CERTIFICATE OF ETHICS APPROVAL

This is to certify that the College of Medicine Research and Ethics Committee (COMREC) has reviewed and approved a study entitled:

P.04/18/2381 - Accurancy and Consequences of using Trial-of-antibiotics for TB diagnosis (ACT-TB Study) by Titus H Divala

On 03-Jul-18

As you proceed with the implementation of your study, we would like you to adhere to international ethical guidelines, national guidelines and all requirements by COMREC as indicated on the next page

03-Jul-18

Dr. YB. Mlombe - Chairperson (COMREC) Date

REQUIREMENTS FOR ALL COMREC APPROVED RESEARCH PROTOCOLS

1. Pay the research overhead fees as required by the College of Medicine for all approved studies.

2. You should note that the COMREC Sub-Committee on Research Participants' Safety will monitor the conduct of the approved protocol and any deviation from the approved protocol may result in your study being stopped.

3. You will provide an interim report in the course of the study and an end of study report.

4. All COMREC approvals of new applications and progress reports are valid for one year only. Therefore all approved studies running for more than one year are subject to continuing review annually. You are required to submit a progress report to COMREC within 90-30 days before the expiration date. Your current expiration date is 03-Jul-19. Studies shall be considered lapsed and inactive if continuing review application is not received one month after the expiry of the previous approval. In that case, all study related operations should cease immediately except those that are necessary for the welfare of subjects.

5. All investigators who are Medical Practitioners must be fully registered with the Medical Council of Malawi.

PHARMACY, MEDICINES & POISONS BOARD

Mission: To promote and improve the health of the population of Malawi through the regulation of Pharmacy Personnel, Pharmacy Businesses, Medicines and Allied Substances

ALL CORRESPONDENCE SHOULD BE ADDRESSED TO THE REGISTRAR

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Chilambula Road
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Capital City
LILONGWE 3, MALAWI

Phone: (+265) 01 755 165
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PMPB/CTRC/III/14062018102
DATE: 4th July, 2018

Department of Infectious Disease Epidemiology
London School of Hygiene and Tropical Medicine
Keppel St
London

Attn.: Dr. Titus Divala

RE: ACCURACY AND CONSEQUENCES OF USING TRIAL-OF-ANTIBIOTICS FOR TB DIAGNOSIS (ACT-TB STUDY).

Refer to your application to register the above mentioned clinical trial with the Pharmacy, Medicines and Poisons Board (PMPB).

The Clinical Trial Review Committee (CTRC), at its meeting held on 22nd June, 2018, issued a **No Objection** to the implementation of the trial after members agreed that the nature of the trial was seen to be outside the scope of trials that should be regulated by PMPB through the CTRC.

Please contact the undersigned if there are any issues that need further clarification.

Yours faithfully,

M. Kawaye
ACTING REGISTRAR

PHARMACY MEDICINES & POISONS BOARD
REGISTRAR
04 JUL 2018
P.O. BOX 30241, LILONGWE 3

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK nord			06.11.2018	2018/1964/REK nord
			Deres dato:	Deres referanse:
			25.09.2018	

Vår referanse må oppgis ved alle henvendelser

Jon Øyvind Odland
Institutt for samfunnsmedisin

2018/1964 En kontrollert klinisk studie for å undersøke responsen til bredspekret antibiotika som en eksklusjonsdiagnose i allmenpraksis mot risiko for antibiotika resistens

Forskningsansvarlig institusjon: UiT Norges arktiske universitet
Prosjektleder: Jon Øyvind Odland

Vi viser til søknad om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK nord) i møtet 25.10.2018. Vurderingen er gjort med hjemmel i helseforskningsloven (hforsknl) § 10.

Prosjektleders prosjektomtale
Det skal undersøkes, ved hjelp av en randomisert, kontrollert studie om respons til bredspekret antibiotika kan brukes som eksklusjonsdiagnose for tuberkulose. Dette skal vurderes opp mot risiko for resistensutvikling knyttet til behandingen. Tre grupper (625 per gruppe) individuelt randomisert (1:1:1), med åpen informasjon undersøkes med standard diagnostisk tilnærming. Kun voksne deltakere, med full brukermedvirkning og informert samtykke. Studien kan forenkle dignostikk og klinikk for en utsatt gruppe mennesker. Studien skal i sin helhet foregå i Malawi. Alle etiske godkjenninger fra Malawi og London er vedlagt.

Komiteen vurderte at Hanne Husom Haukland var inhabil og hun fratrådte møtet da saken ble behandlet, jf. fvl. § 6.

Om prosjektet
Prosjektet er en del av en PhD. Studenten skal avlegge sin PhD i London.

Dette er et samarbeidsprosjekt mellom Universitetet i Malawi, London School of Hygiene and Tropical Medicine, og Universitetet i Tromsø.

Prosjektet skal gjennomføres i Malawi og er et «Tuberkulose initiativ» fra Helse Nord.

Det foreligger godkjenning fra London School of Hygiene and Tropical Medicine, og University of Malawi.

Data
Det skal hentes data fra pasientjournal og fra lokale poliklinikker. Data er standard medisinske opplysninger knyttet til infeksjoner og sykehistorie.

Nye helseopplysninger er respons på behandling av infeksjoner.

Besøksadresse: MH-bygget UiT Norges arktiske universitet 9037 Tromsø
Telefon: 77646140
E-post: rek-nord@asp.uit.no
Web: http://helseforskning.etikkom.no/

Data avidentifiseres med koblingsnøkkel. Database oppbevares i 5 år i Malawi.

Deltakere/rekruttering
Voksne deltakere fordeles i tre grupper voksne deltakere (625 per gruppe), individuelt randomisert. Deltakere rekrutteres gjennom behandling på poliklinikkene.

REK har ingen innvendinger til prosjektet

Vedtak
REK har gjort en helhetlig forskningsetisk vurdering av alle prosjektets sider og godkjenner det med hjemmel i helseforskningsloven § 10. REK forutsetter at prosjektet også har godkjenning fra Malawi.

Sluttmelding og søknad om prosjektendring
Prosjektleder skal sende sluttmelding til REK nord på eget skjema senest 21.03.2022, jf. hfl. § 12. Prosjektleder skal sende søknad om prosjektendring til REK nord dersom det skal gjøres vesentlige endringer i forhold til de opplysninger som er gitt i søknaden, jf. hfl. § 11.

Klageadgang
Du kan klage på komiteens vedtak, jf. forvaltningsloven § 28 flg. Klagen sendes til REK nord. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK nord, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Med vennlig hilsen

May Britt Rossvoll
sekretariatsleder

Kopi til:jon.oyvind.odland@uit.no

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Keppel Street, London WC1E 7HT
United Kingdom
Switchboard: +44 (0)20 7636 8636

www.lshtm.ac.uk

Observational / Interventions Research Ethics Committee

Dr Titus Divala
LSHTM

9 May 2018

Dear Titus ,

Study Title: RCT investigating if benefits of using response to broad spectrum antibiotics as an exclusion diagnostic for tuberculosis in primary care adult patients outweigh the risk of antimicrobial resistance

LSHTM ethics ref: 15232

Thank you for your application for the above research, which has now been considered by the Interventions Committee.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type	File Name	Date	Version
Safety Information	ACT_PackageInsertAzithromycin	14/03/2013	JUNE 2013
Safety Information	ACT_PackageInsertAmoxicillin	21/12/2015	DEC 2015
Sponsor Letter	2018-KEP-077_Sponsor Confirmation_13.03.18	13/03/2018	1
Other	GCP Cert_LSHTM_TDivala_21.03.18	21/03/2018	1
Investigator CV	ACT-CV1_TitusDivala	30/03/2018	1
Investigator CV	ACT-CV2_KatherineFielding	30/03/2018	1
Investigator CV	ACT-CV3_LizCorbett	30/03/2018	1
Information Sheet	ACT-20180330InformedConsentEnglish	30/03/2018	1.0
Information Sheet	ACT-20180330InformedConsentChichewa	30/03/2018	1.0
Protocol / Proposal	ACT-20180330Protocol	30/03/2018	1.0

After ethical review

The Chief Investigator (CI) or delegate is responsible for informing the ethics committee of any subsequent changes to the application. These must be submitted to the Committee for review using an Amendment form. Amendments must not be initiated before receipt of written favourable opinion from the committee.

The CI or delegate is also required to notify the ethics committee of any protocol violations and/or Suspected Unexpected Serious Adverse Reactions (SUSARs) which occur during the project by submitting a Serious Adverse Event form.

An annual report should be submitted to the committee using an Annual Report form on the anniversary of the approval of the study during the lifetime of the study.

At the end of the study, the CI or delegate must notify the committee using an End of Study form.

All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at: http://leo.lshtm.ac.uk

Additional information is available at: www.lshtm.ac.uk/ethics

Yours sincerely,

Professor John DH Porter
Chair

ethics@lshtm.ac.uk
http://www.lshtm.ac.uk/ethics/

Improving health worldwide

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Observational / Interventions Research Ethics Committee

Dr Titus Divala
LSHTM

12/04/2019

Dear Titus,

Project Title: RCT investigating if benefits of using response to broad spectrum antibiotics as an exclusion diagnostic for tuberculosis in primary care adult patients outweigh the risk of antimicrobial resistance

Project ID: 15232

Thank you for your annual report application for the continuation of your research dated 09/04/2019 12:01 , which has now been considered by the Chair on behalf of the Ethics Committee.

Confirmation of ethical opinion

This application is approved by the committee for a further year.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

After ethical review

Any changes to the application must be submitted to the committee via an Amendment form.

The CI or delegate is also required to notify the ethics committee of any protocol violations and/or Suspected Unexpected Serious Adverse Reaction (SUSARs) which occur during the project by submitting a SUSAR and Protocol Violation form.

An annual report should be submitted to the committee using an Annual Report form on the anniversary of the approval of the study during the lifetime of the study.

At the end of the study, the CI or delegate must notify the committee using an End of Study form.

All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at http://leo.lshtm.ac.uk.

Additional information is available at: www.lshtm.ac.uk/ethics.

Yours sincerely,

Professor John DH Porter
Chair

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