

CLINICAL INVESTGATIONAL PLAN (CIP)

Clinical Investigation Title:	<u>Z</u> ip <u>A</u> rthroplasty <u>P</u> atient <u>S</u> atisfaction Evaluation
Clinical Investigation Acronym:	ZAPS
Clinical Investigation Number:	011
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Revision History

Date	Author	Changes
2-Oct-2017	E. Storne	Initial Release

1 Protocol Synopsis

Study Purpose:	To evaluate patient satisfaction of closure method used after joint knee arthroplasty
Study Design:	Prospective, randomized, single center study to evaluate Zip Closure Device in subjects undergoing knee arthroplasty.
Study Endpoints	Primary: Patient and Observer Scar Assessment Scale (POSAS) at 6 weeks post procedure. Secondary: Subject Experience and Satisfaction results at 6 weeks post procedure.
Subject Population:	Patients identified as candidates for knee arthroplasty and meet the study selection criteria
Number of Subjects	40
Number of Sites	Single Center
Study Procedure:	Closure Method used immediately after Arthroplasty
Device Name:	Zip Surgical Closure Device
Duration of Study	Anticipated enrollment duration to meet sample size: _____ Total Duration of Study: _____
Follow-Up Schedule	3 weeks and 6 weeks post arthroplasty surgery
Inclusion Criteria	<ol style="list-style-type: none"> 1. Patients undergoing primary elective knee arthroplasty. 2. Willing and able to provide informed consent and/or obtain legal guardian authorization 3. Willing and able to comply with the subject-specific requirements outlined in the study protocol
Exclusion Criteria	<ol style="list-style-type: none"> 1. Patients that do not meet the conditions listed in the wound closure device warnings, precautions, and contraindications (Appendix A) 2. Patients with comorbidities or conditions that the investigator deems to be ineligible for the study 3. Patients without the capacity to give informed consent (e.g., dementia)

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2 Introduction

2.1 Background

Sutures and metal staples are considered standard of care methods for surgical skin closure. The Zip® Surgical Skin Closure device from ZipLine Medical, Inc. (Campbell, CA USA) is a more recent method of skin closure that utilizes skin adhesive and adjustable ratcheting straps to achieve and maintain tension necessary for wound closure and healing. The Zip device was designated Class I, 510(k) Exempt by the US FDA in 2010, and the CE Mark was affixed in 2014. Clinical studies comparing the Zip device to staples and sutures have demonstrated several benefits, including:

- Fewer wound-related readmissions compared to staples on TKA patients¹
- Can eliminate a home health nurse visit compared to staples on TKA patients²
- 3x faster wound closure compared to subcuticular sutures on pacemaker patients³
- Superior cosmetic scar quality compared to subcuticular suture for pediatric cardiac sternotomy patients⁴
- Less patient pain during removal compared to subcuticular suture (Prolene®) for pediatric cardiac sternotomy patients⁵
- Superior protection of wound from extrinsic distraction forces compared to sutures⁶

Limited patient-reported satisfaction data exists for the Zip device as compared to staples and sutures, so this study will attempt to address this need.

2.2 Purpose of the study

To evaluate patient satisfaction of closure method used after knee joint arthroplasty. Metal staples and the Zip® Surgical Skin Closure device are approved methods in regular use. Selection of method is generally based on physician preference. This study is to determine what, if any, differences exist in patient satisfaction amongst the two methods.

¹ Alberto Carli, M.D., Sara Spiro, M.D., Alejandro Gonzalez Della Valle, M.D., Steven B. Haas, M.D. Hospital for Special Surgery - New York City, USA. Novel Non-Invasive Secure Skin Closure Following Total Knee Arthroplasty Leads to Fewer Wound Complications and No Patient Home Care Visits Compared to Surgical Staples. Presented at 2015 ISTA Conference, Vienna, Austria October 1, 2015

² *ibid.*

³ LALANI, G. G., SCHRICKER, A. A., SALCEDO, J., HEBSUR, S., HSU, J., FELD, G. and BIRGERSDOTTER-GREEN, U. (2016), Cardiac Device Implant Skin Closure with a Novel Adjustable, Coaptive Tape-Based Device. *Pacing and Clinical Electrophysiology*. Accepted Author Manuscript.

⁴ Tanaka Y1, Miyamoto T2, Naito Y2, Yoshitake S2, Sasahara A2, Miyaji K3. Randomized Study of a New Noninvasive Skin Closure Device for Use After Congenital Heart Operations. *Ann Thorac Surg*. 2016 May 31. pii: S0003-4975(16)30204-1. doi: 10.1016/j.athoracsur.2016.03.072. [Epub ahead of print]

⁵ *ibid.*

⁶ Levi K, Ichiryu K, Kefel P, et al. (October 12, 2016) Mechanics of Wound Closure: Emerging Tape-Based Wound Closure Technology vs. Traditional Methods. *Cureus* 8(10): e827. DOI 10.7759/cureus.827

3 Device Description

3.1 Device Overview

ZipLine Medical, Inc. has developed a novel, non-invasive skin closure device called “Zip Surgical Skin Closure” to replace sutures, staples and glue for closure of the skin layer for surgical incisions or laceration repair. The device is designed to provide closure speed superior to sutures, while resulting in a suture-like cosmetic outcome. Both pre-clinical feasibility study data and feedback from over 2000 human cases during the device’s commercial use in the USA suggest that these design intentions are correct. This study will test these assertions in a controlled clinical setting, with the goal of providing results with statistical significance.

The Zip device is a single use, sterile medical device.



Figure 1. Zip Surgical Skin Closure Device

The Zip Surgical Skin Closure Device is applied to clean, dry skin after deeper tension-relieving (i.e., dermal or subcutaneous) sutures have been applied.

The device adheres to the skin adjacent to an incision by use of pressure-sensitive skin adhesives. A combination of acrylic and hydrocolloid adhesives are used to provide a skin-friendly environment while providing the necessary tack to maintain skin adhesion during the recommended wear time of the device. The Zip device will be placed on the incision as the surgeon approximates the incision edges and tensions the wound by adjusting the ratcheting straps located along the device. Once the desired tension is achieved, the excess strap ends are trimmed with scissors, and a conventional absorptive dressing may be applied. The Zip will remain on the skin for 3 weeks, at which point it will be removed.



Figure 2. Adjusting Incision Closure Tension

After application, patients may shower (but not soak in a tub or pool) with the device on. The device is removed by lifting the edge of the device and gently peeling along the incision, taking care not to apply stress to the incision. If there is a risk of skin stripping, an adhesive removal agent may be used during removal.

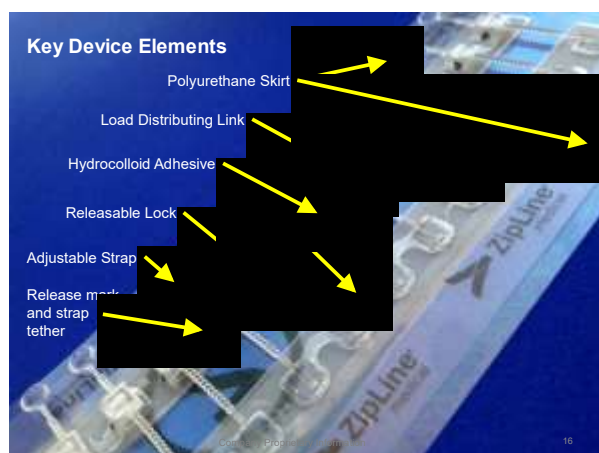


Figure 3. Key Components of the Zip Surgical Skin Closure Device

In addition to the pressure-sensitive adhesives, the device's closure and force distribution components are made up of polyurethane monofilm, polyethylene tape, polyester and nylon.

4 Regulatory Status

4.1 The Zip Surgical Skin Closure is a FDA Class I, 510(k) Exempt Device.

In 2010, ZipLine Medical, Inc. submitted a "513(g)" request for product classification to the U.S. Food and Drug Administration (FDA). In July 2010, ZipLine Medical received a letter from the FDA indicating that FDA reviewers "believe the ZipLine 1 System falls within Title 21 of the Code of Federal Regulations (CFR) 880.5240, Medical adhesive tape and adhesive bandage (Product Code- KGX). A Medical adhesive tape and adhesive bandage is a Class I type device, exempt from the premarket notification [510(k)] requirements of the Act, subject to the limitations of the exemption found in 21 CFR 880.9."

4.2 Quality System Regulations

The Zip Surgical Skin Closure Devices have been developed and are manufactured in full compliance with FDA Title 21 CFR Part 820 Quality System Regulations, including design controls, document controls, purchasing controls, identification and traceability, production and process controls, acceptance activities,

nonconforming product, corrective and preventive action, labeling and package control, handling, storage, distribution and installation, record keeping, servicing, and statistical techniques.

Origin of Manufacture: The Zip® brand Surgical Skin Closure Devices are manufactured in the USA.

Company Registration: ZipLine Medical, Inc. is registered with the FDA in compliance with Title 21 Code of Federal Regulations (CFR) Part 807, Subparts A-D.

4.3 Indication For Use

The Zip Surgical Skin Closure Device is indicated for use during and after skin incision procedures to approximate skin and hold together the skin edges until healing can take place

5 Study Design

Prospective, randomized, single center, study to evaluate Zip Closure Device in subjects undergoing knee arthroplasty.

5.1 Study Population

Patients identified as candidates for knee arthroplasty and meet the study selection criteria.

5.2 Sample Size

Knee Arthroplasty of 40 subjects will be enrolled. 20 subjects will receive ZipLine and 20 subjects will receive Staples.

5.3 Statistical Analysis Plan

General Summary

All variables of interest including subject demographics, baseline characteristics, POSAS scores and patient satisfaction of closure method used will be summarized descriptively by assigned closure groups. Mean, standard deviation, range, and Coefficient of Variation (CV) will be reported across the POSAS Scale attributes, plus comparative “t” test applied between the treatment groups across POSAS attributes. Results will include significance testing (t test) for Knee Arthroplasty study.

5.4 Study Criteria

There will be no gender-based enrollment restrictions. It is expected that the proportion of male to female subjects will be similar to the normal proportion related to the procedure type.

No vulnerable subjects shall be considered for enrollment. This includes children, pregnant women, nursing home residents or other institutionalized persons, students, employees, fetuses, prisoners, and persons with decisional incapacity.

There will be no restrictions on subject age.

There will be no restrictions or selection criteria based on subject racial and ethnic distribution.

5.4.1 Inclusion Criteria

Candidates for the study must meet all the following criteria:

1. Patients undergoing primary elective knee arthroplasty.
2. Willing and able to provide informed consent and/or obtain legal guardian authorization

3. Willing and able to comply with the subject-specific requirements outlined in the study protocol

5.4.2 Exclusion Criteria

Candidates for the study must not meet any of the following criteria. If any one of the following is met, the patient is not eligible to participate in the study.

1. Patients that do not meet the conditions listed in the wound closure device warnings, precautions, and contraindications (Appendix A)
2. Patients with comorbidities or conditions that the investigator deems to be ineligible for the study
3. Patients without the capacity to give informed consent (e.g., dementia)

6 Study Phases

The study will be conducted in phases as subjects are consented, determined eligible by meeting the study selection criteria, receive treatment and followed as standard after the arthroplasty procedure and exited from the study

6.1 Screen / Informed Consent Process

Patients considered to be eligible candidates for the study will be approached to understand their willingness and interest of volunteering for the study. The informed consent process will then be performed in the following manner:

Informed Consent

Informed consent will be obtained as outlined in 21 CFR Part 50 and the Good Clinical Practice: Consolidated Guidance (ICH, April 1996).

Eligible patients will be introduced to the study opportunity during a pre-operative visit. Patients will be given the opportunity to have their questions answered, either at the time of their visit, or after the visit via phone or email. Patients will be given the opportunity to provide consent at the time of their visit or at a later time if they need time to consider participating. A research study member at the approved study site will speak with the study candidate about the purpose of the study. Explanation of the study background, study procedure, follow up visit schedule, study procedure risks and benefits will be reviewed in detail with the patient. Patients will be given the time they need to read through the study information and informed consent document and ask as many questions as necessary to make them comfortable with the study and the requirements.

For those potential candidates who agree to participate in the study by signing the IRB approved Informed Consent Form (ICF), a baseline evaluation will be conducted. Consent may be obtained by the investigator or staff member authorized by the investigator.

If a patient does not have the capacity to give informed consent, they will be excluded from consideration for enrollment. If an enrolled subject loses the capacity to reasonably complete the study questionnaire surveys during the study, they shall be discharged from the study.

The investigator will ensure that prospective subjects have sufficient knowledge and comprehension of the information represented by the elements of informed consent to enable them to make an informed and enlightened decision whether or not to participate or allow participation in research. The investigator shall, based on clinical judgment, determine if the study candidate understood the information presented

The investigator shall be responsible for ensuring that valid consent is obtained and documented for all subjects. All study records including the completed consent forms and patient satisfaction questionnaires shall be maintained in a secure location in the investigator's clinic and handled in a manner that maintains confidentiality of the data.

6.2 Baseline Evaluation / Eligibility Determination / Enrollment

The study investigator or study staff member will conduct a formal evaluation for study eligibility which may include reviewing medical history and understanding general health. When the subject is determined eligible and scheduled for the arthroplasty procedure they will be enrolled into the study.

6.3 Random Assignment

The subject will be randomized to a closure assignment prior to the procedure. A study staff member will open a sealed randomization envelope consisting of closure assignment and a subject study identification number. The subject is considered enrolled into the study at this time and the subject disposition will be accounted for in study reports.

Subjects will be assigned in consecutive order in a 1:1 ratio for closure assignment (Metal Staples:Zip Closure Device) until all subjects are enrolled.

6.4 Procedure

Arthroplasty will be performed as standard and the assigned closure method will be applied and documented on the procedure Case Report Form (CRF). Subjects will be reminded of their follow-up visits to the study office.

6.5 Follow Up / Study Exit

The follow-up period of the study will begin after the arthroplasty procedure. All follow-up visits will be scheduled from the date of the arthroplasty procedure and should be within the study visit windows as indicated in the Table of Assessments (Table 1).

6.6 Study Evaluations and Assessments

The following assessments will be made during each study visit:

Subject Satisfaction Questionnaire – to evaluate subject experience and outcome of incision closure

POSAS (Patient and Observer Scar Assessment Scale) – the subject and investigator will rate commonly described scar characteristics from a patient and observers perspective.

Table 1: Schedule of Assessments

Assessments	Screening / Baseline	Study Procedure	3-Week Follow-Up (+/- 3 days)	6-Week Follow-Up (+/- 7 days)
Screen and Informed Consent Process	X			
Medical Hx, Demographics, Eligibility	X			
Randomization Assignment	X			
Study Procedure and Closure Method		X		
Subject Satisfaction Questionnaire			X	X
POSAS: Subject and Impartial rater Assessment			X	X
Photo of closure of incision		X	X	X
Adverse Event review			X	X
Study Exit				X

7 Subject Compensation

Participating study subjects will not incur any costs as a result of participating in the study and will not receive reimbursement or payments for participation.

8 Study Withdrawal

Subjects may be terminated or withdrawn from the study for the following reasons:

- Voluntary withdrawal – meaning that the subject voluntarily chooses not to further participate in the study
- Lost to follow-up – meaning that the subject is more than one month late (beyond the late visit window) to a study visit and 3 documented attempts to contact the subject are unsuccessful. A subject who misses a study visit but attends a subsequent visit will no longer be considered lost to follow-up.
- In the physician's opinion, it is not in the best interest of the subject to continue study participation.
- Subject death.

Any study subject who does not attend a scheduled follow-up visit should be contacted by site personnel to determine the reason for the missed appointment(s). The reason for the missed visit should be determined and documented in the subject's study records. All subjects enrolled (including those withdrawn or lost to follow-up) shall be accounted for with appropriate documentation.

9 Adverse Events

Adverse events (AEs) may occur during the procedure phase or the follow-up phase of the study. Adverse events occurring after the baseline assessment but before the arthroplasty procedure will be documented in the subject's medical record but will not count as related to the closure device.

Each adverse event will be recorded in the corresponding subject's CRF. Each adverse event will be judged by the Investigator as to its relationship and level of relatedness to the closure device. In addition, the Investigator will identify the date of onset, severity and duration of the AE. All adverse events will be monitored until they are adequately resolved or explained. If a subject reaches the final follow-up visit and is experiencing a new or ongoing adverse event, the study sponsor should be contacted to discuss the need and/or methods for continued surveillance of the event.

The Investigator must submit to the Sponsor a report of any Serious Adverse Event (SAE), Serious Adverse Device Effect (SADE) or Unanticipated Adverse Device Effect (UADE) within 24 hours of knowledge of the event.

Sponsor Contact:	Eric Storne
Telephone:	(408) 684-0747
Mobile	(650) 464-5073
Email:	estorne@ziplinemedical.com

In addition, the Investigator will report adverse events to the reviewing IRB / EC (*as applicable*) according to the local reporting requirements.

10 Study Size Determination

Knee Arthroplasty: 2 groups: Zipline to Staples (2 groups, paired data) with POSAS Scale data est. delta ~ 1.5, and Est. SD ~ 1.41

Alpha error = .05

Power = 0.9, sample n = 19 pairs, or 38 total subjects with estimated 5% subject study loss, **n = 40 total subjects, or 20 per group.**

11 Methods and Procedures

1. Study investigator and designated staff shall be trained on study procedures by the sponsor or sponsor delegate.
2. Patients shall be screened prior to surgery for study eligibility by the investigator or staff member designated by the investigator.
3. Eligible patients shall be presented with the study opportunity during a pre-operative consultation visit to the study site, and will be given the opportunity to read the informed consent form and receive answers to any questions about the study. If the patient is able and willing to participate, they will sign the consent form and become an enrolled subject.
4. Randomization will be assigned in permuted block so that even numbers of each closure method is assigned
5. Immediately after the arthroplasty procedure the assigned closure method will be applied and documented on the procedure data form

6. During the subject's scheduled (i.e., standard of care) 3-week post-operative clinic visit and immediately AFTER the wound closure device is removed (e.g., Zip or staples), clinic staff will:
 - a. Administer the first patient satisfaction questionnaire
 - b. POSAS will be performed by an impartial rater
 - c. Photograph the scar in a well-lighted room at a distance of approximately 12-14", capturing the entire scar. Ensure the knee joint is flexed at approximately 45 degrees for the photo.
7. During the subject's scheduled (i.e., standard of care) 6-week post-operative clinic visit, clinic staff will:
 - a. Administer the second patient satisfaction survey
 - b. POSAS will be performed by an impartial rater
 - c. Photograph the scar in a well-lighted room at a distance of approximately 12-14", capturing the entire scar. Ensure the knee joint is flexed at approximately 45 degrees for the photo.
8. Once enrollment is complete and all subjects have completed the patient satisfaction questionnaires, the data will be analyzed and results will be evaluated by the investigator.

12 Risk/Benefit Assessment

Risk Category. This is a minimal risk study. The probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Potential risks associated with the use of the closure methods in this study as standard of care do not differ from those commonly used for closing wounds, incisions or lacerations.

Potential risks associated with the closure methods used in this study are listed below. Subjects will be monitored closely as part of this study to allow for detection of symptoms, should they be present. This, in turn, should allow for early treatment or intervention, if necessary.

The following are side effects that may occur as a result of use of closure methods used to repair incisions after the arthroplasty procedure:

- Blistering from overtightening of the Zip Closure Device causing excessive stretch force applied to the epidermis
- Edema which can cause skin shearing, skin blistering or loss of adhesion to occur
- Skin stripping upon removal as a result of any surgical tape or adhesive applied to skin
- Allergic reaction to the adhesive product including hypopigmentation or hyperpigmentation following removal
- Infection resulting from any bacteria introduced into the incision
- Dehiscence requiring intervention
- Device failure / malfunction
- Edema
- Wound site pain / discomfort
- Excessive scarring including:
 - Step-off
 - Contour irregularities
 - Excessive distortion
 - Poor cosmetic appearance

Protection Against Risks

This is a minimal risk study. Nonetheless, all efforts will be made to minimize any potential risk. Risks will be minimized through the use of an Investigator with a high degree of experience in orthopaedic surgery. The Investigator has received sponsor-led training in proper use of the device, prior to study initiation and as warranted throughout the study. The sponsor will monitor the study for any trends that would indicate a safety

issue.

Potential Risks to Patient Confidentiality

In all clinical studies, confidentiality of protected health information may be breached due to study-related activities beyond those of routine clinical care. This risk will be minimized by not collecting personally identifying information on Case Report Forms (CRFs) or other study-related documentation to be provided to the study sponsor

Potential Benefits to the Subjects

There are no potential benefits to the subjects other than the satisfaction of having helped improve the body of knowledge on the study subject, which may lead to future preference towards a superior wound closure modality in a subsequent surgery.

Alternatives to Participation

Since this is a patient-participation survey and not an experimental study, the only alternative to participation is to not participate.

13 Quality Assurance and Supervision by Authorities

This study will be conducted in accordance with elements of E6 Good Clinical Practice Consolidated Guidance, ICH, April 1996, abbreviated requirements of 21 CFR 812.2(b) for Non-significant Risk (NSR) device studies, the Declaration of Helsinki, the Belmont Report, and IRB/EC requirements.

All documents and data shall be produced and maintained in such a way to assure control of documents and data to protect the patient's privacy as far as reasonably practicable. The Sponsor and representatives of the FDA or other regulatory authorities are permitted to inspect the study documents (e.g., study protocol, CRFs, and original study-relevant medical records/files) as needed. All attempts will be made to preserve patient confidentiality.

The clinical site is subject to audit by study sponsor personnel or designee for protocol adherence, accuracy of CRFs and compliance with applicable regulations. Any evident pattern of non-compliance with respect to these standards will be cause for corrective action.

The study protocol, data-recording procedures, data handling as well as study reports are subject to an independent clinical Quality Assurance audit by the study sponsor, its designee, or health authorities.

14 Ethical Considerations

The rights, safety and well-being of clinical investigation subjects shall be protected consistent with the ethical principles outlined in the Declaration of Helsinki. This shall be understood, observed and applied at every step in this clinical investigation.

It is expected that all parties will share in the responsibility for ethical conduct in accordance with their respective roles in the investigation. The Sponsor and the Investigator shall avoid improper influence or inducement of the patient, study monitor, clinical investigator or other parties participating in or contributing to the clinical investigation.

15 Patient Confidentiality

At all times throughout the clinical investigation, confidentiality will be observed by all parties involved. All data shall be secured against unauthorized access. Privacy and confidentiality of information about each patient shall be preserved in the reports and in any publication. Each patient participating in this study will be assigned a unique identifier. All CRFs will be tracked, evaluated, and stored using only this unique identifier.

The study site will maintain a confidential study patient list (paper or electronic) identifying all enrolled patients. This list will contain the assigned study patient's unique identifier and name. The Site Principal Investigator (PI) bears responsibility for keeping this list confidential. This list will not be provided to the study sponsor and is only to be used at the study center.

Monitors and auditors will have access to the study patient list and other personally identifying information of study patients to ensure that data reported in the CRF corresponds to the person who signed the ICF and the information contained in the original source documents. Such personal identifying information may include, but is not limited to the patient's name, address, date of birth, gender, race and medical record number.

NOTE: The patient's name, medical record number or address will NOT be recorded in the monitor's visit report or the database; demographic data that may be recorded includes age, race, and gender.

Any source documents copied for monitoring purposes by the Sponsor will have patient identifiable information redacted and be identified by using the assigned patient's unique identifier in an effort to protect patient confidentiality.

16 Data Analysis and Data Monitoring

The study sponsor or designated clinical research associate or professional, shall monitor the site regulatory study documents and study data as needed. All study records including the completed patient satisfaction questionnaires shall be maintained in a secure location in the investigator's clinic and handled in a manner that maintains confidentiality of the data. Data analysis shall be performed by the study statistician using appropriate analysis tools.

17 Data Storage and Confidentiality

All study records including the completed patient satisfaction questionnaires shall be maintained in a secure location in the investigator's clinic and handled in a manner that maintains confidentiality of the data.

18 Definitions and Acronyms

Adverse Events

Adverse Event (AE) – any untoward medical occurrence in a subject (ISO 14155).

NOTE: This definition does not imply that there is a relationship between the adverse event and the device under investigation.

Serious Adverse Event (SAE) – an adverse event that (ISO 14155):

- led to a death,
- led to a serious deterioration in the health of the subject,
- resulted in a life-threatening illness or injury,
- resulted in a permanent impairment of a body structure or a body function,
- required hospitalization or prolongation of existing hospitalization,
- resulted in medical or surgical intervention to prevent permanent impairment to body structure or function,
- led to fetal distress, fetal death, a congenital abnormality, or birth defect.

Adverse Device Effect (ADE) – any untoward and unintended response to a medical device (ISO 14155)

NOTE: This includes any event resulting from insufficiencies or inadequacies in the instructions for use or the deployment of the device. This definition also includes any event that is a result of user error.

Serious Adverse Device Effect (SADE) – an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event or that might have led to any of these consequences if suitable action had not been taken or intervention had not been made or if circumstances had been less opportune (ISO 14155).

Anticipated Adverse Device Effect (AADE) – an adverse device effect which by its nature, incidence, severity or outcome has been previously identified in the previously identified in nature, severity, or degree of incidence in the investigational plan or application

Unanticipated Adverse Device Effect (UADE) – any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects (21CFR812.3.s and ISO 14155).

NOTE: The occurrence of a diagnostic or elective surgical procedure for a pre-existing condition, unless the condition becomes more severe or increases in frequency, would not be considered procedure or device-related.

Adverse Device Effect (ADE)

See Adverse Events.

Case Report Form (CRF)

Printed, optical or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject

Confidentiality

Prevention of disclosure, to other than authorized individuals, of a sponsor's proprietary information or a subject's identity (GCP Consolidated Guidance).

Ethics Committee (EC) / Institutional Review Board (IRB)

Synonyms. An independent body constituted of medical, scientific and nonscientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trials, of protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects (GCP Consolidated Guidance).

Good Clinical Practice (GCP)

An international quality standard for conducting clinical trials that is provided by International Conference on Harmonisation (ICH) to protect trial subjects rights, safety, and welfare, as well as provide integrity to the overall study data.

Informed Consent

The process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated consent form (GCP Consolidated Guidance).

Informed Consent Form (ICF)

A document disclosing the risks, benefits, and alternatives of a clinical trial and documents the subject's voluntary willingness to participate in a clinical trial.

Monitoring

The act of overseeing the progress of a trial, and of ensuring that it is conducted, recorded and reported in accordance with the protocol, procedures and the applicable regulatory requirements.

Patient and Observer Scar Assessment Scale (POSAS)

The POSAS is a comprehensive scale that deals with the most commonly described scar characteristics from a patient and observers perspective

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Serious Adverse Device Effect (SADE)

See Adverse Events.

Serious Adverse Event (SAE)

See Adverse Events.

Source Data

All information in original and identified records and certified copies of original records of clinical findings, observations, or other activities in a clinical investigation, necessary for the reconstruction and evaluation of the clinical investigation. Source data are contained in source documents (ISO 14155 and GCP Consolidated Guidance).

Source Documents

Original documents, data and records (ISO 14155).

NOTE: This may be, for example, hospital records, laboratory notes, pharmacy dispensing records, copies or transcriptions certified after verification as being accurate copies, photographic negatives, radiographs, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical investigation.

Unanticipated Adverse Device Effect (UADE)

See Adverse Events.

Appendix A
ZipLine Instructions for Use



LA10099 Rev B

Zip[®] Surgical Skin Closure Device INSTRUCTIONS FOR USE

EN

Description

The Zip[®] Surgical Skin Closure Device is a single-use non-invasive skin closure device. The number in the device name on the label represents the maximum length of incision in centimeters that a single device may be used to close. Multiple devices may be applied end to end as needed for longer incisions, and the device may be cut for shorter incisions. The device is applied to clean, dry skin prior to skin closure. The device remains on the skin during wound healing. The device is removed by lifting one edge and peeling the device from the skin. The device is made of polymeric materials and utilizes a non-latex, pressure sensitive skin adhesive. The device contents are provided sterile in an intact and unopened package.

Caution

Federal (USA) law restricts this device to sale by or on the order of a physician.

Intended Use

The Zip[®] Surgical Skin Closure Device is indicated for use during and after skin incision procedures to approximate skin and hold together the skin edges until healing can take place.

Contraindications

- Do not use where adhesion cannot be obtained. Potential causes of inadequate adhesion are presence of exudate, skin oils, moisture or hair.
- Do not use on infected wounds.
- Do not use in high tension wounds which cannot be easily approximated with fingers or forceps.

Warnings

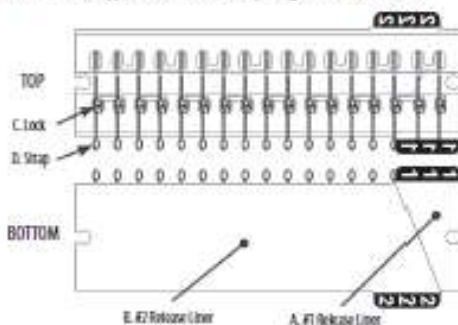
- The development of postoperative edema may cause skin shearing, skin blistering or loss of adhesion to occur.
- Application of any surgical tape or adhesive skin closure may result in skin stripping upon removal.
- As with all adhesive products applied to the skin, a small percentage of individuals may experience allergic reaction and/or hypopigmentation or hyperpigmentation following removal.
- The effect of petroleum based ointments when used in conjunction with this device is unknown.
- Do not use if device becomes damaged during the procedure. Risk of device failure if device is damaged.
- Single use device. Do not reuse. Risk of device failure or infection if reused.

Precautions

- Skin should be clean, dry and free of exudate, skin oils, excess prep residue or hair for adequate adhesion.
- If applied to regions such as joints where the skin surrounding the incision is substantially strained, carefully monitor wound closure integrity as mobility is increased.
- In areas of high body contour, the ability of the device to conform and adhere to the application site should be assessed carefully prior to application.
- Do not swim, soak the device in a bath, or allow direct, constant, shower water pressure on the device to avoid adhesive failure.
- Do not unnecessarily rub, flex or continuously lay on the closure device as this may weaken the adhesives or otherwise damage the device.
- If dressings are not used, avoid clothing edges catching or pulling on device.
- If used for a midline knee incision, apply the device with the knee at approximately 45-60 degrees of flexion.

Device Components

Illustrations in this document show a Zip[®] 16 Surgical Skin Closure device but this document may also apply to other sizes of the Zip[®] Surgical Skin Closure device.



Directions for Use

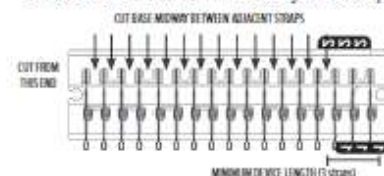
PREPARATION OF PATIENT AND DEVICE

- Remove excess hair where the device will be applied. Prepare skin per facility protocol and ensure that antimicrobial prep solution is completely dry. Remove any excess prep residue for best adhesion.
- Inspect the product and packaging prior to use. Do not use if the sterile barrier is opened or damaged, or if the product is damaged.
- Open the device pouch using sterile technique and remove the device.
- PERFORM SURGICAL PROCEDURE AND APPLY SUPPORTING SUTURES: Upon closure, apply any subcutaneous and/or deep, tension reducing sutures normally used for the procedure as appropriate. For best results, the distance between adjacent incision edges should be 5 mm or less.
- If a surgical incise barrier is used, remove the barrier film from the post-incisional skin to expose an area of skin slightly larger than the device.
- Ensure that skin is clean and completely dry for adequate device adhesion.

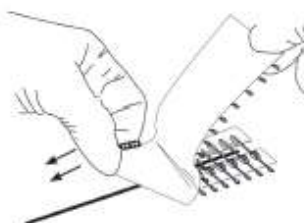
APPLY DEVICE AND CLOSE INCISION

7. OPTIONAL: CUT DEVICE FOR SHORTER INCISION

If needed, the device may be reduced in length in 1 cm increments. Use scissors to cut midway between adjacent straps, so that the resulting segment intended for use contains the #1 Release Liner (A). The minimum device length is three (3) straps.



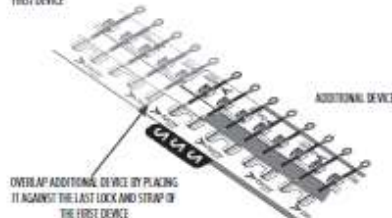
- Lift the #1 Release Liner (A) to expose the skin adhesive. Do not touch the adhesive.
- Align the device so that the end of the incision does not extend beyond the first strap. Place the exposed adhesive on skin, centered on the incision. Press firmly where the exposed adhesive contacts skin.
- Lift the distal end of the device and slowly pull the tab on the #2 Release Liner (B) with one hand while pressing the device down onto the skin with the other hand. Ensure that the device is centered on the incision. Press firmly over entire device.



11. OPTIONAL: USING ADDITIONAL DEVICES FOR LONGER INCISIONS

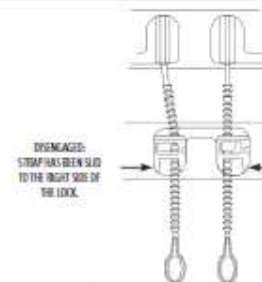
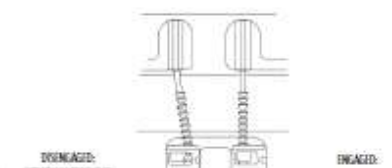
If needed, multiple devices may be applied in series as needed for longer incisions. Follow step 10 prior to placing an additional device. Apply all devices before closing incision. When placing an additional device, overlap the devices by placing the adhesive strip of the additional device next to the last lock and strap of the first device. Press firmly and continue to apply the remainder of the additional device.

FIRST DEVICE



OVERLAP ADDITIONAL DEVICE BY PLACING IT AGAINST THE LAST LOCK AND STRAP OF THE FIRST DEVICE.

- CLOSE WOUND: Close the wound by gently squeezing the device sides together and pulling on each Strap (D) until the desired incision edge approximation and closure tension are achieved. The device is supplied with all of the straps engaged in the locks. To disengage a Strap (D): note that when engaged, the strap is oriented to one side of the Lock (C); to release, slide the strap to the opposite side of the Lock (C). In the illustration below, to disengage, the strap is slid to the right side of the lock. To engage, the strap is slid to the left side of the lock until it snaps into position. Re-tension the incision as needed.



- TRIM STRAPS: Lift each strap vertically away from the skin. Lay the blade of surgical scissors flat against the top of each lock (similar to cutting excess suture), and trim the straps. It is important to trim the straps as short as possible.



- Clean the device of any residue and dry thoroughly.

DRESSING

Device may be covered with an absorbent or protective dressing if desired. Do not place dressing adhesive or tape in direct contact with the device. If contact between the wound dressing adhesive and the Zip device is possible or likely to occur (e.g. island wound dressing), then the Zip[®] DS should be used to protect the Zip from damage caused by contact with wound dressing adhesive.

INSTRUCTIONS FOR CARE

As necessary, the wound area may be rinsed and dried carefully. Patient should not swim, soak the device in a bath, allow direct, constant shower water pressure on the device or unnecessarily rub, flex or continuously lay on the closure device as this may weaken the adhesives or otherwise damage the device. If a dressing is not used, patients should avoid clothing edges catching or pulling on device. Provide patient or caregiver with the appropriate post procedure care instructions.

DEVICE REMOVAL

Patients should be advised that the device will need to remain in place until the wound/incision is properly healed (typically 7-14 days). Device removal time should be based on physician's judgement. Care should be used to not disrupt the incision during removal. To remove device, begin at one end of the incision and gently peel device along the length of the incision. Do not use excessive force or pull away from the incision. The Zip may break into separate pieces as it is removed. In aid in the removal of the device and adhesive residue, medical adhesive remover or baby oil may be used. Continuously wipe a soaked cotton ball or swab along the lifted edge of the device as it is gently pulled along the incision.

Explanation of Symbols Used

Rx Only	Federal law (USA) restricts this device to sale by or on order of a physician		Keep dry
	See instructions for use		Expiration Date
STERILE R	Sterilized Using Irradiation	REF	Catalog Number
	Latex Free	LOT	Lot Number
	Single Use Only		Legal Manufacturer
	Do not use if package is damaged or open	EC REP	EU Authorized Representative
	Keep away from sunlight and heat		Do Not Reuse

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Patent protected/pending: www.ziplinemedical.com/patents

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