Protocol Number: ZX-ZP-0113

A Randomized, Controlled Clinical Trial Evaluating A Novel Perioperative Patient Skin Antiseptic Preparation

Sponsor:	Zurex Pharma, Inc. 2113 Eagle Drive Middleton, WI 53562
Sponsor's Representatives	[redacted] [redacted] Executive Vice President RA/Clinical/Compliance [redacted]
Principal Investigator:	[redacted] Division of Vascular and Endovascular Surgery Froedtert Hospital Medical College of Wisconsin [redacted] Milwaukee, Wisconsin 53226 [redacted]
Study Coordinator:	[redacted] Division of Vascular and Endovascular Surgery [redacted] Milwaukee, Wisconsin 53226
Infection Control Expert:	[redacted]

Study monitoring, data management, and biostatistics:	[redacted]
Medical Monitor:	[redacted]

STATEMENT OF COMPLIANCE

The study will be carried out in accordance with Good Clinical Practice (GCP) as required by the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CRF Part 46, 21 CFR Part 50, 21 CFR Part 56 and 21 CFR Part 312)
- International Conference on Harmonisation (ICH) E6

All key personnel (all individuals responsible for the design and conduct of this study) have completed Human Subjects Protection Training.

SIGNATURE OF APPROVAL

1. Protocol Synopsis

Name of Sponsor: Zurex Pharma Inc.
Name of Investigational Product: [redacted] 26-mL Applicator (70% isopropyl alcohol)
Name of Reference Control Product: [redacted] 26-mL Applicator (chlorhexidine gluconate 2% w/v and 70% isopropyl alcohol)
Protocol Number: ZX-ZP-0113
Study Title: A Randomized, Controlled Clinical Trial Evaluating A Novel Perioperative Patient Skin Antiseptic Preparation
Principal Investigator (PI): Joseph P. Hart, M.D., F.A.C.S., D.F.S.V.S.
Clinical Center: Froedtert Hospital, Medical College of Wisconsin (MCW), Milwaukee, Wisconsin
Study Period: Approximately 1 year
Objectives: The primary efficacy objective of this study is to determine the efficacy of two skin preparation products, [redacted] on the rates of surgical site infections (SSI). The primary safety objectives are to determine the rates of skin irritation or allergic reactions attributed to each product and all other adverse events (AEs).
Methodology: This study is a 2-arm, randomized, parallel group, single-site study designed to determine the SSI rates within 30-days post-surgery of pre-surgical skin cleansing with [redacted] and [redacted] on patients who are planning to undergo clean (class I wound) or clean-contaminated (class II wounds) surgery based on medical chart review will be approached to consent for the study (see Appendix A for wound classification definitions and types of surgical procedures to be included). After consenting to the study, screening will be conducted to determine patient eligibility. Eligibility will be determined from chart review and conducting any procedures for information not in the medical chart (e.g., signs of infection at the surgical site where an incision will be performed or patient reported allergies to components of the surgical scrubs). Pre-operative data to be collected on electronic case report forms (eCRFs) include patient's demographics, medical history, current antibiotics (last 4 days), adherence to [redacted] standard preop surgical instructions, and record of planned surgery. Eligible patients will be randomized with stratification by type of surgery (clean versus clean-contaminated) in a 1:1 ratio to receive skin pretreatment with either [redacted] 26-mL Applicator or [redacted] and will undergo surgery. The surgical site will be examined for signs of infection and local skin reactions at least once a day during hospitalization, and at discharge. The patient will be contacted by telephone approximately 3-to-5 days post hospital release and at 30-days post the day of surgery. During these telephone contacts, the patient will be asked about signs of local skin or systemic allergic reactions and a general question about how they are feeling to determine if any other adverse events (AEs) may have occurred. If during these queries, the patient reveals any events that may be indicative of an SSI, they will be asked to see a study doctor to determine if an SSI has occurred. If they have visited another doctor for an evaluation, the patient will be asked to provide any relevant medical records to include in the study files. At any time after discharge up to 30 days post-surgery, the patient will be encouraged to call a study nurse or doctor and arrange for a prompt clinical evaluation if an infection is suspected.
Number of Patients (Planned): 200 (100 in each treatment group)
Main Inclusion/Exclusion Criteria: Patients will be males and females at least 18 years of age scheduled to undergo clean (class I wound) or clean-contaminated (class II wounds) surgeries (see Appendix A for examples).

Investigational Product, Dosage and Mode of Administration:

[redacted] 26-mL Applicator will be applied topically to the region of surgical incision using repeated back and forth strokes. For dry surgical sites such as the abdomen or arm, the product will be applied for a period of at least 30 seconds and for moist surgical sites (such as the inguinal fold) for 2 minutes. The application area should be allowed to air dry for approximately 3 minutes.

Reference Therapy, Dosage and Mode of Administration: [redacted] will be applied according to the prescribing information.

Duration of Study: Each patient will participate in the study for up to 51 days, including up to 21 days for screening and 30-days of post-surgical follow-up for evidence of any SSI or other AEs.

Criteria for Evaluation:

Primary Efficacy Endpoint: The primary efficacy endpoint is the occurrence of any SSI within 30 days after surgery. A secondary analysis of the primary efficacy endpoint are subgroup analyses including:

- Different types of SSI classified as superficial incisional infection, deep incisional infection, or organ-space infection
- Clean (class I wound) or clean-contaminated (class II wounds) surgeries

Safety Endpoints: Safety endpoints will be analyzed over the entire treatment and follow-up period.

- AEs (including local application site reactions and allergic reactions)

Statistical Methods:

Analysis Populations: The full analysis set includes all patients who were randomized to study treatment, received the study treatment, and underwent surgery. The per-protocol (PP) subset includes all full analysis set patients who had final follow-up at 30 days post-surgery. The safety subset will include all patients who were randomized to the study and received a study treatment and will be analyzed as they were treated.

Statistical Analyses: All baseline data and efficacy and safety endpoints will be presented by descriptive statistics including numbers and percentages for categorical variables and mean, standard deviation (SD), median, minimum and maximum values for continuous variables. All data will be presented for all three of the analysis sets.

AEs will be coded using the most recent version of the Medical Dictionary of Regulatory Activities (MedDRA) preferred terms and will be grouped by system, organ, and class (SOC) designation. The severity, frequency, and relationship of AEs to investigational products will be presented by preferred term by SOC grouping. Listings of each individual AE including start date, stop date, severity, relationship, outcome, and duration will be provided. Each AE (based on preferred terminology) will be counted once only for a given study patient. If the same AE occurred on multiple occasions, the highest severity and relationship to investigational product will be assumed. Thus, study participants are not counted multiple times in a given numerator in the calculation of frequencies for a specific AE. The frequency and severity of skin irritation or allergic reactions at least possibly attributed to each product will also be presented. The number and percentage of patients who were prescribed prophylactic antibiotics and antibiotics to treat an infection as well as patient's adherence to the [redacted] standard preop surgical instructions, will also be summarized.

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2. List of Abbreviations and Definition of Terms

Table 1: List of Abbreviations and Definition of Terms

Abbreviation	Definition
AE	adverse event
CDC	Centers for Disease Control and Prevention
CFR	Code of Federal Regulations
CFU	colony forming units
[redacted]	[redacted]-mL Applicator
cm	centimeter
eCRF	electronic case report form
EDMS	electronic data management system
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HAI	healthcare-associated infection
HIPAA	Health Insurance Portability Accountability Act
ICH	International Conference on Harmonization
IND	Investigational New Drug
IRB	Institutional Review Board
IWRS	interactive web-based randomization system
MBC	minimum bactericidal concentration
MCW	Medical College of Wisconsin
MedDRA	Medical Dictionary for Regulatory Activities
MIC	minimum inhibitory concentration
mL	milliliter
NHSN	National Healthcare Safety Network
NNIS	Nosocomial Infections Surveillance System
PHI	Protected Health Information
PI	principal investigator
PP	per-protocol
preop	preoperative
PT	preferred term
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SOC	System, organ, class
SSI	surgical site infection
US	United States
v/v	volume/volume
WHO	World Health Organization
w/v	weight/volume
[redacted]	[redacted] Solution Applicator
Zurex	Zurex Pharma, Inc.

3. Introduction

Surgical site infections (SSI) are one of the most common complications in the post-operative patient, and the second most common health care associated infection overall [redacted] The Agency for Healthcare Research and Quality reported that in 2014, a total of 14.2 million operative procedures were performed in the inpatient setting in United States hospitals [redacted]. The Centers for Disease Control and Prevention (CDC) healthcare-associated infection (HAI) prevalence survey found that there were an estimated 157,500 surgical site infections (SSIs) associated with inpatient surgeries in 2011 [redacted]. The National Healthcare Safety Network (NHSN) database included 16,147 SSIs following 849,659 operative procedures in all groups reported, for an overall SSI rate of 1.9% between 2006-2008 [redacted] This rate, however, is likely underestimating the true burden of the disease, as the Nosocomial Infections Surveillance System (NNIS) collects data only until discharge from the hospital.

Rates of infection vary considerably depending on type of operation, difficulty, and pre-operative risk. Some SSI rates that have been reported in the literature in randomized controlled trials are shown in Table 2. These trials have in common that SSI's were followed for up to 30 days post-surgery and used CDC criteria to identify and classify SSI [redacted]. Depending on the preventative measure and type of surgery, rates ranged from 3% to 45%.

Table 2: SSI Rates Post Surgery for Various Types of Surgeries

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Type of Surgery	Pretreatment / SSI Rates	References
[redacted]	[redacted]	[redacted]

[redacted] percent of procedures are now done on an outpatient basis [redacted] and hospital stays have become progressively shorter and shorter. While many wound infections arise within the first 5 post-operative days [redacted], an SSI can occur at any time within 30 days of the operation [redacted], thus it is important to follow SSI rates for this duration. For example [redacted] reported that 45 of 176 (26%) patients undergoing colorectal surgeries experienced a SSI and nearly half (44%) of the SSIs diagnosed in their study were discovered only at outpatient follow-up.

3.1. Preventative Measures for Surgical Site Infections- Skin Preparation Agents

Chlorhexidine gluconate is a commonly used microbicide. Effective against bacteria and parasites, it has been shown to be more effective against fungi and biofilms than iodine [redacted], but less effective against germinating spores. [redacted] a pre-packaged swab of 2% chlorhexidine /70% isopropyl alcohol is commonly used brand of surgical skin preparations and is the comparator product in this study.

One disadvantage of chlorhexidine is that hypersensitivity reactions have been reported in 3.2% of men, and 1.9% of women in a sample of 2061 subjects [redacted]. A review of the literature found 40 documented cases of anaphylaxis due to chlorhexidine exposure, of which, 85% were male [redacted]

3.2. [redacted]

Zurex Pharma, Inc. (Zurex) has developed [redacted] Isopropyl Alcohol (70% v/v) Solution as an antiseptic/antimicrobial agent used to aid in the reduction of infective agents (ie, microorganisms) found among a patient's own skin flora. Effective skin antisepsis is essential in preventing or reducing the incidence of healthcare-associated infections occurring with surgical procedures. The [redacted] applicator, containing [redacted] solution is FDA approved as a preoperative skin preparation solution for use in pre-surgical settings as an antiseptic/antimicrobial agent to help reduce the bacteria that potentially can cause skin infection.

[redacted] This product, called [redacted] applicator is the subject of this clinical trial.

[redacted] Applicator is composed of [redacted]

[redacted] has been tested in [redacted] subjects exposed to [redacted] from [redacted] completed clinical studies with a pivotal trial of the [redacted] applicator [redacted]. [redacted] met the standards for this product type outlined in the December 2017 Final Rule on the Safety and Effectiveness of Health Care Antiseptics: Topical Antimicrobial Drug Products for Over-the-Counter Human Use. In the [redacted] pivotal studies, efficacy was observed for multiple, pre-specified efficacy measures (eg, responder rate and log10 colony forming units [CFU]/cm^2 reduction from baseline) and evaluation times (30 seconds, 10 minutes, and 6 hours post application) on both the abdomen and the groin. Moreover, [redacted] was superior to [redacted] and non-inferior to [redacted], based on average treatment effect. Thus, the efficacy of [redacted] was demonstrated consistently across efficacy endpoints and studies. Effectiveness was observed at 30 seconds and 10 minutes post application and persisted for 6 hours.

3.3. Risks and Benefits

All study subjects will receive a pre-surgical skin preparation free of charge that has been shown to be effective in killing skin bacteria and fungi. Chlorhexidine, which is part of the standard of care [redacted] product, can cause a rare but serious allergic reaction that may be life-threatening. Patients will be instructed to obtain emergency medical help if they have signs of an allergic reaction: hives, severe skin rash; wheezing, difficult breathing; cold sweats, severe dizziness; swelling of the face, lips, tongue, or throat.

3.4. Safety of [redacted]

All components in [redacted] solution are either noted within the FDA's Inactive Ingredients Database as safe or have a long history of safe and effective use. The safety of [redacted] Isopropyl Alcohol (70% v/v) Solution was demonstrated in the clinical program. Across the [redacted]

[redacted]

4. Study Objectives

The primary efficacy objective of this study is to determine the efficacy of two skin preparation products, [redacted] Applicator and a standard of care [redacted] Applicator ([redacted]) on the rates of SSI.

The primary safety objectives are to determine the rates of skin irritation or allergic reactions attributed to each product and all other AEs.

5. Investigational Plan

This study is a 2-arm, randomized, parallel group, single-site study designed to determine the SSI rates within 30-days post-surgery of pre-surgical skin cleansing with [redacted] Applicator or [redacted] on patients who are planning to undergo clean (class I wound) or clean-contaminated (class II wounds) surgery based on medical chart review will be approached to consent for the study (see Appendix A for wound classification definitions and types of surgical procedures to be included). After consenting to the study, screening will be conducted to determine patient eligibility. Eligibility will be determined from chart review and conducting any procedures for information not in the medical chart (e.g., signs of infection at the surgical site where an incision will be performed or patient reported allergies to components of the surgical scrubs). Pre-operative data to be collected on electronic case report forms (eCRFs) include patient's demographics, medical history, antibiotics in the last 4 days, and record of planned surgery. Eligible patients will be randomized with stratification by type of surgery (clean versus clean-contaminated) in a 1:1 ratio to receive skin pretreatment with either [redacted] Applicator or [redacted] and will undergo surgery. A total of 200 patients is planned (100 in each group). The surgical site will be examined for signs of infection and local skin reactions at least once a day during hospitalization, and at discharge. The patient will be contacted by telephone approximately 3-to-5 days post hospital release and at 30-days post the day of surgery. During these telephone contacts, the patient will be asked about signs of local skin or systemic allergic reactions and a general question about how they are feeling to determine if any other AEs may have occurred. If during these queries, the patient reveals any events that may be indicative of an SSI, they will be asked to see a study doctor to determine if an SSI has occurred. If they have visited another doctor for an evaluation, the patient will be asked to provide any relevant medical records to include in the study files. At any time after discharge up to 30 days post-surgery, the patient will be encouraged to call a study nurse or doctor and arrange for a prompt clinical evaluation if an infection is suspected. Study assessments and procedures will be performed as outlined in the Schedule of Assessments (Table 3).

Table 3: Schedule of Assessments

Study Day	-21 to 1	2 – 30 if hospitalized (daily)	3 to 5 days post hospital release (telephone follow-up)	Outpatient follow-up visit – if conducted	Any time patient reports possible SSI or clinician reports SSI and visits a doctor's office or comes to the hospital or other clinic	30 (telephone follow-up)
Informed Consent	X					
Locator Form	X					
Medical History / Surgical Plan	X					
Physical Exam Per Standard of Care[a]	X	X		X	X	
Prescribed antibiotics	X	X	X	X	X	X
Demographics	X					
Pregnancy test in women of childbearing potential	X					
Eligibility Checklist[b]	X					
Randomization, Treatment and Surgery	X					
Adherence to MCW standard preop surgical instructions	X					
AEs (open ended question) and elicited AE questions[c]	X	X	X	X	X	X
SSI Evaluation		X	X	X	X	X
Final Patient Disposition[d]						X

[redacted]

6. Study Interventions

6.1. Investigational Products

Investigational products include:

- [redacted] Applicator
- [redacted] Applicator (reference product)

[redacted] Applicator contains as the active ingredient isopropyl alcohol (70% v/v) with other ingredients including [redacted]

[redacted] contains 2% chlorhexidine gluconate (w/v), 70% isopropyl alcohol (v/v), and FD&C Yellow #6.

6.2. Investigational Product Labeling and Storage

Zurex will label, package and provide the [redacted] Applicator to the study site. The [redacted]. The applicators should be stored as per labeling at 15 to 30°C (59 to 86°F). The product supplies will be provided in their regular packaging. An example of the [redacted] label is shown in Figure 1.

Figure 1: Example of [redacted] Applicator Label

[redacted]

6.3. Investigational Product Administration

[redacted] or [redacted] will be applied to the site of the surgical incision in accordance with their respective Directions for Use as described below.

[redacted] Solution will be applied topically to the region of surgical incision using repeated back and forth strokes. For dry surgical sites such as the abdomen or arm, the product will be applied for a period of at least 30 seconds and for moist surgical sites (such as the inguinal fold) for 2 minutes. The application area should be allowed to air dry for approximately 3 minutes. More than one applicator should be used if the coverage area exceeds 13.2 in x 13.2 in (1126 cm^2).

[redacted] will be applied topically to dry surgical sites (e.g., abdomen or arm) using gentle repeated back-and-forth strokes for a period of at least 30 seconds, then allowing the area to air dry for approximately 3 minutes. For moist surgical sites (e.g., inguinal fold), [redacted] will be applied using gentle repeated back-and-forth strokes for 2 minutes and allowing the area to air dry for approximately 3 minutes. More than one applicator should be used if the coverage area exceeds 13.2 in x 13.2 in (1126 cm^2).

6.4. Investigational Product Accountability

Zurex requires Investigators to maintain accountability and adequate inventory security of the study material at all times. The Investigator or designee will:

- Complete a Confirmation of Release and Receipt of Study Materials form upon receipt of the shipment and maintain and account for inventory on the Study Material Disposition form
- Keep study materials in a secure storage area, accessible only to authorized individuals.
- Dispense study material only to patients properly enrolled into the study.
- Return all unused study materials to Zurex Pharma, Inc. at the end of the study or dispose of unused study materials as agreed upon.

7. Study Procedures

7.1. Recruitment of Patients

Patients anticipating undergoing clean (class I wound) or clean-contaminated surgery (class 2 wound) will be identified during chart review. See Appendix A for a description of wound classifications. If the potential participant is planning one of these procedures and otherwise appears to be eligible (e.g., ≥ 18 years old, no medical exclusions from chart review), the PI or designee will explain the study to the patient and if the patient is interested he/she will go through the informed consent procedure.

7.2. Eligibility Screening

Preliminary eligibility for study participation will be assessed as described above. If the patient appears to be an appropriate candidate for the study, a member of the study staff trained in human subjects' protections will perform the informed consent process by explaining the nature and scope of the study and the potential risks and benefits of participation. The study will be explained to the potential subject in lay terms and in a quiet, private setting. Potential subjects will be given as much time and privacy as necessary to review the informed consent and ask any

questions. The potential subject will be provided with an opportunity to discuss participation with others outside the study team. If the potential subject agrees to participate, the subject must read, sign, and date the informed consent form, which must also be signed and dated by the person completing the consent process. A copy of the signed and dated consent will be provided to the subject and the original will placed in the subject's medical record.

Once a patient signs the informed consent form, the patient will be considered enrolled in the study and will be assigned a unique patient number. Demographic data (age, gender, race, and ethnicity) and medical history data will be collected. The type of surgery planned and results of a physical examination will be collected. Antibiotics taken in the past 4 days will be recorded. Then an eligibility checklist will be reviewed to determine if the patient is eligible for the study.

7.3. Selection of Patients

7.3.1. Inclusion Criteria

To be eligible, the patient must:

1. Be male or female and at least 18 years of age.
2. Be able to verbalize an understanding of the consent form, able to provide written informed consent, verbalize willingness to complete study procedures, able to understand written and oral instructions in English
3. Be planning to undergo clean (class I wound) or clean-contaminated (class II wounds) surgery (see Appendix A)
4. Expect to be available for up to 30-days after the surgery

7.3.2. Exclusion Criteria

Patients must not have any of the following:

1. Active infection or fever including evidence of infection at or adjacent to the operative site
2. Immunosuppressed
3. Kidney/liver failure
4. Immunosuppressive therapy (chemotherapy, steroids) within the previous 1 week
5. Any history of allergy to chlorhexidine or isopropyl alcohol or any other component in [redacted] Solution including c[redacted]
6. If female of childbearing potential and pregnant, positive pregnancy test, or breastfeeding.

7.4. Measures Taken to Minimize/Avoid Bias

7.4.1. Randomization (Day 1)

If eligible for the study, patients will be randomized in an approximate 1:1 ratio to have the skin at the surgical site scrubbed with the [redacted] or [redacted] applicator. A

stratified permuted block randomization procedure will be performed via an interactive web-based randomization system (IWRS) with type of surgery [clean (class I wound) or clean-contaminated (class II wounds) surgery]) as the stratification variable.

If the patient is randomized and is never treated with one of the investigational products or never underwent surgery, then the patient will be considered a randomization failure and an additional patient will be randomized with the next randomization sequence at the time he/she is randomized. The reason(s) that a patient was considered a randomization failure or screen failure will be documented in source documents and eCRFs.

7.4.2. Preoperative Surgical Instructions

Each patient undergoing surgery at the MCW is instructed to shower with an antiseptic agent before the day of surgery. Additionally, the surgical staff follows standard preoperative surgical orders while prepping the patient for surgery. The patient will be asked about adherence to the instructions before surgery and the source documents will be checked for adherence to the standard preoperative surgical orders / activities the day of surgery.

7.5. Interventions (Day 1)

Patients will have the region surrounding the surgical site scrubbed with the assigned product as described in section 6.3.

7.6. Assessments During the Inpatient Period

During the post-surgical period while the patient is still in the hospital, the surgical site and surrounding area will be examined for signs of infection or other deep incisional infection and if evident, this will be recorded. Local skin reactions (erythema, rash, or pruritus) or other systemic allergic reactions to the investigational product will be recorded. Other AEs will be assessed by asking the patient an open ended question: How are you feeling? If any antibiotics are prescribed for prophylaxis or treatment of an AE, these will be reported. On the day of hospital discharge, all of the above assessments will also be performed. The patient will be given standard discharge instructions and a card with the name of study nurse or doctor to contact in the event of any post-surgical complications. Patients will be scheduled for an examination appointment or possibly to come to the emergency room if any possibly serious complications have occurred.

7.7. Assessments During the Outpatient Period

If an outpatient follow-up visit has been scheduled, a physical examination should be performed including inspection of the surgical site for signs of an SSI and the skin at the application site for signs of an allergic reaction and new antibiotic prescriptions. Other AEs should be assessed with an open ended question and data will be recorded.

7.8. Telephone Assessments

Three-to-five days after hospital release, on study Day 30 or at any time a patient calls with a complaint, a telephone scripted interview will be completed that assesses AEs and the patient should be queried if they had any other doctor’s office visits that might be indicative of a post-surgical problem indicative of an SSI or AE. If the patient cannot be contacted at Day 30, a person that they listed on the locator form should be called to determine if the patient died or is

otherwise hospitalized or to the best of their knowledge has had no medical issues requiring hospitalization, emergency care, or other doctor's office visit. Also, if the patient cannot be contacted on Day 30, it is permissible to continue to try to reach the patient up to 7 days later to collect the data on the scripted interview reminding the patient that the data is only for the period up to Day 30.

7.9. Duration of Patient Participation

Each patient will participate in the study for up to 51 days including up to 21-days after consenting to the study for screening up to the day of surgery and a Day 30 post-surgical follow-up telephone call or visit (if needed) to determine if there is any evidence of an SSI or other AE.

7.10. Patient Withdrawal or Discontinuation Procedures

Each patient has the right to withdraw consent and withdraw from the study at any time. As each patient receives a single study treatment over the course of a few minutes, once the patient has received a treatment, the investigator should not withdraw the patient from the study and should try to complete all safety follow-up assessments including examinations for SSIs.

In the event that a patient withdraws, the reason(s) for the discontinuation from the study will be recorded. At the time that the patient withdraws, he/she should be asked to complete the safety assessments in accordance with the schedule in Table 3, if possible.

7.11. Study Termination Criteria

Zurex or the Investigator has the right to discontinue the study at any time for medical and/or administrative reasons. As far as possible, this should occur after mutual consultation.

7.12. Product Evaluation Survey

8. Study Endpoints

8.1. Efficacy Endpoints

8.1.1. Primary Efficacy Endpoint

The primary efficacy endpoint is the occurrence of any SSI within 30 days after surgery.

A secondary analysis of the primary efficacy endpoint include subgroup analyses as follows:

- SSI rates by different types of SSI classified as superficial incisional infection (which involves only skin and subcutaneous tissue and excludes stitch related abscesses),

deep incisional infection (which involves fascia and muscle), or organ-space infection (which involves any organ or space other than the incised layer of body wall that was opened or manipulated during the operation) (definitions in accordance with CDC-2019 will be used).

- SSI rates by type of surgery including clean (class I wound) or clean-contaminated (class II wounds) surgeries

8.2. Safety Endpoints

Safety endpoints will be analyzed over the entire treatment and follow-up period.

- AEs (including specifically local application site reactions and allergic reactions)

9. Safety Monitoring Plan

Safety monitoring will be conducted throughout the study; therefore safety concerns will be identified by continuous review of the data by the PI, clinic staff, clinical monitor, medical monitor, and Zurex.

The IRB, Medical Monitor, PI, Clinical Monitors and Zurex will review any safety concerns throughout the trial. The roles of these individuals are described below.

Medical Monitor: A Medical Monitor has been appointed for the study. The Medical Monitor will be available for making recommendations to the investigator and Zurex on the severity of any SAEs, and the relatedness to the study interventions. The Medical Monitor will also be responsible for tracking and assessing trends in the AEs reported.

Clinical Monitors: The PI will allow representatives of Zurex to periodically monitor, at mutually convenient times during and after the study, all study data. These monitoring visits provide Zurex with the opportunity to evaluate the progress of the study and to obtain information about potential problems. The monitors will assure that submitted data are accurate and in agreement with any medical records or paper source documentation used; verify that investigational products are properly stored and accounted for, verify that patients' consent for study participation has been properly obtained and documented, confirm that research subjects entered into the study meet inclusion and exclusion criteria, and assure that all essential documentation required by Good Clinical Practices (GCP) guidelines are appropriately filed.

Monitors will conduct a site initiation visit prior to the start of the study. At this visit, they will assure that proper study-related documentation exists, assist in training investigators and other site personnel in study procedures and GCP guidelines, confirm receipt of study supplies, and assure that acceptable facilities are available to conduct the study.

Routine monitoring visits by Zurex's representatives will be scheduled at appropriate intervals but more frequently at the beginning of the study. At these visits, the monitors will verify that study procedures are being conducted according to the protocol guidelines, monitor eCRFs against source documents, review AEs and SAEs, and perform drug accountability. At the end of the study, they will confirm that the site has the appropriate essential documents on file, advise on storage of study records, and inspect the return and destruction records for unused investigational products.

10. Assessment Methods

All study assessments will be performed at the time points outlined in the Schedule of Assessments (Table 3) that is somewhat flexible due to different lengths of hospitalization after surgery and depending on the needs of the patient. The following sections outline the details and procedures associated with the assessments. All specified assessments will be recorded on a source document or the medical record and appropriate data will be transcribed into electronic case report forms (eCRFs).

10.1. Adverse Events and Serious Adverse Events

The investigator and study site staff are responsible for the detection, documentation, classification, reporting, and follow up of events meeting the definition of an AE or SAE.

10.1.1. Adverse Event Definition

An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and may not necessarily have a causal relationship with the administered treatment. An AE can therefore be any unfavorable and unintended sign (including a clinically significant laboratory abnormality), symptom, or disease temporally associated with the use of an investigational product, whether or not related to the investigational product. Pre-existing conditions, diseases, or disorders are not considered AEs unless there is a change in severity or frequency. Planned surgeries will not be considered an AE.

10.1.2. Serious Adverse Events and Serious Unexpected Adverse Events Definition

An SAE is any untoward medical occurrence that meets one of the following:

- Results in death
- Is life-threatening (at the time of the event)
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect

A serious and unexpected AE is an SAE that is not identified in nature, intensity, or frequency in the risk information included in the Product Label for the drug.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the study patient and may require medical or surgical intervention to prevent one of the outcomes listed in the definition.

10.1.3. Methods/Timing for Assessing, Recording, and Analyzing Safety Endpoints

AEs will be assessed starting after the first administration of investigational product until the final follow-up at Day 30. General symptoms will be collected via an open ended question: How have you been feeling since the last time we spoke? Elicited AEs will be assessed as described in section 10.1.4.

AEs will be documented in the medical/source records, and recorded on the eCRF using accepted medical terms and/or the diagnoses that accurately characterize the event. When a diagnosis is known, the AE term recorded on the eCRF will be the diagnosis rather than a constellation of symptoms. The investigator will assess all AEs for seriousness, relationship to investigational product, and severity. When an event has not resolved by study closure, it will be documented on the AE CRF as "ongoing".

All AEs, including clinically significant abnormal findings on laboratory evaluations, regardless of severity, will be followed by study physicians until satisfactory resolution (the event either resolved or stabilized and is not expected to resolve in the near term). At the follow-up telephone contact, AEs will be recorded and followed to resolution only if they are serious, or if the study physician assesses them to be clinically significant.

10.1.4. Elicited Adverse Events

In addition to asked the open ended question regarding AEs, local application site reactions will be assessed by physical examination or querying the patient. These include the appearance of erythema or rash, or patient reported pruritus (itching).

10.1.5. Classification of Adverse Event Severity and Relationship to Investigational Product

For each recorded AE or SAE, a physician-investigator must make an assessment of severity according to the following criteria:

Mild: An event that is usually transient, requiring no special treatment, and does not generally interfere with the patient's daily activities.

Moderate: An event that interferes with usual activities of daily living, causing discomfort but poses no significant or permanent risk of harm to the patient. The event is usually ameliorated with additional specific therapeutic intervention.

Severe: An event that interrupts usual activities of daily living or significantly affects clinical status. The event poses a significant risk of harm to the patient and hospitalization (prolonged) may be required, and typically requires intensive therapeutic intervention.

Life-threatening An event that puts the patient into imminent risk of death without intervention.

The severity of application site reactions will be scored as shown in Table 4.

Table 4: Severity Rating Scale for Application Site Reactions

Reaction	Grade 0	Grade 1 - mild	Grade 2 - moderate	Grade 3 - severe
Erythema	None	Target lesions covering <10% BSA [a] and not associated with skin tenderness	Target lesions covering 10 - 30% BSA and associated with skin tenderness	Severe or medically significant but not immediately life-threatening; IV intervention indicated

Reaction	Grade 0	Grade 1 - mild	Grade 2 - moderate	Grade 3 - severe
Rash	None	Macules/papules covering <10% BSA with or without symptoms (e.g., pruritus, burning, tightness)	Macules/papules covering 10 - 30% BSA with or without symptoms (e.g., pruritus, burning, tightness); limiting instrumental ADL; rash covering > 30% BSA with or without mild symptoms	Macules/papules covering >30% BSA with moderate or severe symptoms; limiting self-care ADL
Pruritus	None	Mild or localized; topical intervention indicated	Widespread and intermittent; skin changes from scratching (e.g., edema, papulation, excoriations, lichenification, oozing/crusts); oral intervention indicated; limiting instrumental ADL	Widespread and constant; limiting self-care ADL or sleep; systemic corticosteroid or immunosuppressive therapy indicated

[a] Abbreviations: ADL = activities of daily living, BSA=body surface area. The above scale is taken from the National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0.

The investigator must make an assessment of relationship of the AE to the investigational product based on the following criteria:

Unrelated: The patient did not receive the investigational product, the temporal sequence of the AE/SAE onset relative to administration of the investigational product is not reasonable, or there is another obvious cause of the AE/SAE.

Unlikely: There is evidence of exposure to the investigational product but there is another more likely cause of the AE/SAE.

Possible: There is evidence of exposure to the investigational product, the temporal sequence of the AE/SAE onset relative to administration of the investigational product is reasonable, but the AE/SAE could have been due to another equally likely cause.

Probable: There is evidence of exposure to the investigational product, the temporal sequence of the AE/SAE onset relative to administration of the investigational product is reasonable, and the AE/SAE is more likely explained by the investigational product than by any other cause.

Definite There is evidence of exposure to the investigational product, the temporal sequence of the AE/SAE onset relative to administration of the investigational product is reasonable, the AE/SAE is more likely explained by the investigational product than by any other cause, and the AE/SAE shows a pattern consistent with previous knowledge of the investigational product or investigational product class.

10.1.6. Outcomes and Actions Taken

For each recorded AE or SAE, the investigator must make an assessment of outcome at the time of last observation, as follows:

Fatal: The patient died.

Resolved without Sequelae: The AE or SAE has ended.

Resolved with Sequelae:	The AE or SAE has ended but changes are noted from baseline.
Unresolved – Ongoing:	The AE has not ended and is ongoing at the end of the reporting period or the investigator deems that further follow up is not medically required
Unknown – Lost to Follow-up:	Lost to follow-up at least 2 repeated, documented (15 days apart) unsuccessful attempts to contact the patient.

In addition, if the AE was treated (medications or other physical measures), this will also be recorded.

10.1.7. Reporting Serious Adverse Events

10.1.7.1. 24-hour Reporting Requirements (Initial Report)

Any SAE, including death due to any cause, which occurs to any patient from the time of signing consent through the final follow-up telephone call whether or not related to the investigational product, must be reported ***within 24 hours*** of knowledge of the event by completing the AE/SAE eCRF. This will trigger an automatic notification of the SAE via an email communication to Zurex and [redacted]. [redacted] will notify the Medical Monitor upon receipt of the notification and coordinate communications with the Medical Monitor.

10.1.7.2. 3-Day Supporting Documentation Requirements

Written documentation for all SAEs must be received by Zurex and [redacted] within 3 business days of reporting the event. Required eCRFs that must be completed include the following:

- AE/SAE eCRF (revised if additional information is available)

In addition, scanned copies of the following may be requested to be uploaded to the data management system.

- Copies of medical records/source documents pertinent to the event (laboratory reports, ECG tracings, medical chart notes, etc.). These should be identified only by Patient number and not include any patient identification information prohibited by Health Insurance Portability Accountability Act (HIPAA).
- Any other relevant information necessary to support the investigator's judgment regarding the SAE's relatedness severity to the investigational product OR by request of the Medical Monitor/Alternate.

These paper documents may be submitted by facsimile, as email attachments, or by attaching them to the patient's eCRF casebook in the electronic data management system (EDMS).

10.2. Demographics

Demographics data include the patient's age, gender, race, and ethnicity. These data will be collected by site staff on a source document and onto an eCRF.

10.3. Eligibility Checklist

An Eligibility Checklist which includes all inclusion and exclusion criteria will be reviewed in after screening measures are completed and on the day of surgery prior to randomization on Study Day 1. If the patient is not eligible for the study, the reasons for ineligibility will be recorded on an eCRF. These patients will be considered screen failures.

10.4. Locator Form

After signing informed consent, patients will be asked to provide names, addresses, and phone numbers of several friends and/or family members who can be contacted if the patient cannot be located (Locator Form). This locator form will be used to assist in contacting patients after hospital discharge and at the final follow-up. This form asks patients his/her name, address, and phone number and to provide names, addresses, and phone numbers of several friends and family members who can be contacted if the patient cannot be located. This information is essential and will be collected during screening, and will be updated on the day of hospital discharge, if needed. This information will remain exclusively at the site.

10.5. Medical History

Medical history will be reviewed during screening to determine patient eligibility and also to record any past or current medical conditions including the reason for the planned surgery and the type of surgery that is anticipated. Any allergies to medications including [redacted], isopropyl alcohol, or other excipients in [redacted] Solution will also be recorded. Medical history findings will be reported on an eCRF. Childbearing potential in females and if currently breastfeeding will be recorded. Females of childbearing potential will have a pregnancy test. Pregnant or breastfeeding females will be excluded from the study.

10.6. Medications

Antibiotics taken up to 4 days prior to surgery or throughout the study until Day 30 will be recorded including the indication (i.e., prophylaxis or to treat an AE), start and stop dates, dose, route and frequency and will be reported on an eCRF.

10.7. Physical Examination

An appropriate pre-surgical physical examination will be conducted as part of screening and any relevant findings will be recorded. Post-surgical physical examinations will include signs of surgical site or other infection and other AEs such as local application site reactions (erythema, or rash). These data will be recorded on a medical record and an eCRF.

10.8. SSI Diagnosis

A study physician will evaluate the patient and medical records for evidence of SSI up to Day 30. A determination of the type of SSI (Superficial Incisional SSI, Deep Incisional SSI, and Organ/Space SSI) will be made in accordance with CDC criteria as summarized in Appendix B.

10.9. MCW/Froedtert Hospital Standard Preoperative Surgical Skin Prep Instructions

MCW/Froedtert Hospital has Standard Preoperative Surgical Skin Prep Instructions/Procedures for patients undergoing surgery that include use of an antiseptic agent before and/or the day of surgery. Additionally, the surgical pre-op staff follows standard preoperative surgical skin prepping orders the day of surgery. As per the MCW/Froedtert Hospital's standard operating skin prepping procedures, this data will be recorded in the patients eCRF.

10.10. Patient Disposition

A patient disposition eCRF will be completed for all patients who are randomized to the study. This eCRF will be used to record the following data:

1. Completion status:
    a. Patient completed full study (i.e., telephone contact was made at Day 30).
    b. Patient was lost to follow-up prior to Day 30.
    c. Patient died before Day 30.
    d. Patient withdrew consent to continued participation in the study prior to Day 30 (with reason if known).
2. Date of release from the hospital

11. Statistical Methods and Determination of Sample Size

A formal statistical analysis plan (SAP) will be finalized prior to locking the database and commencing with the analysis.

11.1. General Approach

For descriptive purposes, dichotomous and categorical variables will be presented as number of observations and percentages; continuous variables will be given as means, standard deviations (SD), median, minimum (min) and maximum (max).

All data will be presented in either a listing, summary table, or both. For summary descriptive statistics, missing data will be represented by counts, will be treated as missing at random, and no adjustments will be made. All statistical analyses will be performed using SAS version [redacted]

11.2. Analysis Sets

The full analysis set includes all patients who were randomized to study treatment, received the study treatment, and underwent surgery. The per-protocol (PP) subset includes all full analysis set patients who had final follow-up at 30 days post-surgery. The safety subset will include all patients who were randomized to the study and received a study treatment and will be analyzed as they were treated. All analyses will be performed for each analysis set.

11.3. SSI Rates

The number and percentage of patients who were diagnosed with an SSI at any time post surgery will be presented to the full analysis set and the PP analysis set. The rates by type of SSI,

superficial incisional, deep incisional, and organ space will also be summarized. A listing will be provided by patient that includes these endpoints as well as the medical findings that contributed to each diagnosis as described in Appendix B.

11.4. Antibiotic Use

The number and percentage of patients who were prescribed prophylactic antibiotics and antibiotics to treat an infection will be summarized by treatment group for each analysis set.

11.5. Preoperative Surgical Skin Prep Instructions

The number of patients prepped following the MCW/Froedtert Hospital's standard pre-operative skin prep procedures using a topical antiseptic agent will be summarized.

11.6. Safety Endpoints

11.6.1. Adverse Events

AEs will be coded using the most recent version of the Medical Dictionary of Regulatory Activities (MedDRA) preferred terms and will be grouped by system, organ, and class (SOC) designation by treatment group. The severity, frequency, and relationship of AEs to investigational products will be presented by preferred term by SOC grouping. Listings of each individual AE including start date, stop date, severity, relationship, outcome, and duration will be provided. Each AE (based on preferred terminology) will be counted once only for a given study patient. If the same AE occurred on multiple occasions, the highest severity and relationship to investigational product will be assumed. Thus, study participants are not counted multiple times in a given numerator in the calculation of frequencies for a specific AE. The frequency and severity of skin irritation or allergic reactions at least possibly attributed to each product will also be presented.

11.7. Baseline Descriptive Statistics

Summaries of the characteristics of the patients and type of surgery performed in each of the study groups at baseline will be prepared for the full analysis set, PP analysis set, and safety analysis set.

12. Quality Control and Quality Assurance

This study will be conducted in compliance with this protocol, GCP including 45 CFR 160 and 164 (Authorization for Use/Disclosure of Protected Health Information (PHI), 21 CFR 50 (Protection of Human Subjects), 56 (Institutional Review Boards), 330 (Over-The-Counter Human Drugs which are generally recognized as safe and effective and not misbranded) and Tentative Final Monograph for Health Care Antiseptic Drug Products, ICH Harmonised Tripartite Guideline E6: Good Clinical Practice, the study protocol and any protocol amendments.

Actions to ensure the accuracy and reliability of data include the selection of qualified investigators and appropriate study center; the review of protocol procedures with the investigator and study personnel prior to study start; the design of suitable source documents

with appropriate instructions for use; the internal audit of source data according to GCP and internal procedures to ensure their accuracy, completeness, and verifiability; as well as the periodic site monitoring by the Sponsor's representatives (clinical monitors). Clinical monitors will review medical records/source documents and eCRFs for accuracy and completeness during on-site monitoring visits; any discrepancies will be resolved with the investigator, as appropriate.

Significant and/or repeated noncompliance will be investigated and remedial action instituted when appropriate. Failure to comply with remedial actions may result in study site termination and regulatory authority notification.

12.1. Study Monitoring

Study monitoring will be the responsibility of designated clinical monitors [redacted]. Monitors will assure compliance with the clinical protocol and ICH GCPs, human subject's protection, drug accountability, maintenance of the site regulatory file, and conformance of CRF data with source documents. Monitoring visits by clinical monitors will be scheduled to take place at the initiation of the study, during the study at appropriate intervals, and after the last patient has completed the study. A report of monitoring observations will be provided to the PI (for corrective actions) and the Sponsor.

12.2. Audits and Inspections

Authorized representatives of the Sponsor and the IRB may visit the site to perform audits or inspections, including source data verification. The purpose of the audit or inspection is to systematically and independently examine all study related activities and documents to determine whether these activities were conducted, and data were recorded, analyzed, and accurately reported according to the protocol, GCP guidelines, and any applicable regulatory requirements.

The PI should contact Zurex Pharma if contacted by a regulatory agency about an inspection.

13. Ethics

13.1. Institutional Review Board

The study will be conducted under a protocol reviewed by the local site IRB; the study is to be conducted by scientifically and medically qualified persons; the benefits of the study are in proportion to the risks; the rights and welfare of the subjects will be respected; the physicians conducting the study will ensure that the hazards do not outweigh the potential benefits; the results to be reported will be accurate; subjects will give their informed consent and will be competent to do so and not under duress; and all study staff will comply with the ethical principles in 21 Code of Federal Regulations (CFR) Parts 50 and 56 and the Belmont Principles.

13.2. Review/Approval of Study Protocol

Zurex Pharma is the IND holder for this product and will submit the protocol to its IND. The site must obtain written approval from the IRB to conduct the study before study initiation. Zurex Pharma will issue a formal authorization letter for the study to be initiated at the site. Progress reports will be submitted to the IRB by the Investigator at the frequency requested by the IRB.

13.2.1. Protocol Modifications

All necessary protocol changes will be submitted in writing as protocol amendments to the IRB for approval prior to implementation. Zurex Pharma will submit all protocol amendments to the FDA. Protocol amendments will be approved by Zurex Pharma prior to IRB submission.

13.2.2. Protocol Deviation Reporting Procedures

All subject-specific deviations from the protocol are to be documented. The PI or designee will be responsible for identifying and reporting all deviations, which are occurrences involving a procedure that did not follow the study protocol. Any protocol deviation that adversely affects the safety or rights of a subject or scientific integrity of the study is considered a major deviation and will be reported immediately to the Zurex Pharma Project Manager and the local IRB.

13.3. Ethical Conduct of the Study

This study will be conducted in accordance with all applicable Federal human research protections requirements and the Belmont Principles of respect for persons, beneficence, and justice.

The procedures set out in this study are designed to ensure that the sponsor's representative and all study personnel abide by the principles of the ICH GCP Guideline and the CFR. The PI confirms this by signing this study protocol and Form FDA 1572.

13.3.1. Confidentiality

13.3.1.1. Confidentiality of Data

Particular attention is drawn to the regulations promulgated by the FDA under the Freedom of Information Act providing, in part, that proprietary information furnished to clinical investigators and IRB will be kept confidential by the FDA only if maintained in confidence by the clinical investigator and IRB.

By signing this protocol the investigator affirms to Zurex Pharma that information furnished to the investigator by Zurex Pharma will be maintained in confidence and such information will be divulged to the IRB or similar or expert committee; affiliated institution; and employees only under an appropriate understanding of confidentiality with such board or committee, affiliated institution and employees.

13.3.1.2. Confidentiality of Patient Records

To maintain patient confidentiality, all laboratory specimens, eCRFs, reports and other records will be identified by a patient number only. Research and clinical records will be stored in a locked cabinet. Only research staff, Zurex Pharma representatives, and [redacted] clinical monitors will have access to the records. Patient information will not be released without written permission, except as necessary for monitoring by representatives of Zurex Pharma.

By signing the protocol, the investigator agrees that within local regulatory restrictions and ethical considerations, Zurex Pharma or any regulatory agency may consult and/or copy study documents in order to verify eCRF data.

13.3.2. Compensation for Participation

There will be no compensation for patient participation in this study.

13.3.3. Written Informed Consent

The informed consent process and document will be reviewed and approved by the IRB and sponsor prior to initiation of the study. The consent document contains a full explanation of the possible risks, advantages, and alternate treatment options, and availability of treatment in the case of injury, in accordance with 21 CFR Part 50. The consent document indicates that by signature, the patient, permits access to relevant medical records by Zurex Pharma or designated clinical monitors.

A written informed consent document, in compliance with 21 CFR Part 50, 32 CFR Part 219, and the Belmont Principles, and HIPAA Authorization will be signed by the patient before any study-related procedures are initiated for each patient.

All potential subjects for the study will be given a current copy of the Informed Consent Form to read. All aspects of the study and informed consent will be explained in lay language to the patient by either the investigator, or a medically trained designee. Any patient who is unable to demonstrate understanding of the information contained in the informed consent will be excluded from study participation.

All study patients will be given a copy of the signed informed consent.

13.3.4. Delegation of Responsibilities and Adequate Resources

The PI should have adequate time to conduct the study properly and should have an adequate number of qualified staff to assist with the conduct of the study.

The term “investigator” used throughout this protocol refers to the PI and/or qualified sub-investigators. The PI may delegate responsibilities to other study site personnel. The PI shall delegate tasks only to individuals qualified by education, training, and experience to perform the delegated tasks. The PI shall have direct oversight of all delegated activities and shall document delegation of responsibilities. The PI is responsible for ensuring all delegated staff has been properly trained on the protocol and their assigned study responsibilities. A delegation log identifying all delegated duties and the individual to whom they have been delegated will be maintained at the study site.

13.3.5. Financial Disclosure

Clinical investigators are required to provide financial disclosure information for the submission of certification or disclosure statements required under 21 CFR § 54. As defined in 21 CFR § 54.2, a clinical investigator is a listed or identified investigator or sub-investigator who is directly involved in the treatment or evaluation of research subjects. The term also includes the spouse and each dependent child of the investigator. In addition, investigators must promptly update financial disclosure information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.

14. Data Handling and Record Keeping

Source documents include but are not limited to original documents, data and records such as hospital/medical records (including electronic health records), clinic charts, laboratory results, data recorded in automated instruments, and pharmacy records, etc. This study will use an EDMS [redacted]) and eCRFs provided by [redacted]. Data will be transcribed from source documentation into web-based eCRFs. The transcribed data will be consistent with the source documents or the discrepancies will be explained.

Clinical monitors will review all source records and compare them to the data entered into the eCRF. All entries, corrections, and alterations will be made by the investigator or other authorized study personnel. Any errors identified during monitoring will have a query posted by monitor for site staff to address. The EDMS system maintains a full audit trail of data entry, data corrections, and data queries.

14.1. Patient Identification and Confidentiality

Patients will be identified on eCRFs by a unique patient number. No personal identifier will be used in any publication or communication used to support this research study. The patient number will be used if it becomes necessary to identify data specific to a single patient. The Sponsor and designated clinical monitors [redacted], the IRB, and the FDA are eligible to review medical and research records related to this study as a part of their responsibility to protect human subjects in clinical research. Personal identifiers will be removed from photocopied or electronic medical and research records.

14.2. Inspection of Records

The sponsor or designee will be allowed to visit the investigation facilities for the purpose of monitoring any aspect of the study. The investigator agrees to allow the monitor to inspect the investigational product storage area, investigational product stocks, investigational product accountability records, patient records, and other records relative to study conduct.

Patients' health information is used to report results of research to the sponsor and Federal regulators and may be reviewed during study audits for compliance with study plans, regulations, and research policies. The consent document indicates that by signature, the patient permits access to relevant medical records by the sponsor's representative and by representatives of the FDA.

Upon a patient's termination from the trial, completed eCRFs will be ready and available for on-site review by the clinical monitors at scheduled monitoring visits.

14.3. Retention of Records

The investigator is responsible for creating and/or maintaining all study documentation required by 21CFR Parts 50, 54, 56, and 312, ICH E6 section 8, as well as any other documentation defined in the protocol. The investigator must provide key documents to the sponsor prior to start of the study.

Federal and local regulations require that the investigator retain a copy of all regulatory documents and records that support the data for this study for whichever of the following is the longest period of time:

- A period of 2 years following the final date of approval by the FDA or other regulatory agency of the study drug for the purposes that were the subject of the investigation; or
- A period of 5 years following the date on which the results of the investigation were submitted to the FDA or other regulatory agency in support of, or as part of, an application for a research or marketing permit for the study drug for the purposes that were the subject of the investigation.

The sponsor will notify investigators once one of the above 2 timeframes has been satisfied.

If the investigation does not result in the submission of the data in support of, or as part of, an application for a research or marketing permit, records must be retained for a period of 2 years following notification by the sponsor that the entire clinical investigation (not merely the investigator's portion) is completed, terminated, or discontinued or 2 years following withdrawal of the Investigational New Drug application/Clinical Trial Authorization or request for marketing approval (New Drug Application/Marketing Authorization Application).

If the investigator retires, relocates, or for other reasons withdraws from the responsibility of keeping the study records, custody must be transferred to a person who will accept the responsibility. The Sponsor must be notified in writing of the name and address of the new custodian. Study records should not be destroyed without consultation with the Sponsor.

14.4. Trial Registration

Zurex Pharma Inc. will register the trial on the National Library of Medicine's Clinical Trials Registry on the World Wide Web at http://www.clinicaltrials.gov.

15. Final Report and Publication Policy

[redacted] will draft and prepare the final report with input provided from the PI and Infection Control Experts reviews and approval of the report. The final report will be a record of the total study conduct and will be subject to review by Zurex Pharma, Inc. The final report will assess and summarize all data collected and include: test material identification, AE's, randomization schedules, dates of study initiation and completion, and data demonstrating SSI outcomes.

Manuscripts or presentations resulting from this study must be reviewed and approved by Zurex Pharma prior to publication.

16. References

Appendix A. Wound Classifications

Classification	Examples of Procedures
Class I: Clean Risk of infection: ≤ 2%	• Hernia repair • Mastectomy • Total hip or knee replacement • Vascular/cardiovascular procedures
Class 2: Clean/Contaminated Risk of infection: 5-15%	• Cholecystectomy (chronic inflammation) • Colectomy

From: [redacted]

Appendix B. SSI Definitions

Superficial Incisional SSI

Infection involves only skin and subcutaneous tissue of the incision

AND

Patient had at least one of the following:

1. Purulent drainage from the superficial incision
2. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision
3. Superficial incision that is deliberately opened by a surgeon, attending physician or other designee and is culture-positive or not cultured (note: a culture negative finding does not meet this criterion)

   AND

   Patient has a least one of the following signs of symptoms of infection:

   a. Pain or tenderness
   b. Localized swelling
   c. Redness
   d. Heat
4. Diagnosis of superficial by a surgeon, attending physician or other designee

Deep Incisional SSI

Infection involves deep soft tissues if the incision (e,g., fascial and muscle layers)

AND

Patient has at least one of the following:

1. Purulent drainage from the deep incision
2. A deep incision that spontaneously dehisces or is deliberately opened by a surgeon, attending physician, or other designee and is culture-positive or not cultured (note: a culture negative finding does not meet this criterion)

   AND

   Patient has at least one of the following signs or symptoms:

   a. Fever > 38°C
   b. Localized pain or tenderness
3. An abscess or other evidence of infection involving the deep incision that is detected on direct examination, during an invasive procedure, or by histopathologic or imaging test.

Organ/Space SSI

Infection involves any part of the body, excluding the skin incision, fascia, or muscle layers, that is opened or manipulated during the operative procedure

AND

Patient has at least one of the following:

1. Purulent drainage from a drain that is placed in the organ/space
2. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space
3. An abscess or other evidence of infection involving the organ/space that is detected on direct examination, during an invasive procedure, or by histopathologic examination or imaging test.

Appendix C. [redacted]