# MINUTES OF THE 44TH CLINICAL STUDIES COMMITTEE MEETING (SUMMARY)

Pharmacy Services Division, Drug Regulatory Authority of Pakistan

File No: 16-44/2023-CSC (PS)

**AUGUST 25, 2023**

**DRUG REGULATORY AUTHORITY OF PAKISTAN**

**Prime Minister's National Health Complex, Park Road, Chak Shahzad, Islamabad**

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44th meeting of the Clinical Studies Committee was held on 25th August, 2023 in the committee room, Drug Regulatory Authority of Pakistan, G-9/4, Islamabad. The meeting was chaired by Dr. Obaidullah, Director Pharmacy Services. The meeting was started with recitation of the Holy Verses.

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

| Sr. No. | Name | Designation | |
|---|---|---|---|
| i. | **Dr. Obaidullah** | Director Pharmacy Services Division. | *Ex-officio Chairman* |
| ii. | **Prof. Dr. Fazal Subhan** | Department of Pharmacy, CECOS University of IT & Emerging Sciences, Peshawar, Khyber Pakhtunkhwa. | Member |
| iii. | **Prof. Munawar Alam Ansari** | Professor of Pharmacology, Dean Faculty of Pharmacy, Liaquat University of Medical Sciences, Jamshoro, Sindh**.** | Member |
| iv. | **Dr. Mirza Tasawer Baig** | Associate Professor in the Department of Pharmacy Practice, Faculty of Pharmacy, Ziauddin University, Karachi & Clinical Pharmacist at Dr. Ziauddin Hospital, Karachi, Sindh. | Member |
| v. | **Dr. Faiza Bashir** | Nominee of Chairman, Pakistan Health Research Council, Islamabad. | Member |
| vi. | **Ahsan Ul Haq Athar** | Deputy Director, Pharmacy Services Division. | *Ex-officio Secretary* |

3. Following members attended the meeting online through Zoom:

| | | | |
|---|---|---|---|
| i. | **Prof. Dr. Saeed Ahmad Khan** | Professor of Medicine Bolan Medical College Quetta presently serving as head of Medicine Department Jhalawan Medical College Khuzdar, Balochistan. | Member |
| ii. | **Mr. Waqas Latif** | Data Analyst/Biostatistician in Quality Enhancement Cell (QEC) at University of Health Sciences, Lahore, Punjab. | Member |

4. Malik Muhammad Asad (Deputy Director), Mr. Nouman Yousuf (Deputy Director), Hafiz Muhammad Jawad Ali (Deputy Director) and Shafqat Hussain Danish assisted the Committee and Secretary in presentation of the agenda.

**AGENDA ITEM I:**

**CONFIRMATION OF THE MINUTES OF THE 38th, 39th, 40th, 41st, 42nd and 43rd CLINICAL STUDIES COMMITTEE MEETING.**

Draft minutes of the subject meetings were shared with CSC members through email/ what's app and CSC members concurred draft minutes as which were then approved by the Chairman, CSC and accordingly decisions of the meeting have been communicated. As these minutes were not placed in subsequent CSC meetings thus minutes are placed as per following details:

| S.No. | Meeting with date | Draft minutes sent via Email | Date of concurrence of CSC members |
|---|---|---|---|
| i. | 38th CSC meeting held on 8th February 2023. | 10th February 2023 | 13th February 2023 |
| ii. | 39th CSC meeting held on 28th February 2023. | 28th February 2023 | 09th March 2023 |
| iii. | 40th CSC meeting held on 17th March 2023. | 18th March 2023 | 21st March 2023 |
| iv. | 41st CSC meeting held on 10th April 2023. | 11th April 2023 | 13th April 2023 |
| v. | 42nd CSC meeting held on 3rd May 2023. | 03rd May, 2023 | 03rd May, 2023 |
| vi. | 43rd CSC meeting held on 2nd June 2023. | 06th June 2023. | 07th June 2023. |

**Decision:**

*All the Members of the CSC confirmed the Minutes of 38th, 39th, 40th, 41st, 42nd and 43rd CSC meetings.*

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**AGENDA ITEM II:**

**APPLICATION FOR APPROVAL OF APPLICATION TO ACT AS CRO AT M/S PLISER RESEARCH, LAHORE F. No.15-41/2023-CRO.**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation, discussion and considering the recommendations of inspection panel decided to approve M/s Paliser Research Pvt. Ltd., 36-C-1 Faisal Town, Lahore to act as Contract Research Organization under the Bio-Study Rules, 2017.*

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**AGENDA ITEM III:**

**APPLICATION FOR LICENCE ACT AS CRO AT M/S PRIME FOUNDATION, PESHAWAR MEDICAL COLLEGE. F. No.15-18/2022 DD (PS)**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation, discussion and considering the recommendations of inspection panel decided to approve M/s Prime Foundation, Peshawar Medical College, Warsak Road, Peshawar to act as Contract Research Organization under the Bio-Study Rules, 2017.*

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**AGENDA ITEM IV:**

**APPLICATION FOR APPROVAL TO ACT AS CRO AT M/S CONTINUUM RESEARCH CENTER, WAH CANTT. F. No.15-20/2022-CRO.**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation and discussion decided the case as follows:*

i. *Directed the same panel (at least two members) to visit the facility & verify the fulfilment of shortcomings as previously communicated.*
ii. *Authorized the Chairman for issuance of the licence after verification of improvements and recommendations of inspection panel.*

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**AGENDA ITEM V:**

**APPLICATION FOR RENEWAL OF LICENSE TO ACT AS CONTRACT RESEARCH ORGANIZATION (CRO) BY DIMENSION RESEARCH CRO & SMO, KARACHI 12-02/2018 DD (PS)) F. No.15-31/2023-CRO.**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation, discussion and considering the recommendations of inspection panel decided to approve the renewal of CRO Licence No. CRO-0004 of M/s Dimension Research CRO, B-84, Block2, Gulsitan-e-Jauhar, Scheme-36, Karachi to act as Contract Research Organization under the Bio-Study Rules, 2017.*

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**AGENDA ITEM VI:**

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

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation, discussion and considering the recommendations of inspection panel decided to approve M/s Pakistan Kidney & Liver Institute & Research Institute, One PKLI Avenue, Opposite DHA Phase-6, Lahore to act as Clinical Trial Site for Phase-III and IV Clinical Trials under the Bio-Study Rules, 2017.*

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**AGENDA ITEM VII:**

**APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE FROM THE DR. AKBAR NIAZI TEACHING HOSPITAL, ISLAMABAD. F. No.15-38/2023 CTS.**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation, discussion and considering the recommendations of inspection panel decided to approve M/s Dr. Akbar Niazi Teaching Hospital, 17 Meel, Main Murree Road, Bhara Kahu, Islamabad to act as Clinical Trial Site for Phase-III and IV Clinical Trials under the Bio-Study Rules, 2017.*

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**AGENDA ITEM VIII:**

**APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE (FOR PHASE III &IV) FROM MEDIX HOSPITAL, LAHORE. F. No.15-33/2023 CTS.**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation, discussion decided to defer the case of M/s Medix Hospital, 17 Km, Main Ferozpur Road, Opposite Main Gate Pak Arab Society, Lahore, upon following recommendations/report of inspection panel:*

> "*The Panel visited the premises and found the team comprising of young and energetic professionals. The CTU is located in the basement. The temperature was very high (Not feasible for working or retaining subjects. No rack/ cabinet and refrigerator was available for storage of IMPs. Phlebotomist was not available. No archiving room, record room was available. No internet or computer was available at the said CTU. No doctor with any specialty/ IRB was available. No patient was present at the time of visit. Although the Medix Hospital has MOU with Shifa Ambulance but no ambulance was present at the time of visit. Documents/ SOPs need improvement. The Medix hospital need improvement stated above and other discussed with CTU team. That's why panel decided to defer the site for improvement.*"

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**AGENDA ITEM IX:**

**APPLICATION FOR RENEWAL OF LICENCE LICENSE TO ACT AS CLINICAL TRIAL SITE FROM M/S AYUB TEACHING HOSPITAL ABBOTABAD F. No.15-29/2019-DD (PS).**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation, discussion and considering the recommendations of inspection panel decided to approve renewal of the site situated at "*Department of Obstetrics and Gynecology, Ayub Teaching Hospital, Abbottabad *to act as Clinical Trial Site, only for ongoing Women-II Clinical Trials, under the Bio-Study Rules, 2017.*

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**AGENDA ITEM X:**

**APPLICATION FOR LICENSE TO ACT AS CLINICAL TRIAL SITE FROM THE AL-KHIDMAT RAZI HOSPITAL, RAWALPINDI. F. No.15-37/2023 CTS**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation, discussion decided to defer the case of M/s Al-Khidmat Razi Hospital, 25/B-1, Satellite Town, Rawalpindi, upon following recommendations/report of inspection panel:*

> *"The panel appreciated the commitment of CTU management towards continuous improvement. It was observed that the site requires dedicated pharmacy for IMPs and rearrangement of subject movement through the site, also the phlebotomy collection center needs to be relocated for compliance of the IPC and proper waste disposal practices. There was no dedicated space for trial related data (archive) available at present. PK/PD lab is not available so the site is not suitable for phase I & II clinical trials. In the light of above mentioned observation the panel decided to defer the site for further improvement."*

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**AGENDA ITEM XI:**

**APPLICATION FOR GRANT OF LICENCE TO THE AGA KHAN HOSPITAL FOR WOMEN & CHILDREN, KHARADAR, KARACHI, TO ACT AS CTS FOR A PHASE-II CLINICAL TRIAL TITLED, "CAN ESOMEPRAZOLE IMPROVE OUTCOMES IN WOMEN AT HIGH RISK OF PRE-ECLAMPSIA? A PHASE-II, PLACEBO-CONTROLLED RANDOMIZED MULTICENTER CLINICAL TRIAL (THE ESPRESSO STUDY)". F. No.15-16/2022 DD (PS)**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation, discussion decided to defer the case of M/s Aga Khan Hospital for Women & Children, Kharadar, Karachi for a Phase-II (ESPRESSO) Clinical Trial upon following recommendations/report of inspection panel:*

> *"The panel comprising of Prof. Dr. Mirza Tasawer Baig, Dr. Abdul Rasool Sheikh and Dr. Ahson Siddiqui visited the Clinical Trial Site of AKH Kharadar. It was found that there was no specific area dedicated for conduction of trial study. No dedicated Pharmacy or Pharmacy area available. For record, there was no specific area."*

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**AGENDA ITEM XII:**

**NOTIFICATION OF GLOBAL END OF TRIAL REPORT, TITLED, "A PHASE 3, MATRIX DESIGN, PARTIALLY DOUBLE-BLIND, RANDOMIZED STUDY OF THE EFFICACY AND SAFETY OF 50 MG LONAFARNIB/ 100 MG RITONAVIR BID WITH AND WITHOUT 180 MCG PEG IFN-ALFA-2A FOR 48 WEEKS COMPARED WITH PEG IFN-ALFA-2A MONOTHERAPY AND PLACEBO TREATMENT IN PATIENTS CHRONICALLY INFECTED WITH HEPATITIS DELTA VIRUS BEING MAINTAINED ON ANTI- HBV NUCLEOS (T) IDE THERAPY (D-LIVR)" F.No.03-08/2019-CT (PS)**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation and discussion decided as follows:*

a. *In view of "Notification of Global End of Trial Report" for instant trial advised the applicant to submit IRB and DSMB reports (if any).*
b. *Acceded to IMPs destruction report of the Clinical Trial.*

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**AGENDA ITEM XIII:**

**IMPs RECONCILLIATION & INCINERATION REPORT FOR CLINICAL TRIAL TITLED, "ANTI-CORONAVIRUS THERAPIES TO PREVENT PROGRESSION OF COVID-19. F. No.03-57/2021-DD (PS)**

The case was presented before CSC. The Committee decided the case as follows:

a. *Acceded to IMPs destruction report for Clinical Trial titled, "Anti-Coronavirus Therapies to Prevent Progression of COVID-19".*
b. *Directed to submit IRB and DSMB reports (if any).*

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**AGENDA ITEM XIV:**

**IMPs RECONCILIATION & INCINERATION REPORT FOR CLINICAL TRIAL TITLED, "A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE-II CLINICAL TRIAL TO EVALUATE THE EFFICACY & SAFETY OF CBP-307 IN SUBJECTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS (UC)" F.NO.03-59/2021 DD (PS).**

The case was presented before CSC. The Committee decided the case as follows:

a. *Acceded to the IMPs destruction report for Clinical Trial titled, "A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase-II Clinical Trial to Evaluate the Efficacy & Safety of CBP-307 in subjects with moderate to severe Ulcerative Colitis (UC)".*
b. *Advised to submit IRB and DSMB reports (if any).*

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**AGENDA ITEM XV:**

**IMPs RECONCILIATION & INCINERATION REPORT FOR CLINICAL TRIAL TITLED, "A MULTICENTER, SEAMLESS, RANDOMIZED, THIRD-PARTY-BLIND CLINICAL TRIAL TO EVALUATE THE SAFETY & EFFICACY OF MEPLAZUMAB (INJECTION) IN ADDITION TO STANDARD CARE FOR THE TREATMENT OF COVID-19 IN HOSPITALIZED ADULTS" F.NO.03-54/2021 DD (PS).**

The case was presented before CSC. The Committee decided the case as follows:

a. *Acceded to the IMPs destruction report for Clinical Trial titled, "A Multicenter, Seamless, Randomized, Third-Party-Blind Clinical Trial to Evaluate the Safety & Efficacy of Meplazumab (Injection) in Addition to Standard Care for the Treatment of COVID-19 in Hospitalized Adults".*
b. *Advised to submit IRB and DSMB reports (if any).*

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**AGENDA ITEM XVI:**

**Case-A:**

**SUSAR & DEVELOPMENT SAFETY UPDATE REPORT (DSUR) & FOR CLINICAL TRIAL TITLED "A PHASE-III, MULTICENTRE. RANDOMIZED, DOUBLE-BLIND, 24-WEEK STUDY OF THE CLINICAL AND ANTIVIRAL EFFECT OF S-217622 COMPARED WITH PLACEBO IN NON-HOSPITALIZED PAI1ICIPANTS WITH COVID-19", FROM AGA KHAN UNIVERSITY HOSPITAL, KARACHI. F. No.03-25/2023-CT (PS)**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation and discussion decided to defer the case for Extension/Amendment in Trial Enrollments Size due to following reasons:*

a. *Submit protocol amendment application with all prerequisites as in approved protocol version 3.0 the trial was designed as per 1490 subjects.*
b. *Protocol amendment approvals from IRB and NBC.*

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**AGENDA ITEM XVII:**

**FINAL SCRIOUS ADVERSE EVENT REPORT OF CLINICAL TRIAL TITLED "EFFECTIVENESS OF NOVEL APPROACHES TO RADICAL CURE WITH TAFENOQUINE AND PRIMAQUINE (EFFORT)- A RANDOMIZED CONTROLLED TRIAL IN P. VIVAX PATIENTS". FROM AGA KHAN UNIVERSITY HOSPITAL, KARACHI. F. No.03-10/2022-DD (PS) FOR 15% EXTRA DRUGS IMPORT LICENSE FOR CLINICAL TRIAL F.NO.03-20/2022-CT (PS)**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation and discussion advised PI to submit IRB and DSMB reports (if any) for Clinical Trial titled, "Effectiveness of Novel Approaches to Radical Cure with Tafenoquine and Primaquine (EFFORT)- A Randomized Controlled Trial in P. Vivax patients",*

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**AGENDA ITEM XVIII:**

**APPLICATION FOR AMENDMENTS IN ALREADY APPROVED CLINICAL TRIAL TITLED "FINDING TREATMENTS FOR COVID-19: A PHASE-II, MULTI-CENTRE, ADAPTIVE PLATFORM TRIAL TO ASSESS ANTIVIRAL PHARMACODYNAMICS IN EARLY SYMPTOMATIC COVID-19 (PLATCOV)", FROM AGA KHAN UNIVERSITY HOSPITAL, KARACHI. F. No.03-18/2022-PS (CT)**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation and discussion decided to approve the amendments in following documents of already approved Clinical Trial titled, "Finding Treatments for COVID-19: A Phase-II, Multi-Centre, Adaptive Platform Trial to Assess Antiviral Pharmacodynamics in Early Symptomatic COVID-19 (PLATCOV)".*

i. *Details of amended documents is as follows:*

a. *PLATCOV CRF V0.5-Pakistan-9JAN23*
b. *PLATCOV CRF VO.4-PAKISTAN-1 DEC22_CLEAN*
c. *PLATCOV PIS-V0.4-Urdu-CLEAN*
d. *PLATCOV-PIS-V.0.4-Pakistan- English-CLEAN*
e. *Final PLATCOV Flyer (Urdu)*
f. *Final PLATCOV Flyer (English)*
g. *04-PLATCOV-Patient diary card-ensitrelvir*
h. *04-PLATCOV-Patient diary card- Fluoxetine-V.2. 0*
i. *04 PLATCOV Patient diary card-molnupiravir-V.2.0*
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s. *Affidavit of Translation (Diary)*
t. *Affidavit of Translation (Flyer)*

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**AGENDA ITEM XIX:**

**APPLICATION FOR EXTENSION IN TRIAL DURATION, FOR THE STUDY TITLE "A PHASE III, RANDOMIZED, OBSERVER-BLIND, MULTICENTER STUDY TO EVALUATE THE EFFICACY, IMMUNOGENICITY AND SAFETY OF SEQIRUS' CELL BASED QUADRIVALENT SUBUNIT INFLUENZA VIRUS VACCINE (QIVC) COMPARED TO A NON-INFLUENZA VACCINE WHEN ADMINISTERED IN HEALTHY SUBJECTS AGED 6 MONTHS THROUGH 47 MONTHS", FROM AGA KHAN UNIVERSITY HOSPITAL, KARACHI. REF NO: F.NO.03-11/2022-DD (PS)**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation and discussion decided to approve the extension in trial duration w.e.f. 27th July 2023 to 26th July 2024 for an already approved Clinical Trial titled, "A Phase-III, Randomized, Observer-Blind, Multicenter Study to Evaluate the Efficacy, Immunogenicity and Safety of SEQIRUS Cell Based Quadrivalent Subunit Influenza Virus Vaccine (QIVC) Compared to a Non-Influenza Vaccine when administered in Healthy subjects aged 6 months through 47 months".*

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**AGENDA ITEM XX**

**APPROVAL FOR 15% EXTRA DRUGS IMPORT LICENSE FOR CLINICAL TRIAL F.NO.03-20/2022-CT (PS)**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation and discussion decided to approve 15% extra IMPs import for already approved Clinical Trial titled, "A Phase-II Randomized, Double-Blinded Study, to Evaluate Ability of the Probiotic Vivomixx to Improve Environmental Enteropathy in Pregnant Women: A Proof of Concept Trial in Bangladesh Pakistan Senegal, and Zambia".*

II. Details of IMPs are as follows:

| ***Sr. No.*** | ***Material Name*** | ***Manufacturer-Company Name*** | ***Supplier PI/Site-Address*** | ***Supplying Country*** | ***Quantity*** |
|---|---|---|---|---|---|
| *1* | *Vivomixx* | M/s Premier Nutraceutical Pvt. Ltd. (PNPL) India. | *Dr. Yakhya Dieye, Pole of Microbiology Institut Pasteur de Dakar, 36 Avenue Pasteur, Dakar, Senegal* | *(Senegal)* | *304 (No. of doses)* |
| *2* | *Placebo* | M/s Premier Nutraceutical Pvt. Ltd. (PNPL) India. | *Dr. Yakhya Dieye, Pole of Microbiology, Institut Pasteur de Dakar, 36 Avenue Pasteur, Dakar, Senegal* | *(Senegal)* | *304 (No. of doses)* |

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**AGENDA ITEM XXI:**

**APPLICATION FOR DRAP GUIDANCE ON CLINICAL TRIAL SUPPLIES AND IMPs MANAGEMENT, FROM M/S IQVIA PAKISTAN, KARACHI. F. No.08-04/2023-Misc (PS)**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed discussion and deliberations decided as follows:*

| *S. No.* | *Query* | *CSC Decision* |
|---|---|---|
| *i.* | *Absence of the list of Ancillaries in the DRAP Study Approval Letter:* | *Advised the applicants to clearly mention details regarding IMPs as well as about all ancillary items in application form (Form-II, point-19) along with requisite documents. Further, it is decided that CT application assessors/evaluator will communicate and ask about IMPs & ancillary items details from applicant in case details are not attached in the application* |
| *ii.* | *Delayed Shipment Clearance NOC Process:* | *A copy of registration letter(s) of Clinical Trials will be shared with respective DRAP-field offices for information and quick processing of DIL and NOC for Clinical Trials.* |
| *iii.* | *DRAP Authorized Service Providers for Bulk Shipments:* | *The matter regarding CROs/PI/Sponsor's role in Importation/Exportation, Storage, Distribution and Reconciliation of IMPs was deferred for further deliberation and discussion as per the Bio-Study Rules, 2017 and current ICH-GCP Guidelines.* |

**AGENDA ITEM XXII:**

**APPLICATION FOR APPROVAL OF CLINICAL TRIAL TITLED, "THERAPY FOR HEPATITIS C VIRUS (HCV) IN PRIMARY TREATMENT FAILURE IN PAKISTAN" FROM THE AGA KHAN UNIVERSITY (AKUH), STADIUM ROAD, KARACHI.**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation decided to approve the clinical trial subject to submission of clarification/justification letter from Sponsor/Manufacturer regarding provision of IMP and its labelling & packaging as per ICH-GCP Guidelines. The trial titled as, "Therapy for Hepatitis C Virus (HCV) in primary treatment failure in Pakistan" at following two (02) sites: -*

| *Sr. #* | *Clinical Trial Site(s)* |
|---|---|
| *i.* | *The Aga khan university (AKUH), Stadium Road, Karachi. (CTS:0003)* |
| *ii.* | *Dow University of Health Sciences (DUHS), SUPARCO Road, Ojha Campus, Karachi. (CTS: 0068)* |

**AGENDA ITEM XXIII:**

**APPLICATION FOR APPROVAL OF CLINICAL TRIAL TITLED AS, "PREVENTION OF IRON DEFICIENCY ANEMIA POST-DELIVERY (PRIORITY TRIAL)" FROM THE AGA KHAN UNIVERSITY HOSPITAL (AKUH), DEPARTMENT OF COMMUNITY HEALTH SCIENCES STADIUM ROAD, KARACHI. F. No.03-43/2023-CT (PS)**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation decided to defer the subject clinical trial due to following deficiencies and clarifications required: -*

i. *Valid license of intended clinical trial site.*
ii. *Provide the valid cGMP certificates of the manufacturers of the IMPs.*
iii. *Provide the Investigational Medicinal Product (IMP) transfer agreement between the sponsor and manufacturer of all the IMPs utilized during the instant trial that clearly mentioning the Principal clinical trial Site.*
iv. *Protocol version 3.0 dated 17th April 2023 is submitted that has neither approved by NBC nor by the IRBs, provide the approval of above versions, if obtained.*
v. *Clarification/ justification for sample size.*
vi. *Correlation between oral and injectable doses in regards of BE analyses.*
vii. *Correlation and justification between hemoglobin values and dose regimen.*

**AGENDA ITEM XXIV:**

**REQUEST FOR APPROVAL OF PROTOCOL AMENDMENT VERSION 3.0 DATE FEBRUARY 17, 2023 SUBMITTED ON DATE 20TH JUNE 2023 TITLED A RANDOMIZED, DOUBLE-BLIND CLINICAL STUDY OF THE EFFICACY AND SAFETY OF BCD-201 (JSC BIOCAD) AND KEYTRUDA® IN PATIENTS WITH UNRESECTABLE OR METASTATIC MELANOMA.**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation and discussion decided to approve the amended protocol version 3.0, dated 17th February, 2023 of already approved Clinical Trial titled, "A Randomized, Double-Blind Clinical Study of the Efficacy and Safety of BCD-201 (JSC BIOCAD) and KEYTRUDA® in Patients with Unresectable or Metastatic Melanoma".*

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**AGENDA ITEM XXV:**

**SERIOUS ADVERSE EVENTS REPORTED FOR CLINICAL TRIAL TITLED, "A MULTI-CENTER, RANDOMIZED, BLINDED, PLACEBO-CONTROLLED, PHASE-III CLINICAL STUDY TO EVALUATE THE EFFICACY, SAFETY AND IMMUNOGENICITY OF SARS-COV-2 BIVALENT mRNA VACCINE (LVRNA021) AS BOOSTER IN PARTICIPANTS AGED 18 YEARS AND OLDER WHO COMPLETED PRIMARY/1 BOOSTER DOSE(S) OF SARS-COV-2 VACCINATION" F.No.03-38/2023-CT (PS)**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed discussion and deliberation decided and directed the CRO to:*

i. *Submit complete DSMB report by giving final recommendation for all 27 cases of SAEs. Including 02 fatal case where two consultants of DSMB have different opinions.*
ii. *If sample size of 3000 in IMP group is sufficient to meet the WHO guideline for safety assessment as per claim in DSMB report, then what was the rationale to take more sample size for the trial as mentioned in protocol.*
iii. *What is the rational to give different amounts of compensation through insurance to family of three deceased people?*
iv. *PI/CRO/Sponsor are advised to submit their final proposal in light of DSMB report.*
v. *The CSC directed Pharmacy Services Division to provide a copy of inspection report of trial sites to NBC.*

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**AGENDA ITEM XXVI:**

**A DOUBLE-BLIND, RANDOMIZED CLINICAL STUDY OF THE EFFICACY AND SAFETY OF BCD-178 AND PERJETA® AS NEOADJUVANT THERAPY OF HER2-POSITIVE BREAST CANCER (PREFER) F.No.03-44/2023-CT (PS)**

The case was presented before CSC. The Committee decided the case as follows:

*CSC after detailed discussion and deliberation decided to as follows:*

i. *To approve the study titled as A DOUBLE-BLIND, RANDOMIZED CLINICAL STUDY OF THE EFFICACY AND SAFETY OF BCD-178 AND PERJETA® AS NEOADJUVANT THERAPY OF HER2-POSITIVE BREAST CANCER (PREFER).*
ii. *Following IMPs subject to Clearance Certificate from I&E department of DRAP.*

| ***Title*** | ***BCD-178 (Test Drug)*** | ***Perjeta (Reference Drug)*** |
|---|---|---|
| *Name* | *INN: Pertuzumab* | *INN: Pertuzumab* |
| *Dosage Form* | *Concentrate for Solution for Infusion* | *Concentrate for Solution for Infusion* |
| *Strength* | *420 mg / 14 ml* | *420 mg / 14 ml* |
| *Quantity* | *368* | *578* |

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**AGENDA ITEM XXVII:**

**APPLICATION FOR AMENDMENTS IN PROTOCOL AND FORM-VI OF APPROVED CLINICAL TRIAL "A PHASE III, RANDOMIZED, COMPARATOR-CONTROLLED, DOUBLE-BLIND, MULTICENTER STUDY TO EVALUATE THE IMMUNOGENICITY, SAFETY AND LOT TO LOT CONSISTENCY OF THREE LOTS OF A PIKA RABIES VACCINE (VERO CELL) FOR HUMAN USE, FREEZE DRIED IN HEALTH ADULTS USING A POST EXPOSURE PROPHYLAXIS SCHEDULE F.NO.03-36/2023-CT (PS) CT-0053.**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed discussion and deliberation decided to approve.*

i. *Amended protocol V3.0 dated 15 May 2023 along with ICF and other documents for study A PHASE III, RANDOMIZED, COMPARATOR-CONTROLLED, DOUBLE-BLIND, MULTICENTER STUDY TO EVALUATE THE IMMUNOGENICITY, SAFETY AND LOT TO LOT CONSISTENCY OF THREE LOTS OF A PIKA RABIES VACCINE (VERO CELL) FOR HUMAN USE, FREEZE DRIED IN HEALTH ADULTS USING A POST EXPOSURE PROPHYLAXIS SCHEDULE*
ii. *Following IMPs subject to Clearance Certificate from I&E department of DRAP.*

| | |
|---|---|
| *Comparator Vaccine* | *Chirorab (Purified Chick Embryo Cell)* |
| *Quantity of PIKA Rabies Vaccine* | *15000* |
| *Quantity of Comparator* | *8000* |
| *Number of Subjects* | *4500 (competitive recruitment)* |
| *Manufacturer's Address of PIKA Rabies vaccine.* | *No. 415 Daoyi North Street, Shenbei, New District, Shenyang city lioning province, China* |

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**AGENDA ITEM XXVIII:**

**CLINICAL TRIAL STUDY SUPPLIES FOR CLINICAL TRIAL TITLED AS "A PHASE III RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY TO EVALUATE THE EFFECT OF BL-26 (STAIN OF BIFIDOBACTERIUM LONGUM, B. INFANTIS) SUPLEMENTATION VS PLACEBO ON WEIGHT GAIN ON UNDER WEIGHT INFANTS No.F.03-31/2023-DD-PS CT-0056.**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation and discussion decided to allow to import of following ancillary medical items as applicant has submitted Declaration of Conformity / Establishment Registration & devices listing of FDA. The applicant is directed to obtain necessary clearance certificate from Import & Export Department of DRAP:*

| ***Sr.*** | ***Product*** | ***Manufacturer Name & Address*** | ***Quantity Required*** |
|---|---|---|---|
| *i.* | *PIPETTE (Standard)* | *Sarstedt 1025 St James Church Rd, Newton, NC 28658* | *180* |
| *ii.* | *SM Pressure Bag (Standard)* | *Vonco Products LLC, 10826 250th Avenue Trevor, WI 53179* | *270* |
| *iii.* | *Blood Collection Set 23G x 3/4* | *Greiner Bio-one, 4238 Capital Dr. # 7681, Monroe, NC 28110* | *408* |
| *iv.* | *Band aid (Standard)* | *BSN medical, Inc. 5825 Carnegie Boulevard Charlotte, NC 28209* | *720* |
| *v.* | *Omnigene Gut Sample Collection Kit* | *DNA Genotek 3000-500 Palladium Drive Ottawa, Ontario, Canada K2V 1C2* | *270* |
| *vi.* | *2ml Clear Cryovial* | *Thermo Fisher Scientific 275 Aiken Rd, Asheville, NC 28804* | *560* |
| *vii.* | *2ml Red Tube* | *Greiner Bio-one 4238 Capital Dr # 7681, Monroe, NC 28110* | *150* |
| *viii.* | *Stretch Latex Free Tourniquet* | *Becton, Dickinson and Company 1 Becton Drive Franklin Lakes, NJ 07417-1880* | *06* |

| | | | |
|---|---|---|---|
| *ix.* | *LG Nitrile Gloves Disposable* | *Fisher Scientific 81 Wyman Street, Waltham, MA* | *60* |
| *x.* | *Flocked Swab* | *Copan Diagnostics 26055 Jefferson Avenue Murrieta, CA 92562* | *600* |
| *xi.* | *Nitrazine Indicator Paper* | *Micro Essential 4224 Avenue H, Brooklyn, New York, 11210* | *06* |

**AGENDA ITEM XXIX:**

**APPLICATION FOR REMOVAL OF CONDITION TO IMPORT ANTIDOT OF THE ANTICOUGULANT FOR THE CLINCAL TRIAL TITLED AS "ANTICOAGULATION FOR STROKE PREVENTION WITH RECENT EPICODES OF PERIOPERATIVE ATRIAL FIBRILLATION AFTER NON-CARDIAC SURGERY – THE ASPIRE-AF TRIAL F.03-34/2023-DD (CT)**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed discussion and deliberation:*

i. *Acceded to request of applicant to remove condition requiring import of antidote from ASPIRE-AF as the trial is of phase-IV and drug is registered and available in market.*
ii. *It is apprised that, as it's a multi-country trial and antidote requirement is not mentioned in international trial protocol*
iii. *Directed the PI to ensure National Standard of Care to subjects of Clinical Trial.*

**AGENDA ITEM XXX:**

**APPLICATION FOR PROTOCOL AMENDMENT OF CLINICAL TRIAL "A RANDOMIZED, PHASE-III PLACEBO CONTROLLED TRIAL OF COLCHICINE FOR THE PREVENTION OF PERIOPERATIVE ATRIAL FIBRILLATION (COP-AF)" CT-0013.**

The case was presented before CSC. The Committee decided the case as follows:

The *CSC after detailed discussion and deliberations decided as follows:*

a. *To defer the application for amendment in protocol and directed the PI to clarify that on which version of protocol, trial was completed as previously application for approval of version 5 of protocol was also submitted.*
b. *IRB and DSMB reports will be provided regarding SAE and deaths of subjects who participated in the trial.*

**AGENDA ITEM XXXI:**

**CLOSEOUT REPORT FROM CRO M/S DIMENSION RESEARCH FOR CLINICAL TRIAL "A GLOBAL MULTI-CENTER, RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED, ADAPTIVE DESIGNED PHASE-III CLINICAL TRIAL TO EVALUATE THE EFFICACY, SAFETY AND IMMUNOGENICITY OF RECOMBINANT NOVEL CORONA VIRUS VACCINE (ADENOVIRUS TYPE-5 VECTOR) IN ADULTS 18 YEARS OF AGE AND OLDER NO.03-40/2020-DD (PS) CT-0015**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed discussion and deliberations decided that IRB and DSMB reports need to be provided regarding close out report of the trial including SAE and deaths of subjects during the trial.*

**AGENDA ITEM XXXII:**

**IMPs RECONCILIATION & INCINERATION REPORT FOR CLINICAL TRIAL TITLED, "A PHASE - III, endTB (EVALUATING NEWLY APPROVED DRUGS FOR MULTIDRUG RESISTANT TB)", AT THE INDUS HOSPITAL KARACHI. F. No.03-04/2019-DD (PS)**

The case was presented before CSC. The Committee decided the case as follows:

*The CSC after detailed deliberation and discussion decided as follows:*

a. *Acceded the IMPs reconciliation & destruction report for Clinical Trial titled, "A Phase-III, endTB (Evaluating Newly Approved Drugs for Multidrug Resistant TB)."*
b. *Approved re-export of IMPS listed under **(Annex-I)** & utilization of IMPs list **(Annex-II)** in already approved endTB-Q CT after its protocol amendment, as per Sponsor & PI request.*

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The Meeting ended with vote of thanks to and from the Chair.