CONFIDENTIAL

CLINICAL INVESTIGATION PLAN (CIP)

CLINICAL INVESTIGATION TITLE: A randomized, controlled, post-market clinical investigation to evaluate Zip Surgical Skin Closure Device in comparison of using Standard of Care sutures for Laceration Repair in Pediatrics in an Ambulatory and Emergency Department
CLINICAL INVESTIGATION CODE:
INVESTIGATIONAL DEVICE: Zip® 4 Surgical Skin Closure Device
PRINCIPLE INVESTIGATOR: Dr Uri Balla , Director of Pediatric emergency medicine Kaplan Medical Center Reovot, Israel
SPONSOR: ZipLine Medical, Inc. 747 Camden Ave., Suite A Campbell, CA 95008 USA
DATE:

Version	Revision history
מתאריך 2 13/07/2018	

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1 SYNOPSIS

NAME OF THE SPONSOR:
ZipLine Medical, Inc.
747 Camden Ave., Suite A
Campbell, CA 95008
USA

CLINICAL INVESTIGATION TITLE:
A randomized, controlled, post-market clinical investigation to evaluate Zip Surgical Skin Closure Device in comparison of using Standard of Care sutures for Laceration Repair in Pediatrics in a Pedaitric Emergency Medicine Department

CLINICAL INVESTIGATION CODE:

INVESTIGATIONAL DEVICE:

Zip® 4 Surgical Skin Closure Device

AIM:
To evaluate the Zip 4 Surgical Skin Closure Device in a pediatric population requiring laceration repair in an Emergency department.

OBJECTIVES:
Primary Objective

- The primary objective of this clinical investigation is to evaluate the time and costs savings of the Zip 4 Surgical Skin Closure Device in comparison to conventional sutures used in a pediatric population presenting for laceration repair.

Secondary Objective

- The secondary objective of this clinical investigation is to evaluate the satisfaction and outcomes of the Zip 4 Surgical Skin Closure Device in comparison to conventional sutures used in a pediatric population presenting for laceration repair.

OVERALL CLINICAL INVESTIGATION DESIGN:
A prospective, randomized, controlled post-market clinical investigation that will enroll pediatric subjects requiring laceration repair. The investigation population will consist of 30 subjects fulfilling the eligibility criteria for the clinical investigation. The subjects will be randomly assigned at a 1:1 ratio to either the Zip 4 Surgical Skin Closure Device group or the Standard of Care sutures group. The duration of the investigation is estimated to 6 months, including a 5-month recruitment period and 1-month follow up period.

INCLUSION AND EXCLUSION CRITERIA:
Inclusion Criteria
The subjects have to meet all of the following criteria to be eligible to participate in the clinical investigation:

1. Between 4 to 18 years of age at the time of laceration repair.
2. Require suture closure as standard of care for simple straight wounds on trunk or extremities or face up to 4 cm long.
3. Low Tension Laceration, e.g. skin can be easily approximated by pinching with fingers.
4. Subject and legal representative(s) are willing and able to comply with the investigational device removal and meet the follow up visit requirements.
5. Subject and legal representative(s) have been informed of the nature, the scope and the relevance of the study.
6. Subject and legal representative(s) have voluntarily agreed to participation and have duly signed the Informed Consent Form.

Exclusion Criteria

Subjects meeting any of the following criteria will not be permitted to participate in the clinical investigation:

1. Known personal or familial history of scar hypertrophy.
2. Known or suspected allergies or hypersensitivity to non-latex skin adhesives.
3. Atrophic skin deemed clinically prone to blistering.
4. Wounds that are easily susceptible to infection as a result of exposure to unsanitary conditions ("dirty wounds").
5. Wounds that require deep dermal closure using sutures.
6. Known or suspected mental problems and/or aggressiveness that indicates that the subject might try to remove the device during the treatment period.
7. Participating in any other clinical investigation.
8. Known health condition that would affect healing in the opinion of the investigator.
9. Any subject that according to the Declaration of Helsinki is deemed unsuitable for study enrolment.

PERFORMANCE AND SAFETY ENDPOINTS:

Primary Endpoint (performance)

- The primary endpoint in this clinical investigation is the mean difference in time to wound closure for the two treatment methods used. These include total treatment time and duration of period starting from the preparation of procedure until protective wound dressing is applied, and including whether or not sedation was used when comparing the Zip 4 Surgical Skin Closure Device and the Standard of Care closure suturing.

Secondary Endpoints (performance)

- Difference in Wound Evaluation Score at 10 days and 30 days post-treatment compare to baseline when comparing scar satisfaction and appearance of the subjects receiving Zip 4 Surgical Skin Closure Device versus Standard of Care closure suturing. The score will be based on digital photographs taken on day 0, day 10 and day 30 and made by an independent panel of blinded physician(s).
- Rate of wound healing satisfaction in subject at 30 days post-treatment when comparing Zip 4 Surgical Skin Closure Device versus Standard of Care closure suturing. The endpoint will utilize a questionnaire for the subject to fill out.
- The level of pain in connection to device application and removal measured by a visual analog scale (VAS) 0-100 mm.

Secondary Endpoint (safety)

- The incidence and severity of adverse events associated with the Zip 4 Surgical Skin Closure Device and Standard of Care closure sutures.

STATISTICAL METHODS:

Performance Analysis and Safety Analyses

Statistical analysis on variables of interest, include subject demographics, baseline characteristics, effectiveness and safety endpoint (adverse events), will be summarized descriptively by randomization arm. A "t" Test will be applied for testing the Hypothesis of the two closure methods, including "p" values for statistical significance. Mean, standard deviation, range, and Coefficient of Variation (CV) will be reported for closure times for both the two closure treatment methods of Suture and Zip for the primary endpoint. For the secondary endpoints, mean, standard deviation, range, and Coefficient of Variation (CV) will be reported for the VAS scale data. Additional analysis will be reported per the attribute satisfaction survey criteria obtained from subject satisfaction data at the 30 day follow-up interval. This will include an analysis of Average Satisfaction Scores, summary statistics, plus a histogram analysis comparing subject satisfaction data for both treatment groups of SoC sutures and Zip 4 device.

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3 DEFINITIONS AND ACRONYMS

ADE	Adverse Device Effect
AE	Adverse Event
ASADE	Anticipated Serious Adverse Device Effect
CA	Competent Authority
CIP	Clinical Investigation Plan
CIR	Clinical Investigation Report
CV	Coefficient of Variation
CRF	Case Report Form
CRO	Contract Research Organization
DEHP	di-(2-ethylhexyl)phthalate
DD	Device Deficiency
DMC	Data Monitoring Committee
DMP	Data Management Plan
DMR	Data Management Report
DVP	Data Validation Plan
EEA	European Economic Area
EU	European Union
FAS	Full Analysis Set
FDA	Food and Drug Administration
ICF	Informed Consent Form
IEC	Independent Ethics Committee
ISO	International Organization for Standardization
MDD	Medical Device Directive
PI	Principal Investigator
PIS	Patient Information Sheet
PPS	Per Protocol Set
Residual Risk	Risk remaining after risk control measures has been taken
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDV	Source Data Verification
SoC	Standard of Care
SOP	Standard Operating Procedure
USADE	Unanticipated Serious Adverse Device Effect
VAS	Visual Analog Scale
Zip device	Zip Surgical Skin Closure Device
WMA	World Medical Association

4 INTRODUCTION

4.1 Background

Every year a significant number of lacerations are managed at the Pediatric Emergency Room (1). Lacerations require proper skin closure in order to heal properly with good cosmetic outcome. Sutures are a common method for laceration closure [2]. With proper preparation of the wound, skilled procedure and compliant post-procedure wound care, outcomes tend to be favorable with good cosmetic outcome. Nevertheless, suturing takes significant time and may require a high degree of skill and experience [3]. The application of sutures may require multiple injections of anesthesia into the wound site, which may cause anxiety in patients, particularly in children [4]. For a child, the thought of needles and sutures may be worse than the actual injury itself. In some cases, pediatric patients may require sedation to reduce anxiety. In the patient-centered health care, it is a matter of course to increase patient satisfaction. One step in this direction might be to replace suturing with non-invasive methods.

According to current clinical routines, suturing should in most cases be performed by physicians [5]. It therefore takes significant resources (time and personnel) to treat a laceration. From diagnosis, consultation, anesthesial injections and sedation (if required) until suturing, it can take more than one hour. Pediatric emergency departments often have a stressful environment with many patients to treat and it would be valuable if this process could be shortened. In addition, treated children may prefer to remove the sutures at a clinic even if it is usually not required with a follow up visit. This additional visit takes time for the medical staff, the child and the parent/guardian. Hence, a faster and more efficient treatment might reduce time and resources, allowing more patients to be treated at the Emergency departments.

ZipLine Medical, Inc. has developed a novel, non-invasive skin closure device called “Zip Surgical Skin Closure Device” (Zip device) as an alternative to conventional sutures, staples and glue for closure of the skin for surgical incisions or laceration repair. The Zip device is a single use, sterile medical device that is designed to provide closure speed superior to sutures, while resulte in a suture-like cosmetic outcome [6]. Feedback from post-market surveillance and evidence from published clinical studies suggest that these design intentions are correct [7].

The Zip device has been commercially available since April 2013, with over 100.000 clinical cases in 30 countries in orthopedics, electrophysiology, dermatology, plastic and reconstructive surgery, vascular surgery, obstetrics and gynecology, and emergency medicine. Thus, the Zip device is not restricted to any particular procedure, and not either to a patient population. Randomized clinical investigations using the Zip device for skin closure in pediatric patients [6] as well as elderly patients [8] have demonstrated good clinical outcome.
Not only has previous studies showed to reduce the time in wound closure, but also that the Zip device is less painful during removal which might be especially beneficial for a pediatric population [6]. The CE-mark of the Zip device was affixed in 2014 and the device is commercially available in Sweden today.

This clinical investigation is designed to evaluate the time and costs savings and the satisfaction and outcomes of the Zip device when used in a Pediatric emergency department setting for repair of lacerations in a pediatric population. Previous studies have mainly showed the benefits when using the Zip device on surgical incisions, both in adults and pediatric patients, but not in a pediatric population requiring laceration repair. The investigation subjects will be

randomized to receive either the Zip device or standard of care wound closure using sutures for 10 days. All subjects will be followed up for 30 days after treatment.

4.2 Clinical data

Previous clinical data, both from randomized investigations, case studies and evaluations, have shown the value of the Zip device in terms of ease of use in a timely manner, good cosmetic outcome and high patient satisfaction.

In 2013, a prospective case study was performed on subjects with skin excisions [9]. The results revealed that the Zip device was easy to use in a time efficient way with no requirements of advanced training to use the device effectively. The cosmetic outcome was good and high patient satisfaction with low ratings of pain during removal. No device-related complications were reported indicating the high safety of using the device.

In 2014, a randomized clinical investigation was performed to compare the Zip device with conventional suturing on patients with basal cell carcinoma, squamous cell carcinoma or dysplastic nevi [10]. The outcome indicated that the Zip device has equivalent cosmetic results as conventional suturing while being more time efficient regarding application and removal. Additionally, the study showed that the device can be removed by the patient, hence eliminating the need for a follow up visit for device removal.

During 2014 and 2015 a randomized clinical investigation was performed on pediatric patients who underwent cardiac operations [6]. The patients either received the Zip device or standard of care sutures as wound closure. The results showed that the greatest advantages with using the Zip device compared to sutures are the good cosmetic outcome and the reduced closure time. In addition, the Zip device was less painful during removal which can be particularly beneficial for a pediatric population.

Another randomized clinical investigation was performed in 2015 where the Zip device was compared with subcuticular sutures on patients undergoing cardiac implantable electronic defibrillator [8]. Results indicated significant time savings when using the Zip device instead of sutures, although scar outcome, pain ratings and patient satisfaction were similar in both groups.

A prospective evaluation was performed in 2015 on patients undergoing total knee arthroplasty and received the Zip device as skin closure system [11]. The results were compared to historical data of patients receiving sutures as wound closure. The outcome showed that the Zip device was easier to apply, had fewer wound complications, and that the device could be removed without a home care visit.

In 2015, a case study was performed on two patients that received wound closure with the Zip device after pacemaker/implantable cardioverter defibrillator surgery [12]. The results showed the device to be especially useful in treatments of infection-prone patients. It was easy both to apply and remove and had a good cosmetic outcome.

Investigations have also been performed to evaluate the Zip device in comparison to staples. In 2015, a randomized investigation was performed on subjects that underwent total knee arthroplasty and thereafter received wound closure in terms of either the Zip device or staples

[13]. Pain score, cosmetic outcome and wound complication rate were compared between the two groups. The Zip group showed less pain especially during removal of the device and better cosmetic outcome. There was no significant difference in wound complication rate between the two groups.

In 2015, a case study was performed on a high-risk patient following total knee arthroplasty with knee surgeries over a 10-year period [14]. During the fourth revision surgery, the Zip device was selected as closure of the incision instead of staples due to the patient's previous experience of severe pain when removing staples. The treatment with the Zip device showed good cosmetic outcome with a comfortable removal and no additional pain for the patient.

5 IDENTIFICATION AND DESCRIPTION OF THE INVESTIGATIONAL DEVICE

ZipLine Medical, Inc. has developed a novel, non-invasive skin closure device, Zip device, to replace sutures, staples and glue for closure of the skin layer for surgical incisions or laceration repair, see *Figure 1*. The device is a CE-marked, single use, sterile medical device that is designed to provide closure speed superior to sutures, while resulting in a suture-like cosmetic outcome.

The device is a class IIa device as per Annex II of the MDD 93/42EEC, as amended by Directive 2007/47/EEC. A CE-mark was affixed in 2014.

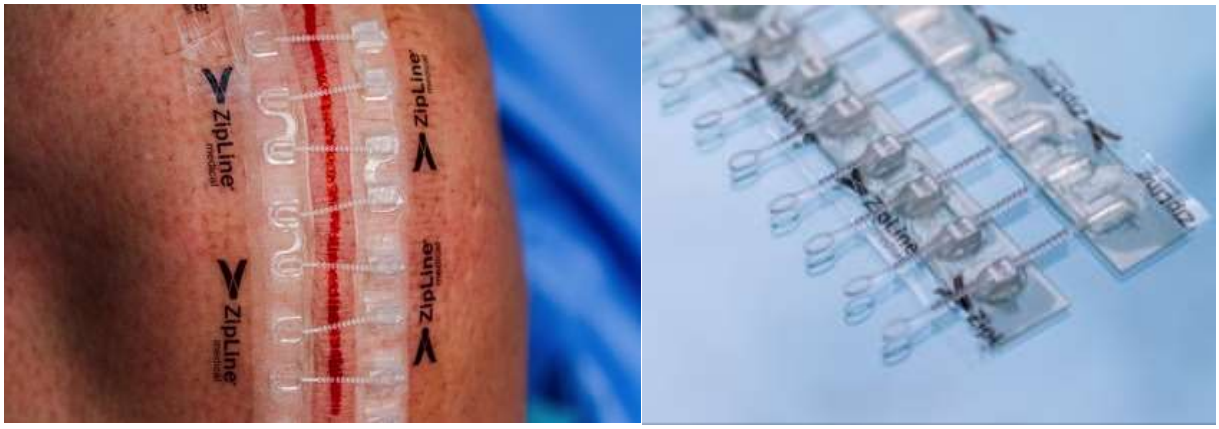

Figure 1. Illustrations of Zip Surgical Skin Closure Device.

The Zip device adheres to the skin adjacent to an incision or laceration by use of pressure-sensitive skin adhesives. A combination of acrylic and hydrocolloid adhesives is used to provide a skin-friendly environment while providing the necessary tack to maintain skin adhesion during a maximum wear time of 14 days. 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. *Figure 2* illustrates the key elements of the Zip device.

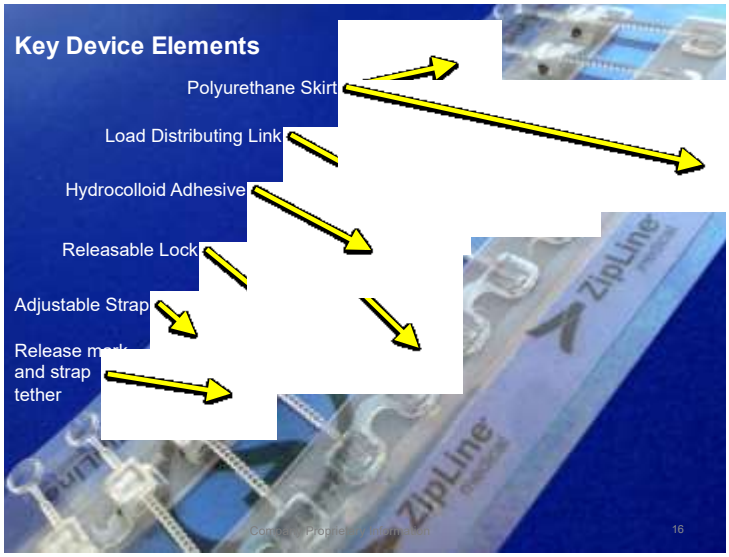

Figure 2. Key components of the Zip Surgical Skin Closure Device.

5.1 Manufacturer

Material fabrication, assembly, packaging and sterilization are all conducted by or for ZipLine Medical, Inc. in the USA.

ZipLine Medical, Inc. authorized representative in the EU is:
Emergo Europe
Molenstraat 15
2513 BH The Hague
The Netherlands

5.2 Identification of clinical investigational medical device

Several different sizes (lengths) of the Zip device are available. In this clinical investigation, the smallest (4 cm) model will be used, Zip® 4 Surgical Skin Closure Device (Zip 4 device).

The Zip devices are provided sterile, each in a sealed pouch designed for aseptic handoff in a sterile field. The devices are provided in boxes of 10 individually packaged devices, and a copy of the Instructions For Use (IFU) accompanies each box of 10 devices.

Each device label includes the device name, part number, lot number and expiration (use by) date. In addition, each individual packaged Zip 4 device to be used in this clinical investigation will be marked "For Clinical Investigation Only, Zip-009".

The Zip 4 devices will be delivered by the Sponsor to the clinical investigation site.

5.3 Device accountability/traceability

The Sponsor and site personnel will keep records documenting the location of all investigational devices from shipment to the site, usage at the site, and return to the Sponsor (if applicable). This will be documented by a shipment log at the Sponsor and in a device accountability log at the investigation site. The device accountability log at site will include the following information:

- Date, Lot No and Expiry date for each delivered device
- Date and Subject No for each dispensed device
- Date for each device returned to sponsor from site (if applicable)

The investigational devices will be handled and stored safely, properly and in agreement with the provided storage conditions. Returned and unused investigational devices are accounted and returned to the Sponsor.

The monitor will verify the accountability process at each site during the site monitoring visits.

5.4 Intended purpose

The Zip device is a CE-marked medical device intended for surgical incisions or laceration repair to approximate skin and hold together the skin edges until healing can take place. In this investigation, the Zip 4 device will be used for laceration repair in a pediatric population.

5.5 Indication and population

The Zip device is not restricted to any particular procedure or patient population. In this investigation, male and female subjects age 4 to 18 that present to the pediatric emergency department with a need of laceration repair and meet CIP eligibility criteria will be enrolled.

5.6 Manufacturing and materials

The material fabrication, assembly, packaging and sterilization of the Zip device are all conducted by or for ZipLine Medical, Inc. The materials used for the different parts of the Zip device is described in *Table 1* below.

Table 1. Detailed description of the material used on the Zip device.

Part of the Zip device	Material
Skin Adhesive	Hydrocolloid and Acrylic
Plastic Film	Polyurethane
Adjustable Straps and Locks	Injection-Molded Nylon
Release Liner	Bottom: Polyethylene, Top: Paper

No latex or di-(2-ethylhexyl)phthalate (DEHP) are used in the manufacturer of the Zip device.

5.7 Training and experience

Investigator and site personnel training will take place prior to subject enrollment to ensure that the Zip 4 device is used in accordance to the IFU, that complete, accurate and timely data are submitted, that protocol requirements are followed and that complications, adverse events and adverse device effects are correctly reported and investigated, as appropriate. The Investigator will ensure that appropriate training relevant to the clinical investigation is given to any other site personnel involved in the investigation and that new information of relevance to the performance of the investigation is forwarded to the staff involved. Staff involved in the research will be trained by use of a laceration simulation model and by application of the device on healthy volunteers.
Staff involved in application of the device or sutures and its removal will be comprised of pediatric emergency physicians will clinical experience in laceration repair.

It is the responsibility of Sponsor to ensure that involved staff is appropriately trained on the Zip 4 device.

5.8 Installation and use

The installation and use of the Zip 4 device shall be done according to the IFU. The Zip 4 device shall be applied to clean, dry skin. After application of the device, the Investigator approximates the laceration edges and tensions the wound by adjusting the ratcheting straps located along the device, see *Figure 3*. Two to three clicks on the straps will provide light tension. Once the desired tension is achieved, the excess strap ends are trimmed as short as possible using scissors. A conventional absorptive dressing will be applied. After application of the device the applying physician will judge the result (Approxiamtion. Eversion, Aversion etc) and if they will not be optimal the device will be removed and the subject will be treated by the standart of care using plain sutures.

Figure 3. Adjusting Laceration Closure Tension.

In this investigation, the Zip 4 device will remain on the skin for 10 days (+/- 2 days), at which point it will be removed. During this time, the subject may not use ointments containing petroleum as well as soak in a tub or a pool with the device on. Furthermore, the subject should not rub or continuously lay on the device since this may weaken the adhesives or damage the device. Further information is described in the IFU, and will also be explained orally for all participating subjects and their legal representative(s) prior discharge.

If at the first follow up at 10 days (+/- 2 days) the treating physician will find a reason to leave the device for additional time to avoid gapping of the wound a new follow up for removal after the extra needed time appreciated by the physician will be set.

The Zip 4 device is removed by lifting the edge of the device and gently peeling along the laceration, taking care not to apply stress to the laceration. If there is a risk of skin stripping, an adhesive removal agent may be used during the removal.

6 JUSTIFICATION OF CLINICAL INVESTIGATION DESIGN

The Zip device is not restricted to any specific procedure or patient population. Previous investigations have been performed on both young and elderly patients with incisions. Another

group of interest is children with lacerations; hence, this study will evaluate the Zip device in a pediatric population with lacerations presented to the Emergency department.

Current practice of suturing in pediatrics is associated with anxiety and often requires sedation. Potential benefits of the Zip device in this population includes reduced anxiety and no need for sedation. Treatment is expected to be easier and faster compared to suturing, efficiency and patient flow will be increased and satisfaction in the pediatric population will be higher.

In order to answer the proposed hypothesis, that the wound closure procedure with the Zip 4 device will result in a mean time that is significantly decreased compared to current standard of care for laceration repair, a prospective, randomized controlled investigation will be performed.

Random treatment assignment will be used to minimize the risk of selection bias and to assure that the Zip 4 group and Standard of Care (SoC) group will be similar at the start of the investigation. The SoC group will be allocated from the same subject population as the Zip 4 group.

Since the Zip 4 device is a CE-marked medical device that will be used within its current intended use, a post-market clinical follow-up design has been deemed appropriate. As such, the clinical setting for this investigation will be in accordance with clinical routine at the investigational site including, but not limited to, preparation of subjects, as well as laceration closure (SoC group) and post-procedure care. The duration of the follow up has been set to 30 days to include both healing period until removal of device and after an additional follow up period.

7 RISKS AND BENEFITS OF THE INVESTIGATIONAL DEVICE AND CLINICAL INVESTIGATION

The risk management related to the Zip device has been conducted in accordance with ISO 14971 and included risk analysis and risk evaluation, risk control and pre-production and post-production review. The risk management process is further described in the risk management report (ref doc RE10100 Rev G).

7.1 Anticipated clinical benefits

The potential benefits of the Zip device over standard of care closure include:

- Improved cosmetic outcome
- Greater patient satisfaction
- No skin piercing
- Reduced procedure time
- Rapid one-person closure time
- Eliminate need for skin sutures
- Improved staff safety – reduced needle stick

The investigation is intended to measure the result of some or all of these benefits.

7.2 Anticipated risks with the device

Complications that may occur include:

- Allergic response
- Infection
- Dehiscence requiring intervention
- Post-operative edema that may cause shearing or blistering
- Wound site pain/discomfort
- Skin stripping upon removal
- Hypo/hyperpigmentation upon removal
- Excessive scarring including:
    - Step off
    - Contour irregularities
    - Excessive distortion
    - Poor cosmetic appearance

Previous evaluations have not shown any additional risks in comparison to those associated with existing wound closure methods [6]. Any adverse event, related as well as un-related to the device, will be reported in the CRF during this investigation and included in the Safety Analysis.

7.3 Residual risks

The residual risks that may occur include:

- The development of post-operative 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.

The described residual risks are understood risks associated with a non-invasive device intended for the closure of wounds.

7.4 Risks associated with participating in the clinical investigation

There are no additional risks to the subjects by participating in this clinical investigation than there would be if the subject was treated with the investigational device (or standard of care) under non-investigational settings. When comparing the risks towards the benefits of using the Zip device, all identified risks are considered to be acceptable. The Zip device is a CE-marked device delivered with IFU and will be used by trained, professional medical staff with experience in using the device as well as standard of care wound closure procedures. The reporting of adverse events and monitoring described in *sections 18* and *11*, respectively, will assure early detection of any increased risk or un-anticipated subject safety concerns.

7.5 Possible interactions with concomitant medical treatments

Subjects participating in the investigation should not use petroleum-based ointments in conjunction with the investigational device since the effects are unknown. No other interactions are anticipated between treatment with the investigational device and concomitant medications and therefore there are no further restrictions of concomitant medications.

7.6 Risk control

The Principal Investigator (PI) will ensure that appropriate training relevant for the investigation is given to the site personnel involved. The Sponsor will provide sufficient training on the specifics of the Zip device prior study enrollment to minimize the risks associated with the device. If needed, the Sponsor will visit the site several times during the investigation for training purpose.

The Investigator and the site personnel will give care instructions to the participating subjects and their legal representatives prior discharge to minimize the risks after the device is placed and during the follow up period.

7.7 Risk-to-benefit rationale

In summary, when compared to the benefits of using the Zip device, there are no unacceptable risks of harm for the subject when used under normal conditions and within its intended use.
The Zip 4 device is supplied with an IFU and the site personnel will be trained on the device, as well as subjects and their legal representatives that will be informed prior discharge about using and handling of the device. Based on this assessment the benefits related to the use of the Zip device have been shown to exceed the risks for the subjects in this clinical investigation.

8 OBJECTIVES AND HYPOTHESES OF THE CLINICAL INVESTIGATION

8.1 Primary Objective

The primary objective of this clinical investigation is to evaluate the time and costs savings of the Zip 4 Surgical Skin Closure Device in comparison to conventional sutures used in a pediatric population presenting for laceration repair.

8.2 Secondary Objectives

The secondary objective of this clinical investigation is to evaluate the satisfaction and outcomes of the Zip 4 Surgical Skin Closure Device in comparison to conventional sutures used in a pediatric population presenting for laceration repair.

8.3 Hypothesis

The hypothesis for the primary endpoint is:
H_0: Mean time for Zip 4 device wound closure procedure = Mean time for standard of care sutures wound closure procedure
H_1: Mean time for Zip 4 device wound closure procedure ≠ Mean time for standard of care sutures wound closure procedure

8.4 Claim of the investigational device to be verified

Claim: Zip device significantly reduces treatment time of lacerations in pediatric population, and the significant reduction translates to a cost reduction for the A&E departments.

The primary endpoint will verify the time reduction of using the Zip device compared to standard of care sutures.

The second endpoints will verify:

- Physician and subject satisfaction of scar outcome and wound healing.
- Pain assessment during application and removal of device.

9 DESIGN OF THE CLINICAL INVESTIGATION

9.1 General

This is a prospective, randomized, controlled post-market clinical investigation to compare the use of Zip 4 device to standard of care skin closure sutures in pediatric subjects requiring laceration repair. 30 subjects will be recruited

The investigation consists of one screening/baseline visits at day 0 and 2 follow ups at day 10 and day 30 (*Figure 4*). After written informed consent has been acquired at the screening/baseline visit the subject will be evaluated and checked for eligibility by a pediatric emergency physician with clinical experience and expertise in laceration repaiar . An eligible subject will be randomized (1:1) to either test or SoC group. Subjects in the test group will be treated with the Zip 4 device, and subjects in the SoC group will instead be treated with conventional sutures as wound closure. After treatment, the subject is scheduled for follow up 10 days and 30 days post-treatment. At day 10 follow up study personnel will remove the Zip device or sutures. During both follow up calls at day 10 (after removal of device) and day 30, the subjects are assessed for the outcome of the laceration repair though subjects interviews and questionnaires filled out by the subject with help of their legal representative(s), if necessary. In addition, a blinded panel of 2 independent plastic surgeons will evaluate the cosmetic outcome of the laceration repair by reviewing digital photographs taken at screening/baseline visits versus 10 days and 30 days follow up.
The investigation consists of one screening/baseline visits at day 0 and 2 follow ups at day 10 and day 30 (*Figure 4*). After written informed consent has been acquired at the screening/baseline visit the subject will be evaluated and checked for eligibility. An eligible subject will be randomized (1:1) to either test or SoC group. Subjects in the test group will be treated with the Zip 4 device, and subjects in the SoC group will instead be treated with conventional sutures as wound closure. After treatment, the subject is scheduled for follow up 10 days and 30 days post-treatment. At day 10 follow up study personnel will remove the Zip device or sutures. During both follow up calls at day 10 (after removal of device) and day 30, the subjects are assessed for the outcome of the laceration repair though subjects interviews and questionnaires filled out by the subject with help of their legal representative(s), if necessary. In addition, a blinded panel of 2 independent plastic surgeons will evaluate the cosmetic outcome of the laceration repair by reviewing digital photographs taken at screening/baseline visits versus 10 days and 30 days follow up.

The overall duration of the clinical investigation is anticipated to be 6 months, including a 5-month enrollment period.

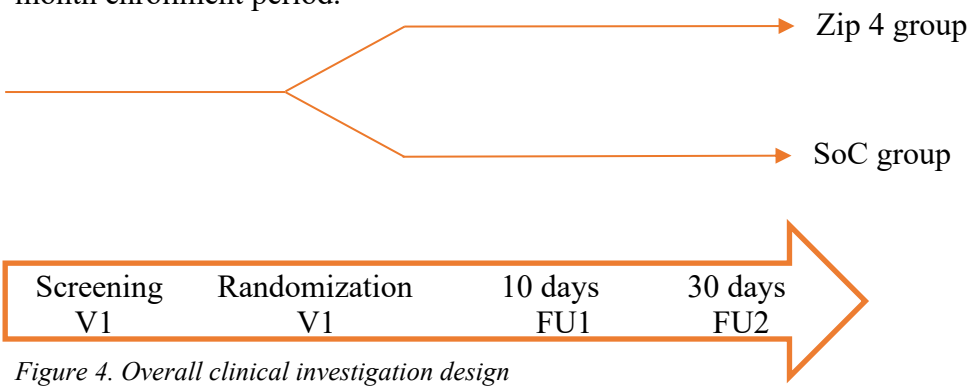

Figure 4. Overall clinical investigation design

9.2 Primary Endpoint (performance)

The primary endpoint in this clinical investigation is the mean difference in time to wound closure, for the two treatment methods used. These include total treatment time and duration of period starting from the preparation of procedure until protective wound dressing is applied, and including whether or not anesthesia and/or sedation was used when comparing the Zip 4 Surgical Skin Closure Device and the standard of care closure suturing.

9.3 Secondary endpoints (performance)

- Difference in Wound Evaluation Score at 10 days and 30 days post-treatment compare to baseline when comparing scar satisfaction and appearance of the subjects receiving Zip 4 Surgical Skin Closure Device versus Standard of Care closure suturing. The score will be based on digital photographs taken on day 0, day 10 and day 30 and made by an independent panel of blinded two specialists in plastic surgery.

- Rate of wound healing satisfaction in subject at 30 days post-treatment when comparing Zip 4 Surgical Skin Closure Device versus Standard of Care closure suturing. The endpoint will utilize a questionnaire for the subject when possible or his caretakers to fill out.

- The level of pain in connection to device application and removal measured by a visual analog scale (VAS) 0-100 mm.

9.4 Secondary endpoints (safety)

The incidence and severity of adverse events associated with the Zip 4 Surgical Skin Closure Device and Standard of Care closure sutures.

9.5 Exposure of investigational device and standard of care

The subjects will be exposed to either the Zip 4 device or standard of care sutures for 10 days (+/- 2 days) until removal. The exposure of both devices will be according to the intended use. Standard of care sutures has been chosen as comparison since it is the current clinical routine for lacerations in the pediatric population focused on in this investigation. A complete description of procedures and assessments performed is described in *Table 3*.

Additional medications, i.e. sedation, local anesthesia (injection or gel) and dressing, will be used according to clinical routine.

9.6 Subjects

9.6.1 Inclusion Criteria

The subjects have to meet all of the following criteria to be eligible to participate in the clinical investigation:

1. Between 4 to 18 years of age at the time of laceration repair.
2. Require suture closure as standard of care for simple straight wounds on trunk or extremities up to 4 cm long.
3. Low Tension Laceration, e.g. skin can be easily approximated by pinching with fingers.
4. Subject and legal representative(s) are willing and able to comply with the investigational device removal and meet the follow up visit requirements.
5. Subject and legal representative(s) have been informed of the nature, the scope and the relevance of the study.
6. Subject and legal representative(s) have voluntarily agreed to participation and have duly signed the Informed Consent Form.

9.6.2 Exclusion Criteria

Subjects meeting any of the following criteria will not be permitted to participate in the clinical investigation:

1. Known personal or familial history of scar hypertrophy.
2. Known or suspected allergies or hypersensitivity to non-latex skin adhesives.
3. Atrophic skin deemed clinically prone to blistering.
4. Wounds that are easily susceptible to infection because of exposure to unsanitary conditions ("dirty wounds").
5. Wounds that require deep dermal closure using sutures.
6. Known or suspected mental problems and/or aggressiveness that indicates that the subject might try to take to take the investigational device off.
7. Participating in any other clinical investigation.
8. Known health condition that would affect healing in the opinion of the investigator.
9. Any subject that according to the Declaration of Helsinki is deemed unsuitable for study enrolment.

9.6.3 Number of Subjects

The study population will be comprised of 60 pediatric patients presented to the Pediatric energency department with need of laceration repair, and eligible to study participation according to the inclusion and exclusion criteria. The subjects will be randomly assigned at a 1:1 ratio to either the Zip 4 group (30 subjects) or to the SoC group (30 subjects).

The sample size calculation was based on preliminary data indicating a difference of approximately 30 minutes in wound treatment procedures between the Zip device and SoC sutures. Alpha = 0.05 and power of the test = .9, indicates a sample size of 24 subjects. Assuming 10% dropout rate, the study will include up to 26 subjects. If for any reason the dropout rate should be higher than this, additional subjects might be enrolled in the study to reach a total of 24 completed subjects. Since different areas of the body are being appreciated we will enroll 60 patients.

9.6.4 Methods of Assigning Subjects to the different treatment arms

When the subjects are consented into the investigation they are given a unique three-digit identification number. If the subject is found eligible he/she will be allocated to the next available randomization number, a code of two digits, and the corresponding randomization envelope opened. The envelope contains information on group allocation in accordance with the randomization list. This is not a blinded investigation and both the Investigator and subject will be aware of the group allocation after randomization. The subject's identification number and randomization number will be noted in applicable investigation logs, Case Report Form (CRF) and in the medical journal system for each subject

Subject withdrawal or discontinuation
Subjects and/or legal representatives are free to discontinue participation in the clinical investigation at any time and are not required to give a reason for their decision. However, they that wish to discontinue the investigation should always be asked about the reason(s) for discontinuation and about the presence of any adverse events/adverse device effects and, if possible, be assessed by an Investigator. Discontinuation from the clinical investigation will not affect the future treatment/care of the subject.

If the subject and/or legal representative(s) will withdraw the consent no further data will thereafter be recorded. Data collected up to the date of window and informed consent will be used in the data analysis and for the Clinical Investigation Report (CIR).

Subjects may be withdrawn from the clinical investigation at any time, if deemed necessary by the PI.
Specific reasons for withdrawal of subjects from this clinical investigation are:

- The decision of a subject and/or legal representative(s) to withdraw from the clinical investigation (including if the subject withdraws informed consent).
- The PI deems the subject is unfit for the investigation or suspects' poor CIP compliance.
- Subject is lost to follow-up.

In case of withdrawal, all AEs/ADEs should be followed up. Any questionnaires should be returned by the subject.

In case of subjects lost to follow up; at least 3 documented attempts to reach the subject shall be made prior to categorizing the subject as “lost to follow-up”.

Incorrectly enrolled or randomized subjects will be withdrawn from further investigation and assessments. A subject may, however, continue the clinical investigation under exceptional circumstances (i.e. if continuation of investigation or follow up are necessary for the subject’s safety and wellbeing, or if only a follow up period remain, and the continuation of the investigation is not expected to be associated with any risk or discomfort for the subject).

9.7 Clinical investigation duration

Table 2. Overview clinical investigation duration.

Point of enrolment:	Q2 2018
Estimated enrolment period	5 months
Expected duration of each subject’s participation:	30 days
Total expected duration of the clinical investigation:	6 months

9.8 Clinical Investigation Procedures

9.8.1 Schedule of clinical investigation procedures/assessments

The assessments and procedures that will be performed during the clinical investigation are illustrated in *Table 3* below.

Table 3. Clinical investigation schedule for assessments and procedures.

Study assessment	**Visit 1 Day 0**	**follow-up 1 Day 10 (+/- 2 days)**	**follow-up 2 Day 30 (+/- 2 days)**
Study information	X		

Informed consent	X		
Demographics	X		
Relevant Medical and Surgical history	X		
Physical examination (Type, size, location of laceration)	X		
Inclusion/Exclusion criteria	X		
Randomization	X		
Wound preparation, e.g. cleansing[1]	X		
Local Anesthesia and/or Sedation[2]	X		
Device application[3]	X		
Dressing application	X		
Study participant instructions[4]	X		
Device and dressing removal[5]		X	
Photographs taken[6]	X	X	X
Visual Analog Scale (VAS)	X	X	
Wound healing satisfaction questionnaire			X
Subject interview		X	X
Adverse event	X	X	X
Medical review / Concomitant medication	X	X	X
Study Exit			X

[1] According to clinical routine.
[2] According to clinical routine. Zip group: Anesthesia and/or sedation only use if deemed necessary by Investigator. Document in Concomitant Medication Log.
[3] Test group will be treated with Zip 4 device and SoC group with conventional sutures as wound closure.
[4] Instructions prior discharge regarding post-treatment and additional follow up visits.
[5] suture ir device removal will be conducted at FU session 1 at the PED or at home by a member of staff of the study
[6] Photographs will be taken at the wound area during Visit 1and follow up visits by the site personnel, . Please be aware of not adding any personal numbers or identifying characteristics on the photographs, only subject identification number and visit information.

9.8.1.1 Visit 1 (Screening/Baseline visit)

The Investigator will introduce the clinical investigation and explain the CIP, procedures and objectives to a potential subject and their legal representative(s). The Investigator will verbally inform about the investigation and provide a Patient Information Sheet (PIS) describing the clinical investigation, potential discomforts, risks and benefits of participation. Potential subjects and their legal representatives will be given adequate time for review of the PIS and time to discuss the investigation and ask questions to the Investigator. Any queries that they may have regarding the investigation will be addressed appropriately by the Investigator. Potential subjects and their legal representatives will be instructed that they are free to obtain further information from the Investigator at any time and that they are free to withdraw their consent and to discontinue their participation in the investigation at any time without prejudice.

If the subject and their legal representative(s) are willing to participate in the investigation, they need to sign and date the informed consent form (ICF) together with the Investigator who gave the verbal and written information. The original ICF will be retained in the Investigator Site File (ISF) and a copy provided to the subject and their legal representative(s). The Investigator must obtain written informed consent before any clinical investigation-related procedures are performed, for further details on the informed consent process please see *section 17*.

After written informed consent has been acquired the subject is considered as enrolled. The subject will be allocated to the available subject identification number, a unique three-digit number, used for the identification of the subject in the investigation.

At visit 1 a physical examination of the laceration will be performed, and relevant medical/surgical history collected together with medication review and information on

subject's demographics. After confirmation of the inclusion and exclusion criteria the subject will be randomly assigned to either test or SoC group. Subject randomization procedure will take place in a block randomized fashion where equal numbers of subjects will receive the Zip 4 device and the SoC suture wound closure (1:1 ratio). The randomization will be performed by opening a sealed envelope containing a randomization card, for further details see *section 10.6.4*. The corresponding device written in the opened randomization envelope will be used as laceration repair.

Prior device application the wound will be cleansed, and for SoC subject local anesthesia and/or sedation will be used according to clinical routine. For Zip subjects, local anesthesia and/or sedation only will be used if deemed necessary by the Investigator. Photographs will be taken of the laceration by the study personnel, and thereafter the devices, Zip 4 device or SoC sutures, will be applied as according to the IFUs. After the devices have been applied appropriate, they will be covered with standard of care dressings to provide protection. Thereafter the subject will fill out the Visual Analog Scale (VAS) with assistance from the legal representative(s), if needed.
Prior discharge:

- Post-treatment information of the Zip 4 device or SoC sutures. The subjects and their legal representative(s) in the Zip 4 group will be informed that the subjects may not use ointments containing petroleum as well as reframe from soaking the device during baths or in swimming pools. Furthermore, the subject should not rub or continuously lay on the device since this may weaken the adhesives or damage the device.
- Removal of the Zip 4 device or SoC sutures will be conducted by the a study personnel either at Kaplan Medical Center ER or at the subjects home depending on the subjects preferences.
- The subject and their legal representative(s) will receive verbally and written information regrding the photgraphs that will be taken at day 10 and day 30.
- The subject and their legal representative(s) will receive questionnaires to be filled out at day 10 (VAS) and day 30 (Wound healing satisfaction questionnaire).
- The subject and their legal representative will be given contact information to the site in case of an adverse event or general questions concerning the investigation.
- Follow up visits will be scheduled and the subject and their legal representative(s) will be reminded of the importance of attending . These will be done either at the subjects home or at the Pediatric Emergency Department at Kaplan Medical Center.

During Visit 1 the following assessments/procedures will be performed:

- Demographics
- Relevant medical and surgical history
- Physical examination of the laceration (type, size, location)
- Medication review
- Verification of subject eligibility (check inclusion/exclusion criteria)
- Randomization
- Wound preparation, e.g. cleansing.
- Anesthesia (if required)
- Sedation (if required)
- Photographs taken at the wound prior device application
- Device application
- Dressing application
- VAS
- Study participant instructions: hand out Zip device removal instructions and photograph instructions

- Hand out questionnaires (VAS and Wound healing satisfaction questionnaire) and self-addressed envelopes to be filled out in conjunction with the telephone follow up 1 and 2.
- Telephone follow ups scheduled

9.8.1.2 Follow up 1 (Day 10 +/- 2 days)

At the first follow up the device, either Zip 4 device or SoC sutures will removed at day 10(+-2 days). Prior discharge at visit 1 the subjects will receive instructions that if:

1) Treated with Zip 4 device the subject and their legal representative(s) will remove the subject themselves at day 10. If necessary, the subject/legal representative(s) may call the A&E for assistance during the removal.
2) Treated with SoC sutures the subject and their legal representative(s) will visit the Pediatric Emergency Department or at home for removal of the sutures. During the follow up after device removal the subject will be asked about any adverse events that may have occurred, and a review of the concomitant medication. The subject will be interviewed about the usage of the device, and will fill out the questionnaire, VAS, and photograph the laceration. Next follow up day 30 will be scheduled if not done at visit 1.

All of the above can be done in assistance by the legal representative(s), if needed.

The following assessments/procedures will be performed at follow up 1:

- Subject interview
- VAS
- Cosmetic Outcome
    - High definition photos will be taken of the laceration
- Registration of any Adverse Events
- Registration of Concomitant Medication

9.8.1.3 Follow up 2 (Day 30 +/- 2 days)

At the second follow up the subjects will be asked about any adverse events that may have occurred and a review of concomitant medication. The subjects will fill out the questionnaire, Wound healing satisfaction, and a subject interview will be performed by the site personnel. Photographs will be taken on the laceration.

All of the above can be done in assistance by the legal representative(s), if needed.

If no pending adverse events the subjects will be assessed as completed and the subject termination page will be filled out in the CRF by the site personnel after the telephone call has been performed.

The following assessments/procedures will be performed at follow up 2:

- Subject interview
- Wound healing satisfaction questionnaire
- Cosmetic Outcome
    - High definition photos will be taken of the laceration
- Registration of any Adverse Events
- Registration of Concomitant Medication

9.8.2 Demographic Data and Baseline Measurements

The demographic data that is collected at the screening/baseline visit will describe the subject population and confirm eligibility. The age, gender and weight will be recorded. In addition,

relevant medical and surgical history, medicine review and physical examination of the laceration prior treatment.

Relevant medical and surgical history is defined as any previous or existing condition that may potentially affect the outcome of the treatment according to the best judgement of the investigator.

9.8.3 Performance Variables and Measurements

9.8.3.1 Time of treatment procedure

The treatment procedure time will be measured at the baseline/screening visit. The time will be recorded starting from the preparation of the wound until the protective wound dressing is applied. The time will be measured in HH:MM:SS, e.g. 01:15:30, and recorded in each subject's CRF.

9.8.3.2 Wound Evaluation Score (WES) –

The Wound Evaluation Score (WES) will be used to evaluate the scar satisfaction and appearance based on the photographs taken at day 0, day 10 and day 30. An independent panel of 2 Plastic Surgeons will objectively rate the photographs based on six categories. For each category, response is binary: either yes=0 or no/no=1.

9.8.3.3 Wound healing satisfaction

The wound healing satisfaction questionnaire will be filled out by the subject with assistance by the legal representative(s) if needed. The questionnaire will be used to achieve a subjective evaluation of the wound healing. The questionnaire will be filled out at day 30, and contain questions where the subject either will mark the most correct answer or rate on a line between 0-100 mm.

9.8.3.4 Visual Analog Scale (VAS)

The pain VAS is an instrument to measure pain intensity (15) to access the subject's subjective experience. The scale in this investigation will be between 0-100 mm, where 0 is no pain and 100 mm is the worst imaginable pain for the subject. The subject will fill out the VAS line at the point that represents their pain intensity at the time. The VAS will be used after device has been applied at day 0, and after device removal at day 10. Legal representative(s) will assist if needed.

9.8.4 Safety Variables and Measurements

The safety measurement will be the onset, severity, duration and frequency of adverse events (anticipated and unanticipated), including determination of causality. The adverse event recordings between the two device groups will be compared. Only events, which are new after the consent has been signed or have increased in severity after the consent has been signed, will be recorded and used in the comparison. All adverse events will be recorded and reported and all data required both to assess the safety and to comply with the Competent Authority (CA) and IEC requirements will be collected.

9.8.5 Potential Confounding Factors

- Dressings will be used on the devices to provide protection, e.g. of accidental loss of device. If the device would be accidentally lost prior to complete healing process the outcome may be less favorable for the subject.

- Petroleum based ointments in conjunction with the Zip 4 device should not be used since the effects are unknown.

9.8.6 Prior and Concomitant Medication and Procedures

The site personnel will record the concomitant medication (using generic names) information in the appropriate section of the CRF.

Note that petroleum based ointments shall not be used in conjunction with this Zip device since the effects are unknown.

No other interactions are anticipated between treatment with the investigational device and concomitant medications and therefore there are no restrictions of concomitant medications.

10 DATA QUALITY ASSURANCE

10.1 Monitoring, Audits and Inspections

During the investigation, the monitor will have regular contacts with the investigation site. These contacts will include visits to confirm that the facilities remain adequate to specified standards and that the site personnel are carrying out the procedure as stated in the CIP. All data must be accurately recorded in the CRF. Source Data Verification (SDV), a comparison of data in the CRF with the subjects' medical records and other records of source data at the investigation site, will also be performed. The CRF and source documents and records must be made accessible during the visit.

The monitor and other Sponsor personnel will be available between visits if the PI or other site personnel needs information and/or advice. Authorized representatives of the Sponsor and/or appropriate regulatory agencies, including IEC, may visit the site to perform audits/inspections, including SDV.

A detailed description of the monitoring activities will be explained in investigation specific monitoring plan.

10.2 Subject Records and Source Data

Subject data recorded directly in the CRF, and not into the medical record, will be considered as source data. It is the responsibility of the PI to record essential information in the medical records, in accordance with national regulations and requirements. The origin of the source data in this clinical investigation will be further specified in a separate document ("Origin of Source Data").

In general, the following information will be recorded in the medical records:

- Clinical investigation code
- Subject identification number
- That informed consent for participating in the clinical investigation was obtained
- Diagnosis
- All visits during the investigation period
- All AEs/ADEs
- Treatments and medications

In the instance where the CRF is considered source data it should be noted on the "Origin of Source Data" document. The PI is responsible for ensuring the accuracy; completeness, legibility and timeliness of the data recorded in the CRFs. Completed sections of CRFs will be monitored and collected on regular basis.

10.3 Access to Source Data and Documentation

The PI should guarantee access to source documents for the monitor and auditors as well as for inspection by appropriate regulatory agencies, and the IEC, if required.

11 STATISTICAL CONSIDERATIONS

11.1 Statistical design, method and analytical procedures

Statistical analysis on variables of interest, including subject demographics, baseline characteristics, effectiveness and safety endpoints will be summarized descriptively by randomization arm. Students 't' Test for comparative testing, will address testing the hypothesis statements, along with p values reported for significance. Mean, standard deviation, range, and Coefficient of Variation (CV) will be reported for closure times for both the two closure treatment methods of SoC suture and Zip 4 device for the primary endpoint.

For the secondary endpoints, mean, standard deviation, range, and CV will be provided for the VAS scale data, plus comparative "t" test will be applied for testing any possible significant differences between the two treatment groups. Additional analysis will be reported per the attribute satisfaction survey criteria obtained from patient satisfaction data at the 30 day follow-up interval. This will include an analysis of Average Satisfaction Scores, summary statistics, plus a histogram analysis comparing patient satisfaction data for both treatment groups of Sutures and Zipline..

11.2 Sample size

Sample sizes for the two treatment groups of Zip 4 device and SoC suture, were determined, and based on prior studies performed for the primary endpoint of mean times for incision closure time. The justification for sample sizes determined, is based on the following delta differences, and pooled Standard Deviation (SD) calculations for mean time differences of closure methods.

Differences and variances are based on prior data, with a delta difference of 30 mins, pooled SD = 22, alpha error = .05, power of the test = .9, the sample size determined for each grouis 12, or 24 subjects total. In consideration is a possible 10% loss calculation, a total maximum number of up 26 subjects or up to a maximum of 13 subjects per group is determined.

11.3 Data Sets to be analyzed

a. Safety data will include all relevant safety data from consenting subjects in this investigation.
b. The Full Analysis Set (FAS) will include randomization (random order) of participant subjects in the study.
c. The Per Protocol Set (PPS) will include the following:
    I. Randomization applied to participating subjects
    II. Completion of PPS to the study endpoint objectives in accordance with this Protocol. This to be performed without any significant protocol deviations, which could have potential erroneous affect on the studies' efficacy, e.g. protocol violation could be a change to specific criteria per the primary and secondary endpoints.

The final criteria specified per the PPS, regarding protocol deviations, if any, that warrant exclusion, will be determined at the time of the database "lock meeting," when all data on any protocol violations or deviations are revealed.

11.4 Level of significance and power

The level of significance, or alpha error selected is equal to .05, which is interpreted as the Type I error for acceptance of Alternative Hypothesis or H_1, with 95% confidence. The power

of the test, is set at .9, which is interpreted as the Type II error (beta), rendering an error of .1 or 10% for incorrect acceptance of the Null Hypothesis or H_0.

11.5 Drop-out rates

The drop-out rate or "Loss" is based on a 10% loss (L) estimate for this study.
Loss calculation = (sample n/ (1-L).

11.6 Interim analysis

At the 10 day interview and data gathering point, an Interim Analysis will provide any meaningful subject feedback or inputs to VAS scores. Additionally, closure time data will be available at that time, for an initial analysis of the Primary Endpoint with mean, standard deviation, and "t" significance testing of the Hypotheses.

11.7 Criteria for termination on statistical grounds

The criteria applicable for termination is based only if an incomplete study subject sample size taken from the population, i.e. not meeting the sample sizes (n) specified for this study, or if the randomization methodology (order) is not adhered to during the administration of the investigation.

11.8 Reporting of deviations from the original Statistical Analysis Plan

Any deviation discovered throughout the study from the original Statistical Analysis Plan (SAP), will be described with justification in a CIP Amendment to the final report, as deemed appropriate.

11.9 Missing, unused or spurious data

Spurious data, also known as outliers or mavericks, will be included in the summary tables, though noted in study as abnormal data. Premature withdrawn subject data will also be inclusive to the analysis, as far into the study as possible. Any missing data discovered will be incorporated to the analysis, and noted accordingly.

11.10 Exclusion of particular information from the testing of the hypothesis

Since the primary endpoint and the testing of the hypothesis is based specifically on mean closure times, there may be exclusion of extraneous data or information not related to the hypotheses being tested, if applicable.

12 DATA MANAGEMENT

Data management will be conducted in accordance with applicable guidelines. A study specific Data Management Plan (DMP) will describe in detail the management of all subject data collected in the study. Any deviations, i.e. discrepancies and additions from the procedures defined in the DMP, will be described in a study specific Data Management Report (DMR).

All subject data will be collected in designated paper CRF and questionnaires. The PI or an authorized person will record subject data in the CRF in a precise and accurate manner. Abbreviations should not be used. The PI is responsible for the data entered and sign off the CRF at the end of the clinical investigation. The data should be recorded as soon as they are generated.

The subject data will be entered into a designated MS SQL database on a secure PFT. The database will be designed for the sole purpose of compiling and handling data from the ZipLine Study. The ZipLine database will be validated prior to study data entry. Responsible data management personnel will receive training and login credentials. Single data entry type will be applied.

Data validation/data cleaning procedures will be performed to assure validity and accuracy of the clinical data. These procedures consist of manual reviewing during data entry, as well as computerized edit checks. For all detected errors, queries will be raised to site for identifying out-of-range data values, CIP deviations, incomplete or inconsistent data.

Upon completion of the Zipline study, all study data will be verified from the original CRFs/ questionnaires and a complete data quality control of the database will be performed. After all discrepancies are resolved and the reconciliation with the SAE database is done, the database will be locked and the data will be analyzed.

12.1 Data Retention

The medical file of clinical investigation subjects must be retained in accordance with local legislation and in accordance with the maximum period permitted by the hospital, institution or private practice.

The Investigator shall retain all clinical investigation records during the investigation and for the period required by the applicable regulatory requirements or for at least 10 years after the premature termination or completion of clinical investigation, whichever is the longer. The PI must take measures to prevent accidental or premature destruction of these documents. The Investigator should contact the Sponsor prior to destruction of any records or reports pertaining to the clinical investigation to ensure they no longer need to be retained. In addition, if the PI leaves the hospital, he/she should provide the Sponsor with the name and address of the person who will look after and be responsible for the clinical investigation-related records. If the records will be transferred to another person/party, the transfer will be documented at the investigation site or at the Sponsor.

13 AMENDMENTS TO THE CIP

Any change to the approved clinical investigation documents will be documented and include a written justification. Any effects of the implemented changes on other clinical investigation documents shall be evaluated and documented. If deemed necessary, affected documents shall be properly updated and relevant parties notified. The version number and date of amendments shall be documented.

Proposed amendments to the CIP shall be agreed upon between he Sponsor and PI. The amendments shall be notified to, or approved by, the IEC.

All amendments to the CIP will be documented in an amendment log and communicated to relevant parties.

14 DEVIATIONS FROM THE CIP

A CIP deviation is a failure to follow, intentionally or unintentionally, the requirements of the CIP. Every effort should be made to comply with the requirements of the CIP and the Investigator is not allowed to deviate from the CIP.

As required by national regulations or guidelines, requests for deviations and reports of deviations will be provided to the IEC if the deviation affects subject's rights, safety and well-being, or the scientific integrity of the clinical investigation.

Under emergency circumstances deviations from the CIP may proceed without prior approval by the Sponsor and favorable opinion of the IEC if the rights, safety and well-being of the human subjects need to be protected. Such deviations will be documented and reported to the Sponsor and IEC as soon as possible in accordance with national regulations.

When the monitor or Sponsor identifies that the PI is out of compliance, this will be notified to the PI in writing, with a request to correct the source of the deviation immediately. Corrective action will be implemented to avoid repeated non-compliance, which will usually include re-training and may include terminating the clinical investigation at the site.

The Sponsor is responsible for analyzing deviations and assessing their significance. Corrective action will be implemented to avoid repeated deviations, which may include suspending the clinical investigation, disqualify the PI.

15 STATEMENTS OF COMPLIANCE

This clinical investigation will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki (*Appendix C*). Furthermore, the clinical investigation will be conducted in compliance with ISO 14155:2011 and applicable regional or national regulations.

15.1 Institutional Ethics Review

The final CIP, including the final version of the ICF, must be approved or given a favorable opinion in writing by an IEC before enrolment of any subject into the clinical investigation. The PI is responsible for informing the IEC of any amendment to the CIP as per local requirements.

Any additional requirements imposed by the IEC shall be followed.

15.2 Insurance

The Sponsor will be responsible for ensuring adequate insurance covering any injuries to the subject caused by the investigational medical device.

16 INFORMED CONSENT PROCESS

All subjects and legal authorized representatives will receive written and verbal information regarding the investigation beforehand. This will emphasize that participation is voluntary and that the subject may withdraw from the investigation at any time and for any reason. If new vital information appears during the clinical investigation the subject will be informed both orally and in writing. All subjects will have the opportunity to ask questions about the investigation and will be given sufficient time to decide whether to participate or not. Before any investigation-related procedures, the information consent will be signed and dated by the subject, their legal acceptable representative(s), and by the Investigator who gave the verbal and written information.

The only exception to the above is if not all legal representative(s) are present at the investigation site at the time for consent. The additional legal representative(s) will receive verbal information about the investigation through the phone, and will give their oral consent prior to any investigation-related procedures. Signed consent will be given as soon as possible thereafter.

The written subject information, PIS, explains that the data will be stored in a computer database, maintaining confidentiality in accordance with national data legislation, and that authorized representatives of the Sponsor, FDA, CA, and/or IEC may require direct access to those parts of the medical records relevant to the investigation, including medical history, for verification of data. Additionally, the written information specifies that data will be recorded, collected, processed and may be transferred (to either EEA countries and/or non-EEA countries). In accordance with the EU Data Protection Directive (95/46/EC), the data will not identify any subjects taking part in the investigation.

17 ADVERSE EVENTS, ADVERSE DEVICE EFFECTS AND DEVICE DEFICIENCIES

The definitions and procedures for reporting Adverse Events (AE), Adverse Device Effects (ADE), Serious Adverse Events (SAE), Serious Adverse Device Effects (SADE), and Unanticipated Serious Adverse Device Effects (USADE) are presented in the subsections below. It is outmost importance that all staff involved in the investigation is familiar with the definitions and procedures and it is the responsibility for the PI to ensure this.

17.1 Definitions

Adverse Event (AE)
Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons whether or not related to the investigational medical device.

Note 1: This definition includes events related to the investigational device or the comparator.
Note 2: This definition includes events related to the procedure involved.
Note 3: For users or other persons, this definition is restricted to events related to investigational medical devices.

Adverse Device Effect (ADE)
Adverse event related to the use of an investigational medical device.

Note 1: This includes any adverse event resulting from insufficiencies or inadequacies in the instructions of use, the development, the implantation, the installation, the operation, or any malfunction of the investigational medical device.

Note 2: This includes any event that is a result of a use error or intentional abnormal use of the investigational medical device.

Device Deficiency (DD)
Inadequacy of an investigational medical device related to its identity, quality, durability, reliability, safety or performance. This may include malfunctions, use error, or inadequacy in the information supplied by the manufacturer.

Serious Adverse Event (SAE)
Adverse event that:

a) Led to a death, injury or permanent impairment to a body structure or a body function.
b) Let to a serious deterioration in health of the subject, that either resulted in:
   - A life-threatening illness or injury, or
   - A permanent impairment of a body structure or a body function, or
   - In-patient hospitalization or prolongation of existing hospitalization, or
   - In medical or surgical intervention to prevent life-threatening illness.
c) Led to foetal distress, foetal death or congenital abnormality or birth defect.

Note: Planned hospitalization for pre-existing condition, or a procedure required by the CIP, without a serious detoration in health, is not considered a serious adverse event.

Serious Adverse Device Effect (SADE)
Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Unanticipated Serious Adverse Device Effect (USADE)
Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

Note: Anticipated SADE (ASADE): an effect which by its nature, incidence, severity or outcome has been previously identified in the risk analysis report.

17.2 Methods for discovering and documenting AE/ADE

All subjects will be carefully monitored for the occurrence of AEs throughout the clinical investigation, from the first day to the completion of follow up. Events prior to randomization will be considered medical history. The PI will collect safety information using non-leading questions such as "Have you experienced any new health problems or worsening of existing conditions?". Events directly observed or spontaneously volunteered by subjects will also be recorded throughout the clinical investigation.

Clearly related signs, symptoms and abnormal diagnostic procedure results should be grouped together and reported as single diagnosis or syndrome, whenever possible.

All AEs, including but not limited to events reported by the subject or reported in response to an open question by the PI or member of the investigation team, which fall into any of the previously defined definitions must be recorded as an AE in the CRF and should include the following information:

- Brief description of the event (diagnosis)
- Date of event onsent (and time, if relevant)
- Date of event resolution (and time, if relevant)
- Severity
- Seriousness
- Causality assessment (i.e. relationship to medical device and/or procedure)
- Event treatment
- Event outcome

Any AE that is ongoing when the subject is withdrawn from the investigation should be followed up until the AE is resolved or the PI decides that the AE is stable and no further follow up is needed.

If the AE meets seriousness criteria it should be subject to expedited reporting as described in *section 18.4*.

17.2.1 Severity

Severity describes the intensity of an AE and will be assessed as:

1. Mild: asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
2. Moderate: minimal, local or non-invasive intervention indicated, limiting age-appropriate instrumental activities of daily living.
3. Severe or medically significant by not immediately life-threatening: hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living.
4. Life-threatening consequences; urgent intervention indicated.
5. Death related to AE.

If an AE changes in severity, it should be reported as an AE of new severity but with the same description and identifier.

17.2.2 Causality

Causality is the relationship between the use of medical device (including the investigational device, the comparator and the medical – surgical procedure) and the occurrence of each AE.

During causality assessment activity, clinical judgment shall be used and the relevant documents, such as the CIP, or the risk analysis report, shall be consulted as all the foreseeable SAEs and the potential risks are listed and assessed there. The presence of confounding factors, such as concomitant medication/treatment, the natural history of the underlying disease, other concurrent illness or risk factors shall also be considered.

For harmonizing reports, each SAE will be classified per five different levels of causality. The Sponsor and the Investigator will use the following definitions to assess the relationship of the SAE:

- Not related: relationship to the device or procedures can be excluded when:
    - The event is not a known side effect of the product category the device belongs to or of similar devices and procedures;
    - The event has no temporal relationship with the use of the investigational device or the procedure;
    - The serious event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;
    - The discontinuation of medical device application or the reduction of the levels of activation/exposure – when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious event;
    - The event involves a body-site or an organ not expected to be affected by the device or procedure;
    - The serious event can be attributed to another cause (e.g. an underlying or concurrent illness/clinical condition, an effect of another device, drug, treatment or other risk factors);
    - The event does not depend on a false result given by the investigational device used for diagnosis when applicable;
    - Harms to the subject are not clearly due to use error;
    - To establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.
- Unlikely: the relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
- Possible: the relationship with the use of the investigational device is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/clinical condition or/and an effect of another device, drug or treatment). Cases were relatedness cannot be assessed or no information has been obtained should also be classified as possible.
- Probable: the relationship with the use of the investigational device seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.
- Causal relationship: the serious event is associated with the investigational device or with procedures beyond reasonable doubt when:
    - The event is known side effect of the product category the device belongs to or of similar devices and procedures;

- The event has a temporal relationship with investigational device use/application or procedures;
- The event involved a body-site or organ that
  - the investigational device or procedures are applied to;
  - the investigational device or procedures have an effect on.
- The serious event follows a known response pattern to the medical device (if the response pattern is previously known);
- The discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of activation/exposure), impact on the serious event (when a clinically feasible);
- Other possible causes (e.g. an underlying or concurrent illness/clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;
- Harm to the subject is due to error in use;
- The event depends on a false result given by the investigational device used for diagnosis, when applicable;
- To establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

The Sponsor and PI will distinguish between the AEs related to the investigational device, the standard of care and those related to any procedure specific to the clinical investigation. An AE can be related to both the procedure and the device. Complications of procedure are considered not related if the said procedure would have been applied to the subjects also in the absence of the device use/application.

17.3 Methods for discovering and documenting DD

Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance shall be reported as a DD without unnecessary delay to the Sponsor by using the investigation specific DD form. The Zip device shall be returned to the Sponsor for analysis, if applicable. If the device has been in contact with the subject or may have been in contact with the subject's bodily fluids, proper biohazard controls and labeling shall be used when handling and transporting the device.

It is the PI's responsibility to record every observed DD together with an assessment. The Sponsor shall review all DDs and determine and document in writing whether they could have led to a SADE. DDs that are assessed to or have SADE potential should be subjected to expedited reporting as described in *section 18.4*.

17.4 Reporting of SAE/SADE and DD with SADE potential

The following events are considered reportable events in according with the Medical Device Directive (MDD) 93/42/EEC and ISO 14155:2011:

- Any SAE,
- Any DD that might have led to a SAE if:
  - Suitable action had not been taken or;
  - Intervention action had not been taken or;
  - If circumstances had been less fortunate;
- New findings/updates in relation to already reported events.

All SAEs/SADEs and DDs that could have led to a SADE must be reported to the Sponsor immediately, but not later than 3 calendar days according to MEDDEV 2.7/3 after site

personnel's awareness of the event, regardless of the time that may have elapsed from the time the event occurred.

The initial report should contain as much information as possible, but as a minimum the following information:

- Subject identification
- Site contact information
- Treatment arm
- Date of procedure
- Date of event onset
- Event type (i.e. SAE or Device Deficiency with SADE potential)
- Description of event
- Action/treatment/subject outcome
- Relationship to investigation procedure
- Relationship to medical device
- Unanticipated SADE (Yes/No)
- Event status

The Sponsor must also promptly receive a completed report. All SAEs have to be reported whether or not they are considered causally related to the investigational medical device.

Since this is a post-market investigation all SAEs will be handled according to the Sponsors vigilance system and in accordance with MEDDEV 2.12/1 Guidelines on Medical Device Vigilance System.

SAE EMERGENCY CONTACT DETAILS – Sponsor's Medical Monitor
Name: Dr. Elisabeth Liljensten, DDS PhD
Phone: +46 (0) 723 611 968
E-mail: elisabeth.liljensten@devicia.se

17.5 Data Monitoring Committee

Since this is a post-market clinical investigation no Data Monitoring Committee (DMC) will be assigned. Any serious adverse events will be part of the Sponsor's vigilance system. The adverse event reporting and monitoring described in *sections 18* and *11*, respectively, will assure early detection of any increased risks or un-anticipated subject safety concerns.

18 Vulnerable population

In this clinical investigation, pediatric subjects will participate in an age between 4 and 18 years. Pediatric subjects are per se described as a vulnerable population according to ISO 14155:2011. Therefore, also the potential subjects' legal representatives will receive information both verbally and written about the study prior any decision about the subjects' participation. If not all legal representative(s) are present at the time of consent, the additional legal representative(s) will receive oral information about the investigation and give oral consent. Written consent will take place as soon as possible thereafter. Both the potential subject and the legal representative(s) need to voluntarily agree to participate. The subject will be informed about the clinical investigation within his/her ability to understand, i.e. additional versions of the PIS have been developed to target the different ages. If the subject will have specific difficulties to understand the contents of participating in the clinical investigation, i.e. as a child may have, additional time will be given for questions regarding the investigation as well as consent procedure.

19 SUSPENSION OR EARLY TERMINATION OF THE CLINICAL INVESTIGATION

If the clinical investigation is terminated early or suspended due to reasons for safety, the Sponsor will promptly inform the PI(s) and the site(s) of the termination or suspension and the reason(s) thereof. The IEC will also be informed promptly and provided with reason(s) for the termination or suspension by the Sponsor or by the PI/investigation site.

In addition, CIP violations may result in termination of the clinical investigation at a site. CIP violations are deviations made without permission because of error or fraud/misconduct. Where the monitor or Sponsor identifies that the PI is out of compliance, this will be noted to the PI in writing, with a request to correct the source of the deviation immediately. Corrective actions will be implemented to avoid repeated non-compliance, including re-training. However, in case of repeated non-compliance despite implemented corrective actions, the clinical investigation will be terminated at the site.

19.1 Subject follow-up

If the clinical investigation is prematurely terminated, the Sponsor and the PI(s) will assure that the adequate consideration is given to the protection of subjects' interest, including subject follow up.

20 PUBLICATION POLICY

The clinical investigation will be registered in a publicly accessible database before recruitment of the first subject.

A final report of the investigation, a ClR, will be completed, even if the investigation is prematurely terminated. The report will be prepared by the Sponsor according to the guideline presented in Annex D of ISO 14155:2011.

All publications and presentations must be based upon the CIR.

All information supplied by the Sponsor in connection with this investigation will remain the sole property of the Sponsor and is to be considered confidential information. No confidential information will be disclosed to others without obtaining prior consent from the Sponsor and will not be used except in the performance of this investigation.

The PI(s) may publish results from this investigation; however, the Sponsor must first be given the opportunity to review any publication manuscript prior to submissions to journals, meetings or conferences.

The Sponsor may choose to publish or present data from this investigation. If a PI is offered first authorship, he/she will be asked to comment and approve the publication. The Sponsor has the right to use the results for registrations and internal presentation and for promotion.

21 REFERENCES

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22 APPENDICES

22.1 Appendix– Clinical Investigation Contact List

PRINCIPAL INVESTIGATOR
Name: Uri Balla , MD.
Address: Kaplan Medical Center, Rehovot Israel
Phone: +972 8 9441 275
+972 52 2326141
E-mail: Uriballa@gmail.com

CLINICAL INVESTIGATION SITE
Kaplan Medical Center
Rehovot
Israel

SPONSOR REPRESENTATIVE
Name: Eric Storne, VP Marketing
Address: ZipLine Medical, Inc.
747 Camden Ave., Suite A
Campbell, CA 95008
USA
Phone: +1 650 464 5073
E-mail: estorne@ziplinemedical.com

SAFETY OFFICER
Name: Amir Belson, M.D.
Address: ZipLine Medical, Inc.
747 Camden Ave., Suite A
Campbell, CA 95008
USA
Phone: +972 846 212 45
E-mail: abelson@ziplinemedical.com

CASE REPORT FORM

Clinical Investigation Title:

A randomized, controlled, post-market clinical investigation to evaluate Zip Surgical Skin Closure Device in comparison of using Standard of Care sutures for Laceration Repair in Pediatrics in a Pediatric Emergency Department

Subject ID No:	|__|__|__|
Sponsor:	ZipLine Medical, Inc. 747 Camden Ave., Suite A Campbell, CA 95008 USA

Instructions how to complete the Case Report Form

- Use a ball point pen

- All data entries must be completed in English
- Always use a 24-hour clock format HH:MM (e.g. 16:00)
- Dates should be documented as follows: DD (numeric)-MMM (alphabetic)-YYYY (numeric). For example: 18-JUL-2014
- If data is missing or impossible to obtain, please fill in as far as possible and fill in the remaining fields as follows: NA (not available, not applicable), or explain the reason why the information is outstanding
- Data that looks inaccurate, but is correct, could be indicated with "sic" mark next to the information
- The investigator or authorized delegate may make changes to the original CRFs. Corrections should be made by drawing a line over the incorrect item. The incorrect information must remain legible. Write the correct information, date for correction and your initials next to it.

Example:	THIS IS THE RIGHT ANSWER ~~THIS WAS WRONG ANSWER~~	NN *18-JUL-2014*

VISIT 1 (Screening)

Date of Visit 1 (DD-MMM-20YY)	|__|__| - |__|__|__| - |2| 0 |__|__|

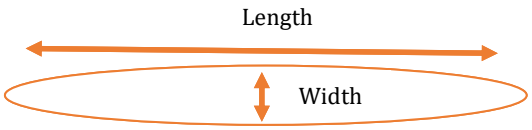
INFORMED CONSENT	
Informed consent has been signed and dated by subject, legal representative(s) and Principle Investigator (or delegate)?	☐ NO ☐ YES
Date of Obtained Informed Consent **Legal Representative(s)** (DD-MMM-20YY)	|__|__| - |__|__|__| - |2| 0 |__|__|
*If Informed Consent was **NOT obtained**, please clarify:*	

DEMOGRAPHICS	
Age	|__|__| years
Gender	☐ Male ☐ Female
Weight	|__|__| kilograms

MEDICATION REVIEW	
Is the subject taking any concomitant medication? *If **YES**, please fill out Concomitant Medication Log.*	☐ NO ☐ YES

RELEVANT MEDICAL AND SURGICAL HISTORY			
Any relevant medical and surgical history? *If **YES**, please specify below.*		☐ NO	☐ YES
Medical Condition	**Details, timeline**	**Ongoing**	**Resolved**
		☐	☐
		☐	☐
		☐	☐

PHYSICAL EXAMINATION LACERATION		
	Anterior	**Posterior**

Laceration location: *Please tick the box describing the body area of laceration location.*	☐ Shoulder ☐ Axillary region ☐ Brachial arm ☐ Antecubital region ☐ Antebrachial arm ☐ Wrist ☐ Palm ☐ Finger ☐ Chest ☐ Abdominal ☐ Inguinal region ☐ Hip ☐ Thigh ☐ Front of knee ☐ Lower leg ☐ Ankle ☐ Dorsal side of foot ☐ Toe ☐ Other: _____	☐ Shoulder ☐ Brachial arm ☐ Elbow ☐ Antebrachial arm ☐ Dorsal side of hand ☐ Back ☐ Loin ☐ Gluteal region ☐ Thigh ☐ Fold of the knee ☐ Calf ☐ Heel ☐ Plantar ☐ Other: _____
Is the laseraction on a bending part of the body?	☐ NO ☐ YES	
Laceration size:	 Length _____mm Width _____mm	
Any foreign material in the laceration?	☐ NO ☐ YES, ***please clarify:*** ☐ Gravel ☐ Splinter ☐ Fragment of glass ☐ Clothing fragment ☐ Other: _____	
Laceration edges:	☐ Rough/jagged ☐ Smooth ☐ Other: _____	
Please provide any other relevant observations:		

INCLUSION CRITERIA

1. Between 4 to 18 years of age at the time of laceration repair.
2. Require suture closure as standard of care for simple straight wounds on trunk or extremities.
3. Low Tension Laceration, e.g. skin can be easily approximated by pinching with fingers.
4. Subject and legal representative(s) are willing and able to comply with the investigational device removal and meet the follow up requirements.
5. Subject and legal representative(s) have been informed of the nature, the scope and the relevance of the study.
6. Subject and legal representative(s) have voluntarily agreed to participation and have duly signed the Informed Consent Form.

EXCLUSION CRITERIA
1. Known personal or familial history of scar hypertrophy.
2. Known or suspected allergies or hypersensitivity to non-latex skin adhesives.
3. Atrophic skin deemed clinically prone to blistering.
4. Wounds that are easily susceptible to infection as a result of exposure to unsanitary conditions ("dirty wounds").
5. Wounds that require deep dermal closure using sutures.
6. Known or suspected mental problems and/or aggressiveness that indicates that the subject might try to remove the device during the treatment period.
7. Ongoing treatment with cytostatic.
8. Known or suspected diagnosis of severe anorexia.
9. Participating in any other clinical investigation.
10. Known health condition that would affect healing in the opinion of the Investigator.
11. Any subject that according to the Declaration of Helsinki is deemed unsuitable for study enrolment.

ELIGIBILITY CONCLUSION	
Does the Subject fulfill all the inclusion- and none of the exclusion criteria? *If **NO** – please terminate subject.*	☐ NO ☐ YES

Date (DD-MMM-YYYY): _____ Investigator signature: _____

VISIT 1 (Randomization)

ALLOCATION OF RANDOMIZATION NUMBER TO SUBJECT
The subject has been allocated the following Randomization Number: |__|__|

ALLOCATION OF TREATMENT		
The subject has been allocated to the following treatment group	☐ Zip 4 device	☐ SoC sutures

VISIT 1 (Post-randomization)

PHOTOGRAPHS TAKEN	
Photographs taken prior laceration repair	☐ NO ☐ YES
*If **NO**, please clarify:*	

LACERATION REPAIR PROCEDURE	
Start Time of preparation of procedure	|__|__|:|__|__|:|__|__| HH:MM:SS
Time of registration to the PED	|__|__|:|__|__|:|__|__| HH:MM:SS
Wound cleaning	
Start Time of wound cleaning: |__|__|:|__|__|:|__|__| HH:MM:SS	**Stop Time** of wound cleaning: |__|__|:|__|__|:|__|__| HH:MM:SS
Cleaning method (***mark all** that applies*):	☐ Sterile water ☐ Soap ☐ Removal of debris ☐ Other: _____
Was anesthesia required for wound cleaning? *If **YES**, please fill out Concomitant Medication Log.*	☐ NO ☐ YES
Was sedation required for wound cleaning? *If **YES**, please fill out Concomitant Medication Log.*	☐ NO ☐ YES
Wound closure	
Was anesthesia required for wound closure? *If **YES**, please fill out Concomitant Medication Log.*	☐ NO ☐ YES, **please specify:** ☐ No new anesthesia used, anesthesia applied during cleaning was adequate. ☐ New or additional anesthesia required for wound closure.
Was sedation required for wound closure? *If **YES**, please fill out Concomitant Medication Log.*	☐ NO ☐ YES, **please specify:** ☐ No new sedation used, sedation applied during cleaning was adequate. ☐ New or additional sedation required for wound closure.
Number of Zip 4 devices used: ***(ONLY APPLICABLE FOR ZIP GROUP)***	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ Other: _____ ☐ N/A

Wound dressing used on the device:	☐ Mepore ☐ Other: _____
Stope Time of procedure, *i.e. after wound dressing been applied.*	|__|__|:|__|__|:|__|__| HH:MM:SS
Time of PED Discharge	|__|__|:|__|__|:|__|__| HH:MM:SS

VAS – Visit 1	
Has the subject completed the VAS form?	☐ NO ☐ YES **VAS Score** _____
*If **NO**, please provide reason:*	

ADVERSE EVENT/ADVERSE DEVICE EFFECT QUESTION	
Has the subject experienced any Adverse Events/Adverse Device Effects during the treatment procedure? *If **YES**, please fill out the Adverse Event/Adverse Device Effect Log.*	☐ NO ☐ YES
Has any device deficiency been detected? *If **YES**, please fill out the Device Deficiency Form.*	☐ NO ☐ YES

FOLLOW UP CALLS SCHEDULED	
Follow-up **1** (10 days +/- 2 days) scheduled? (Home/PED)	☐ NO ☐ YES
Follow-up **2** (30 days +/- 2 days) scheduled?*(Home/ PED)*	☐ NO ☐ YES

Date (DD-MMM-YYYY): _____ Investigator signature: _____

FOLLOW UP 1 (10 DAYS +/- 2 DAYS)

Date (DD-MMM-20YY) and Time (HH:MM)	|__|__| - |__|__|__| - |2|0|__|__| |__|__|:|__|__|

DEVICE REMOVAL	
Has the device been properly attached during the healing period?	☐ NO ☐ YES
*If **NO**, please provide a reason:*	
Date (DD-MMM-20YY) and Time (HH:MM) of device removal:	|__|__| - |__|__|__| - |2|0|__|__| |__|__|:|__|__|
Device removed as scheduled (10 days +/- 2 days)?	☐ NO ☐ YES
*If **NO**, please provide a reason:*	
Adhesive remover used for Zip removal? ***(ONLY APPLICABLE FOR ZIP GROUP)***	☐ NO ☐ YES ☐ N/A

INTERVIEW	
If the subject would need laceration repair again, would the subject prefer the treatment he/she received in this study?	☐ NO ☐ YES ☐ I do not know
How satisfied is the subject with the removal procedure?	☐ Very satisfied ☐ Satisfied ☐ Neither satisfied nor dissatisfied ☐ Somewhat satisfied ☐ Very dissatisfied
Any additional comments the subject would like to inform about the treatment he/she received:	
Has the legal representative(s) helped out to answer the interview questions?	☐ NO ☐ YES

CONCOMITANT MEDICATION QUESTION	
Has there been any new or changes to the concomitant medication since last time? *If **YES**, please fill out the Concomitant Medication Log.*	☐ NO ☐ YES

ADVERSE EVENT/ADVERSE DEVICE EFFECT QUESTION	
Has the subject experienced any Adverse Events/Adverse Device Effects since last time? *If **YES**, please fill out the Adverse Event/Adverse Device Effect Log.*	☐ NO ☐ YES
Has any device deficiency been detected? *If **YES**, please fill out the Device Deficiency Form.*	☐ NO ☐ YES

VAS – FOLLOW UP 1	
Has the subject/legal representative(s) completed the VAS form ?	☐ NO ☐ YES **VAS Score ____**
*If **NO**, please provide a reason:*	

PHOTOGRAPHING – FOLLOW UP 1	
photographs on the laceration?	☐ NO ☐ YES
*If **NO**, please provide a reason:*	

FOLLOW UP SCHEDULED	
Has the follow up **2** (30 days +/- 2 days) been scheduled?	☐ NO ☐ YES
*If **NO**, please provide a reason:*	

Date (DD-MMM-YYYY): _____ Investigator signature: _____

FOLLOW UP 2 (30 DAYS +/- 2 DAYS)

Date (DD-MMM-20YY) and Time (HH:MM)	|__|__| - |__|__|__| - |2|0|__|__| |__|__|:|__|__|

CONCOMITANT MEDICATION QUESTION	
Has there been any new or changes to the concomitant medication since last time? *If **YES**, please fill out the Concomitant Medication Log.*	☐ NO ☐ YES

ADVERSE EVENT/ADVERSE DEVICE EFFECT QUESTION	
Has the subject experienced any Adverse Events/Adverse Device Effects since last time? *If **YES**, please fill out the Adverse Event/Adverse Device Effect Log.*	☐ NO ☐ YES
Has any device deficiency been detected? *If **YES**, please fill out the Device Deficiency Form.*	☐ NO ☐ YES

WOUND HEALING SATISFACTION QUESTIONNAIRE – FOLLOW UP PHONE CALL 2	
Has the subject completed the Wound Healing Satisfaction form ?	☐ NO ☐ YES
*If **NO**, please provide a reason:*	

PHOTOGRAPHING – FOLLOW UP 2	
photographs on the laceration?	☐ NO ☐ YES
*If **NO**, please provide a reason:*	

Date (DD-MMM-YYYY): _____ Investigator signature: _____

Wound Evaluation Score (WES) Results from Photos

BASELINE

Date of photo evaluation(DD-MMM-20YY)	|__|__| - |__|__|__| - |2| 0 |__|__|

RESULTS	
1. Step-off of laceration edges	☐ NONE=1 ☐ YES=0 _____mm
2. Contour irregularity - puckering	☐ NONE=1 ☐ YES=0
3. Scar width – greater than 2 mm	☐ NONE=1 ☐ YES=0
4. Edge inversion – sinking, curling	☐ NONE=1 ☐ YES=0
5. Inflammation – redness, discharge	☐ NONE=1 ☐ YES=0
6. Overall cosmesis	☐ Acceptable=1 ☐ POOR=0
- **Total score:**	

Additional observation/comments made by independent observer:

_____
_____
_____
_____
_____

FOLLOW UP 1

Date of photo evaluation (DD-MMM-20YY)	|__|__| - |__|__|__| - |2| 0 |__|__|

RESULTS	
1. Step-off of laceration edges	☐ NONE=1 ☐ YES=0 _____mm
2. Contour irregularity - puckering	☐ NONE=1 ☐ YES=0
3. Scar width – greater than 2 mm	☐ NONE=1 ☐ YES=0
4. Edge inversion – sinking, curling	☐ NONE=1 ☐ YES=0
5. Inflammation – redness, discharge	☐ NONE=1 ☐ YES=0
6. Overall cosmesis	☐ Acceptable=1 ☐ POOR=0
- **Total score:**	

Additional observation/comments made by independent observer:

_____
_____
_____
_____
_____

FOLLOW UP 2

Date of photo evaluation (DD-MMM-20YY)	|__|__| - |__|__|__| - |2| 0 |__|__|

RESULTS	
1. Step-off of laceration edges	☐ NONE=1 ☐ YES=0 _____mm
2. Contour irregularity - puckering	☐ NONE=1 ☐ YES=0
3. Scar width – greater than 2 mm	☐ NONE=1 ☐ YES=0
4. Edge inversion – sinking, curling	☐ NONE=1 ☐ YES=0
5. Inflammation – redness, discharge	☐ NONE=1 ☐ YES=0
6. Overall cosmesis	☐ Acceptable=1 ☐ POOR=0
- **Total score:**	

Additional observation/comments made by independent observer:

_____
_____
_____
_____
_____

Date (DD-MMM-YYYY): _____ Investigator signature:

_____

STUDY TERMINATION

Date of completion or discontinuation (DD-MMM-20YY)	|__|__| - |__|__|__| - |2|0|__|__|

TERMINATION BEFORE RANDOMIZATION, i.e. screening failures
Due to inclusion or exclusion criteria, please specify: ☐ Inclusion criterion Please specify which criterion/criteria: _____ ☐ Exclusion criterion Please specify number of criterion/criteria: _____
TERMINATION AFTER RANDOMIZATION
Study completed according to protocol? ☐ NO ☐ YES
*If **NO**, please select one of the options below:* ☐ Unacceptable AE/ADE or SAE/SADE according to the opinion of the Investigator ☐ The decision of a subject and/or legal representative(s) to withdraw from the investigation (including if the subject/legal representative(s) withdraws informed consent) ☐ Subject withdrawn by Investigator for protocol non-compliance ☐ Subject lost to follow up. Number of attempts to contact subject/legal representative(s): |__|__| ☐ Other reason, ***please specify***:

In case of premature discontinuation, AEs/ADEs as well as SAEs/SADEs should be followed up.

ADVERSE EVENT/ADVERSE DEVICE EFFECT LOG

This is the last page of the AE/ADE log ☐

No	Description of event (diagnosis)	Is this event an AE or ADE?	Start date and Stope date (DD-MMM-20YY)	Severity of AE/ADE **1** Mild **2** Moderate **3** Severe	Serious *If YES, please complete the SAE Form and assign report No.*	Device Deficiency *If YES, please complete the Device Deficiency Form**	Relation-ship **0** Unlikely **1** Possibly **2** Likely	Action taken **0** None-required **1** Medication** **2** Intervention **3** Other	Outcome of AE/ADE **1** Resolved **2** Stable condition **3** Death **4** Other
01		AE ☐ ADE ☐	**Start:** |__|__|-|__|__|__|-|2|0|__|__| **Stop:** |__|__|-|__|__|__|-|2|0|__|__|	|__|	YES NO ☐ ☐ *If YES, state Report No:* _____	YES NO ☐ ☐	|__| Procedure |__| Device	|__| If 2 or 3, specify: _____ _____	|__|
02		AE ☐ ADE ☐	**Start:** |__|__|-|__|__|__|-|2|0|__|__| **Stop:** |__|__|-|__|__|__|-|2|0|__|__|	|__|	YES NO ☐ ☐ *If YES, state Report No:* _____	YES NO ☐ ☐	|__| Procedure |__| Device	|__| If 2 or 3, specify: _____ _____	|__|
03		AE ☐ ADE ☐	**Start:** |__|__|-|__|__|__|-|2|0|__|__| **Stop:** |__|__|-|__|__|__|-|2|0|__|__|	|__|	YES NO ☐ ☐ *If YES, state Report No:*	YES NO ☐ ☐	|__| Procedure |__|	|__| If 2 or 3, specify:	|__|

[הקלד טקסט]

					_____		Device	_____ _____	

* All device deficiencies related to the identity, quality, durability, reliability, safety or performance of an investigational medical device shall be documented.

** Please provide information on the Concomitant Medication Log.

Please note that an ongoing adverse event should be followed-up until the AE is resolved or until the Prinicpal Investigator decides that the AE is stable and needs no further follow up.

CONCOMITANT MEDICATION LOG

This is the last page of the CM log ☐

Please record all medications used at or during Visit 1. During follow-up calls, any changes or new medications must be recorded.

No	Generic Drug Name	Dosage	Indication	> 3 months prior to study start *	Start Date / Stop Date (if applicable) (DD-MMM-20YY)	Ongoing at the end of study
1				☐	Start date |__|__| - |__|__|__| - |2|0|__|__| Stop date |__|__| - |__|__|__| - |2|0|__|__|	☐
2				☐	Start date |__|__| - |__|__|__| - |2|0|__|__| Stop date |__|__| - |__|__|__| - |2|0|__|__|	☐
3				☐	Start date |__|__| - |__|__|__| - |2|0|__|__| Stop date |__|__| - |__|__|__| - |2|0|__|__|	☐
4				☐	Start date |__|__| - |__|__|__| - |2|0|__|__| Stop date |__|__| - |__|__|__| - |2|0|__|__|	☐

5				☐	Start date |__|__| - |__|__|__| - |2| 0 |__|__| Stop date |__|__| - |__|__|__| - |2| 0 |__|__|	☐

** Start date not applicable to fill out if the subject has been treated with the medication > 3 months*

SIGN OFF

SIGN OFF
By signing this page, I declare that all information on page 1 – page 17 (as well as the SAE/SADE form and/or Device Deficiency form, if applicable) of this Case Report Form has been reviewed and is correct and complete to the best of my knowledge as of the date below.
Date (DD-MMM-20YY): |__|__| - |__|__|__| - |2| 0 |__|__|
Principal Investigator signature:
Printed name of Principal Investigator:

WOUND HEALING SATISFACTION QUESTIONNAIRE
Study: ZIP-009

1. How satisfied are you with your mark/scar as a result of your wound?
    a. Very Satisfied
    b. Satisfied
    c. Okay
    d. Somewhat dissatisfied
    e. Very dissatisfied
    -
2. What do you think of the mark/scar as a result of your wound?

Very good ——————————— Very bad

3. How does your mark/scar feel?
    a. Very good
    b. Good
    c. Okay
    d. Not so good
    e. Very bad
    -
4. How much pain do you have on your mark/scar?

No pain ——————————— Worst

5. How did you think it was when the physician/nurse treated your wound?
    a. Very good
    b. Good
    c. Okay
    d. Not so good
    e. Very bad

6. Has the guardian assisted the child in filling out the questionnaire?
    a. Yes
    b. No

7. Date when the questionnaire was filled out

8. Additional comments