MINUTES OF THE 48TH CLINICAL STUDIES COMMITTEE MEETING (SUMMARY)

Pharmacy Services Division, Drug Regulatory Authority of Pakistan

File No: 16-48/2024-CSC (PS)

MARCH 28, 2024
DRUG REGULATORY AUTHORITY OF PAKISTAN
Prime Minister Health Complex, Park Road, Chak Shahzad,
Islamabad.

The 48th meeting of the Clinical Studies Committee was held on 28th March, 2024 in the Conference Room, Drug Regulatory Authority of Pakistan, Prime Minister Health Complex, Park Road Chak Shahzad, Islamabad. The meeting was started with recitation of the Holy Verses of Quran.

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 and Emerging Sciences, Peshawar, Khyber Pakhtunkhwa.	Member
iii.	Prof. Dr. Munawar Alam Ansari.	Professor of Pharmacology, Dean Faculty of Pharmacy, Liaquat University of Medical Sciences, Jamshoro. ***(Sindh)***	Member
iv.	Dr. Faiza Bashir	Nominee of Chairman, Pakistan Health Research Council, Islamabad.	Member
v.	Prof. Dr. Mirza Tasawer Baig	Department of Pharmacy Practice, Faculty of Pharmacy, Ziauddin University, Karachi and Clinical Pharmacist at Dr. Ziauddin Hospital, Karachi, Sindh.	Member
vi.	Mr. Ahsan Ul Haq Athar	Deputy Director, Pharmacy Services Division.	*Ex-officio Secretary*

3. Following members attended the meeting online through Zoom application.

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
iii.	Dr. Sadia Asim	Representative of PPMA (Observer), Director IBBPS (Institute of Biological, Biochemical & Pharmaceuticals Sciences) Dow University of Health Sciences OJHA Campus, Karachi.	Observer
iv.	Dr. Raeefuddin Ahmed.	Representative of Pharma Bureau (Observer), 107/II, Khayaban-e-Roomi, Phase-8, DHA Karachi. Pakistan	Observer

4. Dr. Nouman Yousuf, Mr. Hafiz Muhammad Jawad Ali and Mr. Shafqat Hussain Danish assisted the Committee and the Secretary in presentation of the agenda.

AGENDA ITEM I:

CONFIRMATION OF THE MINUTES OF THE 47th CLINICAL STUDIES COMMITTEE MEETING.

The minutes of the 47th CSC meeting held on 22nd December, 2023. Minutes were shared with CSC members through email. The CSC members submitted their consent and no comments/queries were received from the members. Accordingly, after approval of the minutes, decisions taken in the meeting have been communicated to all applicants and are placed for confirmation by members.

2. Minutes of the 47th CSC meeting were placed before the Committee.

Decision:

All the Members of the CSC confirmed the Minutes of 47th CSC meetings.

AGENDA ITEM II:

DRAP's AUDIT BY WHO FOR GLOBAL BENCHMARKING FOR LEVEL-III NATIONAL REGULATORY AUTHORITY.

Decision:

The Committee acknowledged the efforts of the entire Clinical trial team especially hard work of Mr. Shafqat Hussain Danish and assistance of Dr. Faiza Bashir for IDPs related to NBC. The CSC further recommended that efforts of the team may be recognized by the Authority and appreciation certificates may be issued.

A. CLASSIFICATION / CATEGORIZATION OF AMENDMENTS FOR PROTOCOL AND OTHER CLINICAL TRIAL RELATED DOCUMENTS AMEDMENTS IN "GUIDELINES FOR CLINICAL RESEARCH IN PAKISTAN"

Decision:

The CSC acknowledged the amended guidelines and delegated the powers to Chairman CSC for decision/ approval of minor/ non-substantial amendments.

B. ANNUAL PLAN OF THE CLINICAL STUDIES COMMEETT TO BE PUBLISHED ON DRAP'S OFFICIAL WEBSITE. F. No. 03-49/2023-CT (PS).

Decision:

The Committee decided that the CSC meetings will be convened after every 45 days and accordingly the following schedule was approved: -

S. No.	*CSC Meeting*	*Proposed Dates*
01	*49th CSC Meeting*	*2nd week of May, 2024*
02	*50th CSC Meeting*	*4th week of June, 2024*
03	*51st CSC Meeting*	*2nd week of August, 2024*
04	*52nd CSC Meeting*	*4th week of September, 2024*
05	*53rd CSC Meeting*	*2nd week of November 2024*
06	*54th CSC Meeting*	*4th week of December, 2024*

2. Further it was decided that, the meeting can be called by the Chairman CSC whenever required, in case a meeting conducted before its scheduled date then scheduled meeting may or may not be convened.

C. NOMINATION AND NOTIFICATION OF SUB-COMMITTEE FOR PROCESSING OF SAEs AND ADRs TO FULFIL IDPs AND GUIDELINES REQUIREMENTS. F. No. 03-49/2023-CT (PS).

Decision:

The CSC nominated following Sub-Committee for review of SAEs / Clinical Study Reports (CSR):

- *Prof. Dr. Munawar Alam Ansari (Chairman)*
- *Dr. Faiza Bashir*
- *Malik Muhammad Asad DD (PS) (Secretary)*

2. The Chairman of sub-committee may co-opt any member with relevant experience /expertise.

AGENDA ITEM III:

APPLICATION FOR APPROVAL OF APPLICATION TO ACT AS CRO AT M/S MEDWATCH GLOBAL PRIVATE LTD., LAHORE (F.No.15-40/2023-CRO).

Decision:

The CSC after detailed deliberation, discussion and on recommendation of inspection panel, decided to grant the licence to M/s Medwatch Global (Pvt.) Ltd., 24-G/4, Johar Town Lahore to act as Contract Research Organization.

AGENDA ITEM IV:

APPLICATION FOR LICENSE TO ACT AS TRIAL SPECIFIC NON-INFERIORITY TRIAL FOR CUTANEOUS LEISHMANIASIS (PHASE-IV) CLINICAL TRIAL SITE FROM GOVERNMENT NASSER ULLAH KHAN BABAR MEMORIAL HOSPITAL, PESHAWER F. No.15-35/2023 DD-CTS.

Decision:

The CSC after detailed deliberation, discussion and on recommendation and verification by inspection panel, decided to grant the licence to act as clinical trial site for Phase-IV clinical trial titled "Randomised, open label, multicenter non-inferiority clinical trial for new treatment modalities for cutaneous leishmaniasis caused by Leishmania tropica" situated at Department of Dermatology of M/s Government Naseer Ullah Khan Babar Memorial Hospital (GNKBMH), Peshawar.

AGENDA ITEM V:

APPLICATION FOR RENEWAL OF LICENSE TO ACT AS BA/BE CENTER FROM INSTITUTE OF BIOLOGICAL, BIOCHEMICAL AND PHARMACEUTICAL SCIENCES (IBBPS), DUHS, KARACHI (F. No.15-10/2019 DD (PS)).

Decision:

The CSC after detailed deliberation, discussion and on recommendation of inspection panel, decided to grant renewal of licence (BA/BE-C-0004) to act as BA/BE Center situated at Dow Institute of Biological, Biochemical & Pharmaceutical Sciences (IBBPS), Dow University of Health Sciences, KDA Scheme 33, Gulzar e Hijri, SUPARCO Road, Ojha Campus, Karachi for the period of three years (w.e.f. 24th December 2023 to 23rd December 2026).

AGENDA ITEM VI:

APPLICATION FOR RENEWAL OF LICENCE NO. CRO-0003, TO ACT AS CONTRACT RESEARCH ORGANIZATION FROM M/S METRICS RESEARCH (PVT) LTD., KARACHI F. No.15-21/2022-CRO.

Decision:

The CSC after detailed deliberation, discussion and on recommendation of inspection panel, decided

i. *to grant the renewal of licence (CRO-0003) to act as Contract Research Organization to M/s M/s Metrics Research (Pvt.) Ltd. Plot No. B-10, Block WCHS, KDA Scheme No.24, Gulshan e Iqbal, Karachi, for the period of three years (w.e.f. 03rd February 2023 to 02nd February 2026).*
ii. *directed the applicant to fulfill/ address following shortcomings/panel recommendations within period of three months and to submit compliance to the Division of Pharmacy Services, DRAP Islamabad;*
    a. *develop the structured mechanism to assess and document personnel competency on an annual basis.*
    b. *Quality Assurance Unit need further strengthening and putting it as an independent unit in the organogram.*
    c. *QC and QA are the same person and suggested for separate setups.*
    d. *SOP for approval and authorization need separation as presently both done by CEO.*
    e. *a current index listing of the SOPs available but need improvement for obsolete SOP.*
    f. *change control system for SOP/Methods need improvement.*

AGENDA ITEM VII:

APPLICATION FOR RENEWAL OF LICENSE TO ACT AS CONTRACT RESEARCHI ORGANIZATION (CRO) FROM IQVIA SOLUTION PAKISTAN (PVT) LTD., KARACHI 15-09/2019 DD (PS)).

Decision:

The CSC after detailed deliberation, discussion and on recommendation of inspection panel, decided to grant the renewal of licence (CRO-0006) to act as Contract Research Organization to M/s IQVIA Solutions Pakistan (Pvt.) Ltd., at Ground Floor, Orient House, Plot No. 194-A, SMCHS, Karachi., for the period of three years (w.e.f. 29th June 2023 to 28th June 2026)

AGENDA ITEM VIII:

APPLICATION FOR RENEWAL OF LICENSE TO ACT AS CLINICAL TRIAL SITE FROM MAROOF INTERNATIONAL HOSPITAL ISLAMABAD F. No.15-02/2021 DD (PS).

Decision:

The CSC after detailed deliberation, discussion and on recommendation of inspection panel, decided to grant the renewal of licence (CTS 0045) to act as Clinical Trial Site at M/s Maroof International Hospital Plot # 8, 10th Avenue, F-10 / Markaz, Islamabad, for a period of three years (w.e.f. 16.02.2024 to 15.02.2027). However, license will be issued after following steps (pts i & ii):

i. *That the Chairman CSC will constitute the two members panel for verification of fulfilments of shortcomings.*
ii. *To authorize the Chairman CSC to approve the grant of licence based on recommendation/ verification of fulfilments of shortcomings by the panel.*
iii. *Recommended improved QMS system for clinical trial site from reputable organization.*

AGENDA ITEM IX:

APPLICATION FOR APPROVAL OF M/S INTEGRATED MEDICAL CARE HOSPITAL, LAHORE TO ACT AS GENERALIZED CLINICAL TRIAL SITE FOR PHASE-I, II, III & IV CLINICAL TRIALS. F. NO.15-15/2022 DD (PS) F. No.15-15/2022-DD (PS)

Decision:

The CSC after detailed deliberation, discussion and on recommendation of inspection panel, decided to give final opportunity to the applicant for improvements/compliance of points given below, (reported by the inspection panel) and advised applicant to submit compliance report to Pharmacy Services Division, DRAP, Islamabad, not later than three (03) months for re-inspection by the panel.

i. *The panel recommended re-organization of different sections of CTU e.g. designated subject waiting area, screening/ physical examination room, phlebotomy, ICF/ subject counselling room, IMP administration, observation room etc. with well-defined layout plan.*
ii. *Dedicated pharmacy for storage and dispensing of IMPs complying to good storage and good clinical practices with research pharmacist required.*
iii. *Dedicated space for trial related data (archiving area) with lock & key and controlled access need to be developed.*
iv. *A proper clinical trial team i.e. Principal Investigator/ Director research, study coordinator, pharmacist, phlebotomist and nurses along with their CVs required.*
v. *Standard Operating Procedures (SOPs) for all aspects of the operations, including document control, SOP creation, revision, computer validation, clinical operations, study start-up, conduct, and closeout/completion, record retention and archival etc. required.*
vi. *Emergency evacuation plan and subject transfer protocol to ICU in case of SAEs need to be developed.*

AGENDA ITEM X:

NATIONAL UNIVERSITY OF MEDICAL SCIENCES, RAWALPINDI REQUEST FOR INCLUSION INSTITUTES IN VACINITY (AFIC, AFIO, AFIRI & AFIMH) IN ALREADY ISSUED LICENCE OF PAK. EMIRATES MILITARY HOSPITAL RAWALPINDI/ EXTENSION OF THE SCOPE OF LICENCE (CTS-0095) ISSUED TO M/S PAK MILTIARY HOSPITAL (PEMS) ISLAMABAD. F. No.15-10/2022 DD (PS).

Decision:

The CSC after detailed deliberation and discussion decided

i. *To refer the case to Legal Affair Division, DRAP for legal opinion on NUMS request to include names of institutes in the vicinity of PEMH (AFIC, AFIO, AFIRI & AFIMH) in already issued CTS No. 0095.*
ii. *To write the letter to applicant for submission of miscellaneous fee of Rs.25,000/- +Rs 25,000 for already submitted miscellaneous requests.*

AGENDA ITEM XI:

APPLICATION FOR APPROVAL OF A PHASE-III CLINICAL TRIAL TITLED "A DOUBLE-BLIND, RANDOMIZED CLINICAL STUDY OF THE EFFICACY AND SAFETY OF MONOTHERAPY WITH BCD-254 AND DARZALEX® IN SUBJECTS WITH RELAPSED AND REFRACTORY MULTIPLE MYELOMA" FROM SHAHEED ZULFIQAR ALI BHUTTO MEDICAL UNIVERSITY, ISLAMABAD. F. No.03-49/2023-CT (PS).

Decision: -

The CSC after deliberation and discussion decided to defer the case for following points:

a. *DSMB report on the review of the Phase I Clinical Study Report (CSR) of the trial.*
b. *submission of CoPP for Darzalex® or confirmation of approval status from website of relevant National Regulatory Authority.*

AGENDA ITEM XII:

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

Decision:

The CSC after deliberation, discussion decided to reject the application as the applicant has not completed / rectified the shortcomings and submitted a new application with prerequisites and the same has been placed at agenda item # XIII.

AGENDA ITEM XIII:

APPLICATION FOR THE USE OF GRANULOCYTE COLONY STIMULATING FACTOR (GCSF) TRIAL PROTOCOL RECORD. FROM AGA KHAN UNIVERSITY HOSPITAL, KARACH. F. No.03-71/2021-DD (PS)

Decision: -

The CSC after deliberation decided to approve Clinical Trial Titled "THE USE OF GRANULOCYTE COLONY STIMULATING FACTOR (GCSF) TRIAL PROTOCOL RECORD" to be conducted at Aga Khan University Hospital, Karachi.

AGENDA ITEM XIV:

REQUEST FOR APPROVAL AND REGISTRATION OF BIOEQUIVALENCE STUDY OF DELANZO™DR 60MG (DEXLANSOPRAZOLE) CAPSULE OF M/S SAMI PHARMACEUTICALS (PVT) LTD WITH DEXILANT® 60MG (DEXLANSOPRAZOLE) CAPSULE. F. No. 14-02/2024-BE (PS)

Decision: -

The CSC after detailed deliberation, decided to defer the case due to following shortcomings:

i. *Application is not on revised/amended Form-IIA, applicant need to submit application on revised/amended Form-IIA along with prerequisites.*
ii. *Prescribed processing fee is not provided.*
iii. *Formulation of Investigational Product is not provided in attached document.*
iv. *Pharmacodynamics and Pharmacokinetics of Investigational Product are not provided.*
v. *Pre-clinical or clinical data or safety studies are not provided.*
vi. *Attached IEC/IRB approval is very old; applicant need to provide a fresh IEC approval. Further, applicant/PI of the trial is also member of IEC, so, in revised approval it should be clarified that the PI/applicant of this application hasn't taken any part in decision.*
vii. *Approval from National Bio-ethics Committee (NBC) is not provided.*
viii. *Attached ICF is not as per format (ICH-GCP) and US FDA, US and Non-US Sites mentioned in the form. No details regarding insurance is provided in ICF.*
ix. *ADR/AE reporting form is attached but should be as per CIOMS Form.*
x. *A copy of valid GMP Certificate and Manufacturing licence need to be provided.*
xi. *Copy of registration letter of the test drug is not provided.*
xii. *Country of origin of the reference product is not specified. Mode of purchase couldn't be direct it can be only through import through Drug Import Licence*
xiii. *Label/packaging of both the investigational & reference product need to be provided.*

AGENDA ITEM XV:

REQUEST FOR APPROVAL OF PHASE-I CLINICAL TRIAL TITLED "RANDOMIZED, DOUBLE BLINDED, PARALLEL PLACEBO CONTROLLED CLINICAL TRIAL", TO EVALUATE THE SAFETY OF DIETRY HERBAL HEALTH SUPPLEMENT-I (DHA-I), DEVELOPED FOR THE TREATMENT AND/OR MANAGEMENT OF PARKINSON'S DISEASE". F. No.03-63/2021-DD (PS)

Decision: -

The CSC after detailed deliberation, decided to defer the case due to following shortcomings and clarifications:

i. *Submission of Composition of IP, Process of standardization of ingredients, their phytochemical analysis and mode of action of the individual ingredient of IP.*
ii. *Pre-clinical data of ingredients of IP.*

iii. *Basis of proposed doses of 6 g and 12 g thrice a day. In preclinical studies, ED:50, TD;50 or LD:50 are not calculated which is the basis for selection of doses and safety of margin.*
iv. *Mechanism of action of ingredients of IP for the treatment and/or management of Parkinson's disease as no scientific mechanism has been proposed regarding use of mixture and its relation with ameliorating the symptoms of the Parkinson's disease except an animal behavioral study.*
v. *Blood concentration level of the IP to produce anti Parkinson effects*
vi. *IRB and NBC approvals are required as IB and Protocol are revised.*
vii. *Clarification as protocol and IB has been revised but its Version is still 1.0 and dated 26th February 2021 and 07th December 2020 respectively.*
viii. *Profile of Dr. Hassan Auj Co PI of the study.*
ix. *Insurance details of the participants.*

AGENDA ITEM XVI:

APPLICATION FOR APPROVAL OF PLACEBO PREPARATION BY PHARMACEUTICAL MANUFACTURER AND APPROVAL OF CLINICAL TRIAL TITLED "A PILOT STUDY OF AN ADAPTIVE, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFECTS OF METFORMIN IN REDUCING FATIGUE IN LONG-COVID ADOLESCENT SUBJECTS WITH PERSISTENT FEATURES" (REVIVE TRIAL) FROM TVI (CRO) KARACHI. F. NO.03-54/2024-CT (PS)

Decision: -

The CSC decided to defer for further deliberation and evaluation of submitted reply and submission of responses for following questions:

i. *Clarification about the status of the study as there is no term "pilot study" for Phase-III Clinical Trial as per ICH-GCP Guidelines.*
ii. *Effective or determined of results due to small sample size.*
iii. *Hypothesis / rationale and mechanism of action for using Metformin in study for treatment of Fatigue.*
iv. *How they are measuring the fatigue as it has many psychological aspects related.*
v. *Fatigue Syndrome have many symptoms, on which symptoms fatigue scale calculated. Moreover, how fatigue will be measured as it has many aspects including psychological orientation.*
vi. *What will be the impact of metformin on the fatigue parameter in diabetic and nondiabetic patients as the study does not segregate diabetic and nondiabetic patient?*

AGENDA ITEM XVII:

APPLICATION FOR AMENDMENT IN ALREADY APPROVED CLINICAL TRIAL TITLED "TRANSNASAL CAPSULE ENDOMICROSCOPY FOR VISUALIZATION OF THE SMALL INTESTINE IN ENVIRONMENTAL ENTERIC DYSFUNCTION (EED) POPULATION IN PAKISTAN. F. No.03-18/2020-DD (PS).

Decision: -

The CSC after detailed deliberation, decided to approve following mentioned IP quantities to be imported and utilized in already approved Clinical Trial Titled "Transnasal Capsule Endomicroscopy for Visualization of the Small Intestine in Environmental Enteric Dysfunction (EED) Population in Pakistan:

ITEM	*QUANTITY*	*HS CODE*
Research Imaging System and accessory tools	*2*	*9013.80.0000*
Research Rotary Junction and accessory tools	*2*	*9013.80.0000*
Imaging Probe (includes optical probe and introduction tube as one entity)	*24*	*9013.90.0000*
Optical Probes	*10*	*9013.90.0000*
Introduction Tubes	*6*	*9013.90.0000*
Luer holders	*10*	*9013.90.0000*
Hemostatis with female/female luer	*10*	*9013.90.0000*
Microbiome Brush and accessory tools	*100*	*9013.90.0000*
Proximal Subsystems	*40*	*9013.90.0000*
pressure gauges	*40*	*9026.20.0000*
Galinstan Bottles	*20*	*9013.90.0000*
60ml syringes	*30*	*9018.31*
10ml syringes	*60*	*9018.31*
5ml syringes	*30*	*9018.31*
IR card	*2*	*9013.90.0000*
Needles (for syringes, covered)	*50*	*9018.31*
Female luer caps	*50*	*9018.31*
Markers	*2*	*9608.20.0000*
Sterile Drapes	*50*	*6304.93.0000*

AGENDA ITEM XVIII:

A.

AMENDMENTS IN PROTOCOL AND RELATED DOCUMENTS IN ALREADY APPROVED CLINICAL TRIAL TITLED "A MULTICENTER, RANDOMIZED, CONTROLLED, OPEN-LABEL PHASE IIB STUDY TO ASSESS EFFICACY AND SAFETY OF HH-003 INJECTION IN SUBJECTS WITH CHRONIC HEPATITIS DELTA VIRUS INFECTION (HH-003-204)", FROM AGA KHAN UNIVERSITY HOSPITAL, KARACHI. F. No.03-45/2023-CT (PS)

Decision: -

*The CSC after deliberation decided to approve Amendments in already approved of Clinical Trial Titled "*A Multicenter, Randomized, Controlled, Open-Label Phase IIB Study to Assess Efficacy and Safety of HH-003 Injection in Subjects with Chronic Hepatitis Delta Virus Infection (HH-003-204)", *and approved the following amended documents:*

- *Information Sheet and Consent Form (English & Urdu)*
- *Final Signed Protocol Amendment*
- *Protocol Amendment summary from v2.0 to v3.0_EN Version-clean*
- *Pharmacy Manual*

B.

APPLICATION FOR NOTIFICATION OF SPONSOR DECISION TO DROP CLINICAL TRIAL SITE NUMBER 203 (CENTRAL PARK TEACHING HOSPITAL) FOR CLINICAL TRIAL TITLED "A MULTICENTER, RANDOMIZED, CONTROLLED, OPEN-LABEL PHASE IIB STUDY TO ASSESS EFFICACY AND SAFETY OF HH-003 INJECTION IN SUBJECTS WITH CHRONIC HEPATITIS DELTA VIRUS INFECTION (HH-003-204)", FROM AGA KHAN UNIVERSITY HOSPITAL, KARACHI. F. No.03-45/2023-CT (PS)

Decision: -

The CSC after deliberation acceded the request of the Sponsor to drop-out the Clinical Trial Site Number 203 (Central Park Teaching Hospital) for Clinical Trial titled "A Multicenter, Randomized, Controlled, Open-Label Phase-IIB Study to Assess Efficacy and Safety of HH-003 Injection in Subjects with Chronic Hepatitis Delta Virus Infection (HH-003-204)".

2. Applicant is directed to submit prescribed processing fee of Rs.25000/- in Miscellaneous head.

AGENDA ITEM XIX:

APPLICATION FOR IPs ACCOUNTABILITY/ UTILIZATION REPORT AND RE-EXPORT OF IPs TO SPONSOR OF 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", FROM AGA KHAN UNIVERSITY HOSPITAL, KARACHI. F. No.03-11/2022-DD (PS)

Decision: -

The CSC deliberated that Chairman CSC has already been authorized for constitution of Inspection Panel for verification and reconciliation of IPs available at trial sites. Further, the Chairman CSC will decide for issuance NOC for re-export by relevant DRAP field office as per panel report.

AGENDA ITEM XX:

CLINICAL VALIDATION OF ICU VENTILATOR "ALNNOVENT AVB-100" MANUFACTURED BY THE M/S. ALSON'S GROUP IN PAKISTAN.

Decision:

On the recommendations of sub-committee on ventilator, the CSC decided to approve the request to extend the trial of Alnovent AVB-100, under the supervision of Prof. Dr. Muhammad Ashraf Zia (Head of Anesthesia ICU Department, Jinnah Hospital, Lahore) under the amended version 1.2, approval Ref: No.4-87/EMD-Vent-03/24/1521, dated 25th March, 2024, at ICU Department Jinnah Hospital Lahore for 5 patients in each category of non-sedated and fully sedated.

AGENDA ITEM XXI:

A. **CLINICAL TRIAL TITLED, "A PHASE III RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY EVALUATE THE EFFECT OF, Bi-26 (STAIN OF BIFIDOBACTERIUM LONGUM, B. INFANTIS) SUPLEMENTATION VS PLACEBO ON WEIGHT GAIN ON UNDER WEIGHT INFANTS", AL-SHIFA TRUST EYE HOSPITAL, RAWALPINDI. F. No.03-31/2023-DD (PS)**

Decision:

The CSC after detailed discussion and deliberation decided that trial will remain suspended and will be re-considered after following steps:

i. *Restoration of trial by National Bio-Ethics Committee.*
ii. *Approval of applied amendments from NBC and respective IRBs.*
iii. *Status of trial in other countries.*
iv. *Conduct training of all PIs, site PIs, CRAs for close monitoring of subjects as per revised inclusion criteria.*
v. *Comprehensive risk based follow up plan of study participants.*
vi. *Plan for medical checkup of subjects before randomization to confirm health status including WAZ score and at every follow up and ensure to stop IMP administration if WAZ score is reduced.*
vii. *Amendment in Informed Consent Form to ensure complete information to parents about trial.*
viii. *GCP audit of sites where deaths have been reported.*

B.

AMENDMENTS FOR CLINICAL TRIAL "A PHASE III RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY EVALUATE THE EFFECT OF, Bi-26 (STAIN OF BIFIDOBACTERIUM LONGUM, B. INFANTIS) SUPLEMENTATION VS PLACEBO ON WEIGHT GAIN ON UNDER WEIGHT INFANTS", AL-SHIFA TRUST EYE HOSPITAL, RAWALPINDI. F. No.03-31/2023-DD (PS).

Decision:

The CSC after deliberations decided to defer the following amendments because the trial is still suspended and NBC and all IRBs approvals are not provided.

New Amended documents
Investigator's Brochure Edition No. 04 dated 22 September 2023
Main ICF V4.0_Pak V1.0 dated 7 November 2023
Ring Cards dated 14 October 2022- English (Principal) – V1.0 for investigators use
2D Animation Video (What is Probiotic) v1.0
2D Animation Video (Understanding Clinical Trials)
Flipchart v1.0 dated 18 Nov 2022
Subject Case Report Form Version 3.0 dated 01 Dec 2023
Dosing Diary V2.0 dated 14th December 2023
Infographics V1.1 dated 22 Feb 2023-Urdu

C.

REQUEST FOR EXTENSION OF DRAP STUDY APPROVAL

Decision:

The CSC after deliberations decided to defer the request for extension of DRAP approval because the trial is still suspended.

AGENDA ITEM XXII:

TRANEXAMIC ACID BY THE INTRAMUSCULAR OR INTRAVENOUS ROUTE FOR THE PREVENTION OF POSTPARTUM HAEMORRHAGE IN WOMEN AT INCREASED RISK: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL (I'M WOMAN)

Decision: -

The CSC after detailed discussion and deliberation decided as follows:

a. *Approved clinical trial titled as "**Tranexamic Acid by the Intramuscular or Intravenous Route for the Prevention of Postpartum Haemorrhage in Women at Increased Risk: A Randomized, Double-blind, Placebo-controlled Trial (I'm woman)"** at* Medicare Hospital Rawalpindi (CTS-0076).

b. *Rest of clinical sites will be considered by CSC after their panel inspection and grant of license.*

i. *Approved request for withdrawal of site of Shifa International Hospital* for IM Woman Trial.

ii. *authorized the Chairman CSC to approve following IMPs for import after provision of COPP or Free Sale Certificate or confirmation of approval status from website of relevant Regulatory Authority of Cyklokapron 100mg /ml solution for injection / infusion (5 ml ampoule) or confirmation of approval status from website of relevant regulatory authority.*

Quantity of investigational products to be imported on Form 6 and Clearance Certificate under The Drugs (Import & Export) Rules, 1976.	***Detail***	***Intervention***	***Placebo***
	Brand	*Cyklokapron 100mg/mL solution for reinjection*	*Sodium Chloride .09%*
	Generic	*Tranexamic Acid*	*Sodium Chloride .09%*
	Manufacturer	*Pfizer Limited, Ramsgate Road, Sandwich, kent, CT13 9NJ, UK*	*Calderdale and Huddersfield NHS Foundation Trust, UK*
	Manufacture (de-labelling, re-labelling and collation) and release of IMP	*Sharp Clinical Services, UK*	*Sharp Clinical Services,UK*
	Quantity	*917 Box* *Each Box contains 24 treatment packs.* *Total: 22,008 treatment Packs* *Total TXA Ampoules: 36, 680* *Total Placebo Ampoules: 51,352* *TXA Kits: 18340* *Placebo Kits: 25676*	

AGENDA ITEM XXIII:

AN OPEN LABEL, SINGLE DOSE, RANDOMIZED, TWO PERIOD, 2X2 CROSSOVER BIOEQUIVALENCE STUDY OF FIXTIL-T DS (CEFIXIME) TABLET 400 MG

Decision: -

The CSC after detailed discussion and deliberation decided as follows:

a. *to approve the BA/BE Study titled, "An Open Label, Single Dose, Randomized, Two Period, 2x2 Crossover Bioequivalence Study of Fixtil-T Ds (Cefixime) Tablet 400 Mg" to be conducted at IBBPS-DUHS, Ojha Campus, SUPARCO Road, Karachi.*
b. *Registration certificate will be issued after submission of Bio-analytical method validation studies and approval status of reference product from website of relevant regulatory authority by the applicant.*
c. *PI will provide details of reference product regarding Import license, mode of purchase and shipment details for record.*

AGENDA ITEM XXIV:

AMENDMENTS IN ANTICOAGULATION FOR STROKE PREVENTION IN PATIENTS WITH RECENT EPISODES OF PERIOPEARATIVE ATRIAL FIBRILLATION AFTER NONCARDIAC SURGERY- THE ASPIRE-AF TRIAL.

Decision: -

The CSC after detailed discussion and deliberation decided as follows:

i. *Approved Protocol version 6.0 (14-09-2023) and other documents.*
ii. *Clarification is required about status of approval of Protocol version 5.0 by IRB, NBC and CSC as last approved version of protocol is 4.0 (29-10-2021).*

AGENDA ITEM XXV:

APPLICATION FOR IP DESTRUCTION OF CLINICAL TRIAL "A RANDOMIZED, PHASE-III PLACEBO CONTROLLED TRIAL OF COLCHICINE FOR THE PREVENTION OF PERIOPERATIVE ATRIAL FIBRILLATION IN PATIENTS UNDERGOING THORACIC SURGERY (COP-AF)" CT-0013 / 03-37/2020-DD (PS)

Decision:

The CSC after detailed discussion and deliberation decided as follows:

a. *Endorsed the IP destruction / disposal report as same was reconciled and witnessed by panel.*
b. *Directed to seek clarification from PI regarding clearance of IPs from Customs without Clearance Certificate from DRAP and will be placed before CSC for its consideration.*

AGENDA ITEM XXVI:

CLOSEOUT REPORT FROM SHIFA INTERNATIONAL HOSPITAL FOR CLINICAL TRIAL "A RANDOMIZED, PHASE-III PLACEBO CONTROLLED TRIAL OF COLCHICINE FOR THE PREVENTION OF PERIOPERATIVE ATRIAL FIBRILLATION IN PATIENTS UNDERGOING THORACIC SURGERY (COP-AF)" CT-0013 / 03-37/2020-DD (PS)

Decision: -

The CSC after deliberations decided to defer Close-out report for review of report by members of CSC and will be placed in forthcoming CSC meeting.

AGENDA ITEM XXVII:

CLOSEOUT REPORT QUERY RESPONSE FROM SITE OF SHIFA INTERNATIONAL HOSPITAL DATED 10.10.2023 OF THE CLINICAL TRIAL "PERI-OPERATIVE ISCHEMIC EVALUATION-3 (POISE-3) TRIAL. F.NO.03-07/2019-CT(PS)

Decision:

The CSC after deliberations decided to defer Close-out report for review of report by members of CSC and will be placed in forthcoming CSC meeting.

AGENDA ITEM XXVIII:

AMENDMENTS IN CLINICAL TRIAL "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)

Decision:

The CSC after deliberations decided to approve following documents.

Documents	**Previous submitted version and effective date**	**Amended Protocol and Study documents**
Clinical Study Protocol	Version 1. September, 02, 2022	Version 3. July 12, 2023 Version 2 was superseded and is not applicable anytime.
Investigator Brochure	Version 1. April 22 2022	Version 2. March 03, 2023
Patient Information Sheet and ICF for female subjects of the clinical study (English)	V1.0 PAK of January 07, 2023	V3.0 PAK of November 17, 2023
Patient Information Sheet and ICF for female subjects of the clinical study (Urdu)	V1.0 PAK of January 07, 2023	V3.0 PAK of November 17, 2023

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