PART 1: Administrative Details	
Full Study Title	Randomized placebo-controlled trial testing 0.2% chlorhexidine mouthwash to reduce lower postoperative respiratory tract infections in abdominal surgeries (ROBOCOW)
Protocol/ Document Number	version 2.1, dated 11/2023
Date of Receipt of the Application	10th January 2023
Phase of Study	Phase II
Study Registration Details	Pan African Clinical Trial Registry Number **PACTR202211513812190** Clinical trial approval certificate no. **FDA/CT/2315**
Name and Address of Applicant(s)	Mohammed Sheriff, Tamale teaching hospital, P. O. Box TL 16, Tamale
Name and Address of Sponsor(s)	(Investigator-led) Mohammed Sheriff, Tamale teaching hospital, P. O. Box TL 16, Tamale
Name and Address of Principal Investigator(s)	Mohammed Sheriff, Tamale teaching hospital, P. O. Box TL 16, Tamale
Study Sites	Tamale Teaching Hospital
Study Duration	6 Months
FAPAR Number	FDA/CT/PAR/CTA/245

PART 2: Investigational Product(s)	
Name of Investigational Product(s) including Comparator(s).	Kamaclox mouthwash (0.2% Chlorhexidine Gluconate) Placebo (water)
Justification for Investigational Product(s) including comparators	Systematic studies and several clinical trials have shown that regular application of chlorhexidine antiseptic mouthwash reduces the incidence of respiratory tract infections by over 25% among mechanically ventilated intensive care unit (ICU) patients and by about 40% when used peri-operatively in cardiac surgery. The study by Segers et-al demonstrated, in a major randomized placebo-controlled clinical trial, a significant reduction of postoperative lower respiratory tract infection for oral and nasopharyngeal chlorhexidine application in cardiothoracic surgery patients by an absolute risk reduction (ARR) of 6.4%. This study showed both statistical and clinical

	superiority of the antiseptic mouthwash intervention with chlorhexidine over no antiseptic mouthwash. Perioperative chlorhexidine mouthwash is a simple inexpensive intervention that can reduce perioperative respiratory tract infection, subsequent deaths, and overall healthcare cost in abdominal surgeries in LMICs. Hence quality clinical trials to test the effectiveness and safety of chlorhexidine mouthwash in major abdominal surgeries in our hospital and Ghana are urgently needed.

PART 3: Study Summary

Study Objectives

Primary Objective

- To determine whether perioperative use of 0.2% chlorhexidine mouth wash reduces the rate of postoperative pneumonia in 30 days postoperative period compared to placebo among patients undergoing midline laparotomy

Secondary Objective (s)

- To assess the impact of the intervention on 30-day postoperative mortality
- To determine the impact of the intervention on length of hospital stay
- To determine whether the intervention impacts on the 30-day unplanned readmission rates due to a respiratory complication
- To assess the effect of the intervention on time to return to normal activities

Study Design

The study will be a prospective one conducted using a 1:1 parallel randomized double-blind placebo-controlled clinical trial design to assess the effect of 0.2% chlorhexidine mouth wash compared to placebo on the desired clinical parameters.

Eligibility Criteria

Inclusion criteria list:

1. Participants who are 10 years and above
2. Participants presenting with either elective or emergency abdominal condition requiring midline laparotomy under general anaesthesia
3. Midline incision of at least 5cm long or more
4. Participants who have given written informed consent and/or assent

Exclusion criteria list

1. Non-midline abdominal incision

PART 3: Study Summary

2. Emergency laparotomy for gynaecological conditions including caesarean sections
3. Patients who have documented allergy or hypersensitivity to chlorhexidine
4. Patients with documented evidence of pneumonia before surgery
5. Incisions less than 5cm
6. Those unable to complete follow up after surgery
7. Patients assessed to have ASA grade V, expected to die with or without surgery, before the commencement of surgery
8. Patients who have had abdominal surgery in another facility and referred to TTH for further management

Sex of participants
Male/Female

Age boundaries
10 years and above

Date of Commencement (Expected or Actual)

25th March 2024 (Actual)

Status of Study

Commenced/Actively recruiting/Enrolment Closed/Analysis/Trial Ended

Actively recruiting

PART 4: Scientific Discussion

Summary of Review Comments

Quality

The Investigational products Kamaclox and Bel-aqua mineral water are registered products. The quality of the IPs has been assessed by the FDA.

Safety

The interventions compared in this trial have been used in a cardiac trial. No adverse effects have so far been reported in most of the studies conducted to evaluate the effectiveness of chlorhexidine gluconate mouthwash in cardiac surgeries. Hence, it is expected that the study intervention will not pose any significant safety concerns and/or affect the participants' well-being.

PART 4: Scientific Discussion

The following documents were reviewed and found satisfactory to fulfill the safety requirement of the trial:

1. Protocol sections on Adverse events reporting guidelines, End of Study definition, Risk to Benefit Ratio Assessment, Management and Accountability of Investigational Products (IP).

Efficacy

Evaluation of the possible efficacy of the intervention was based on previous studies as stated in the protocol:

The study by Segers et-al demonstrated, in a major randomized placebo-controlled clinical trial, a significant reduction of postoperative lower respiratory tract infection for oral and nasopharyngeal chlorhexidine application in cardiothoracic surgery patients by an absolute risk reduction (ARR) of 6.4%. This study showed both statistical and clinical superiority of the antiseptic mouthwash intervention with chlorhexidine over no antiseptic mouthwash. This intervention's effectiveness has not been studied extensively among other patient populations such as those undergoing elective or emergency abdominal surgeries in low- and middle-income and high-income countries.

The endpoint for the study is to measure the rate of pneumonia in patients who undergo a midline laparotomy for an intra-abdominal condition.

Overall comments

After initial review, the application was deferred with queries to be addressed by the applicant. Following the satisfactory response to all queries on the submission, the study was approved and issued a clinical trial certificate.

The applicant is committed to ensuring that the study is conducted in compliance with Good Clinical Practice (GCP) and applicable regulatory requirements.

All participants will consent to the protocol prior to participation in any study-related activity.

Based on the assessment of medical and ethical principles, the anticipated benefits to the participant justify the foreseeable risks and inconveniences related to the conduct study.

PART 5: Application Review Process

The application was reviewed under the routine approval pathway with a decision taken in 26 working days.

PART 6: Status after Review

Study was approved on 20th December 2023.

References

1. Protocol version 2.1, dated November 2023
2. Segers P, Speekenbrink RGH, Ubbink DT, Van Ogtrop ML, De Mol BA. Prevention of nosocomial infection in cardiac surgery by decontamination of the nasopharynx and oropharynx with chlorhexidine gluconate: A randomized controlled trial. J Am Med Assoc. 2006;296(20):2460–6.
3. Adult Participant Information Leaflet version 2.0 dated 1st July 2021
4. IP Label for Kamaclox Mouthwash
5. FDA's Clinical Trial Assessment form version for Clinical Trial Application version 1.0 dated 2nd September 2019
6. Guidelines for Authorization of Clinical Trials of Medicines, Food Supplements, Vaccines and Medical Devices in Ghana
7. Guidelines for Good Clinical Practice in Ghana