019, applicant submitted that upon direction of DRAP inspection panel they are limiting their scope to only BA/BE Study Centre, and requested that merge their BA/BE Studies Centre& CRO application and fee.

2.6.7. Mrs. Sadia Asim requested vide letter dated 6th August, 2019, for reconsideration of their CRO application separately.

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

**2.6.9 Decision of 5th CSC Meeting:-**

"***The CSC after deliberation, deferred the case till provision of Layout plan, equipment list along with calibration certificate used at BA/BE studies centre, Fee & reinspection by the same panel as constituted in the 3rd CSC meeting."***

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

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

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

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

**2.7.2. Description of shortcomings:**

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

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

2.7.3 Application was discussed in the 4th CSC meeting after inspection and CSC decided as follows:

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

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

2.7.4. Applicant submitted their reply regarding shortcomings, dates 09th July, 2019, as follows:

| S.No. | Shortcomings | Reply / Status |
|---|---|---|
| 1 | Particulars regarding the legal status of the applicant/firm are not provided. | Public Sector University. |
| 2 | Details of premises including layout plan is not provided. | Attached. |

2.7.5. Applicant requested to merge this application along with its fee for BA/BE Studies approval application.

2.7.6 Mrs. Sadia Asim requested vide letter dated 6th August, 2019, for reconsideration of their CRO application separately.

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

**2.7.6. <u>Decision of 5th CSC Meeting</u>:-**

"***The CSC after deliberation, deferred the case & decided that the panel constituted for BA/BE Centre will also inspect the Contract Research Organization (CRO).”***

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

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

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

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

**2.8.2. Description of shortcomings:**

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

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

2.8.3 Application was discussed in the 4th CSC meeting after inspection and CSC decided as follows:

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

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

2.8.4. Applicant submitted their reply regarding shortcomings, dates 09th July, 2019, as follows:

| S.No. | Shortcomings | Reply / Status |
|---|---|---|
| 1 | Particulars regarding the legal status of the | Public Sector University. |

| | | |
|---|---|---|
| | applicant/firm are not provided. | |
| 2 | Details of premises including layout plan is not provided. | Attached. |

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

**2.8.6. <u>Decision of 5th CSC Meeting</u>:-**

"***The CSC after deliberation, deferred the case & decided that the panel constituted for BA/BE Centre will also inspect the Bio Analytical Laboratory."***

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**<u>AGENDA ITEM NO. III:</u> <u>CLINICALTRIALS/STUDIESREGISTRATION. (Discussed in previous CSC Meeting, Ongoing Cases)</u>**

All the following cases for registration of Clinical Studies under agenda item no. III were discussed in the 4thCSC meeting and most of them were deferred due to Clinical Trial Site approval from DRAP.

**3.1) <u>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).</u>**

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

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

The trial comprises of two primary objectives;

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

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

| S. No. | Document | Remarks |
|---|---|---|
| 1 | Application on prescribed Form-I | Attached |
| 2 | Fee | Attached |
| 3 | Investigator Brochure (s) | Attached |
| 4 | Final protocol | Attached |
| 5 | Informed consent and participant information sheet (Urdu to English) | Attached |
| 6 | List of participating countries | Georgia, Lesotho, Kazakhstan, Kyrgyzstan, Peru, South Africa and Pakistan |
| 7 | Phase of trial. | Phase – III |
| 8 | Quantity of drug / trial material to be imported on Form 4 under the Drugs (Import & Export) Rules, 1976 and application for import of trial material. | Attached |
| 9 | Site of the trial | The Indus Hospital.<br>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.<br>Explanatory note regarding two ancillary medicine attached regarding their GMP status |
| 14 | Pre-clinical/clinical safety studies | Attached |
| 15 | Summary of Protocol | Attached |
| 16 | Summary of Investigator Brochure | Attached |
| 17 | Adverse Event Reporting Form | Attached |
| 18 | No of patients to be enrolled in each centre. | 108 |

| | | |
|---|---|---|
| 19 | Name of Monitors & Clinical Research Associate | Attached |
| 20 | Evidence of registration in country of origin. | Attached.<br>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 |

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

| **S. No** | **International Nonproprietary Names (INN) for Pharmaceutical Products** | **Manufacturer** | **Country of origin** | **Shelf life (months)** | **Total Quantity** |
|---|---|---|---|---|---|
| | **Investigational Medicinal Products (IP) TB Drugs** | | | | |
| 1 | AMIKACIN sulfate, eq. 250 mg/ml base, 2 ml, amp. | **MEDOCHEMIE** | CYPRUS | 48 | 1200 |
| 2 | BEDAQUILINE, 100 mg, tab. | **JANSSEN** | BELGIUM | 36 | 27833 |
| 3 | CLOFAZIMINE, 100 mg, soft caps. | **NOVARTIS** | SWITZERLAND /FRANCE | 60 | 28350 |
| 4 | CYCLOSERINE 250 mg caps. | **MACLEODS** | INDIA | 36 | 23100 |
| 5 | DELAMANID, 50mg, tab., blister | **OTSUKA** | GERMANY | 60 | 71971 |
| 6 | ETHIONAMIDE, 250 mg, tab., blister | **MACLEODS** | INDIA | 48 | 10290 |
| 7 | LEVOFLOXACIN hemihydrates, eq. 250 mg base, tab. | **HETERO** | SPAIN | 36 | 8400 |

| | | | | | |
|---|---|---|---|---|---|
| 8 | LEVOFLOXACIN hemihydrates, eq. 500 mg base, tab. | **MACLEODS** | INDIA | 48 | 38115 |
| 9 | LINEZOLID, 600 mg, coated tab. | **HETERO** | INDIA | 36 | 28245 |
| 10 | MOXIFLOXACIN hydrochloride eq. to 400 mg base , tab. | **HETERO** | INDIA | 36 | 12322 |
| 11 | PARA-AMINOSALICYLIC acid (PAS),del.rel.gran, 4g, sach.(25°C) | **JACOBUS** | US | 24 | 2583 |
| 12 | ETHAMBUTOL hydrochloride (E), eq. 400 mg base, tab. blister | **MACLEODS** | INDIA | 36 | 11550 |
| 13 | ISONIAZID (H), 300 mg, tab., blister | **MACLEODS** | INDIA | 36 | 3150 |
| 14 | PYRAZINAMIDE (PZA), 400 mg, tab., blister | **MACLEODS** | INDIA | 48 | 132653 |
| | **Ancillary medicines** | | | | |
| 1 | AMITRIPTYLINE hydrochloride, 25 mg, tab. | **REMEDICA LTD** | CYPRUS | 60 | 4000 |
| 2 | BECLOMETASONE dipropionate, 0.10mg/puff, 200 puffs,aerosol | **LABORATORIO ALDO-UNION S.L.** | SPAIN | 36 | 8 |
| 3 | TRIHEXYPHENIDYL hydrochloride, 2 mg, tab. | **REMEDICA LTD** | CYPRUS | 60 | 100 |
| 4 | CARBAMAZEPINE, 200 mg, tab. | **MEDOCHEMIE** | CYPRUS | 60 | 1000 |
| 5 | CHLORPHENAMINE maleate, 4 mg, tab. | **CADILA** | INDIA | 48 | 2000 |
| 6 | FLUOXETINE, 20mg, caps. | **MYLAN** | FRANCE | 48 | 900 |
| 7 | HALOPERIDOL, 5 mg, tab. | **REMEDICA LTD** | CYPRUS | 60 | 1500 |
| 8 | IBUPROFEN, 400 mg, tab. | **REMEDICA LTD** | CYPRUS | 60 | 16000 |
| 9 | LEVOTHYROXINE SODIUM, 0.025 mg, tab. | **Mercury Pharmaceuticals Ltd** | UK | 24 | 5376 |
| 10 | LOPERAMIDE hydrochloride, 2 mg, tab. | **REMEDICA LTD** | CYPRUS | 60 | 1000 |

| | | | | | |
|---|---|---|---|---|---|
| 11 | MAGNESIUM OXIDE 270 mg, eq. to 150 mg Magnesium, efferv. tab | **ARROW GENERIQUE** | FRANCE | 36 | 8940 |
| 12 | METOCLOPRAMIDE hydrochloride anhydrous, 10 mg, tab. | **REMEDICA LTD** | CYPRUS | 60 | 1000 |
| 13 | OMEPRAZOLE 20 mg, enteric caps. | **MEDOCHEMIE** | CYPRUS | 36 | 3752 |
| 14 | ONDANSETRON hydrochloride, eq. 8 mg base, tab. | **PLIVA** | UK | 60 | 60 |
| 15 | PARACETAMOL (acetaminophen), 500 mg, tab. | **REMEDICA LTD** | CYPRUS | 60 | 16000 |
| 16 | POTASSIUM chloride, 600 mg, sustained release tab. | **LABORATOIRE LEO** | FRANCE | 60 | 44700 |
| 17 | PREDNISOLONE, 5mg, tab. | **REMEDICA LTD** | CYPRUS | 36 | 1000 |
| 18 | PROMETHAZINE hydrochloride, eq. 25 mg base, tab. | **REMEDICA LTD (CY)** | CYPRUS | 60 | 1000 |
| 19 | PYRIDOXINE hydrochloride (vitamin B6), 50 mg tab. | **MACLEODS** | INDIA | 24 | 268000 |
| 20 | RISPERIDONE, 1 mg, tab. | **REMEDICA LTD** | CYPRUS | 36 | 540 |
| 21 | SULBUTAMOL sulfate, eq.0.1mg base/puff, 200 puffs, inhaler | **LABORATORIO ALDO-UNION S.L.** | SPAIN | 36 | 108 |
| 22 | CLOTRIMAZOLE, 500 mg, vaginal tab. + applicator | **REMEDICA LTD** | CYPRUS | 36 | 45 |
| 23 | MICONAZOL nitrate, 2%, cream, 30 g, tube | **MEDOCHYME** | CYPRUS | 36 | 10 |
| 24 | EPOETIN ALFA 10000 IU/ml, 1ml, syringe | **JANSEEN** | FRANCE | 18 | 144 |

| | | | | | |
|---|---|---|---|---|---|
| 25 | MEGNESIUM sulfate, 0.5 g/ml, 10ml, vial. | **AURUM PHARMACEUTICALS** | UK | 36 | 420 |
| 26 | POTASSIUM chloride 100 mg/ml, 10 ml amp. | **AGUETTANT LABORATOIRE** | FRANCE | 36 | 850 |
| 27 | SODIUM chloride, 0.9%, 250 ml, plastic pouch. | **BAXTER S.L.** | SPAIN | 24 | 750 |
| 28 | VALPROATE SODIUM, 500 mg, enteric coated tab. | **SANOFI** | UK | 36 | 600 |
| 29 | WATER for injection, 10ml, plastic amp | **B.BRAUN** | GERMANY | 36 | 10700 |

**3.1.5.** **Decision of 3rdCSC Meeting:-**

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

3.1.6. After inspection of the site, CSC approved the Clinical Trial Site for the trial in its 4th meeting.

3.1.7. Dr. Mehrun Nisa Hameed, representative from The Indus Hospital, delivered the presentation of the endTB Clinical Studies before CSC in the 4th CSC meeting.

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

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

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

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

### 3.1.10 EXPERT OPINION

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

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

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

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

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

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

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

### 3.1.13. Decision of 5thCSC Meeting: -

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

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

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

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

i) Baqai Institute of Diabetes and Endocrinology, Karachi.

ii) National Defence Hospital, Lahore.

iii) University of Health Sciences, Lahore.

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

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

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

| S. No. | Required Documents | Remarks |
|---|---|---|
| 1. | Application on prescribed Form-II | Attached |
| 2. | Fee | Not provided |
| 3. | Investigator Brochure | Not provided & claimed that it's an observational study. |
| 4. | Final Protocol | Protocol Version 1.1.0 dated 20th November, 2017. |
| 5. | Informed consent form (English & Urdu) | Attached |
| 6. | List of participating countries (If applicable) | 09 countries including Bangladesh, India, Indonesia, Malaysia, Saudi Arab, United Arab Emirates, Kuwait, Egypt and |

| | | |
|---|---|---|
| | | Pakistan. |
| 7. | Phase of trial | Phase-IV |
| 8. | Quantity of Drug(s) to be imported/procured/manufactured for the trial | Details not provided. Applicant claimed as it is an observational study, there is no need to import medicines. |
| 9. | Site(s) of the trial | Trial will be conducted at following five sites in Pakistan;<br><br>1. Baqai Institute of Diabetes and Endocrinology, Karachi.<br>2. National Hospital& Medical Centre, Lahore.<br>3. Akram Medical Complex, Lahore.<br>4. Diabetes Institute of Pakistan, Jail Road, Lahore.<br>5. Hayatabad Medical Complex (Medical Teaching Institute), Peshawar. |
| 10 | C.Vs of investigator(s) | Attached. |
| 11 | Ethical committee approval with complete composition of committee i.e. Name and designations of the members | Ethical Committee Composition and approval from each Clinical trial Site is not provided. |
| 12 | Approval from National Bio-ethics Committee (PHRC) | NBC Approval vide letter No.4-87/NBC-302( 2nd yr Exten+Amed/19/360) Dated 4th January, 2019, is attached. |
| 13 | GMP certificate along with Free Sale Certificate/Certificate of Pharmaceutical Product (Note: For locally manufactured product GMP Cert., COA of the Product and Registration Letter will be required) | Not Provided. |
| 14 | Pre-clinical, clinical data and safety studies. | Not provided & claimed that it's an observational Study. |
| 15 | Summary of the protocol | Attached |
| 16 | Summary of the Investigator Brochure | Not provided. |
| 17 | Adverse Event Reporting form | Attached |
| 18 | No. of Patients to be enrolled in each centre | 20 patients at each site. |
| 19 | Name of monitors/clinical research associate | Mr. Faheem Shehzad. |

| | | |
|---|---|---|
| 20 | Evidence of registration of study drug in country of origin | Not provided. |
| 21 | Copy of registration letter (if drug is registered in Pakistan) | Attached. |
| 22 | Sample of label of drug | Not provided, and claimed that the product is already registered in Pakistan, so Not applicable |
| 23 | Duration of trial | 06 Months |
| 24 | Undertaking on stamp paper | Not provided |

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

| S.No. | Shortcomings | Reply |
|---|---|---|
| 01 | Investigator Brochure is not provided and claimed that it is an observational studies. | Investigators Brochure is the requirement for an Investigational Drug (Phase II-III). For phase IV studies already available product leaflet is used. |
| 02 | Quantity of Drug(s) to be imported/procured/manufactured for the trial, is not described. | As this is an observational (Phase IV) study using the already available medicines in the market (having being prescribed and patient already using) and since we are not going to import any medicines hence the quantity of the medicines were not mentioned. |
| 03 | Ethical committee approval with complete composition of committee i.e. Name and designations of the members for the clinical trial sites are not provided. | Complete composition of the IRB with names and designations were attached as Appendix B (the checklist given in the Bio-Study Rules 2017 at number 10). This is being provided again. (Annexure 1) |
| 04 | Approval from NBC attached, but it is for second year extension and amendments, previous approval is not provided. | The initial approval by the NBC is being provided. (Annexure 2) |
| 05 | GMP Certificate and Free Sale Certificates are not provided, and claimed that as the drug registered in Pakistan so not applicable. | Gliclazide 60 mg MR (Diamicron 60 mg MR) was registered in Pakistan in 2009 (as per the registration letter dated 9th September 2009-copy attached). The GMP certificate of the production facility is attached. This is a locally manufactured drug and hence does not require a free sale certificate. |
| 06 | Pre-clinical, clinical data and safety studies are not provided and claimed it is an observational study. | Pre-clinical, clinical data and safety studies again is a requirement for investigational drug and if the drug is registered and marketed (as |

| | | |
|---|---|---|
| | | is the case with Gliclazide 60 mg MR since 2009) and its pharmacology is widely understood by medical practitioners, an extensive IB is not necessary and the leaflet suffices. |
| 07 | Summary of Investigator brochure is not provided. | Not required for a registered and marketed drug (as given above) |
| 08 | Evidence of registration in country of origin is not provided, as the drug registered in the Pakistan | The requirement of registration in the country of origin is also for an unapproved investigational drug. This is an approved drug in Pakistan since 2009 and is being locally manufactured since then hence this is not required. (Registration letter attached—Annexure 3) |
| 09 | Sample of label of drug is not provided. | This (leaflet of the drug) was provided and is being sent again. (Annexure 4) |

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

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

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

3.2.6. The applicant replied that there is some mistake / typographic error in Clinical Trial Sites names, following five sites should be considered and application for Clinical Trial Sites approval also submitted:

i) Baqai Institute of Diabetes and Endocrinology, Karachi.
ii) National Hospital & Medical Centre, Lahore.
iii) Akram Medical Complex, Lahore.
iv) Diabetes Institute of Pakistan, Jail Road, Lahore.
v) Hayatabad Medical Complex (Medical Teaching Institute), Peshawar.

3.2.7. Applications for the approval of the Clinical Trial Sites were included and discussed in the 4th CSC meeting and CSC constituted the panel for inspection.

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

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

**3.2.9.** Following three Clinical Trial Sites were inspected by the panel and submitted their reports with recommendation for approval and are included in the agenda.

i) National Hospital & Medical Centre, Lahore.
ii) Akram Medical Complex, Lahore.
iii) Diabetes Institute of Pakistan, Jail Road, Lahore.

3.2.10 Submitted for perusal, discussion and decision of CSC.

3.2.11 Dr. Aatif Mirza, President Clinical Operations, M/s DRK Pharma Solutions, Lahore, presented the case before CSC on behalf of applicant.

**3.2.11. <u>Decision of 5th CSC Meeting:</u> -**

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

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

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

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

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

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