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UZ-CTRC
University of Zimbabwe - Clinical Trials Research Centre
Saving Lives Through Innovative Research Strategies

University of Zimbabwe,
Faculty of Medicine and Health Sciences

SOP Title:	UZ-CTRC CTU SOP for Managing and Documenting Regulatory Communication with Regulatory Bodies		
SOP # 001	SOP Version/No:8.0	Date SOP first adopted:	13 March 2017
Title of Author(s):	Name:	Signature:	Revision Date:
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1. Purpose

1.1 The purpose of this Standard Operating Procedure (SOP) is to ensure that all Clinical Research Sites (CRS) follow a standardized process of obtaining regulatory approval to conduct medical research in Zimbabwe.

1.2 It functions to guide Clinical Research Site (CRS) staff in preparing regulatory documents for submission to the various regulatory authorities and Institutional Review Boards (IRBs).

1.3 Specifically, the purpose is to seek institutional and regulatory approvals from regulatory bodies including Ministry of Health and Child Care, Harare City Council, Chitungwiza City Council, Parirenyatwa Hospital, Zimbabwe National Family Planning Council, Joint Research Ethics Committee, Medical Research Council of Zimbabwe, Medicines Control Authority of Zimbabwe, Research Council of Zimbabwe, University of California San Francisco Committee on Health Research, University of Zimbabwe Clinical Trials Research Centre Institutional Biosafety Committee and National Biotechnology Authority of Zimbabwe as required(ZNFPC), JREC, MRCZ, MCAZ, RCZ and UCSF CHR, UZ-CTRC IBC & NBAZ

2. References

2.1 Charter for the UZ-CTRC Institutional Biosafety Committee

2.2 National Biotechnology Authority Act [*Chapter 14.31*]

2.3 Health Professions Act. Act 6/2000, 22/2001 (s. 4), 14/2002 (s. 43), 28/2004 (s. 29) Zimbabwe (2004)

2.4 https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf

2.5 www.nbaz.ac.zw

2.6 UZ-CTRC Document and Specimen Storage , Retention and Disposal SOP Version 7.0 dated February 2021

2.7 ICH-GCP guidelines E6 (R2) dated March 2018

2.8 MCAZ GCP guidelines Revision 2 dated 30 June 2020

2.9 http://www.rcz.ac.zw/

2.10 http://www.mrcz.org.zw/

2.11 http://www.jrec.uz.ac.zw/

2.12 http://www.mcaz.co.zw

2.13 https://irb.ucsf.edu/submitting-covid-19-research-irb-new-studies-modifications

2.14 www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidanceInformationSheetsandNotices/ucm219433.htm

2.15 https://www.hhs.gov/ohrp/regulations-and-policy/guidance/alphabetical-list/index.html

3. Scope

This SOP applies to all staff involved in the generation of communication with regulatory bodies, these include but not limited to Regulatory Officers, IoRs, PoRs and CRS Coordinators. This SOP applies only to the processing of applications to be made that affect study conduct, the obligations of the CRS to the study networks/sponsors, the safety of participants, study results, data management, and subject matter relevant to meeting regulations of the FDA in-country regulations on clinical trials, ICH Guidelines, NIH requirements and any other sponsor required guidance.

The SOP is applicable to all research studies affiliated to or operating under the UZ-CTRC. The SOP will be used during a study's preparatory phase before contact with participants, during the study's activation, enrolment, follow-up till study close-out as appropriate and applicable.

4. Allowable Exceptions

This SOP is meant to be followed without deviation. However, it is an allowable exception to follow procedures specified in a protocol or Study Specific Procedure Manual (SSP) that may deviate from this SOP.

5. ABBREVIATIONS AND DEFINITION OF TERMS

CRS	Clinical Research Site
CRO	CTU Regulatory Office
CTU	Clinical Trials Unit
CV	Curriculum Vitae
DAIDS	Division of AIDS
DHHS	Department of Human Health Services
DPRS	DAIDS Protocol Registration Services
DSMB	Data and Safety Monitoring Board
EC	Ethics Committee
FAQ	Frequently Asked Question/s
FDA	Food and Drug Administration, USA
GCP	Good Clinical Practices
IB	Investigator's Brochure
IBC	Institutional Biosafety Committee
ICF	Informed Consent Form(s)
IEC	Institutional Ethics Committee
IoR	Investigator of Record
IRB	Institutional Review Board
IoR	Investigator of Record
IRB	Institutional Review Board
JREC	Joint Research Ethics Committee for the University of Zimbabwe, Faculty of Medicine and Health Sciences and Parirenyatwa Group of Hospitals
MCAZ	Medicines Control Authority of Zimbabwe
MoHCC	Ministry of Health and Child Care
MRCZ	Medical Research Council of Zimbabwe
NBAZ	National Biotechnology Authority of Zimbabwe
NIH	National Institutes of Health, USA
OCSO	Office of Clinical Site Oversight
OHRP	Office of Human Research Protection
PoR	Pharmacist of Record
PI	Principal Investigator
RCZ	Research Council of Zimbabwe

STA	Specimens Transfer Agreement
UCSF CHR	University of California, San Francisco Committee on Human Research
ZNFPC	Zimbabwe National Family Planning Council

Initial Application
Initial application is the first application submitted for a protocol which has not yet gone through the process of review by an IRB or a regulatory authority.

Renewal Application
An approved protocol that requires continuing review approval by an IRB or a regulatory authority not more than 12 months after the initial approval.

CRS Regulatory Team
This is a team situated at a CRS composed of the Investigator of Record, Study/CRS Coordinator, Medical Officer(s), Pharmacist of Record, Regulatory Officer (if present), and Administrative Assistant (if present). Note: A team leader should always be appointed for accountability per protocol (usually the IoR.)

6. Role and Responsibilities

Responsibility	Role
Central Regulatory Officer	• Making submissions to regulatory bodies on behalf of IoR • Developing tracking systems for all regulatory submissions and responses • Review of application packages and approval letters for accuracy, completeness and quality. • Track all required approvals to ensure all protocols have valid approvals at all times. • Support the PI and IoR to finalize the Regulatory Work Plan document. • Raise payment request(s) for all regulatory bodies and Institutional Review Boards and indicate the timeline for payment to each. • Perform Quality Audit Checks on master file documents. • Prepare required files for IRB/Regulatory submission • Follow up of submissions. • Ensuring that reminders for renewal applications are sent to IoR, Coordinators and other designated key staff. Use of automated reminders and follow up emails can be utilized.
Principal Investigator	• Overseeing the regulatory submissions process • Assigning tasks to competent staff in support of the regulatory submission process • Ensure all protocols have valid approvals at all times.
IoR	• Preparing submissions to regulatory bodies • Assigning tasks to CRS team • Ensuring that protocol implementation is only commenced following receipt of regulatory approvals
Administrative Assistants	• Assisting the IoR and CRO with administrative tasks in preparing regulatory applications
CTU Coordinator	• Overseeing the regulatory submission process to ensure submissions made are of acceptable standard, are complete and accurate

Quality Affairs Manager	• Ensuring that Shipment transfer Agreements are available for submission to regulatory body(ies)

7. GENERAL GUIDANCE

IRB/ Regulatory Authority Application Process

7.1 Submissions can be stratified into initial submissions, interim submissions, renewals, and close-out.
7.2 All submissions are the responsibility of the IoR
7.3 Please ensure that the correct letterhead is used for all submissions
7.4 Prior to any research activity being conducted it is a requirement that the relevant IRB and regulatory authority approvals be in place.
7.5 The Office of Human Research Protections (OHRP) requires that all federally funded research studies undergo continuing IRB/EC review at intervals appropriate to the degree of risk, but NOT LESS than once per year within 30 days of each IRB/EC continuing Review meeting where study was approved.
7.6 If review of any protocol is deemed necessary by IRB/EC at any interval of less than one year, then required timeframes of review (3-month, 6 months, etc.) will be noted on the approval letter at the time of initial review.

7.7 The renewal is expected to be in place preferably prior to or on the date of expiry of the current approval to avoid a lapse in approval. Lapses in approvals:
  7.7.1 Per the DHHS regulations 13 and OHRP guidance on continuing review, if there is a lapse in continuing review (i.e., If an investigator has failed to provide continuing review information to their IRB/EC or the IRB/EC has not reviewed and approved a research study by the Continuing/Annual review date specified by the IRB/EC), the research at the CRS must stop, unless the IRB/EC finds that it is in the best interest of individual participants to continue participating in the research interventions or interaction. Enrollment of new participants cannot occur after the expiration of IRB/EC approval(s).
  7.7.2 CRSs should contact their DAIDS Office for Clinical Site Oversight (OCSO) representative and/or DAIDS Program Officer when there is any lapse and for additional guidance and information.
  7.7.3 CRSs should submit IRB/EC lapse documentation (i.e., the site's documentation of the lapse to the IRB/EC and the IRB/EC's response) to the DAIDS PRO.

7.8 If the current approval expires before the investigator applies for continuing review the IRB must be immediately notified for guidance.
7.9 All protocols must be renewed on a yearly (unless specified) basis even if participants are no longer being seen and/or only data is being analysed until the close out report is submitted to the IRBs and regulatory authorities
7.10 It is generally advised to submit initial applications at least four weeks prior to the next IRB meeting date.
7.11 With any application should the IRB or regulatory authority raise queries, CRSs are advised to respond to these queries in 7 days (if this is not possible sites should document the reasons and communicate with the CRO)
7.12 It is strongly recommended that all MRCZ renewal applications are submitted 12 weeks prior to expiry of current approval
7.13 Central Regulatory Office to make follow-up on all applications to the different regulatory bodies
7.14 For all submissions retain a stamped copy of submission package for your records. However, if for any reason, submission has to be made online or via email, an email submission print out can be used as evidence of submission. The email submission should be done from the Central Regulatory Office copying the relevant CRS coordinator, administrative assistant and any other designated person. Ensure that the email submission text is concise and specific. The subject line of the email should reflect what is being submitted in the body of the email.

7.14.1 Please note ALL reviewed and finalized submissions with signatures should be converted to PDF and be sent to 'regsubmissions@uz-ctrc.org.'

7.15 Once approval letters have been received from JREC, MRCZ, MCAZ, RCZ and IBC & NBAZ (where applicable) the stamped approval letters should be uploaded within one week to: DAIDS Protocol Registration Office if the protocol is NIH funded. Commercial, industry and other Non- NIH funded protocols must follow sponsor requirements to complete the protocol registration process for site activation.

7.16 ALL regulatory/ IRB study submissions should be done from the Regulatory Office for accountability, centralized tracking and quality control. In cases where the CRO or designee is unavailable, applications can be submitted by site (admin assistant, coordinator, IoR, PoR or PI) but the CRO must be notified and copied in such email correspondence.

7.17 Where required, application fees should be made in consultation with the current fee schedules for the regulatory bodies.

7.18 Where an Investigator is a member of a regulatory body, recusal letters should be obtained to verify that they were not part of the review.

7.19 It is advisable for sites to circulate draft submissions copying CRO to ensure that review before finalization is all inclusive.

7.20 Submissions to IRBs / Regulatory authorities will be made on days and times as stipulated by the bodies. CRO will provide updates CRSs of any changes in submission times as advised by the regulators. of Unless otherwise directed,

Note:

- Ministry of Health and Child Care support letters are required for health research conducted in the country.
- It is important to note that, the Regulatory System in Zimbabwe is a stepwise process.
- Approval from institution where the research will be conducted should be sought first followed by JREC and IBC (where applicable).
- Simultaneous initial submissions can be made to MRCZ, MCAZ, NBAZ (where applicable) except for RCZ which requires prior regulatory approvals before accepting application. Where regulatory bodies raise comments which affect documents such as ICFs, Implementation materials, it is advisable to defer response to all bodies until a time where all comments are available so that revisions to materials can be done at once across all regulatory bodies.
- Ensure that the final approved protocol, Informed Consent Forms, Data Collection Instruments and all relevant materials are affixed with an MRCZ approval stamp before use. On the consent documents, please ensure that all pages which include the signature portions are affixed with an approved stamp.
  NB:- There is no need to obtain the 'APPROVED' stamp from other regulatory bodies on protocol documents

8. INITIAL APPLICATIONS

Pre-Submission Preparations
Background

- There are multiple steps necessary to collect all documentation required for submitting a new protocol to the regulatory authorities.
- Some steps may not apply to a protocol. The order of steps may vary, by protocol needs, or may begin simultaneously.
- The individuals assigned to work on specific steps may differ by protocol and by site preference.
- The underlying principle is that the process of preparing the regulatory submissions should be planned, coordinated, and monitored to maximize efficiency and address any anticipated matters likely to be queried by reviewers.
- This section outlines what the required steps may be, indicating an approach to developing a work plan and how that plan could be executed and monitored.

8.1 Pre-submission Activities for CRS Regulatory Team

8.1.1 Assemble Protocol documents.

a. In general, the protocol team releases the protocol materials by email to the key staff e.g. CTU PI, CRS Leader, CRS Coordinator
b. For studies being conducted within multiple sites, the person to be the local lead Principal Investigator for the protocol is assigned by the CTU and site leadership and carries ultimate responsibility for assembling the required protocol documents. Subsequently, site Investigators of Record/designees are assigned.
c. It is usual to receive in the initial release the following protocol documents:
   - Protocol
   - ICFs
d. IoR to request from the protocol team any additional protocol documents required to complete regulatory submissions. These may include the following:
   - FAQs
   - Consent comprehension quiz
   - Questionnaires that will be administered to the participants.
   - Other study implementation materials e.g., adverts, brochures, specimen collection instructions, tools for home use, laboratory, and study product information.
   - **Section 5** below presents a template form to communicate with the protocol team about these pre-submission needs.
e. Create site specific ICFs for translation, as per Part 3 below.
f. Create an electronic store of protocol documents accessible to the team working to prepare the regulatory submissions (e.g.: on an external hard drive, network folder, Microsoft SharePoint or Dropbox).
g. The CRS Regulatory team should accumulate Investigator documents required, such as:
   - PI and IoR professional registration
   - PI and IoR(s) CVs updated for this protocol.
   - PI and IoR(s) GCP certificates
   - PI and IoR(s) declarations for MCAZ

8.1.2 Develop Regulatory Work Plan with CTU Departments

The IoR is to distribute the protocol materials received within 5 working days to and convene a round-table meeting with relevant CTU personnel within 10 working days, such as:

8.1.2.1. Local PI and IoR(s)/designee

- ✓ Appoint the IoR(s) and assign one to coordinate the regulatory submissions with the Regulatory Officer.
- ✓ Appoint a signatory for all payment requests related to regulatory submissions and communicate that to the Head of Finance.
- ✓ Inform protocol team of the IoR in Zimbabwe to serve as the point contact for all communications about this protocol.
- ✓ Develop Stakeholders' Engagement Plan and arrange appointments or communicate with stakeholders who need to supply Letters of Support to accompany regulatory submissions (e.g.: Ministry of Health and Child Care AIDS and TB Director, central hospital Clinical Directors).
- ✓ Send the list of additional documentation required to complete regulatory submissions, per Section 5

8.1.2.2. CRS Leader(s) and CRS Coordinator(s)

- ✓ Support the protocol PI/IoR(s) to complete their responsibilities.
- ✓ Identify retention activities that need IRB approval (e.g.: differential participant reimbursement amounts, incentive package)

8.1.2.3. Central Laboratory, Central Pharmacy and Site Heads of Division

Review the relevant information in the protocol and identify additional documentation required to complete regulatory submissions, per **Section 5.**

8.1.2.4. Community Coordinator

Assign a date for the IoR to sensitize the relevant Community Advisory Board (CAB) about the protocol and timelines and receive their input about any sensitive issues identified for this protocol.

8.1.2.5 Finance, Grants and CTU Coordinator

- ✓ Verify whether the protocol is listed in the CRS Notice of Award for the financial year and inform the IoR.
- ✓ If it is not listed, write a letter to cover the requirement to submit a study budget and proof of funding.
- ✓
- ✓ Determine the foreign laboratories to receive specimens collected from the protocol.
- ✓ Develop plan for obtaining signed Specimen Transfer Agreements from the recipient laboratories and order of their priorities.

8.1.2.6. Regulatory Office

- ✓ Support the PI and IoR to finalize the Regulatory Work Plan document.
- ✓ Raise initial submission payment request(s) for all regulatory bodies and Institutional Review Boards and indicate the timeline for payment to each.
- ✓ Perform Quality Audit Checks on master file documents.
- ✓ Prepare required files for IRB/Regulatory submission
- ✓ Submit and follow up applications

8.1.3. Execute Regulatory Work plan

Table 1 (Regulatory workplan)

ITEM	Responsibility	Maximum Activity timeline (Weeks)	Comments
Protocol Summary	IoR/Designee	2	This should present the local PI's plan to implement a multi-site protocol in the context of the current Zimbabwean setting and differs from the Protocol Schema supplied.
Regulatory Body Specific Application Forms	IoR/Designee	2	Input from Central Pharmacy, Central Lab and site HODs, as necessary
DPRS Clinical trial Application Form	IoR/Designee	2	This should be submitted together with the application for approval to all regulatory bodies, ie, JREC, MRCZ, MCAZ, RCZ and NBAZ)

Translation	Translation team	2	• IoR and CRS Coordinator assign site staff to review the Shona ICFs, back translate them and reconcile against the English version. • The Translation team makes necessary revisions with the site staff input. • The final document is formatted, and a version date is assigned. • IoR signs the Translation Verification Statement to scan and upload to DAIDS PRO once all regulatory approvals are in place. • Translation team forwards completed translation certificates and invoices to the Central Regulatory Office for payment processing
Specimen Transfer Agreements	IoR/Lab/CTU Coordinator/QA and QC/CRO	4	• Develop STA annexures • Contact recipient labs /protocol teams for developing STA annexures and requesting for signed STAs Send them the RCZ template and annexure
Protocol Team request for additional documents	IoR/Designee	N/A	Refer to Section 7.1.5
Reg Submissions tracker	IoR/CRO	1	Refer to Table 2
Request for risk designation	IoR/Designee	2	• Should be signed off by IoR. • For studies involving minors less than 18 years of age, a separate risk designation request letter should be submitted at initial application. This applies to JREC and MRCZ applications only. • For studies involving pregnant women, foetuses and neonates, a separate request for confirmation of whether a study conforms to research involving pregnant women, foetuses and neonates should be submitted at initial application. This applies to JREC and MRCZ applications only.
Cover letters (Application Letter/Application for risk designation)	IoR/Designee	1	• Should be signed off by IoR. • For studies involving minors less than 18 years of age, a separate risk designation request letter should be submitted at initial application. This applies to JREC and MRCZ applications only. For studies involving pregnant women, foetuses and neonates, a separate request for confirmation of whether a study conforms to research involving pregnant women, foetuses and neonates should be submitted at initial application. This applies to JREC and MRCZ applications only.

8.1.4. Monitor Progress

In the initial Application process, the Central Regulatory Officer monitors progress in executing the regulatory work plan by updating the regulatory trackers and circulating to relevant CTU personnel monthly via emails and/ or meetings.

8.1.5. Application Preparation

This is the process where site together with CRO consolidates all the work stated above from protocol receipt , inception preparation and planning. Data Collection: Pre-submission input needed from protocol team and sponsor.

If additional documentation is required from the protocol team and sponsor, this need is communicated by the IoR to the protocol team upon receipt of the email with the protocol released to the sites. A template of appropriate text for use when drafting a request letter appears below for adaptation to suit the specific protocol. Refer to appendix 6 for template

8.1.6. Setting Submission Timeline Goals and Maintenance of Regulatory Submission Tracker

- The CRO and the Admin Assistant are responsible for developing the Regulatory timelines and submissions tracker/s.
- This tracker is used by the local team to assign target timelines for submission to each regulatory body and assess possible start dates for the protocol.
- It is modified to suit the specific needs of a protocol and team.
- It is updated by both the CRO and Admin Assistants (for comparison) whenever a submission is made (actual submission date), comments are received (comments) or an approval is received (actual approval date).
- It may be shared with the protocol trials specialist to present progress in reaching the regulatory targets and highlight the timeline for receipt of documents that are not available to the site, as per example in the template below. (*Look at next section on IRB Application Process when completing this template for guidance when setting dates.)*

Table 2 (Regulatory Tracker)

EC/ IRB/ REGULATORY AUTHORITY	TARGET SUBMISSION DATE	ACTUAL SUBMISSION DATE	TARGET APPROVAL DATE	ACTUAL APPROVAL DATE
Ministry of Health and Child Care				
Chitungwiza City Council				
Harare City Council				
Parirenyatwa Hospital				
UZ IBC				
NBAZ				
UCSF CHR				
JREC				
MRCZ				
MCAZ				
RCZ				

8.2. Initial/New Study Application Requirements

Table 3 (New Study Applications)

Regulatory Body	Required documents	Meeting dates	Submission process	Review timelines	Comments
Ministry of Health and Child Care (MoHCC), Harare City Council, Chitungwiza city Council,	• Application letter • Full Protocol • Protocol summary • ICFs and Data Collection tools for Chitungwiza City Council only)	N/A Protocols reviewed on a rolling basis when submitted	Hard copy submission	4 weeks	These are permission granting institutions which provides support and participant access to the UZ-CTRC. Please note that these do not constitute an Ethics Committee

Parirenyatwa Hospital					
UZ CTRC Institutional Biosafety Committee	• Application letter • Application form • Full protocol • Protocol summary • Investigator's Brochure • Curriculum Vitae(s) • FDA 1572 or Sponsor/Investigator Agreement • Other materials requested	N/A Protocols reviewed on a rolling basis when submitted	Electronic/hard copy submission	4 weeks	The IBC ensures that recombinant and synthetic nucleic acid research conducted at the CTU is in compliance with applicable local and international requirements. All clinical trials that involve study products involving bioengineered molecules, which according to the National Biotechnology Act [Chapter 14:31], NIH Guidelines or any relevant biosafety legislation requires approval by a competent biosafety review committee.
NBAZ Trials Release Application	• Same as UZ CTRC IBC but additional requirement is Application fee	N/A Protocols reviewed on a rolling basis when submitted	Electronic/hard copy submission	4-6 weeks	National Biosafety Authority of Zimbabwe is responsible for supervising the contained use, trial release and general release of biotechnology products like GMOs as per the National Biotechnology Act (Chapter 14.31). All protocols involving GMOs e.g. vaccines are regulated by this authority.
NBAZ Facility Registration	• application fee for registration. • application form and return • Institutional Biosafety manual, if any amendments have been made to the copy approved by NBA • Invite the Authority's inspectorate for an inspection audit.	N/A	Electronic/hard copy submission	4-6 weeks	National Biosafety Authority of Zimbabwe is responsible for supervising the contained use, trial release and general release of biotechnology products like GMOs as per the National Biotechnology Act (Chapter 14.31). All facilities managing GMOs e.g. vaccines are regulated by this authority.
UCSF CHR	• Protocol • Informed Consent Form (English and Shona) • Investigator's Brochure • Package inserts	N/A	Electronic	8 weeks	This is an independent ethics committee at UCSF. Submissions to UCSF CHR are only applicable for studies where Prof ZM Chirenje or

	• Implementation materials including Guides, recruitment materials etc				other UCSF Investigator is a Principal Investigator or Investigator of Record. Trials being conducted in response to a health emergency qualify for expedited review following set guidelines.
JREC	• Refer to appendix 1	Protocols reviewed on a rolling basis when submitted	Hard copy/Electronic submission	4-6 weeks	The JREC is constituted as an independent ethics committee through the Deanery of University of Zimbabwe- Faculty of Medicine and Health Sciences (UZ-FMHS) and the Parirenyatwa Group of Hospitals Refer to www.jrec.uz.ac.zw for application forms and other requirements Trials being conducted in response to a health emergency qualify for expedited review following set guidelines.
MRCZ	• Refer to appendix 2 • If application for exemption from full ethical review, it is only submitted to MRCZ. Exemption requirements are:- o Cover letter o Full protocol o Study summary o Permission letters • Studies which qualify for exemption include; use of de identified stored data, use of samples in storage, minimal risk procedures, procedures ordinarily experienced during routine settings.	Last Thursday of every month	Email/hard copy submission	4-6 weeks	This an independent body set up to provide ethical review. It serves as the National Ethics Committee Refer to www.mrcz.org.zw for application forms and other requirements Trials being conducted in response to a health emergency qualify for expedited review following set guidelines. These include review within 10 working days.

MCAZ	• Refer to appendix 3	1st Wednesday of every month	Online application	8-12 weeks	MCAZ is the Drug Regulatory Body in Zimbabwe responsible for review and approval of all clinical trials involving medicines on human participants Trials being conducted in response to a health emergency qualify for expedited review following set guidelines. These include review within 15-30 days. Refer to www.mcaz.co.zw Please note the online platform for submission is www.e-ctr.mcaz.co.zw
RCZ	• Refer to appendix 4	Last Thursday of every month	Hard copy submissions	4-6 weeks	The Investigator shall also ensure that he/she is registered with the Research Council of Zimbabwe and if the protocol involves any collection and shipment of biospecimens outside Zimbabwe, a bio-specimen shipment permit should also be obtained from the RCZ. According to the Research ACT of 1986 (Chapter 10:22), all foreign researchers must be registered with the Council before commencing any research in Zimbabwe. The council defines foreign researchers as "A non-Zimbabwean citizen who conducts a systematic investigation designed to discover or contribute to generalizable knowledge using specimens/data collected in Zimbabwe" or any person who wishes to conduct research in Zimbabwe on behalf of a foreign institution /person, whether as an employee or otherwise or any local research conducted research funded by a foreign sponsor e.g. NIH of the USA, WHO, UNICEF etc. The body which regulates the conduct of researches in Zimbabwe

					being conducted by foreign researchers or being conducted in collaboration and on behalf of foreign researchers. RCZ also regulates the shipment of research samples by reviewing shipment applications. We can only submit initial registration application to RCZ when MRCZ, JREC and MCAZ approvals are available

9. RENEWAL APPLICATIONS

9.1 General guidance

9.1.1 Renewal Applications should be instituted well in advance before expiry (refer to table 2)

9.1.2 Refer to OHRP guidelines for the avoidance of lapse, maintenance of fixed anniversary dates, scenarios where expedited or full board review is required.

9.1.3 Continuing review is required for UCSF CHR, JREC, RCZ and MCAZ even if data analysis or participant follow up is underway

9.1.4 Ensure that the correct version and date of the protocol and ICFs is quoted or submitted

9.1.5 Ensure required application fees are processed in line with current fee schedules

9.1.6 Ensure submission is correctly labelled with submission type, name of PI, Full protocol title, details of contact person)

9.1.7 Ensure that correct forms are used.

9.2 Renewal Application Requirements

Table 4 (Renewal Applications)

Regulatory Body	Required documents	Meeting dates	Submission process	Submission timelines	Comments
IBC	• Cover letter • Progress report • Biosafety Incident report • SAE Log	N/A Protocols reviewed on a rolling basis when submitted	Electronic/hard copy submission	4-6 weeks before expiry	IBC renewal applications are not required if there is no more Investigational Product management or administration being carried out
NBAZ Trial Release and Facility Registration	• Cover letter • Renewal Application Form • Biosafety incident report	N/A Protocols reviewed on a rolling basis when submitted	Electronic/hard copy submission	4-6 weeks before expiry	NBAZ renewal applications are not required if there is no more Investigational Product management or administration being carried out. These requirements apply to both renewal of permits of trial release and the facility registration permits which expire bi annually.

UCSF CHR	• Renewal Application form	N/A	Electronic	8 weeks before expiry	
JREC	• Application letter • Application form • Approved Full protocol • Approved Informed Consent Form (English and Shona) where applicable • Request for risk designation for studies enrolling minors • Application fee	Protocols reviewed on a rolling basis when submitted	Hard copy/Electronic submission	4 weeks before expiry	
MRCZ	• Same as for JREC	Last Thursday of every month	Email/hard copy submission	12 weeks before expiry	
MCAZ	• Cover Letter • Annual Progress report Form	1st Wednesday of every month	Online application/hard copy	At the anniversary of initial approval	Annual reports will be required to be submitted to the Authority in line with Section 23 and 24 of the Medicines and Allied Substance Control Act, as long as the study final report has not been submitted and the study has not been officially closed.
RCZ	• Refer to appendix 4	Last Thursday of every month	Hard copy submissions	4-6 weeks before expiry	NB- RCZ renewal Forms are signed by the Dean of UZ FMHS, Registrar of UZ and VC of UZ. Initiate completion and signing of the RCZ renewal form 4 weeks prior the target submission date.

10. Interim Submissions

10.1 AMENDMENTS

General Guidance

- In cases where there is a change to be necessitated to the original application package submitted for regulatory review, an application for amendment should be submitted to IRBs/ Regulatory Authorities before the changes can be implemented. However, changes which need to be effected immediately for the safety and wellbeing of the participant can be implemented before approval by regulatory bodies but this should be reported forthwith to regulatory bodies detailing the nature of the

amendment and justification for effecting changes before approval **(refer to http://www.mrcz.org.zw/faqs/ and MCAZ guidelines Revision 1 dated June 2020**).

- Documents affected by the amendment need to be submitted (these can be the protocol, Informed Consent Forms, Data Collection Tools, addition of Data Collection Tools etc.)
- Where an amendment is received while the parent protocol initial application is still under review, the amendment can be submitted to IRBs/ Regulatory Authorities. However, the approval date of the amendment should not precede the initial application approval date.
- All amendments should be submitted in real time to JREC, MRCZ as well as MCAZ and NBAZ where applicable.
- Application for risk designation should be made for JREC and MRCZ only
- Consult the fee schedules for processing of payments
- If allowable, expedited review can be applied for.

Table 5 (Amendment Applications):

Regulatory Body	Required documents	Meeting dates	Submission process	Response turnaround	Comments
IBC	• Cover letter • Amendment description • Revised documents	N/A Protocols reviewed on a rolling basis when submitted	Electronic/Hard copy	4-6 weeks	
NBAZ	• Cover letter • Amendment Description • Revised documents	N/A Protocols reviewed on a rolling basis when submitted	Electronic/hard copy submission	4-6 weeks	Do not submit amendment applications for protocols which are no longer actively administering or preparing study product
UCSF CHR	• Amendment Form • Revised documents	N/A	Electronic	8 weeks	Trials being conducted in response to a health emergency qualify for expedited review following set guidelines.
JREC	• Application letter • Application form • Revised documents • Request for risk designation for studies enrolling minors • Application fee	Protocols reviewed on a rolling basis when submitted	Hard copy/Electronic submission	3-4 weeks	Trials being conducted in response to a health emergency qualify for expedited review following set guidelines.
MRCZ	• Same as for JREC	Last Thursday of every month	Email/hard copy submission	4-6 weeks	Trials being conducted in response to a health emergency qualify for expedited review following set guidelines.
MCAZ	• Cover Letter • Amendment Form • Revised documents	1st Wednesday of every month	Online application/hard copy	4-8 weeks	Trials being conducted in response to a health emergency

					qualify for expedited review following set guidelines.
RCZ	• Amended documents submitted at the point of Annual Renewal for their Information	Last Thursday of every month	Hard copy submissions	4- 6 weeks	This is a submission for RCZs noting and not approval before implementation

11. Termination and Close-Out

General principle

- To terminate IRB and Regulatory authorities' approval, all research related to protocol must have ceased, including participants enrollment, participants follow-up, and work with identifiable information related to the study participants, including medical or research records and data analysis utilizing identifiable data collected from study participants.
- **If protocol is still at the data analysis stage, valid IRBs and applicable regulatory approval letters are required.**
- Completed termination form/close-out form and final comprehensive report to include: Dissemination plan or report if it has already been carried out, and a list of publications from the study. This should be done within 30 days of study close out.

Table 6 (Study Close-out)

Regulatory Body	Required documents	Meeting dates	Submission process	Comments
IBC	• Cover letter • Progress report • List of Publications • Results dissemination plan • Biosafety Incident log	N/A Protocols reviewed on a rolling basis when submitted	Electronic/hard copy submission	
NBAZ	• Cover letter • Study report • Destruction certificates of remaining products	N/A Protocols reviewed on a rolling basis when submitted	Electronic/hard copy submission	
UCSF CHR	• Cover letter • Study report if available • Study publications if available	N/A	Electronic	
JREC	• Application letter • Close out Application form • Publications if available	Protocols reviewed on a rolling basis when submitted	Hard copy/Electronic submission	Forms can be accessed from www.jrec.uz.ac.zw
MRCZ	• Same as for JREC	Last Thursday of every month	Email/hard copy submission	Forms can be accessed from www.mrcz.org.zw
MCAZ	• Cover Letter • Close Out Report • Publications available	1st Wednesday of every month	Online application/hard copy	

RCZ	• Cover letter • Close out Form • Publications available • Destruction certificates of samples outside Zimbabwe	Last Thursday of every month	Hard copy submissions	Forms can be accessed from www.rcz.ac.zw

12. IRB/Regulatory Authority Contact Details and Fees

Table 7 (Regulatory contact details and fees)

Regulatory Body	Address & Contact Details	Fees Schedule
MoHCC, Chitungwiza or Harare City Council, Spilhaus	Check address for relevant committee	Contact the body directly
UCSF IRB	Human Research Protection Program & IRB 3333 California St., Suite 315 San Francisco, CA 94118, USA Website: https://irb.ucsf.edu/ Email: irb@ucsf.edu Tel: 1-415-476-1814	No fees are charged for UCSF investigators
JREC	The Chairman JREC Office #4, 5th Floor, Health Sciences Building. e-mail jrec.office@gmail.com jrec@medsch.uz.ac.zw website www.jrec.uz.ac.zw . Tel: +263-4-791631/ 708127/707707/730553	Initial Application ➢ Normal review $100 USD ➢ Expedited review USD 200 Renewal Application ➢ Normal review $50USD Penalty for late renewals ➢ $50USD Amendment Application ➢ USD75
MRCZ	The Chairperson Medical Research Council of Zimbabwe Josiah Tongogara and Mazowe Street PO Box CY573 Causeway Harare Tel: +263-242-791792/ 791193/792747, Telefax: +263-242-253979 Website: www.mrcz.org.zw	Initial Application ➢ Normal review -$500USD ➢ Expedited review - $1000USD ➢ 1% of study budget levy fee Annual Renewal & Amendments ➢ Normal review - $100USD ➢ Expedited review -$200USD Shipment of non-research samples ➢ $20 USD
MCAZ	The Director General Medicines Control Authority of Zimbabwe 106 Baines Avenue Harare Tel : 263-242-736981-5, 708255/792165, 2901327-31, 0772 145 191/2/3 E-mail : mcaz@mcaz.co.zw	**Protocol Administration Fees** a) Refer to fee schedule on MCAZ website: http://www.mcaz.co.zw/index.php/downloads/category/26-fee-schedule

Regulatory Body	Address & Contact Details	Fees Schedule
	Website: www.mcaz.co.zw	
IBC	The Director University of Zimbabwe College of Health Sciences Research Support Center P.O Box A 178 Avondale Harare Tel:- +263 242 708020	Contact the IBC directly
NBAZ	The CEO NBAZ 21 Princess Drive Newlands Harare Tel: +263-242 -782155, 782167, 782856/9 E-mail: marketing@nba.ac.zw / enquiries@nba.ac.zw / nba@nba.ac.zw Website: http://www.nba.ac.zw	Use CTRC negotiated rates (letter from NBAZ dated 01 February 2018) ➢ Initial application $1500 ➢ Amendment $300 ➢ Annual Renewal $500 ➢ Non-compliance $1000
RCZ	The Executive Director Research Council of Zimbabwe 11 Stafford Road Mt Pleasant Harare Email: secretary@rcz.ac.zw, website: www.rcz.ac.zw	Initial & Renewal Applications: ➢ PI registration only - $500 USD ➢ PI registration & one STA - $500USD ($500 for any additional STA) ➢ Penalty - $500 per month after expiry of PI registration

13. Regulatory Communication Documentation, Storage and Retention

Please refer to the current Document and Specimen Storage , Retention and Disposal SOP.

- **LIST OF APPENDICES**

APPENDIX 1: JREC INITIAL APPLICATION CHECKLIST (COORDINATOR)

DOCUMENT	MARK ONCE AVAILABLE
Shona and English Consent Forms where necessary	☐
Shona and English Questionnaire where necessary	☐
Approval letters from Clinical Directors-Parirenyatwa, Harare or Chitungwiza Hospitals	☐
A covering letter from the researcher	☐
A completed JREC application form signed and dated	☐
Clinical Trial Application Form	☐
A Full protocol	☐
A Protocol Summary (if main protocol is more than 5 pages)	☐
Researchers'/ Investigator(s) curriculum vitae (signed, and dated)	☐
*All supplemental material (e.g. questionnaires and other assessment tools)	☐
Permission from the institution where the research will be done	☐
*The most recent investigators brochure for clinical trials	☐
*An itemized budget	☐
*Any other relevant correspondence	☐
*Any other supplemental material necessary for the decision-making process	☐

INSTRUCTIONS

Mark all boxes once available

All documents with an asterisk (*) if unavailable mark N/A

_____**PI or designee date**

_____**checked and signed at CRO**

APPENDIX 2

MRCZ INITIAL APLICATION CHECKLIST (COORDINATOR)

DOCUMENT	MARK ONCE AVAILABLE
Completed MRCZ application form	☐
Clinical Trial Application Form	☐
Research proposal summary *(maximum 4 pages)*	☐
Full research proposal and an electronic version as well. (includes LoAs and CMs)	☐
Informed consent forms: *English & Vernacular Versions (Appropriate vernacular language)*	☐
Data Collection Tools (English and Shona) If available	☐
Recruitment Materials (English and Shona) if available	☐
CVs for the P.I and Co-Investigators	☐
PI GCP certificates	☐
PI application/Cover Letter	☐
JREC approval/Submission	☐
Drug brochure or supplementary information if applicable.	☐
Permission letter from head of institution where data is to be collected (*For research in schools, a letter from ministry of Education is a requirement).*	☐
Proof of funding on Sponsor's Letterhead	☐

INSTRUCTIONS

NOTE THAT ONCE ALL BOXES HAVE BEEN MARKED THE PACKAGE IS READY FOR REVIEW AND FINAL SUBMISSION TO MRCZ

_____PI or designee date

_____checked and signed at CRO

APPENDIX 3

MCAZ APPLICATION CHECKLIST (COORDINATOR)

DOCUMENT	MARK ONCE AVAILABLE
Cover Letter	☐
Application fee	☐
Copies of letters applying for ethics committee approvals	☐
Clinical Trial Application Form	☐
Fully completed Application form (MC 10) to be submitted in triplicate	☐
All documents and electronic copies to be submitted in duplicate	☐
Final version of the Clinical Trial Protocol including relevant questionnaires	☐
Patient Information Leaflet and Informed Consent Form	☐
Investigators Brochure and /or Package Insert	☐
Signed investigator(s) CV (s) in required format	☐
Signed Declaration by Principal investigator (s)	☐
Signed Joint Declaration by Sponsor/National Principal Investigator	☐
Signed declaration by Co-or Sub-investigators	☐
Signed declaration by regional monitor and/ or study coordinator	☐
Pharmacy Plan for the local trial site MCAZ Pharmacy License	
Indemnity and Insurance Certificate and/or letter endorsing generic insurance certificate	☐
Copies of recruitment advertisements if applicable	☐
Ethics Committee (s) approval in country of origin and local MRCZ approval/Proof of Submission	☐
Proof of approval of study by the National Regulatory Authority in country of origin	☐
Electronic versions of the application form plus all the relevant protocol materials on CD or flash drive.	☐
Financial Declaration by sponsor and Principle Investigator	☐
Proof of provision of Data and Safety Monitoring Board/Committee	☐
Proof of application to the local Bio Safety Board for biological products e.g. Vaccines	☐
Abbreviated pharmaceutical dossier for a new investigational drug (IND) product including stability data generated from 3 batches to support the shelf life claim and storage conditions. (N.B) if study products are generic products not yet registered and specifically manufactured as 'trial batches' for the study then a pharmaceutical dossier is also required.	☐

INSTRUCTIONS

NOTE THAT ONCE ALL BOXES HAVE BEEN MARKED THE PACKAGE IS READY FOR REVIEW AND FINAL SUBMISSION TO MCAZ

_____**PI or designee date**

_____**checked and signed at CRO**

APPENDIX 4 RCZ Checklist

Document	MARK ONCE AVAILABLE
Application letter from Institution of Affiliation	☐
MRCZ Cover letter	☐
Valid MRCZ approval letter	☐
RA1(registration) & RA2 (renewal)	☐
Clinical Trial Application Form	☐
Proof of funding	☐
PI and Co-investigators' CVs	☐
Study summary	☐
Study protocol	☐
English & Shona informed consent forms	☐
Questionnaire if applicable	☐
Research report if application is for renewal	☐
Current registration certificate if application is for renewal	☐
GCP certificate	☐
Temporary Employment Permit where applicable	☐
Identification Documents if applicant is a Permanent Resident	☐
Proof of payment of RCZ registration fee.	☐
To be completed if application is for shipment of bio-specimens.	
Application letter from Institution of Affiliation	☐
MRCZ Cover letter	☐
Valid MRCZ approval letter	☐
Valid RCZ registration certificate if study is registered	☐
Specimens Transfer Agreement form (This should be submitted without alterations)	☐
Shipment Logs if shipment application is for renewal	☐
Employee verification letter if recipient(s) have not provided their National ID Numbers	☐
Study summary	☐
Study protocol	☐
English & Shona informed consent forms	☐
PI CV and GCP certificate	☐
Stated finite date of destruction of left over bio-specimen in annexure III	☐
Commitment to avail a copy of the record of destruction within two months of date stated above	☐

APPENDIX 5

INTERIM SUBMISSIONS

DOCUMENT	UCSF IRB	JREC	MRCZ	MCAZ	RCZ	SPONSOR	NBAZ	REPORTING TIME FRAME	Documents required
1. Letter of Amendment (LoA)	YES	YES	YES	YES	N/A	N/A	Yes	≤5 working days of receipt	Refer to table 5
2. Risk designation	YES	YES	YES	N/A	N/A	N/A	N/A	When applying for new study, annual renewal and amendments	Cover letter
3. Shipment outside Zimbabwe of non-research samples	N/A	N/A	Yes	N/A	N/A	N/A	N/A	When shipment is due	Cover letter describing samples to be shipped, destination laboratory and justification
4. Revised protocol	YES	YES	YES	YES	YES	N/A	Yes	≤30 days from receipt, annually to RCZ	Refer to table 5
5. Clarification MEMO (CM)	YES	YES	YES	YES	N/A	N/A	Yes	≤5 working days of receipt	Cover letter Clarification Memo
6. DSMB report/s	YES	YES	YES	YES	N/A	N/A	N/A	≤5 working days.	Cover letter DSMB Report
7. Safety MEMOs	YES	N/A	YES	YES	N/A	N/A	N/A	≤3 working days of receipt	Cover letter Safety Memo
8. Adverse Event report/s	YES	N/A	YES	YES	N/A	YES	N/A	Unless exemption is granted, ≤7 working days of site awareness to MRCZ and MCAZ. SAE log also submitted annually to MRCZ and JREC	Cover letter AE report NB: For MCAZ submit via online platform https://e-pv.mcaz.co.zw/
9. Serious Adverse report/s	YES	N/A	YES	YES	YES	YES	N/A	≤3 working days of site awareness to MRCZ and MCAZ. SAE log also submitted annually to MRCZ and JREC	Cover letter AE report NB: For MCAZ submit via online platform https://e-pv.mcaz.co.zw/
10. Expedited adverse events report/s	YES	N/A	YES	YES	N/A	YES	N/A	≤3 working days of awareness	Cover letter AE report NB: For MCAZ submit via online

11. Protocol deviations	YES	YES	YES	YES	N/A	YES	N/A	≤7 working days of awareness to MRCZ, MCAZ	platform https://e-pv.mcaz.co.zw/ Cover letter PD report
12. Protocol violations	YES	YES	YES	YES	N/A	YES	N/A	≤ 3 working days of site awareness	Cover letter PD report
13. Initial Investigator Brochure	YES	YES	YES	YES	N/A	YES	N/A		Cover letter Initial Investigator's Brochure
14. Updated investigator's brochure/ package inserts	YES	N/A	YES	YES	N/A	N/A	N/A	≤30 days from receipt	Cover letter Updated Investigator's Brochure
15. Updated/revised informed consent forms	YES	YES	YES	YES	N/A	YES	YES	Prior to implementation	Cover letter Revised ICFs
16. Updated/revised recruitment materials	YES	YES	YES	YES	N/A	YES	N/A	Prior to implementation	Cover letter Revised recruitment materials
17. Shelf life Extension of a drug	N/A	N/A	YES	YES	N/A	N/A	N/A	≤ 7 working days of receipt	Cover letter Stability data for the product
18. Study Implementation materials	Yes	Yes	Yes	Yes	N/A	N/A	N/A		Cover Letter Study Implementation materials
19. PI/Investigator of Record changes	N/A	YES	YES	YES	YES	YES	N/A	Prior to implementation	Cover letter Amendment form/Change in PI Form CV and GCP for new Investigator Acceptance of role by new Investigator
20. Study extension	N/A	YES	YES	YES	YES	N/A	N/A	Prior to current approval expiry	Cover letter Extension application form
21. Study Close out	YES	YES	YES	YES	YES	YES	YES	Prior to approval expiry	Cover letter Close out Form Study report (if available) Study publications
22. Withdrawal of Application before implementation	YES	YES	YES	YES	YES	YES	YES	≤ 14 working days of notification	Cover letter Withdrawal form if available

Note: For Adverse Events and Serious Adverse Events, only submit to UCSF IRB if the event is related to study participation. Safety memos will be submitted to UCSF IRB on a case-by-case basis; contact the UCSF Research Coordinator.

In cases where sites are not sure if a submission is supposed to be made, kindly consult the individual regulatory bodies for guidance

Appendix 6 Template letter to request for additional documents

Dear Protocol Team,

We are in receipt of protocol version [X.0] for [protocol title] and look forward to implementing this project at our site. For the local team to complete regulatory submissions efficiently, we request your assistance to source additional documents.

These documents are specified in the attached checklist which we will use to track our progress in receiving them.

Once again, we thank you for this opportunity to work with you.

Revision History:	Version	Effective Date	Description
	7.0	30 October 2020	Version 7.0