Appendix A: Standardized Intranasal Dosing

**Study:** Comparison of sub-dissociative intranasal ketamine plus standard pain therapy versus standard pain therapy in the treatment of pediatric sickle cell disease vasoocclusive pain crises in resource-limited settings

**Standardized Intranasal Dosing**

*Syringe contents: ketamine (50 mg/mL) OR Normal Saline (0.9%)*

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Syringe 1 (mL)</th>
<th>Syringe 2 (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-11.9</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>12-13.9</td>
<td>0.26</td>
<td></td>
</tr>
<tr>
<td>14-15.9</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>16-17.9</td>
<td>0.34</td>
<td></td>
</tr>
<tr>
<td>18-19.9</td>
<td>0.38</td>
<td></td>
</tr>
<tr>
<td>20-21.9</td>
<td>0.42</td>
<td></td>
</tr>
<tr>
<td>22-23.9</td>
<td>0.46</td>
<td></td>
</tr>
<tr>
<td>24-25.9</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>26-27.9</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>28-29.9</td>
<td>0.58</td>
<td></td>
</tr>
<tr>
<td>30-31.9</td>
<td>0.62</td>
<td></td>
</tr>
<tr>
<td>32-33.9</td>
<td>0.66</td>
<td></td>
</tr>
<tr>
<td>34-35.9</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>36-37.9</td>
<td>0.74</td>
<td></td>
</tr>
<tr>
<td>38-39.9</td>
<td>0.5</td>
<td>0.28</td>
</tr>
<tr>
<td>40-41.9</td>
<td>0.5</td>
<td>0.32</td>
</tr>
<tr>
<td>42-43.9</td>
<td>0.5</td>
<td>0.36</td>
</tr>
<tr>
<td>44-45.9</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>46-47.9</td>
<td>0.5</td>
<td>0.44</td>
</tr>
<tr>
<td>48-49.9</td>
<td>0.5</td>
<td>0.48</td>
</tr>
<tr>
<td>50-51.9</td>
<td>0.5</td>
<td>0.52</td>
</tr>
<tr>
<td>52-53.9</td>
<td>0.5</td>
<td>0.56</td>
</tr>
<tr>
<td>54-55.9</td>
<td>0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>56-57.9</td>
<td>0.5</td>
<td>0.64</td>
</tr>
<tr>
<td>58-59.9</td>
<td>0.5</td>
<td>0.68</td>
</tr>
<tr>
<td>60-61.9</td>
<td>0.5</td>
<td>0.72</td>
</tr>
<tr>
<td>62-63.9</td>
<td>0.75</td>
<td>0.5</td>
</tr>
<tr>
<td>64-65.9</td>
<td>0.75</td>
<td>0.55</td>
</tr>
<tr>
<td>66-67.9</td>
<td>0.75</td>
<td>0.6</td>
</tr>
<tr>
<td>68-69.9</td>
<td>0.75</td>
<td>0.64</td>
</tr>
<tr>
<td>70-71.9</td>
<td>0.75</td>
<td>0.68</td>
</tr>
<tr>
<td>72-73.9</td>
<td>0.75</td>
<td>0.72</td>
</tr>
<tr>
<td>74 or above</td>
<td>0.75</td>
<td>0.75</td>
</tr>
</tbody>
</table>
Appendix B: Standardized Treatment Protocol

PROPOSED PEDIATRIC SICKLE CELL PAIN CRISIS TREATMENT PROTOCOL

Section I. *Initial Assessment:*

- Assess vital signs and clinical hydration status
- Supplemental O2 as needed to maintain SpO2 > 92%
- If clinically dehydrated, give NS bolus (10-20 ml/kg, max: 2L)
  - Encourage PO fluids
  - 1-1.5 MIVF if unable to tolerate PO
- If pain, administer ibuprofen 10 mg/kg PO (max: 600mg)
  - Give paracetamol (PCM) 15 mg/kg PO (max: 1000mg) if has already taken an NSAID within 6 hours
  - This marks TIME ZERO (see Section II below)
- Baseline laboratory investigations:
  - CBC, reticulocyte count, additional studies as indicated
- Proceed with pain management as outlined in Section II.
- If fever or concern for other sickle cell disease sequelae (i.e.: acute chest, acute osteomyelitis, septic joint, splenic sequestration, stroke, etc.), please follow algorithm in Section III.

Section II. *Pain Management: Assess, Intervene, and Reassess*

* Pain assessment should precede each medication administration and also be used to evaluate for effect of each intervention

- **Time Zero:** perform FPS-R and administer ibuprofen or PCM
- **30 Minutes:** repeat FPS-R and treat as per pain assessment below
- **60 Minutes:** repeat FPS-R and treat as per pain assessment below
- **120 Minutes:** repeat FPS-R and treat as per pain assessment below
- Continue pain assessments with all routine vitals and treat accordingly

**Pain Assessment: FPS-R**

<table>
<thead>
<tr>
<th>Mild Pain (0-4)</th>
<th>Moderate Pain (5-7)</th>
<th>Severe Pain (8-10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCM 15 mg/kg PO Q6H (max: 1000 mg/dose)</td>
<td>Diclofenac 0.5-1 mg/kg/dose IM Q8H (max: 50 mg/dose)</td>
<td>Pentazocine 0.5 mg/kg/dose IM Q4H (max: 15mg/dose)</td>
</tr>
<tr>
<td>Ibuprofen 10 mg/kg PO Q6H (max: 600 mg/dose)</td>
<td>Morphine 0.2-0.5 mg/kg/dose PO Q4-6H (max: 10 mg/dose)</td>
<td>Morphine 0.1-0.2 mg/kg/dose IV Q2-4H (max: 5 mg/dose)</td>
</tr>
<tr>
<td></td>
<td>Tramadol 1-2 mg/kg/dose PO Q4-6H (max: 100 mg/dose)</td>
<td>Pethidine 1 mg/kg/dose IM/IV Q2-3H (max: 75 mg/dose)</td>
</tr>
</tbody>
</table>
Section III. *Clinical Considerations:*

- If fever, consider:
  - CXR, UA, malaria evaluation, CSF, etc.
  - Evaluate for acute chest syndrome (ACS)/pneumonia, osteomyelitis or septic joint

- If severe abdominal pain or altered mental status:
  - Labs: BMP and LFTs, +/- lipase
  - Abdominal US – evaluate for splenic sequestration, cholelithiasis/cholecystitis/pancreatitis

- Limb pain:
  - Routine pain management as above
  - X-rays and orthopedics consult if concern for osteomyelitis and/or septic joint

- If chest pain or respiratory distress:
  - CXR and supplemental O2
  - Evaluate for acute chest syndrome

- Neurologic symptoms:
  - Consider head CT, evaluate for infection and/or stroke
Faces Pain Scale – Revised

**English:** These faces show how much something can hurt. This face [left most face] shows no pain. The faces show more and more pain [point to each face from left to right] up to this one – it shows very much pain. Point to the face that shows how much you hurt right now.

**Piggin:** Dis face dem di show how something di hot you. Dis face (point to left-most face) di show sey hot no dey. Dis face dem di show plenty plenty hot (point to each from right to left) sotee dis one (point to right most face) – di show over plenty hot. Put your finger for di face wey e di show how you di over feel hot now.

**French:** Ces visages montrent combien on peut avoir mal. Ce visage (montrer celui de gauche) montre quelqu’un qui n’a pas mal du tout. Ces visages (les montrer un à un de gauche à droite) montrent quelqu’un qui a de plus en plus mal, jusqu’à celui-ci (montrer celui de droite), qui montre quelqu’un qui a très très mal. Montre-moi le visage qui montre combien tu as mal en ce moment."

**Fulfulde:** Fodu go nawdum hageecce. Geceee doh holla hano honde nanta nawdum. Yee-so ko heddi nano holla nawdum wallah. Geceee doh don holla diga nano nawdum wallah. Toh adon dila farugo nyamo, nawdum don besda wanee. Holla babal dji nawata jonta wanee.

**Swahili:** Hizi nyuso zaonyeshi jinsi kitu kinaweza umiza. Uso ulio kushoto hauonyeshi uchungu. Nyuso hizo zaonyeshi uchungu zaidi na zaidi kuanzia kushoto kuelekea kulia hadi uso ulio kulia – inaonyeshi uchungu ulio mwingi zaidi. Lenga uso unaonyeshi jinsi unavyoumia sasa hivi.
Faces Pain Scale – Revised Validation References:


Appendix D: Side Effect Definitions

Side effects are common and anticipated effects often experienced by patients receiving a medication, which do not alter outcomes, but may affect patient experience or willingness to receive the medication in the future. Typical ketamine side effects evaluated in this study are listed below.

- **Bad taste in mouth**: subjective agreement by the patient noted by purposeful expulsion of the medicine, grimacing in response to a foul taste, and/or when asked “did you experience a bad taste in your mouth after the medicine?”

- **Drowsiness**: subjective agreement by the participant or family members that s/he appears drowsy. Drowsiness is distinguished from altered mental status by awakening to voice alone.

- **Dizziness**: subjective agreement by the participant or family that s/he feels or appears lightheaded, vertiginous, or has new onset unsteady gait.

- **Itchy nose**: subjective agreement by the participant or family that s/he has an itchy nose.

- **Nausea**: subjective agreement by the participant or family that s/he feels the urge to vomit.

- **Dysphoria**: subjective agreement by the participant or family that s/he demonstrates an unpleasant or irritable sensation after medication administration.

- **Novel subjective negative experiences**: verbally expressed symptomatology by the participant or family members not already addressed above.
Appendix E: Serious Adverse Event Definitions

Adverse events include unintended or unfavorable signs, symptoms, or components of the subjective patient experience temporally related to administration of the study drug. For the current study, adverse events (AEs) include the following:

- Well-described, specific AEs previously reported in the literature related to ketamine administration by any route (intravenous, intramuscular, intranasal, per os, or per rectum). These include the following:
  - **Apnea**: cessation of respirations recognized by clinical examination requiring bag valve mask ventilation.
  - **Assisted Ventilation**: use of bag valve mask ventilation or intubation secondary to loss of protective airway reflexes as a consequence of drug administration.
  - **Bradypnea**: decreased respiratory rate with associated cyanosis requiring physical stimulation, regardless of presence of true apnea or need for assisted ventilation.
  - **Cyanosis**: bluish discoloration of the skin as noted on clinical exam, believed secondary to insufficient blood oxygenation.
  - **Dissociative dosing**: new onset nystagmus observed on clinical examination.
  - **Emergence reaction**: hallucinations, odd behaviors, or subjective reports of an uncomfortable emotional experience that occurs during observation period post-study drug administration.
  - **Hypotension**: systolic blood pressure less than 70 plus 2x age (in mmHg) or less than 90 mmHg for patients over 10 years of age.
  - **Laryngospasm**: obstructive breathing pattern with respiratory distress as noted on clinical examination.
  - **Myoclonus**: muscle stiffening noted on clinical examination.
  - **Seizure**: generalized tonic and/or clonic movements associated with altered level of consciousness.
• **Vomiting:** emesis occurring after study drug administration.

- Novel AEs not previously reported in the literature associated with ketamine administration that occur during the study AE reporting period.

- Participant complications that occur during study period secondary to study procedures, including dosing errors, medication administration, or other study protocols.

- Worsening of preexisting medical conditions secondary to study interventions as determined by clinical staff.
Appendix F: Modified PedsQL-SCD and Validation Reference

Enrollment and Data Collection Form

Comparison of sub-dissociative intranasal ketamine plus standard pain therapy versus standard pain therapy in the treatment of pediatric sickle cell disease vasoocclusive pain crises in resource-limited settings.

Subject ID: ___ ___ ___ ___ ___ ___

<table>
<thead>
<tr>
<th>Pain and Hurt (problems with…)</th>
<th>Never</th>
<th>Almost Never</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Hurting a lot</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. Hurting all over his/her body</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. Hurting in his/her arms</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. Hurting in his/her legs</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. Hurting in his/her stomach</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6. Hurting in his/her chest</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7. Hurting in his/her back</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8. Having pain every day</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>9. Having so much pain that he/she has to take medicine</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
Enrollment and Data Collection Form

Comparison of sub-dissociative intranasal ketamine plus standard pain therapy versus standard pain therapy in the treatment of pediatric sickle cell disease vasoocclusive pain crises in resource-limited settings.

Subject ID: ___ ___ ___ ___ ___ ___

<table>
<thead>
<tr>
<th>Pain Impact (problems with...)</th>
<th>Never</th>
<th>Almost Never</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. It is hard for him/her to do things because he/she might get pain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. Missing school when he/she has pain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. It is hard for him/her to run when he/she has pain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. It is hard for him/her to have fun when having pain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. Having trouble moving around when he/she has pain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6. It is hard for him/her to stay standing when he/she has pain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7. It is hard for him/her to take care of himself/herself when he/she has pain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8. It is hard for him/her to do what others can do because he/she might get pain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>9. Waking up at night when he/she has pain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>10. Getting tired when he/she has pain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Pain Management and Control (problems with...)</td>
<td>Never</td>
<td>Almost Never</td>
<td>Sometimes</td>
<td>Often</td>
<td>Almost Always</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>-------</td>
<td>--------------</td>
<td>-----------</td>
<td>-------</td>
<td>---------------</td>
</tr>
<tr>
<td>1. It is hard for him/her to manage his/her pain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. It is hard for him/her to control his/her pain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
**Enrollment and Data Collection Form**

Comparison of sub-dissociative intranasal ketamine plus standard pain therapy versus standard pain therapy in the treatment of pediatric sickle cell disease vasoocclusive pain crises in resource-limited settings.

**Subject ID:** ___ ___ ___ ___ ___ ___

<table>
<thead>
<tr>
<th>Treatment (problems with...)</th>
<th>Never</th>
<th>Almost Never</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Not liking how he/she feels after taking medicine</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. Not liking the way his/her medicine tastes</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. Medicine making him/her sleepy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. Worrying about whether his/her medicine is working</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. Worrying about whether his/her treatments are working</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6. Medicine not making him/her feel better</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

---

Study Clinician Name: __________________________

Date: ______________
PedsQL-SCD Validation Reference:

Appendix G: Data and Safety Monitoring Board Members

- Kaleab Abebe, PhD  
  o Assistant Professor of Medicine, Center for Research on Health Care Data Center, University of Pittsburgh, Pittsburgh, PA

- Randy Cordle, MD  
  o Director Pediatric Emergency Medicine, Carolinas Medical Center, Charlotte, NC

- Ify Osunkwo, MD, MPH  
  o Medical Director Sickle Cell Program, Levine Cancer Institute, Carolinas HealthCare System, Charlotte, NC

- Natalie Strickland, MD  
  o Assistant Professor of Anesthesiology, Pediatric Pain Management, Egleston Children’s Hospital, Atlanta, GA
Appendix H: Cameroon Baptist Convention IRB

CAMEROON BAPTIST CONVENTION HEALTH BOARD
INSTITUTIONAL REVIEW BOARD
Baptist Centre, Nkwen, P.O. Box 1, Bamenda, Northwest Region

1 October, 2015

James Robert Young, MD
Young.james.r@gmail.com

Re: IRB2015-07, "Comparison of sub-dissociative intranasal ketamine plus standard pain therapy versus standard pain therapy in the treatment of pediatric sickle cell disease vaso-occlusive pain crisis"

Dear Dr. Young,

Your proposed research will study the efficacy and safety of IN ketamine as an adjunct for sickle cell pain crises in children served in resource-limited settings measured by changes in pain scale assessments and rates of reported adverse events.

You will also measure the impact of adjunctive IN ketamine on the hospital length of stay and total analgesia use (morphine equivalent/kg body weight, total NSAID and acetaminophen dose/kg body weight).

Your study protocol was reviewed by two members of the CBC Health Board IRB and has been granted expedited approval, but will be presented to the entire Board during our next Board meeting to get the final approval. An email will be sent to you to inform you of the final decision by the Board.

However, your protocol approval has the following contingencies:

1. Please add the name and phone number of one IRB member with the information: "To ask questions about your rights as a research participant, contact Dr. Nancy Palmer, phone 677 500 480."

2. On your informed consent form, state consequences of withdrawal from the research; explain how confidentiality will be maintained; your consent form needs to be restated to signify parental consent (that is parental consent and assent for minors is lacking)

Upon our receipt of this information and receipt of the revised consent form, we will inform you that you have the IRB approval to begin data collection.

Please understand that this is the ethical and safety approval for your study. You must present this IRB approval letter and the email stating the contingencies have been met to the Hospital Administrator and Chief Medical Officer for approval to do the study in that institution.

If you make any changes in the research protocol, please immediately send the IRB an amendment specifying the changes proposed.

The Board grants approval for this study for a one-year time period. Thereafter, before October 1, 2016, you will complete our renewal formfinal report which will be attached to an email and return it to me. The completed form must be reviewed and approved by the Institutional Review Board prior to the expiration date of the current approval period. The fee to renew a study protocol is 10,000 CFA.

Your protocol has been assigned the above reference IRB protocol number. All correspondence to us should include 1) the IRB protocol number 2) Name of the principal investigator and 3) full title of the study.

Finally, all abstracts, manuscripts, posters and presentations pertaining to the above protocol, must be submitted to the IRB for pre-publication approval.

Please feel free to contact me with any questions and/or concerns regarding the above. Copies of all correspondence regarding this proposal should be sent to me and to Zita Acha secretary, e-mail CBCHIRB@gmail.com.

Sincerely,

Nancy Palmer, Ph.D.

Nancy Palmer, Ph.D., Chairperson, palmernancyela@gmail.com

Mrs. Acha Zita, Secretary, cbcchirb@gmail.com
Appendix I: Muhimbili National Hospital IRB

MUHIMBILI NATIONAL HOSPITAL

ETHICAL CLEARANCE CERTIFICATE

Dr. Hendry Sawe
Emergency Medicine Department
Muhimbili University of Health and Allied Sciences
P.O Box 65001
DAR ES SALAAM.

Certificate Reference Number: MNH/IRB/I/2015/14

Project Title: Comparison of sub-dissociative intranasal ketamine plus standard therapy versus standard therapy alone in the treatment of painful crises among paediatric sickle cell patients in resource limited settings.

Principal Investigator: Hendry Sawe

Date of Approval: 11/02/2016

Expiration Date: 10/02/2017

On behalf of the Muhimbili National Hospital’s Institutional Review Board (MNH-IRB), I am pleased to inform you that ethical approval has been granted in respect to the undertakings of the above-mentioned project.

The Principal investigator must ensure the following conditions are fulfilled:
1. Progress report is submitted to the MNH-IRB where applicable, annually, and final report at the conclusion of the project
2. Amendments to the approved project (including change of personnel) are not effected before submission of request for amendment to MNH-IRB and a written approval from MNH-IRB.
3. Other investigators are aware of the terms of this approval and the project is conducted as approved by MNH-IRB

We wish you well in your research.

Dr. Faraja Chiwanga
Ag. Head of Teaching, Research and Consultancy unit

Prof. Lawrence M. Musuru
Ag. Executive Director

HEAD, TEACHING RESEARCH & CONSULTANCY UNIT
MUHIMBILI NATIONAL HOSPITAL
P. O. BOX 65000
DAR ES SALAAM

EXECUTIVE DIRECTOR
MUHIMBILI NATIONAL HOSPITAL
P. O. BOX 65000
DAR ES SALAAM
Appendix J: National Institute for Medical Research, Tanzania, Approval Letter

THE UNITED REPUBLIC OF TANZANIA

National Institute for Medical Research  
3 Barack Obama Drive  
P.O. Box 9653  
11101 Dar es Salaam  
Tel: 255 22 2121400  
Fax: 255 22 2121360  
E-mail: headquarters@nimr.or.tz  
NIMR/HQ/R.8a/Vol. IX/2299

Ministry of Health, Community  
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14th September 2016

Dr. Juma A Mfnanga,  
Muhimbili National Hospital,  
Department of Emergency Medicine,  
P O Box 65000  
DAR ES SALAAM

CLEARANCE CERTIFICATE FOR CONDUCTING MEDICAL RESEARCH IN TANZANIA

This is to certify that the research entitled: Comparison of Sub-dissociative Intranasal Ketamine plus Standard Pain Therapy Versus Standard Pain Therapy in the Treatment of Pediatric Sickle Cell Diseases vaso-oclusive Pain Crises in Resource-limited Settings (Mfnanga JA et al) has been granted ethical clearance to be conducted in Tanzania.

The Principal Investigator of the study must ensure that the following conditions are fulfilled:

1. Progress report is submitted to the Ministry of Health, Community Development, Gender, Elderly & Children and the National Institute for Medical Research, Regional and District Medical Officers after every six months.
2. Permission to publish the results is obtained from National Institute for Medical Research.
3. Copies of final publications are made available to the Ministry of Health, Community Development, Gender, Elderly & Children and the National Institute for Medical Research.
4. Any researcher, who contravenes or fails to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine. NIMR Act No. 23 of 1979, PART III Section 10(2).
5. Site: Muhimbili National Hospital, Dar es Salaam

Approval is for one year: 14th September 2016 to 13th September 2017.

Name: Dr Mwelecele N Malecela  
Signature  
CHAIRPERSON  
MEDICAL RESEARCH  
COORDINATING COMMITTEE

Name: Prof. Muhammad Bakari Kambi  
Signature  
CHIEF MEDICAL OFFICER  
MINISTRY OF HEALTH, COMMUNITY DEVELOPMENT, GENDER, ELDERLY & CHILDREN

CC: RMO  
DED  
DMO
Appendix K: Tanzania Food and Drugs Authority Approval Letter

TANZANIA FOOD AND DRUGS AUTHORITY

Ref. No. TFDA0015/CTR/0015/9

Dr. Dr. Hendry R. Sawe,
Muhimbili National Hospital,
P.O. Box 65000,
DAR ES SALAAM.

RE: APPROVAL TO CONDUCT A STUDY ENTITLED “COMPARISON OF SUB-DISSOCIATIVE INTRANASAL KETAMINE PLUS STANDARD PAIN THERAPY VERSUS STANDARD PAIN THERAPY IN THE TREATMENT OF PEDIATRIC SICKLE CELL DISEASE VASO-OCCLUSIVE PAIN CRISES IN RESOURCES-LIMITED SETTINGS, TANZANIA”

1. Approval is hereby granted for you to conduct the above study.

2. The approved study site is Muhimbili National Hospital at the Emergency Department.

3. The approval is subject to the following conditions;
   a. Complying with all provisions of the Tanzania Food, Drugs and Cosmetics Act, Cap 219 and Tanzania Food, Drugs and Cosmetics (Clinical Trials Control) Regulations, 2013.
   b. Complying with the approved protocol MNH/IRB/1/2015 version 1.1 of 08th February 2016.
   c. If for any reason the trial is prematurely terminated or suspended, a detailed written explanation must be submitted to TFDA not later than 15 days after the date of the discontinuance.
   d. The Authority may withdraw the approval already given if it is dissatisfied with the conduct of the study or there are breaches of any conditions prescribed in this letter.
   e. Six monthly progress and final reports should be submitted to TFDA, including interim analyses done by the Data Safety Monitoring Board (DSMB) or related Committee. The progress reports should be submitted within three weeks after the end of the period being reported and the final report within 60 days of conclusion of the trial.

02nd November, 2016

MISSION
To protect and promote public health by ensuring quality, safety and effectiveness of food, drugs, cosmetics and medical devices.
f. All relevant information, documents and records pertaining to the trial should be retained at the clinical trial site for a period of not less than 20 years after completion of a trial and made available upon request by TFDA.

g. Any amendment of the protocol, product or Investigators Brochure should be reported to TFDA and approval obtained before its implementation.

h. All serious adverse events should be reported in writing within 14 days and for fatal ones within 24 hours of their occurrence in any of the study sites.

i. Permits for Importation of Investigational Medicinal Product(s) should be obtained before importation. The product(s) should be inspected and approved at the port of entry.

j. Copies of publication(s) of any part of the study should be submitted.

4. The validity of this permit expires on **01st November, 2017**.

5. Looking forward to your continued cooperation.

\[Signature\]

C. N. Ugullum  
Ag. DIRECTOR GENERAL

C.c Dr. Juma Mfinanga,  
Emergency Physician,  
Muhimbili National Hospital,  
P.O. Box 54235,  
DAR ES SALAAM

Cmu/km/afn