Abbreviations

Acronyms / Abbreviations	Terms
ACP	Acyl carrier protein
ACS	American College of Surgeons
AE	Adverse event
CDC	Centers for Disease Control and Prevention
CRO	Contract Research Organization
EC	Ethics Committee
EMS	Express Mail Service
EQ-5D-5L	European Quality of Life-5 Dimensions, 5 Levels Scale
e-CRF	Electronic Case Report Form
FAS	Full analysis set
FPG	Fasting plasma glucose
ICF	Informed Consent Form
IFU	Instructions for Use
LLC	Limited Liability Company
[redacted]	[redacted]
[redacted]	[redacted]
PP	Per Protocol
SAE	Serious adverse event
SOP	standard operating procedure
SSI	Surgical site infection
VAS	Visual Analogue Scale
WHO	World Health Organization

Study Device	[redacted] absorbable surgical suture is an antibacterial monofilament, synthetic absorbable device consisting of dyed (violet) polyester, i.e. poly(p-dioxanone), the empirical molecular formula of which is $(C_4H_6O_3)_X$. As the device is designed with barbs, it allows tissue approximation without the need to tie surgical knots. The device contains IRGACARE® MP (triclosan), a broad spectrum antibacterial agent, at no more than 2,360 μg/m. The pigment for the violet dye is D&C Violet No.2. Polydioxanone polymer has been found to be nonallergenic, nonpyrogenic and elicits only a slight tissue reaction during absorption. [redacted] absorbable surgical suture is an antibacterial monofilament, synthetic absorbable device prepared from a copolymer of glycolide and ε-caprolactone (Poliglecaprone 25). As the device is designed with barbs, it allows tissue approximation without the need to tie surgical knots. The device contains IRGACARE® MP (triclosan), a broad spectrum antibacterial agent, at no more than 2,360 μg/m. Poliglecaprone 25 copolymer has been found to be nonpyrogenic and elicits only a slight tissue reaction during absorption.
Inclusion Criteria	Subjects will be included if ALL of the following inclusion criteria applies: 1) The subject is ≥18, and <70 years old 2) Planned open thyroid surgery, adopting an anterior cervical curved incision (Kocher's incision); 3) Subject who volunteers to participate in this study, follows the study requirements and follow-up visit and signs the written Informed Consent Form voluntarily; 4) Subject who agrees to not schedule any elective surgical operation except the study surgery before the study is completed; 5) The investigator considers the subject's expected postoperative survival time is not less than 3 months.
Exclusion Criteria	Subjects will be excluded if ANY of the following exclusion criteria applies: 1) Female subjects who are pregnant or lactation at screening; 2) Preoperative clinical staging shows stage IV thyroid cancer, or cervical lymph nodes dissection is planned; 3) Suspected or confirmed anaplastic thyroid cancer; 4) Peripheral vascular disease affecting blood supply of the

The study population includes 501 cases of subjects who plan to receive thyroid surgery. The subjects are randomized into the investigational group 1 (using [redacted]), investigational group 2 (using [redacted]) and control group (using [redacted] and [redacted] according to the ratio of 1:1:1. See the table below for the specific suture levels, materials and techniques of each group.

Level	Suture Material (Technique)		
	Investigational group 1	Investigational group2	Control group
Ribbon muscles	[redacted] **(Continuous)**	[redacted] **(Continuous)**	[redacted] **(Continuous)**
Platysma	[redacted] (Interrupted)		
Intradermal	[redacted] **(Continuous)**	[redacted] **(Continuous)**	[redacted] **(Continuous)**

The above subjects will be followed up on Day 5-7 and Day 28-35 post-surgery, respectively. The primary endpoint is the proportion of subjects achieving Grade A healing of surgical incision in each group, central blinded evaluation will be performed on the incision pictures taken on Day 5-7 post-surgery; secondary endpoints include: incision suturing time, modified Hollander Wound Evaluation Scale, postoperative incision pain score, health related quality of life scale; safety endpoints include: incidence of postoperative surgical site infection (SSI), ASEPSIS score, incidence of incisional wound separation or wound dehiscence requiring intervention, incidence of delayed incisional wound healing events, incidence of other adverse events (AE), and product complaints.

4. Background Information of Clinical Trial

4.1 Introduction to the Condition and Investigational Products

Thyroid surgery is a very common type of wound cleaning surgery and with the development of surgical techniques and continuous improvement in people's pursuit of beauty, patients pay more and more attention to the appearance of incision after thyroid surgery. Surgeons have to choose appropriate surgical incision and approach, suture technique and material, minimize damage at different anatomical layers, reduce incision scar, decrease penetrance of scar and improve patients' quality of life, on the condition that the quality of thyroid surgery is guaranteed. At present, from the perspective of surgical approach, thyroid surgery is mainly done via open and endoscopic approaches and if an open surgery is done, an anterior cervical curved incision (Kocher's incision) is mainly adopted, while other incisions are not as commonly used as before. Since open thyroid surgery has a big base, there has been certain consensus on the use of intradermal continuous suture to reduce penetrance of scar clinically, and therefore the anterior cervical curved incision is selected for the thyroid surgery in this study.

In this study, the investigational products are two types of absorbable surgical sutures, and compared to traditional sutures, these two sutures are both knotless, surgical sutures containing an antibacterial agent (triclosan), except one of them consists of poly(p-dioxanone) and another is prepared from a copolymer of glycolide and ε-caprolactone.

The knotless function of the investigational products is realized by forming barbs via cutting the suture body, and such a design has been extensively applied in knotless sutures and has been demonstrated to be qualified for wound stitching (including high tensile tissues) and to reduce surgery (suture) time by lots of clinical studies and literature [1-5]. Besides, the decrease in surgery time is also related to the reduction of wound complications, especially SSI [6].

control group use different shapes and usages of suture, it is impossible to blind investigators who are responsible for suturing.

- Central evaluator: Imaging data will be submitted to Imaging Center for assessment to assess the primary endpoint and the modified Hollander score among secondary endpoints. The Central Imaging evaluators will be blinded.
- Monitor: As the product information is specified on the detachable label supplied with the product and instrument counting and source document verification is - done with the study product inventory records and subject's medical record, the monitor will not be blinded.

In addition, this study will collect data about objective measures, study related information will be recorded in the source medical records as detailed as possible, the monitor will pay attention to verifying the data in the source medical records during the monitoring process, investigator training will be strengthened, and investigators will closely communicate with subjects to improve compliance of subjects. This will help to reduce the informational bias.

7.1.4 Investigational Medical Devices and Control Medical Devices

	Investigational Device 1 [redacted]	Investigational Device 2 [redacted]	Control Device [redacted] or [redacted]
Picture	[redacted]		
Launch the global market (year)	Global: 2016	Global: 2016	Global: 2006 China: 2014
Indications	Indicated for use in soft tissue approximation where the use of absorbable sutures is appropriate	Indicated for use in soft tissue approximation where the use of absorbable sutures is appropriate	[redacted]: Indicated for use in soft tissue approximation, including use in pediatric cardiovascular tissue where growth is expected to occur and ophthalmic surgery (other than contact with cornea and sclera). [redacted] suture is not indicated in adult cardiovascular tissue, microsurgery and neural tissue. These sutures are particularly useful where the combination of an absorbable suture and extended wound support (up to six weeks) is desirable. [redacted]: Indicated for use in general soft tissue approximation and/or ligation, but not for use in cardiovascular or neurological tissues, microsurgery or ophthalmic surgery.
Components	Suture, surgical needle	Suture, surgical needle	Suture, surgical needle
Size	4-0 to 1	4-0 to 2-0	[redacted]:6-0 to 1

7.1.7 Safety Evaluation Method

1) Description of safety parameters

Safety Endpoints include:

1. Incidence of postoperative SSI, which is defined as follows according the standard of US Centers for Disease Prevention and Control [16]:

1) Superficial incisional SSI:

Involves skin or subcutaneous tissue, occurs within 30 days postoperatively, and must fulfill one of the following additional criteria:

- Purulent drainage from the superficial incision with or without diagnostic laboratory testing;
- Microorganisms isolated from aseptically obtained culture of fluid or tissue from the superficial incision;
- At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness or heat, and the superficial incision is deliberately opened by a surgeon (unless culture of incision is negative);
- Diagnosis of a superficial incisional SSI by a surgeon or attending physician.

Do not report the following conditions as SSI:

- Stitch abscess (minimal inflammation and discharge confined to the points of suture penetration);
- Infection of an episiotomy or newborn circumcision site;
- Infected burn wound;
- Incisional SSI that extends into the fascial and muscle layers (see deep incisional SSI).

Note: Specific criteria are used for identifying episiotomy and newborn circumcision sites and infected burn wounds.

2) Deep incisional SSI:

Infection occurs within 30 days after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation, infection involves deep soft tissues (e.g., fascial and muscle layers of the incision) and at least one of the followings:

- Purulent drainage from the deep incision but not from the organ/space component of the surgical site;
- A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38°C), localized pain, or tenderness, except that the incision is culture-negative;
- An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination;
- Diagnosis of a deep incisional SSI by a surgeon or attending physician.

Note:

- Report infection that involves both superficial and deep incision sites as deep incisional SSI;
- Report an organ/space SSI that drains through the incision as a deep incisional SSI.

3) Organ/space SSI:

Infection occurs within 30 days after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation, and infection

involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation, and at least one of the followings:

- Purulent drainage from a drain that is placed through a stab wound into the organ/space;
- Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space;
- An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination;
- Diagnosis of an organ/space SSI by a surgeon or attending physician.

It is unnecessary to conduct any confirmatory culture, unless the physician considers it necessary to provide subjects with appropriate treatment according to the local standard of care.

2. ASEPSIS score (only assessed in subjects with confirmed SSI):

The severity of incision infection is assessed by numeric scores (determining the presence or absence of SSI and types relative to CDC standard). The ASEPSIS incision score is used to evaluate the visual characteristics of incision and if additional treatment can be an incentive of infection or not when the subject leaves the hospital. The predictors include: serous discharge, erythema, purulent exudate, separation of deep tissues, antibiotics, drainage of pus, debridement of wound, isolation of bacteria, and requirement of inpatient care. Surgeons should assess each parameter and provide a numeric score based on the objective standard of incision appearance and the clinical outcome of infection. The following additional points are added: antibiotic treatment of SSI (10 points), drainage of pus under local anesthesia (5 points), debridement of wound under general anesthesia (10 points), isolation of bacteria from incision (10 points), and stay in hospital over 14 days (5 points). The total score, ranged from 0 to 100, is calculated to define the severity of incision according to the percentage of each characteristic's impact on incision [18,19]. Please refer to Annex 6.

3. Incidence of incisional wound separation or wound dehiscence requiring intervention;

4. Incidence of delayed incisional wound healing events;

5. Incidence of other adverse events;

6. Product complaints.

2) Selection of method and time to evaluate, record, and analyze the safety parameters

The safety parameters are recorded on the e-CRF according to the Investigator's record, medical record, and examination results, which are collected at each follow-up visit 2, 3, 4 and 5. See Section 8 for the Analysis Method of Safety Parameters.

7.2 Trial Flow Chart

7.2.1 Flow diagram of clinical trial

The schedule and events table of the trial is as follows:

Project	V1	V2	V3	V4	V5	Withdraw visit
Event/time point	Screening /baseline: within 14 days prior to surgery	Randomization: prior to surgery	Surgery	5-7 days after surgery	28-35 days after surgery	For subjects randomized but without any of study sutures used and for subjects who withdraw ICF[i]

Informed consent	X					
Demographic information	X					
Randomization		X				
Inclusion & Exclusion Criteria	X	X				
Fasting plasma glucose test [a]	X					
Blood/urine pregnancy test [b]	X					
Medical Record/ Surgical history [c]	X	X				
Physical examination	X					
Concomitant Medications [d]	X	X	X	X	X	
Surgical data [e]			X			
Concomitant treatment			X	X	X	
Imaging data of incision [f]				X	X	
Discharge date				X		
Wound healing grade assessment [g]				X		
Modified Hollander Wound Evaluation Scale [g]					X	
Postoperative incision pain score				X	X	
EQ-5D-5L	X			X	X	
SSI/ASEPSIS score				X	X	
Complications of incision [h]				X	X	
Adverse event		X	X	X	X	X
Product complaint			X	X	X	X
End of study					X	X

a. The result of the examination should be completed within 7 days prior to the signing of ICF.
b. Applicable to female subjects of childbearing age (less than 2 years post-menopausal). The result of the examination completed within 7 days prior to the signing of ICF is acceptable.
c. Disease newly diagnosed or existing within the period from 30 days prior to the signing of ICF to randomization are collected.
d. Concomitant medications used within the period from 7 days prior to the signing of ICF to the end of the study will be documented, excluding medications for surgical anesthesia.
e. The surgical data should include suturing time, length of operation, total operating room time, intraoperative suture performance indicators (collected data of the second case using [redacted] and [redacted] from each Investigator), and intraoperative use of suture devices.
f. At V4, a picture of complete neck anterior view containing full length of the incision should be collected; at V5, 5 pictures of incision should be collected [including a picture of complete neck anterior view containing full length of the incision, a picture taken parallel to the incision plane, a picture taken at a 45° angle to the incision plane, and incision lateral view pictures of both sides (one for each)] for assessment done by independent Central Imaging evaluators.
g. Assessed by Central Imaging evaluators using imaging data provided by study sites.
h. Including incisional wound separation or wound dehiscence requiring intervention, target incisional wound healing delay, etc.

the two group comparisons, the p-value associated with the non-inferiority test will be calculated using the Normal approximation Z (pooled) statistic. If the smaller p-value is smaller than 0.0125, then the null hypothesis associated with this p-value will be rejected and it will be concluded that the associated Test product is non-inferior to Control; subsequently, the larger p-value will be compared to 0.025 in order to test the non-inferiority of the other Test product to Control. If the smaller p-value is larger than 0.0125, then neither of the null hypotheses can be rejected and it will be concluded that, for both investigational devices, the study failed to demonstrate non-inferiority to Control.

The primary endpoint will be analyzed using the Full Analysis Set (FAS) and Per-Protocol (PP) sets. The PP analysis will be considered the primary analysis, while the FAS analysis will be considered supportive. The analysis sets for this study are defined in section 8.8.

The following **secondary efficacy endpoints** will be summarized descriptively by treatment group for the FAS:

1. Incision suturing time, defined as the time required from the first needle insertion for stitching ribbon muscles to the completion of intradermal suture (min);
2. Modified Hollander Wound Evaluation Scale;
3. Postoperative incision pain score (VAS Scale);
4. Health related quality of life scale (EQ-5D-5L).

In addition, the following safety endpoints will be summarized descriptively t by treatment group for the Safety analysis set:

1. Incidence of postoperative SSI;
2. ASEPSIS score (only assessed in subjects with confirmed SSI);
3. Incidence of incisional wound separation or wound dehiscence requiring intervention;
4. Incidence of delayed incisional wound healing events;
5. Incidence of other AEs;
6. Product complaints.

The incidence of AEs will be assessed according to the classification of event and summarized descriptively by treatment groups. Incidence of AEs will also be assessed by onset time (intraoperative or postoperative), relationship to study surgical procedure, relationship to the study product, severity, and seriousness.

All continuous variables will be summarized by number of subjects, mean, standard deviation, median, minimum and maximum. All categorical data will be summarized by frequencies and associated percentages. No inferential statistics will be generated for secondary efficacy and safety endpoints.

8.2 Calculation of Sample Size

8.2.1 Total Sample size

This clinical study will enroll approximately 501 subjects, 167 for each treatment group.

One hundred fifty (150) evaluable subjects per study arm will achieve 80% power to detect a non-inferiority margin difference in group proportions of -0.05 for each of the two comparisons using a Pearson Chi-square test with a one-sided significance level of 0.0125. The proportion of successes in the Control group is assumed to be 0.98. The proportion of successes in Test group ([redacted] or [redacted]) is assumed to be 0.93 under the null hypothesis of inferiority. The power was computed for the case when the actual proportion of successes in the Test group is 0.98.

In order to account for a potential 10% dropout rate, approximately 167 subjects per arm will be enrolled, for a total of approximately 501 subjects.

8.2.2 Number of Subjects for Clinical Trial of Each Disease Entity and Reasons for

The severity of AE will be separated into the following grades:

Mild: Awareness of sign or symptom that does not interfere with the subject's usual activity or is transient, resolved without treatment and with no sequelae,

Moderate: Interferes, but does not hinder, the subject's usual activity and may require treatment;

Severe: Causes severe discomforts, results in major impact on the subject's activities of daily living and requires treatment or intervention.

The causal relationship should be assessed as follows:

Unrelated	There is no correlation between the AE and the use of medical device
Possibly unrelated	The occurrence of AE is more likely to be associated with other factors, e.g.: concomitant medication or concomitant disease, or the occurrence time of the event does not suggest a causal relationship with the use of study-related device.
Possible:	The occurrence of AE may be caused by study-related device. Other factors may have contributed to the event, e.g.: concomitant medication or concomitant disease. The event occurs within a reasonable time after the use of study-related device and the causal relationship between the event and the use of study-related device cannot be ruled out.
Probable	The occurrence of AE is probably caused by the use of study-related device. The event occurs within a reasonable time after the use of study-related device, e.g.: it is confirmed after the medical device is taken out. It is unlikely to have another explanation for the event (e.g. concomitant medication or concomitant disease).
Definitely Related:	The occurrence of AE has been confirmed as a definite side effect of the medical device and cannot be explained by other reasons (e.g. concomitant medication and concomitant disease). The occurrence time of the event highly suggest a causal relationship (e.g. reaction after removal of medical device and replantation of medical device).

14.2 Serious Adverse Event

SAE refers to any untoward medical occurrence in a clinical trial that results in death or serious deterioration of health status, including life-threatening conditions or damage, permanent defect of body structure or body function, events requiring inpatient hospitalization or prolongation of existing hospitalization, those requiring medical or surgical intervention to avoid permanent defect of body structure or body function; and those resulting in fetal distress, fetal death or congenital anomaly/birth defect, etc.

A planned hospitalization and/or medical intervention for pre-existing conditions, or a procedure required by the protocol, without serious deterioration in health, is not considered to be a serious adverse event.

14.3 Device Complaints

A product complaint is defined as any written, electronic or oral communication that alleges deficiencies related to the identity, labelling, quality, durability, reliability, safety, efficacy, or performance of a device after it is released for distribution. In the event of any device complaint, the study site must inform the monitor and track and report it according to the process stipulated by the Sponsor. The study site must inform the study monitor of all device complaints of the study groups and control group. The monitor will track and report device complaints according to the method and time limit stipulated by the Sponsor and China's laws and regulations and return related products to the quality department of J[redacted] upon the request of the Sponsor.

14.4 Device Defects

Device defects refer to unreasonable risks of medical device existing during the clinical trial

under normal use, which may endanger human health and life safety, such as labeling error, quality problem, malfunctioning, etc.

In the event of any device defect that may lead to SAE, the Sponsor should report it to the Food and Drug Administration Department and Health Planning Department at the same level within 5 working days after the awareness of the defect. The Sponsor will notify other clinical trial institutions and investigators participating in the trial and notify the EC of the clinical trial institution involved in a timely manner via its medical device clinical trial management department. The investigator should record all AEs occurring and device deficiencies found in the process of clinical trial, work with the Sponsor to analyze the causes of the events, generate the written analysis report, present the comments on the continuation, discontinuation or termination of the trial, and report to the Ethics Committee by the administrative department for clinical trial of medical device of clinical trial institution for review.

14.5 Reporting Procedure and Contact Person Information

The investigator should ensure sufficient treatment is given for any AE experienced by a subject, including clinically significant laboratory test values related to this study.

Once a subject is randomized, his/her AE should be followed up, until they are resolved or stabilized and the clinical outcome has been determined, or until his/her last follow-up visit (the earliest one shall prevail). If the investigator considers the AE is related to the study product, the subject must be followed up until the event is resolved and stabilized.

The investigator must report the AE to the Sponsor via e-CRF within 2 weeks after its awareness. The Investigator should record the nature, severity, treatment and outcome of AE and determine whether the AE is related to the study device, medication, or surgical procedure defined in the study protocol or not.

All the SAEs must be followed up until they are resolved (with or without sequela). When the event is not resolved or stable at the end of study, the medical monitor in this clinical study will decide whether it is necessary to collect the further follow-up information. The Investigator should send a report to regulatory agencies at different levels, EC and the Sponsor within 24 hours after the awareness of a SAE.

The Investigator must report any SAEs and any device defects possibly leading to SAE that occur during the study to the Sponsor and related regulatory department required by laws and regulation within 24 hours after the awareness of the event or defect; and provide further information upon the sponsor’s request.

For any SAE and device defect that may lead to SAE, the Investigator should report it to the regulatory authorities, EC and the Sponsor within the time limit defined by the Sponsor. According to the requirements of No.25 Decree, the Sponsor should report the SAE or defect to the Food and Drug Administration Department and Competent Department of Health and Family Planning at the same level within 5 working days after its awareness. – The Sponsor will notify other clinical trial institutions and investigators participating in the trial and notify the EC of the clinical trial institution involved in a timely manner via its medical device clinical trial management department.

The investigator should record all AEs occurring and device deficiencies found in the process of clinical trial, work with the Sponsor to analyze the causes of the events, generate the written analysis report, present the comments on the continuation, discontinuation or termination of the trial, and report to the Ethics Committee by the administrative department for clinical trial of medical device of clinical trial institution for review. Once a device complaint is found, the site should inform the Sponsor as soon as possible, and report the device related information on the relevant CRF.

In the event of a device failure, the study site must notify the clinical monitor as soon as possible.

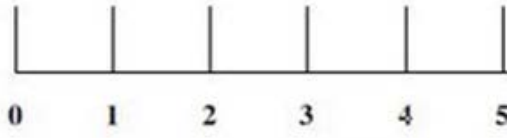
Annex 4: Vas Scale

1. Postoperative Incisional Pain

Score 0 means no pain;
Score 10 means unbearable: severely affects sleep with other symptoms, or passive position;

2. Intraoperative suture performance indicators

   Survey to be completed for the second case using [redacted] and [redacted] for each Investigator.



- Ease to pass through tissues

Score 0 means very easy to pass through tissues;
Score 5 means very difficult to pass through tissues;

- Surgical operation profile (including surgical “handfeel”)

Score 0 means the best “handfeel”;
Score 5 means the worst “handfeel”;

- Suture memory

Score 0 means no suture memory;
Score 5 means the suture memory is very serious;

- Wear resistance of suture

Score 0 means the wear resistance is very good;
Score 5 means the wear resistance is very bed.

Synopsis

<table>
<tr><td>Study Title</td><td>A Prospective, Multi-center, Randomized Controlled Study Evaluating the Efficacy and Safety of Two Types of Absorbable Surgical Sutures in the Suturing of Thyroid Surgery Incision</td></tr>
<tr><td>Study Objective</td><td>The primary objective of this study is to evaluate the efficacy and safety of two types of absorbable surgical sutures -- [redacted] Knotless Plus Tissue Control Device and [redacted] Knotless Tissue Control Device (hereinafter referred to as [redacted] and [redacted]) used in thyroid surgery to suture surgical incision.</td></tr>
<tr><td>Number of Study Sites</td><td>Planned selection of 10 sites</td></tr>
<tr><td>Number of subjects</td><td>Planned enrollment of 501 subjects</td></tr>
<tr><td>Study Design</td><td>This study adopts a multicenter, prospective, randomized controlled design. The study population are subjects who undergo thyroid surgery.
Before the surgery, subjects are randomized in 1:1:1 ratio to the investigational group 1 (using [redacted]), investigational group 2 (using [redacted]) and control group. See the table below for the specific suture levels, materials and techniques of each group.
<table>
<tr><td rowspan="2">Level</td><td colspan="3">Suture Material (Technique)</td></tr>
<tr><td>Investigational group 1</td><td>Investigational group2</td><td>Control group</td></tr>
<tr><td>Ribbon muscles</td><td>[redacted] (Continuous)</td><td>[redacted] (Continuous)</td><td>[redacted] (Continuous)</td></tr>
<tr><td>Platysma</td><td colspan="3">[redacted] (Interrupted)</td></tr>
<tr><td>Intradermal</td><td>[redacted] (Continuous)</td><td>[redacted] (Continuous)</td><td>[redacted] (Continuous)</td></tr>
</table>
A blinded central imaging evaluation will be performed on the healing condition of surgical incision on Day 5-7 post-surgery. The subjects will be blinded to the type of suture used for wound closure.</td></tr>
</table>

	neck; 5) Active infectious collagenosis (e.g. scleroderma), or any other disease that would interfere with wound healing; 6) Fasting plasma glucose ≥7.7 mmol/L; 7) History of coagulation diseases; 8) Current oral or intravenous antibiotic therapy for existing disease or infection; 9) History of immunosuppressant use (e.g. steroids) within the last 6 months; 10) Chemotherapy or radiotherapy within the last 6 months, or planned chemotherapy or radiotherapy during the study; 11) Personal or family history of keloid formation or hyperplasia; 12) Current participation in any other drug (within 30 days or within 5 half-lives of the investigational drug) or device clinical study; 13) History of any thyroid surgery, except thyroid fine-needle aspiration biopsy; 14) Planned use of skin adhesive at the incision site; 15) The subject is not suitable for participating in this study for any other reasons, as judged by the investigator.
Endpoints	Primary Efficacy Endpoint: Proportion of subjects achieving Grade A healing of surgical incision(success) in each group. Wound healing grade will be assessed by independent, blinded Central Imaging evaluators using (a picture of complete neck anterior view, containing full length of the incision) on Day 5-7 post-surgery. Secondary Efficacy Endpoints: 1. Incision suturing time, defined as the time required from the first needle insertion for stitching ribbon muscles to the completion of intradermal suture (min) 2. Modified Hollander Wound Evaluation Scale [assessed by Central Imaging evaluators using pictures, including a picture of complete neck anterior view containing full length of the incision, a picture taken parallel to the incision plane, a picture taken at a 45° angle to the incision plane, and incision lateral view pictures of both sides (one for each)]; 3. Postoperative incision pain score (Visual Analogue Scale, VAS); 4. Health related quality of life scale (EQ-5D-5L).

In addition, the investigational product also contains an antibacterial agent to resist SSI (nonantibacterial launched products have been marketed in China). The antibacterial agent contained is triclosan, which, at a low concentration, can interact with the acryl carrier protein (ACP) reductase (FabI) of sensitive bacteria and subsequently inhibit the formation of sensitive bacterial fatty acids to achieve an antibacterial effect [7]. It has been confirmed both in in vivo and in vitro experiments that, triclosan-containing sutures can effectively resist colonization of sensitive bacteria, including *Staphylococcus aureus*, *Staphylococcus epidermidis*, methicillin-resistant *Staphylococcus aureus*, methicillin-resistant *Staphylococcus epidermidis*, *Klebsiella pneumoniae* and *Escherichia coli* [8-10]. In the meantime, it has also been shown by clinical studies that, such an effect also works in human body to reduce about 30% of SSIs [11-12]. Based on the great clinical efficacy and safety in clinical application of such sutures, World Health Organization (WHO), American College of Surgeons and US Centers for Disease Control and Prevention (CDC) all recommend the application of knotless sutures in surgeries to prevent SSI in their guidelines [13-15].

To sum up, the investigational products will be new products with two kinds of relatively mature suture processes applied in the same type of suture. This study will demonstrate the investigational products' efficacy in wound closure in thyroid surgery and safety in clinical application, to support the marketing of the products in China.

4.2 Application of Investigational Products and Control Products

The investigational products have been granted with 510K clearance by the country of origin USA in 2015. Currently the products have been marketed in many countries, however, due to the short marketing time, they have not been reported in literature yet.

Both the control products [redacted] and [redacted] are non-barbed, triclosan-coated sutures. Such sutures have been marketed in China since 2014. As mentioned above, the efficacy and safety of such sutures have been sufficiently validated [11-12, 16].

4.3 Product Registration and Reason for Clinical Trial Registration in China

The investigational products were granted with 510K marketing clearance by the country of origin USA in 2015 and was granted with EU marketing authorization (CE certificate) in 2016. To support the marketing of the investigational products in China and according to the requirements of China's *Guidelines for Medical Evaluation of Medical Devices*, the study selects non-barbed [redacted] and [redacted] as launched products. The difference between the investigational products and launched products lies in whether they contain barbs or not. Therefore, the clinical trial design is to demonstrate that the barbed nature of the suture does not have any adverse impact on the safety and efficacy of the products.

5. Features, Structural Composition, Operation Principle, Mechanism of Action, and Study Population

5.1 Features

Type	Name of device	Design Features	Characteristics of Material
Investigational Product 1	[redacted]	This product is an antibacterial monofilament absorbable suture consisting of barbed suture material. Its barbs allow tissue approximation without the need to tie surgical knots. The suture contains triclosan, an antibacterial agent, which is only used to inhibit colonization of bacteria on sutures.	The suture material is polyester, i.e. poly(p-dioxanone), the empirical molecular formula of which is $(C_4H_6O_3)x$.

			[redacted]:6-0 to 1
Materials	Poly(p-dioxanone)	Poliglecaprone 25 (i.e. a copolymer of glycolide and ε-caprolactone)	[redacted]: Poly(p-dioxanone) [redacted]:Poliglecaprone 25 (i.e. a copolymer of glycolide and ε-caprolactone)

7.1.5 Subject Selection

1) Inclusion criteria

1. The subject is ≥18, and <70 years old
2. Planned open thyroid surgery, adopting an anterior cervical curved incision (Kocher's incision);
3. Subject who volunteers to participate in this study, follows the study requirements and follow-up visit and signs the written Informed Consent Form voluntarily;
4. Subject who agrees to not schedule any elective surgical operation except the study surgery before the study is completed;
5. The investigator considers the subject's expected postoperative survival time is not less than 3 months.

2) Exclusion Criteria

1. Female subjects who are pregnant or lactation at screening;
2. Preoperative clinical staging shows stage IV thyroid cancer, or cervical lymph nodes dissection is planned;
3. Suspected or confirmed anaplastic thyroid cancer;
4. Peripheral vascular disease affecting blood supply of the neck;
5. Active infectious collagenosis (e.g. scleroderma), or any other disease that would interfere with the wound closure;
6. Fasting plasma glucose (FPG) ≥7.7 mmol/L;
7. History of coagulation diseases;
8. Current oral or intravenous antibiotic therapy for existing disease or infection;
9. History of immunosuppressant use (e.g. steroids) within the last 6 months;
10. Chemotherapy or radiotherapy within the last 6 months, or planned chemotherapy or radiotherapy during the study;
11. Personal or family history of keloid formation or hyperplasia;
12. Current participation in any other drug (within 30 days or within 5 half-lives of the investigational drug) or device clinical study;
13. History of any thyroid surgery, except thyroid fine-needle aspiration biopsy;
14. Planned use of skin adhesive at the incision site;
15. The subject is not suitable for participating in this study for any other reasons, as judged by the investigator.

3) Criteria and procedure of Study Discontinuation

The criteria for Subject's Discontinuation from Study include, but are not limited to:

1. Withdrawal of consent: Subject decides to withdraw from the study. This decision must be "self-determination" and should be documented;
2. Investigator's judgement: The Investigator may determine the withdrawal of subjects from the study according to reasonable medical judgement and such withdrawal may benefit the subject mostly.
3. Adverse event (AE)/Serious Adverse event (SAE: The AE or SAE may not cause the subjects to discontinue the study treatment. If the investigator decides to withdraw a subject from the study, this subject must be followed up, until the AE/SAE is resolved or until the stable clinical endpoint is reached;

i. For subjects who are randomized but without any of study sutures used for incision closure, this visit is conducted as early as possible. For subjects who withdraw ICF, this visit is conducted as early as possible with subjects' permission. Telephone visit is acceptable.

7.2.2 Specifications for Use of Devices

According to Instructions for Use (IFU) and technical manual of the product, the requirements for the use of study product are as follows:

1) **Indications/Scope of Application of Product**

Investigational products ([redacted] and [redacted]): indicated for use in soft tissue approximation where the use of absorbable sutures is appropriate

Control products:

[redacted]: It is indicated for use in soft tissue approximation, including use in pediatric cardiovascular tissue where growth is expected to occur and ophthalmic surgery (other than contact with cornea and sclera). [redacted] suture is not indicated in adult cardiovascular tissue, microsurgery and neural tissue. These sutures are particularly useful where the combination of an absorbable suture and extended wound support (up to six weeks) is desirable.

[redacted]: It is indicated for use in general soft tissue approximation and/or ligation, but not for use in cardiovascular or neurological tissues, microsurgery or ophthalmic surgery.

2) **Recommended Methods of Operation**

[redacted] device is designed to be used in continuous suture patterns. [redacted] device is intended to be used without anchoring knots to begin or terminate the device line.

Use as required per surgical procedure.

1. Secure the fixation loop portion to robust tissue by taking a bite in the designated tissue, passing the needle through the loop and pulling tautly around the anchoring tissue.

2. After [redacted] Device is anchored into the tissue, grasp the strand and approximate tissue to the desired tension. Bites, or passes through the tissue, can be taken in a continuous suturing technique to approximate the wound. Care should be taken to utilize the [redacted] Device on the barbed segments only. Do not attempt to approximate wounds using the non-barbed segment near the needle, as the barbs are required for successful wound approximation with the [redacted] Device

3. (1) To complete the closure in subcuticular closure, take at least one pass in the reverse direction. Then pass the needle across the incision and take a split thickness bite perpendicular to the incision and exit the skin.

(2) To complete the closure in all other tissue layers, take at least two passes in the reverse direction to complete the closure.

4. Then gently pull on the free end of the device and cut flush with the surface of the tissue.

To remove the entire [redacted] Device: Cut the [redacted] Device at the end anchored with the loop, and then pull the distal end to remove the device.

[redacted] device is designed to be used in continuous suture patterns. [redacted] Device is intended to be used without anchoring knots to begin or terminate the device line.

Use as required per surgical procedure.

1. Secure the fixation loop portion to robust tissue by taking a bite in the designated tissue, passing the needle through the loop and pulling tautly around the anchoring tissue.

Determination

A total of approximately 501 Chinese subjects who undergo thyroid surgery will be included in the study. With consideration to the angle of incision, subjects with stage IV thyroid cancer and anaplastic thyroid cancer are excluded, but there are no restrictions on other disease.

8.2.3 Minimum and Maximum Number of Subjects in Each Clinical Trial Institution and Reasons for Determination

In China, total of approximately 501 subjects undergoing thyroid surgery in approximately 10 study sites will be enrolled into the study. Each site should enroll more than 125 subjects (25% of the total number).

During the implementation of the study, the Sponsor will try to ensure the consistency of number of subjects among sites in order to reduce the variation of the primary endpoint (and subject safety indicators) among sites.

8.3 Significance Level and Power of Clinical Trial

Determination of the sample size was performed assuming 80% power and a significance level of 0.0125 for each comparison. To control the overall Type I error rate at a 0.025 level for the two hypotheses being tested, Holm's stepdown multiple comparison procedure is being utilized.8.4 Expected Dropout Rate

The expected dropout rate in this study is 10%.

8.5 Criterion of Acceptability/Unacceptability of Clinical Trial Result

For the primary endpoint analysis, the Holm's step-down procedure will be used. For each of the two group comparisons, the p-value associated with the non-inferiority test will be calculated. If the smaller p-value is smaller than 0.0125, then the null hypothesis associated with this p-value will be rejected and it will be concluded that the associated Test product is non-inferior to Control; subsequently, the larger p-value will be compared to 0.025 in order to test the non-inferiority of the other Test product to Control. If the smaller p-value is larger than 0.0125, then neither of the null hypotheses can be rejected and it will be concluded that, for both test devices, the study failed to demonstrate non-inferiority to Control.

8.6 Criteria and Reason for Terminating the Trial Based on the Statistical Results

No interim analysis and corresponding early termination criteria, are planned for this trial; therefore this section does not apply. All the statistical analyses will be done after all the data are collected, and after study database lock. A Statistical Analysis Plan will be finalized prior to database lock and the performing of any final analyses.

8.7 Statistical Method of All Data, together with the Handling Method of Missing, Unused and Error Data (including Termination and Withdrawal Halfway) and Unreasonable Data

All study endpoints will be analyzed using the available data. There will be no missing data imputation in this study.

8.8 Selection Criteria and Reason of Subjects Included in the Analysis

All subjects that meet the inclusion/exclusion criteria are considered to meet the requirements for recruitment.

Three analysis sets in the study are defined for this study, as follows:

- FAS consists of all the enrolled subjects who were randomized and for whom the randomized suture materials were used for incision closure.
- PP (evaluable) Set contains all the subjects in the FAS who have no major protocol

The monitor should coordinate related departments and return the product to the quality department of [redacted] according to the Sponsor's schedule.

The contact persons for AE and device defect reporting are as follows:

AE: [redacted].com [redacted].com
Device Complaints: [redacted].com

15. Deviation From Clinical Trial Protocol And Regulations For Clinical Trial Protocol Amendment

The study protocol deviations are defined as the circumstances that fail to comply with the requirements of clinical trial protocol intentionally or unintentionally.

All protocol deviations should be reported as protocol deviations to the Sponsor via protocol deviation form and monitoring visit report. The reporting should include the date and reason for protocol deviations. The Investigator should also report the protocol deviations to hospital's medical device clinical trial management department, and report to EC via them, in accordance with the procedures and regulations and the requirements of the hospital.

If a protocol amendment occurs, the Sponsor or designated person should submit a summary of changes of the study protocol to the Investigator, regulatory authority, and the Ethics Committee, etc. according to the relevant laws and regulations. All major amendments must be approved by the Ethics Committee and regulatory authority (if needed) prior to implementing any changes to study procedures.

An amendment is regarded substantial when they are likely to have a significant impact on:

- The safety or physical or mental integrity of the subjects;
- Scientific value of trial;
- Conduct or management of the trial;
- Quality or safety of investigational medical device specified in the trial.

16. Direct Access to Source Data and Document

The source data is defined as all information in the subject's original medical record and its approved copy regarding the clinical findings, observations and other activities in the clinical trial, which can be used for reproduction and evaluation of clinical trial. The source documents are documents on which the source data is recorded, including printed, paper or electronic documents.

The subject's medical record and other study related documents (source documents) must be maintained and retained by the Investigator. The Investigator should allow the monitors and auditors/inspectors to review all relevant subject records, including but not limited to the following information:

- Medical/physical condition of the study subject that meets the inclusion criteria prior to participating this study;
- Medical record documenting the informed consent process;
- Operational description of use and implantation of the study product;
- All inspection results and follow-up;
- Examined printed output file or report (for example, X-ray film) that is dated and signed;
- Imaging or video data of wound healing status;
- Description of AE and follow-up of AE (description of event, severity, date of occurrence, duration, correlation with the study device, study procedure, outcome, and treatment of the AE, concomitant medications when the AE occurs);

Health Questionnaire

Simplified Chinese Version for China

(Simplified Chinese version for China)