PROTOCOL COVER PAGE

Protocol Title	The effect of wound irrigation with Irrisept™ delivery system on abscess healing in patients presenting to the emergency department
Protocol Short Title	The effect of wound irrigation with Irrisept on abscess healing (Irrisept UF Study)
Sponsor Name	Irrimax Corporation, Sam Zaidspiner
Sponsor Address	1665 Lakes Parkway, Suite 102, Lawrenceville, GA 30043
Investigator (PI) Responsible for Conducting Research	Richard Petrik, MD, Clinical Assistant Professor
Research Site	University of Florida/Shands Emergency Department College of Medicine Department of Emergency Medicine 1329 SW 16th Street P.O. Box 100186 Gainesville, FL 32610 352.265.5911
Date of IRB Approval for Protocol	31 JULY 2012

EXHIBIT A

THE EFFECT OF WOUND IRRIGATION WITH *IRRISEPT™ delivery system* ON ABSCESS HEALING IN PATIENTS PRESENTING TO THE EMERGENCY DEPARTMENT

Sponsor Name and Address:
Irrimax Corporation
Sam Zaidspiner
1665 Lakes Parkway Suite 102
Lawrenceville, GA 30043

Investigator(s) (PI) Responsible for Conducting Research::
Richard Petrik, MD
Clinical Assistant Professor

Research Site:
University of Florida/Shands Emergency Department
College of Medicine
Department of Emergency Medicine
1329 SW 16th Street
PO Box 100186
Gainesville, Florida 32610
352.265.5911

- **Purpose of the Study and Background:**

Study Purpose: The purpose of this study is to *determine the effect of wound irrigation with IrriSept™ delivery system on abscess healing in healthy patients presenting to the Emergency Department (ED).*

The Specific Aims of the Study are:

1: To determine f use of pressurized irrigation with IrriSept delivery system in uncomplicated abscesses improves wound healing when compared to pressurized irrigation with normal saline.

2: To determine if use of IrriSept delivery system reduces (or eliminates) the need for oral antibiotics in patients with uncomplicated abscesses presenting to the ED.

3: To determine if use of pressurized irrigation with IrriSept delivery system in uncomplicated abscesses improves wound healing in patients that have MRSA-positive wounds compared to pressurized irrigation with normal saline.

Background: The current standard of care for the ED management of uncomplicated abscesses is to incise and drain (I&D), irrigate, and pack the wound. Oral antibiotics are commonly prescribed despite little evidence to support this practice. Based on published literature on this subject, a 6% to 16% re-infection rate occurs with this standard of care.

Since 2004, Irrimax Corporation has marketed a saline-based product (Max-101) which includes a novel compressible bottle design and splashguard. The product is used in EDs and other acute wound care sites to irrigate wounds with a pressurized dispersed stream of saline. In February 2009, Irrimax Corporation received notice that IrriSept, a new delivery system containing Chlorhexidine Gluconate (CHG), was cleared by the FDA for wound cleansing and debridement.

In early anecdotal studies conducted by Irrimax Corporation, an improvement in healing

rates and signs of infection were observed with use of these products. Most notably, a reduction in exudate from infected abscesses was observed within 24-48 hours of using IrriSept delivery system on wounds.

- **Criteria for Subject Selection:**

Number of subjects: The total number of consented ED subjects will be 628, 314 per arm. With an expected attrition rate of 66% for the return appointments, the total final number, who return for a 48-hour follow-up appointment and complete the entire study, will be 214 (n=214). The current attrition rate of subjects returning to the ED for recheck of uncomplicated abscesses at Shands/University of Florida ED is 66%.

A sample size of approximately 107 subjects in each arm will provide a power of 80% to detect a 20% improvement in subjects treated with IrriSept with an alpha of 0.05.

Gender of Subjects:

Male and female subjects will be included. Pregnant women or women who think they may be pregnant will be excluded.

Age of Subjects:

Immunocompetent patients aged 12 and older with uncomplicated abscesses will be eligible for study inclusion.

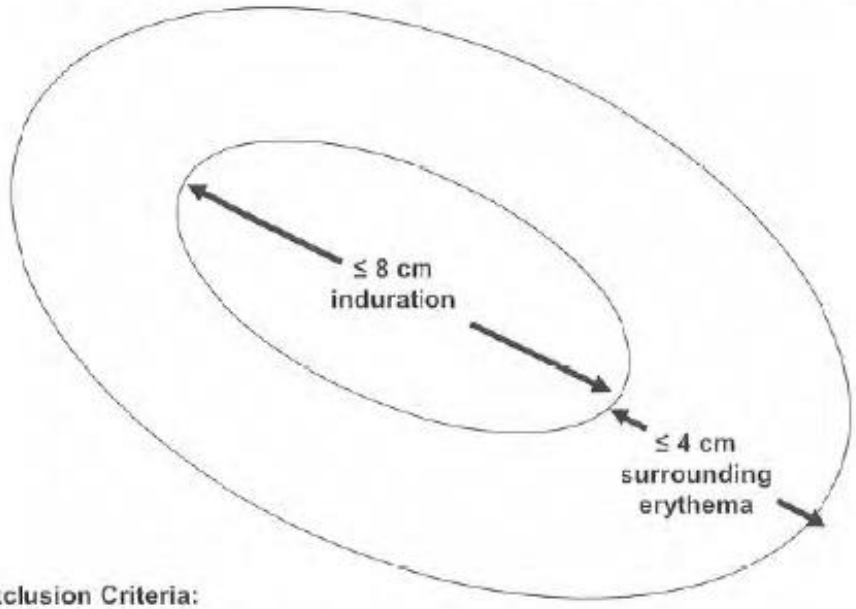
Racial and Ethnic origin:

There are no exclusions based on racial or ethnic origin.

Inclusion Criteria:

Immunocompetent individuals, 12 years of age or older, with an uncomplicated abscess are eligible for study inclusion. An uncomplicated abscess is defined as ≤8 cm of induration (defined as firmness to touch) at the greatest diameter with ≤4 cm of surrounding erythema (redness). A defined area of central fluctuance may or may not be present. Please see diagram below. The patient must be able to answer questions, be

medically stable as defined by the ED physician, and participate voluntarily in the study.



Exclusion Criteria:

Patients with any of the following are excluded:

- Currently receiving antibiotics or received antibiotics within the last 72 hours.
- Evidence of systemic infection (fever, aches, chills, nausea)
- Requires admission to the hospital for infection or for any other reason(s).
- Abscess caused by a human or animal bite.
- Prior history of hypersensitivity or allergy to Chlorhexidine Gluconate (CHG).
- Immunodeficiency (Examples: HIV Positive, Crohns Disease, Systemic Lupus Eythematosus, Addison's disease, psoriasis, splenectomy, leukemia, cancer on chemotherapy)
- Currently on any immune-modifying medication. (Examples – prednisone, antivirals)
- History of chronic skin infection (3 or more in the past year).
- Chronic medical problem, for example end-stage heart, liver, kidney or lung disease, diabetes mellitus, peripheral vascular disease, history of organ transplant
- Mental illness including but not limited to substance abuse, dementia, schizophrenia or mentally handicapped or challenged.

- Incarcerated.
- Patient is pregnant or thinks she may be pregnant.

Vulnerable Subjects:

Children older than 12 years of age, students, and employees may be included in the study, not because they are targeted, but because they may need care for abscesses.

- **Methods and Procedures:**

The study will be a prospective, randomized, controlled, double-blind, 2-arm study.

General Study Design: The two arms of the study will include an IrriSept arm and a normal saline arm. *IrriSept will be used to irrigate the abscess wound of patients in one arm of the study. In the second or normal saline arm, patients will have the abscess irrigated with normal saline using the same proprietary abscess irrigator cap in both arms.* The population will be randomly divided between the two arms. IrriMax will use a table of random numbers to randomize the study devices. Each device will be coded prior to being sent to the study site. IrriMax and the PI will have access to the code in case of an adverse event. Both IrriSept and the proprietary abscess irrigator cap are FDA cleared (Appendix A-include 510K)

Example: The randomizer indicates that bottles 3, 4, 5 contain treatment and 1,2,6 contain control or saline. The study site will use devices in order, but are blinded to treatment or control device. The informed consent forms will be numbered and the device number and informed consent number will match.

Bottle	Code	Randomizer
1	120120	control
2	120121	control
3	120121	Treatment
4	120121	Treatment
5	120122	Treatment

6	120123	control

This study will target healthy, immune-competent patients over 12 years of age with moderate abscesses that are treated on an outpatient basis. The patient who presents with an uncomplicated abscess and meets inclusion criteria will be approached for informed consent. Following consent to participate in the study, the patient will undergo abscess I &D using standard techniques and standard of care. A culture of the wound will be obtained and sent for microbiology analysis as defined by standard of care. The patient will be randomly assigned to group 1 or group 2. For the study to be double-blinded, both arms will use the same FDA-cleared device – a proprietary abscess irrigator cap for abscess irrigation. Group 1 will be irrigated with the *IrriSept* delivery system and group 2 will be irrigated with normal saline. Both study arms will undergo a saline rinse step since according to the FDA clearance, IrriSept requires the saline rinse step. Patients will have their abscesses photographed before, after initial treatment, and at each follow-up. Patients in this study will not receive antibiotics as part of their initial wound management. Those requiring antibiotics on the initial visit will be excluded from the study.

Technique: To achieve the double blind objective, the solution in both arms of the study will be applied under pressure using a proprietary abscess irrigator cap that delivers irrigant at a pressure of 7-8 psi as currently recommended. Bottles will be labeled with numbers only and codes for these numbers will be kept in the sponsor's corporate office. Study staff and patients will not be able to distinguish the control from the treatment because the solutions will look the same.

The prescribed treatment technique for both arms of the study is the following:

1: Employ universal precautions when cleansing open wounds, to include but not limited to gloves and eye protection.
2. Thoroughly cleanse the skin overlying the abscess with chlorhexidine swabs.

3: Anesthetize the skin overlying the abscess with 1% lidocaine.

4: Make a linear incision into the abscess cavity at a point of maximal fluctuance or in the center of induration if no fluctuance.

5: Insert forceps or other blunt instrument into abscess cavity and break up loculations. (if required)

6: Insert the tip of the irrigator cap into the abscess at the incision site.

7: Thoroughly cleanse entire abscess ensuring that exudate is clear and the solution contacts all inner surfaces of the abscess cavity.

8: Repeat until 450 cc of irrigant is usec and the abscess is clear of exudate.

9: Wait at least one minute.

10: Rinse the abscess using the same technique as above with an equal volume of normal saline.

11: Loosely pack the abscess cavity with plain packing strip.

12: Apply a non-occlusive dressing to the wound.

After initial treatment, the physician will complete the patient data collection form through the 'treatment" section and ensure that the patient understands the recuirements for follow-up return and immediate return for worsening. The patient will follow-up every 48 hours for repeat examination until clinical resolution. This practice of frequent follow-up is consistent with the current standard of care. At each visit, the physician will complete the patient data collection form examining for fever, wound exudate, erythema, induration, warmth, fluctuance, pain, and abscess reformation. If at the first 48-hour evaluation, the patient's abscess is in category 1 or 2 (see Wound Resolution scale below), then the clinical data collection is complete. If the patient is in category 3, 4, or 5, there will be additional data collection every 48 hours until the patient's abscess is in category 1 or 2.

If signs of worsening or systemic infection are present, appropriate antibiotic treatment will be given. If necessary, a surgical consultation will be obtained or the patient will be admitted to the hospital for further treatment. This is at the discretion of the treating physicians.

Wound Swab and Culture: The abscess cavity will be cultured at presentation to assess the types of bacteria present with specific testing for MRSA. Wound culture is consistent with the current standard of care. MRSA positive isolates will be sent to the Emerging Pathogens Institute at the University of Florida for DNA fingerprinting and identification of specific MRSA isotypes.

Data Collection: Patients will be evaluated at 48 hours and at 48-hour intervals until abscess healing. The wound will be compared to previous data collected for wound exudate, erythema, induration, warmth, fluctuance, and pain. If the patient requires antibiotics, this will be recorded. Results from the wound culture and MRSA culture will also be recorded.

Primary Outcome Measures:

Oral Antibiotics:

Oral antibiotics required at 48 hours?

☐Yes

☐No

Wound Improvement:

Wound improvement will be assessed on a 5-point Likert scale using the clinical scale outlined below.

☐ 1: Clinically resolved, no signs of active infection.

☐ 2: Markedly improved, resolving infection and healing.

☐ 3: Improved with some remaining signs of active infection.

☐ 4: Unchanged, stable without signs of worsening clinical infection.

☐ 5: Worsening conditions.

Exudate:

Exudate will be assessed using a 5-point Likert scale as outlined.

☐ 1 = none

☐ 2 = scant

☐3 = minimal

☐ 4 = moderate

☐ 5 = copious.

Patient Comfort:

Pain Scale – A subjective patient-assessed measure using a 10 cm Visual Analog Scale.

NO PAIN MOST SEVERE PAIN

Secondary Outcome Measures:

Erythema – Circle the area of redness surrounding the abscess with a marker at treatment and at follow-up. Measure the longest and shortest axes of the most lateral edges.

Abscess Size:

Initial Measurement: [cm] x [cm]

1st Follow Up Measurement: [cm] x [cm]

2nd Follow Up Measurement: [cm] x [cm]

Warmth –

☐ Yes

☐ No

Fluctuance –

☐ Yes

☐ No

Patient Data:

Prior to Treatment:

- Patient's name, phone number, gender, age, medical record number (MRN), address including zip code, name of school (if applicable), organized sports activities, and pertinent medical history. Geographic mapping techniques will be used by the Emerging Pathogens Institute at the University of Florida to track MRSA isotypes to specific schools, neighborhoods or zip codes.
- Date and time when wound noticed.

Treatment:

- The date and time of treatment.
- Additional treatments, protocol deviations, techniques, antibiotics, consult, admission, or other comments.

Data Analysis and Data Monitoring:

The Statistical package for the Social Sciences (SPSS, v 17.0) will be used for data analysis. Descriptive statistics will be recorded as means ± standard deviation or proportions as appropriate. Categorical variables will be compared using Chi-square and continuous variables will be compared with two-sided Student's t tests or analysis of variance as appropriate. For all analyses, a p value < 0.05 will be considered significant. Data Monitoring: The PI will be notified of all adverse events. There is no data monitoring committee for this study because the risk is low and no adverse events have emerged in previous cases and studies (in vivo and in vitro).

The sponsor employs a doctorally prepared registered nurse, with clinical trial/research experience, who holds an active Florida risk management license. She will provide desk top reviews for adverse events, if any.

Data Storage and Confidentiality: Information obtained in this research contains identifying patient information. Data collection forms will be secured in the ED in a locked file cabinet and removed when the patient has completed treatment (abscess in clinical stage 1 or 2) and stored in the PI's office in a locked file cabinet. The PIs office is locked at night assuring a double locked situation. Each unique patient ED visit will be assigned a code. Patient identifiers and key-codes will be kept exclusively within a password and encrypted protected spreadsheet that will be stored on the University of Florida Emergency Department server. Only those directly involved in this research will have access to the study data. Papers stemming from this work will not include identifying patient information. The key code will be destroyed at the end of the study.

Patient Data Reporting: The information from the patients will be "de-identified for research purposes" following HIPAA guidelines for the patient's privacy protection (in accordance with 45 CFR 164.502(d) and 164.514(a)-(c) of the Rule). The data will be collected on a paper copy as described above and assigned a unique identifier. De-identified forms will then be scanned and sent digitally to the sponsor.

- **Risk/Benefit Assessment:** Patient involvement in this study presents minimal risk beyond those associated with standard treatment for uncomplicated abscesses. The possibility of hypersensitivity or allergic reaction to Chlorhexidine gluconate exists but it is a dilute, topically applied solution and thus, represents minimal risk. Patients will be monitored for hypersensitivity or allergic reaction to the irrigant solution in the ED.

Potential Benefit to the Subjects: Anecdotal evidence suggests that patients currently treated with IrriSept delivery system have more rapid abscess healing than standard of care. It is possible that patients treated with IrriSept delivery system will have more rapid abscess resolution than those not treated with the experimental device.

Alternatives to Participation: Participation in this research is entirely voluntary. Subjects electing not to participate will be treated according to the current standard of care, including

I&D of the abscess.

- **Subject Identification, Recruitment and Consent/Assent:**

All patients 12 years and older presenting to the Shands/UF ED who are immunocompetent and meet inclusion criteria will be eligible for participation. Residents, Faculty and Physician extenders in the Shands/University of Florida ED will obtain written informed consent prior to patient enrollment. Eligible subjects will be informed of the study in a private area or treatment bay of the ED and allowed up to 30 minutes to decide on participation. Participation is entirely voluntary and refusal to participate will not affect medical care rendered. There will not be any threat of harm or adverse consequences if the subject does not agree to participate in the study and the information provided during the consent process will be presented in a balanced way with equal emphasis on all elements of consent (e.g. there will not be over-emphasis of benefits or under-emphasis of risks).

Only those who are cognitively able, as determined by triage personnel and the treating physician, to provide informed consent will be approached. Children age 12 years and older will be asked to provide assent and parents will provide written informed consent. Only patients with signed informed consent will be entered into the study. Informed consent documents will be retained in the PI's locked office and file cabinet.

There will be no cost to subjects for participation in the study outside of that incurred for standard of care. Sponsor will provide the study devices. Initial wound culture is part of standard of care. The patient will be mailed a $50.00 gift card as nominal token of appreciation, once the 48 hour return visit is completed.