Protocol No.: 20256031708

Clinical Trial on Performance and Safety of Disposable Powered Articulating Endoscopic Linear Cutter Stapler in Gastrointestinal Tissue Cutting and Anastomosis

(Prospective, multi-center, stratified block randomization, incomplete blinding, parallel positive control, non-inferiority testing)

Study Device: Disposable Powered Articulating Endoscopic Linear Cutter Stapler

Product Specifications: See the IFU for details.

Regulatory Category of Study Medical Device: Class III medical device

Requiring Clinical Trial Review and Approval: Yes☐ No☑

Similar Product(s) Existing in China: Yes☑ No☐

Protocol Version No.: 1.1

Protocol Version Date: 2019.01.25

Leading Site: Yangzhou First People's Hospital

Coordinating Investigator: Ni Qing

Sponsor: Fengh Medical Co., Ltd.

Agent :/

Affiliated Hospital of Yangzhou University
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Confidentiality Statement

All information contained in this report is proprietary to Fengh Medical Co., Ltd. Therefore, it is only provided to the investigators, co-investigators, ethics committees, regulatory authorities and other relevant medical institutions for review. Without the written approval of the sponsor, no information should be given to any third party not involved in the study, except for necessary explanation when signing the informed consent form with the subjects who may participate in the study.

Notes:

1. To carry out clinical trials of medical devices, clinical trial protocols shall be developed.
2. The clinical trial protocol is jointly designed and developed by the investigators of the clinical study institution and the sponsor. The sponsor shall sign the clinical trial protocol approved by both parties, and clinical study agreement or contract with the clinical study institutions and investigators.
3. The clinical trial protocol shall be approved by the ethics committee of this institution.
4. The clinical study of investigational medical devices listed in the *Catalogue of Class III Medical Devices Requiring Clinical Trial Review and Approval* shall not be implemented until approved by NMPA.
5. Clinical trial institutions and investigators shall jointly formulate the case number and duration of clinical study for each disease according to clinical statistical methods, characteristics of investigational medical devices, existing data and evidence with the sponsor, thereby ensuring to achieve the intended purpose of the study and reduce the waste of resources.
6. For a multi-center clinical trial, only the leading site should be filled in for the "clinical study institution" on the cover, and other institutions should be listed in the protocol.
7. For a multi-center clinical trial, the coordinating investigator shall be filled in for the "investigator" on the cover.

Content

Abstract of Trial Protocol

Trial Name	Clinical Trial on Performance and Safety of Disposable Powered Articulating Endoscopic Linear Cutter Stapler in Gastrointestinal Tissue Cutting and Anastomosis
Sponsor	Fengh Medical Co., Ltd.
Device Name	Study/investigational device: Disposable Powered Articulating Endoscopic Linear Cutter Stapler Control device: ECHELON Flex Powered Articulating Endoscopic Linear Cutters
Regulatory Category	Class III medical device
Trial Scope	The trial is intended for patients to be subject to gastrointestinal tissue cutting and anastomosis
Clinical Trial Indication	Gastrointestinal tissue cutting and anastomosis
Trial Design	Prospective, multi-center, stratified block randomization, incomplete blinding, parallel positive control, non-inferiority testing
Trial Purpose	By comparing the effectiveness and safety of Disposable Powered Articulating Endoscopic Linear Cutter Stapler (product under application) manufactured by Fengh Company with the similar product (ECHELON Flex Powered Articulating Endoscopic Linear Cutters manufactured by Johnson & Johnson Company) in gastrointestinal tissue cutting and anastomosis, it is demonstrated that the product under application can be used for anastomosis of digestive tract, and the clinical trial meets the requirements of *Good Clinical Practice for Medical Devices* and *Guidelines for Technical Review of Endoscopic Stapler Registration*, which can be used for product registration application.
Sample Size	164 cases, randomly divided into the test group and the control group, with 82 cases in both the test group and control group, respectively
Center Number	5
Follow-up period:	37 days
Test Time	(1) Enrollment date of the first subject: June 2018 (2) Duration of subject recruitment: 6 months (3) Completion date of the last subject: December 2018
Primary Effectiveness	(1) Success rate of anastomosis

Evaluation Indicator	
Secondary Effectiveness Evaluation Indicator	(1) Conversion rate due to stapler-related causes (2) Number of stitches for anastomotic repair (3) Operation time (4) Anastomosis time (5) Anastomotic healing time (6) First flatus time (7) First bowel movement time (8) Semi-liquid diet time
Safety Evaluation Indicator	(1) Incidence of anastomotic dehiscence (2) Incidence of anastomotic bleeding (3) Incidence of anastomotic leakage (4) Incidence of anastomotic stricture (5) Incidence of anastomotic infection (6) Incidence of SAEs (7) Incidence of AEs
Operational Performance Evaluation	(1) Stapler operational performance evaluation
Inclusion Criteria	(1) Subjects aged 18-75 years old, male or female; (2) Subjects who are intended to undergo gastrointestinal tissue cutting and anastomosis with linear stapler; (3) Subjects or their guardians are able to understand the purpose of the study, show adequate compliance with the trial protocol, and sign an informed consent.
Exclusion Criteria	(1) Subjects who are scheduled to receive gastrointestinal emergency surgery; (2) Subjects with moderate malnutrition (BMI < 17 kg/m^2) and severe anemia (Hb < 60 g/L); (3) Subjects with a BMI ≥ 28 kg/m^2; (4) Subjects who have a platelet (PLT) < 60 × 10^9/L or international normalized ratio (INR) > 1.5; (5) Subjects with forced expiratory volume in one second (FEV1)/predicted value ≤ 50%, or forced expiratory volume in one second (FEV1)/forced vital

	capacity (FCV) ≤ 60%; (6) Subjects with ejection fraction ≤ 50%; (7) Subjects with important organ failure or other serious diseases (e.g., the subject's aspartate aminotransferase (AST), alanine aminotransferase (ALT), or serum creatinine (Scr) is more than 3 times of the upper limit of normal before surgery; the subject's fasting blood glucose value before surgery is ≥ 10.0 mmol/L); (8) Subjects who are pregnant or lactating women; (9) Subject who have participated in other drug or device clinical trials within 3 months prior to the trial; (10) Other situations not suitable for inclusion judged by investigators.
Device Usage Specification	According to the results of random allocation, the investigators apply the investigational medical device to the subjects who enter the test group, and the control medical device to the subjects who enter the control group. If a subject required the use of a circular stapler during the trial, the brand and model of the circular stapler are required to be recorded.
Concomitant medication/concomitant treatment	If a subject receives any medication or treatment for an adverse event during the study for any reason, the investigators are required to record such occurrence on the case report form (CRF) for easy access.
Inspection Items	**Medical history and vital signs, etc.:** (1) Demographic data: gender, date of birth; (2) History of present illness: admission time, etiology; (3) Past medical history: history of allergy, dysfunction of vital organs (heart, lung, liver and kidney), surgery and previous medication history (within 1 month); (4) Vital signs: height, weight, blood pressure, pulse, body temperature, respiration, BMI; **Laboratory examinations:** (1) Blood routine: hemoglobin (Hgb), red blood cell count (RBC), white blood cell count (WBC), neutrophil count (NEUT), neutrophil ratio (NEUT%), platelet count (PLT); (2) Coagulation blood routine: prothrombin time (PT), activated partial thromboplastin time (APTT), international normalized ratio (INR);

(3) Blood biochemistry: aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum total bilirubin (STB), serum albumin (ALB), serum creatinine (Scr), blood urea nitrogen (BUN);

(4) Fasting blood glucose;

(5) Fecal examination: occult blood test;

(6) Cardiac ultrasonography: cardiac ejection fraction;

(7) Pulmonary function test: forced expiratory volume in one second (FEV1)/predicted value, forced expiratory volume in one second (FEV1)/forced vital capacity (FCV);

(8) Blood pregnancy test: applicable for women of childbearing age (18-50 years old).

Preoperative imaging:

(1) CT examination: tumor stage, whether there is liver metastasis, whether there is pelvic metastasis, whether there is lung metastasis;

Post-operative imaging:

(1) Angiography: whether there is anastomotic bleeding;

(2) Upper gastrointestinal radiography: whether there is anastomotic leakage and stricture;

(3) Gastrointestinal endoscopic examination: whether there is anastomotic leakage and stricture;

(4) Abdominal CT: whether there is abdominal effusion and the amount of abdominal effusion;

Other tests:

(1) Intraoperative observation items: name of operation, start time of operation, end time of operation, start time of anastomosis, end time of anastomosis and intraoperative blood loss;

(2) Observation of the study product: whether the digestive tract is successfully transected and stapled, whether the cutting anastomosis ring/staple line is complete, whether there is leakage of cutting anastomosis ring/staple line, whether there is bleeding of cutting anastomosis ring/staple line, whether there is bubble overflow at the anastomotic stoma, whether there are indicators of conversion to laparotomy, number of needles for anastomotic repair, whether there is anastomotic dehiscence, whether there are other

	complications, whether the staple line or tissue buttressing materials are used, and the operating performance of stapler; (3) Device use: model and specification of electric stapler, model of cartridge, use condition, cutting and stapling tissues, device defects; (4) Postoperative follow-up observation: first anus exhaust time, semi-liquid feeding time, first defecation time, bowel sound recovery time, whether there is anastomotic bleeding, whether there is anastomotic leakage, whether there is anastomotic stenosis, whether there are other complications, whether there is abdominal effusion and the abdominal effusion volume; (5) Routine observation items: adverse events, concomitant medication, protocol deviations.
Statistical Analysis	Statistical analysis is performed using SAS 9.1 software. Perform statistical description on all data, including demographic data, baseline data, all efficacy indicators and all safety data. Measurement data include the mean, standard deviation, minimum, maximum, median, 25^{th} percentile and 75^{th} percentile; enumeration data include frequency and corresponding percentage. The primary effectiveness evaluation indicators are evaluated using the confidence interval method. For secondary evaluation indicators, the difference test is adopted. Two independent samples t test is adopted for measurement data. Difference test is used for safety evaluation indicators. Two independent samples t test is used for measurement data. Pearson *X*2 test or Fisher's exact test is used for enumeration data. The adverse events and device defects occurred in this trial are described in list. Difference test is used to evaluate the operating performance of the stapler. Pearson *X*2 test or Fisher exact test is used to analyze enumeration data. Center effect is considered during the analysis process. General linear model is used for measurement data. CMH is used for enumeration data.

Trial Flow Chart

Visit Time / Visit Item	Visit 1 Before surgery (Day -7 ~ 0)	Visit 2 During surgery (Day 0)	Visit 3 After surgery (Day 7 ± 2 days)	Visit 4 After surgery (Day 30 ± 5 days)
Informed consent	▲			
Subject screening	▲			
Demographic data	▲			
History of present illness	▲			
Past medical history	▲			
Vital signs	▲	▲	▲	▲
Blood routine	▲		▲	
Coagulation routine	▲		▲	
Blood biochemistry	▲		▲	
Cardiac examination	▲		▲	▲
Pulmonary function test	▲			
Arterial blood gas analysis	▲			
Preoperative imaging	▲			
Blood pregnancy test	▲			
Randomization		▲		
Intraoperative observation record		▲		
Use of device		▲		
Postoperative imaging			▲	
Postoperative follow-up observation			▲	▲
Concomitant medication	▲	▲	▲	▲
Adverse events	▲	▲	▲	▲
Device defect		▲		

List of Abbreviations

Abbreviation	English	Chinese
AE	Adverse Events	不良事件
CRF	Case Report Form	病例报告表
EC	Ethics Committee	伦理委员会
FAS	Full Analysis Set	全分析集
GCP	Good Clinical Practice	医疗器械临床试验质量管理规范
ICF	Informed Consent Form	知情同意书
PPS	Per-Protocol Set	符合方案集
SAE	Serious Adverse Events	严重不良事件
SOP	Standard Operating Procedure	标准操作规程
SS	Safety Set	安全数据集

Text of Study Protocol

1. Sponsor Information

1.1 Sponsor Name

Fengh Medical Co., Ltd.

1.2 Sponsor Address

Address/production address: D3 No. 6 Dongsheng West Road, Jiangyin National High-tech Zone, 214437 Jiangsu, P.R. China

1.3 Sponsor Contact

Contact Person	Liu Jiao		
Tel	(86) 510-81695550	Mobile	13815132106
Fax	(86) 510-81695550	E-mail	liuj_fenghmedical@163.com

1.4 Sponsor-Related Qualification Documents

Social credit code	91320281583765063L
Registration inspection report	2017ZC2908, 2017ZC2908-EMC, 2017QW0247

2. List of All Clinical Trial Institutions and Investigators in Multi-Center Clinical Trial

Code number	Name of clinical trial institution	Investigator	Title	Contact information
01	Yangzhou First People's Hospital	Ni Qing	Chief Physician	Tel: 13951056866 E-mail: yzniqing@163.com
02	Affiliated Hospital of Jiangsu University	Sanrong Xu	Chief Physician	Phone: 13775531799 E-mail: zjxsrong@163.com
03	Quzhou People's Hospital	Mao Xinglong	Chief Physician	Tel: 13757055369 E-mail: qzryjgb@126.com
04	Lishui Central Hospital	Hongtao Xu	Chief Physician	Tel: 15024622762 E-mail: xht0071@sina.com
05	Shanghai Tongren Hospital	Sun Peng	Chief Physician	Tel: 18121225835 E-mail: sp2082@shtrhospital.com

3. Purpose and Content of Clinical Trial

3.1 Purpose

By comparing the effectiveness and safety of Disposable Powered Articulating Endoscopic Linear Cutter Stapler (product under application) produced by Fengh Company with the similar product (ECHELON Flex Powered Articulating Endoscopic Linear Cutters manufactured by Johnson & Johnson Company) in gastrointestinal tissue cutting and anastomosis, it is proved that the product under application can be used for alimentary tract anastomosis, and the clinical trial meets the requirements of *Good Clinical Practice for Medical Devices* and *Guidelines for Technical Review of Endoscopic Stapler Registration*, which can be used for product registration application.

3.2 Content

This clinical trial is a prospective study. The patients scheduled for gastrointestinal tissue cutting and anastomosis were selected as the study subjects. The subjects were randomly divided into the test group and control group. Subjects in the test group received the Disposable Powered Articulating Endoscopic Linear Cutter Stapler manufactured by Fengh Company, and the subjects in the control group received the similar product (ECHELON Flex Powered Articulating Endoscopic Linear Cutters) manufactured by Johnson & Johnson Company. The subjects were blinded and were followed up for 4 visits within 1 month. The collected data were analyzed and compared to evaluate the effectiveness and safety of the Disposable Powered Articulating Endoscopic Linear Cutter Stapler manufactured by Fengh Company in gastrointestinal tissue cutting and anastomosis.

4. Background Data of Clinical Trial

Since laparoscopic surgery is increasingly and widely used in the treatment of gastric cancer, the stapler cooperating with laparoscopic surgery is also widely used in clinical practice. Stapler is an alternative manual suture device used in medicine. Its main operating principle is to use titanium nail for transection or anastomosis of tissues, which is similar to book stapler. According to different applicable scopes, it can be divided into skin stapler, linear stapler, circular stapler, circular hemorrhoidal stapler, circumcision stapler, vascular stapler, hernia stapler, etc.

Compared with the traditional manual suture, the advantages of anastomosis suture include: ① simple and convenient operation, saving operation time; ② disposable use, avoiding cross-infection; ③ tight and moderate suture using titanium nail or stainless steel nail (skin stapler); ④ few side effects and effectively reducing surgical complications.

In order to provide clinicians with a more convenient thoracoscopic linear stapler, Fengh Company develops one kind of Disposable Powered Articulating Endoscopic Linear Cutter Stapler according to market demands.

This linear stapler is driven by electric motor, which can better reduce the surgical intensity of doctors and save surgical time.

The Disposable Powered Articulating Endoscopic Linear Cutter Stapler designed and developed by Fengh Company according to the clinical treatment characteristics have passed the test by Jiangsu Institute for Medical Device Testing of NMPA (original CFDA) [2017ZC2908, 2017ZC2908-EMC, 2017QW0247].

This clinical trial is to test the safety and effectiveness of the device by evaluating the success rate of anastomosis of the device after use, so as to provide trial basis for the product registration.

5. Product Model, Structural Composition, Operating Principle, Mechanism of Action and Trial Scope

5.1 Product Model/Specification

Table 1 Model and specification of Electric stapler

Model/specification of electric stapler	Arm length (L3)	Length of reload-resisting base (L1)	Overall length (L)
FSMS30	192 ± 20	66.3 ± 2.5	538.6 ± 20
FSMS45	192 ± 20	78.3 ± 2.5	547.6 ± 20
FSMS60	192 ± 20	90.3 ± 2.5	562.6 ± 20
FSMM30	252 ± 20	66.3 ± 2.5	538.6 ± 20
FSMM45	252 ± 20	78.3 ± 2.5	547.6 ± 20
FSMM60	252 ± 20	90.3 ± 2.5	562.6 ± 20
FSML30	352 ± 20	66.3 ± 2.5	538.6 ± 20
FSML45	352 ± 20	78.3 ± 2.5	547.6 ± 20
FSML60	352 ± 20	90.3 ± 2.5	562.6 ± 20
FSAS30	192 ± 20	66.3 ± 2.5	538.6 ± 20
FSAS45	192 ± 20	78.3 ± 2.5	547.6 ± 20
FSAS60	192 ± 20	90.3 ± 2.5	562.6 ± 20
FSAM30	252 ± 20	66.3 ± 2.5	538.6 ± 20
FSAM45	252 ± 20	78.3 ± 2.5	547.6 ± 20
FSAM60	252 ± 20	90.3 ± 2.5	562.6 ± 20
FSAL30	352 ± 20	66.3 ± 2.5	538.6 ± 20
FSAL45	352 ± 20	78.3 ± 2.5	547.6 ± 20
FSAL60	352 ± 20	90.3 ± 2.5	562.6 ± 20
FNMS30	192 ± 20	66.3 ± 2.5	538.6 ± 20
FNMS45	192 ± 20	78.3 ± 2.5	547.6 ± 20
FNMS60	192 ± 20	90.3 ± 2.5	562.6 ± 20
FNMM30	252 ± 20	66.3 ± 2.5	538.6 ± 20
FNMM45	252 ± 20	78.3 ± 2.5	547.6 ± 20
FNMM60	252 ± 20	90.3 ± 2.5	562.6 ± 20
FNML30	352 ± 20	66.3 ± 2.5	538.6 ± 20
FNML45	352 ± 20	78.3 ± 2.5	547.6 ± 20
FNML60	352 ± 20	90.3 ± 2.5	562.6 ± 20
FNAS30	192 ± 20	66.3 ± 2.5	538.6 ± 20
FNAS45	192 ± 20	78.3 ± 2.5	547.6 ± 20
FNAS60	192 ± 20	90.3 ± 2.5	562.6 ± 20
FNAM30	252 ± 20	66.3 ± 2.5	538.6 ± 20
FNAM45	252 ± 20	78.3 ± 2.5	547.6 ± 20

Model/specification of electric stapler	Arm length (L3)	Length of reload-resisting base (L1)	Overall length (L)
FNAM60	252 ± 20	90.3 ± 2.5	562.6 ± 20
FNAL30	352 ± 20	66.3 ± 2.5	538.6 ± 20
FNAL45	352 ± 20	78.3 ± 2.5	547.6 ± 20
FNAL60	352 ± 20	90.3 ± 2.5	562.6 ± 20
DSMS30	192 ± 20	66.3 ± 2.5	538.6 ± 20
DSMS45	192 ± 20	78.3 ± 2.5	547.6 ± 20
DSMS60	192 ± 20	90.3 ± 2.5	562.6 ± 20
DSMM30	252 ± 20	66.3 ± 2.5	538.6 ± 20
DSMM45	252 ± 20	78.3 ± 2.5	547.6 ± 20
DSMM60	252 ± 20	90.3 ± 2.5	562.6 ± 20
DSML30	352 ± 20	66.3 ± 2.5	538.6 ± 20
DSML45	352 ± 20	78.3 ± 2.5	547.6 ± 20
DSML60	352 ± 20	90.3 ± 2.5	562.6 ± 20
DSAS30	192 ± 20	66.3 ± 2.5	538.6 ± 20
DSAS45	192 ± 20	78.3 ± 2.5	547.6 ± 20
DSAS60	192 ± 20	90.3 ± 2.5	562.6 ± 20
DSAM30	252 ± 20	66.3 ± 2.5	538.6 ± 20
DSAM45	252 ± 20	78.3 ± 2.5	547.6 ± 20
DSAM60	252 ± 20	90.3 ± 2.5	562.6 ± 20
DSAL30	352 ± 20	66.3 ± 2.5	538.6 ± 20
DSAL45	352 ± 20	78.3 ± 2.5	547.6 ± 20
DSAL60	352 ± 20	90.3 ± 2.5	562.6 ± 20
DNMS30	192 ± 20	66.3 ± 2.5	538.6 ± 20
DNMS45	192 ± 20	78.3 ± 2.5	547.6 ± 20
DNMS60	192 ± 20	90.3 ± 2.5	562.6 ± 20
DNMM30	252 ± 20	66.3 ± 2.5	538.6 ± 20
DNMM45	252 ± 20	78.3 ± 2.5	547.6 ± 20
DNMM60	252 ± 20	90.3 ± 2.5	562.6 ± 20
DNML30	352 ± 20	66.3 ± 2.5	538.6 ± 20
DNML45	352 ± 20	78.3 ± 2.5	547.6 ± 20
DNML60	352 ± 20	90.3 ± 2.5	562.6 ± 20
DNAS30	192 ± 20	66.3 ± 2.5	538.6 ± 20
DNAS45	192 ± 20	78.3 ± 2.5	547.6 ± 20
DNAS60	192 ± 20	90.3 ± 2.5	562.6 ± 20
DNAM30	252 ± 20	66.3 ± 2.5	538.6 ± 20
DNAM45	252 ± 20	78.3 ± 2.5	547.6 ± 20
DNAM60	252 ± 20	90.3 ± 2.5	562.6 ± 20
DNAL30	352 ± 20	66.3 ± 2.5	538.6 ± 20
DNAL45	352 ± 20	78.3 ± 2.5	547.6 ± 20
DNAL60	352 ± 20	90.3 ± 2.5	562.6 ± 20

Table 2 Model and specification of cartridge components

Unit: mm

Model/specification of reload	Reload color	Reload number	Anastomosis length (L2)
FMCC30	Gray	36	35.2 ± 2
FMCC45	Gray	70	49.3 ± 2
FMCC60	Gray	88	61.3 ± 2

Model/specification of reload	Reload color	Reload number	Anastomosis length (L2)
FMCW30	White	36	35.2 ± 2
FMCW45	White	70	49.3 ± 2
FMCW60	White	88	61.3 ± 2
FMCT30	Brown	36	35.2 ± 2
FMCT45	Brown	70	49.3 ± 2
FMCT60	Brown	88	61.3 ± 2
FMCB30	Blue	36	35.2 ± 2
FMCB45	Blue	70	49.3 ± 2
FMCB60	Blue	88	61.3 ± 2
FMCG30	Green	36	35.2 ± 2
FMCG45	Green	70	49.3 ± 2
FMCG60	Green	88	61.3 ± 2
FMCP30	Purple	36	35.2 ± 2
FMCP45	Purple	70	49.3 ± 2
FMCP60	Purple	88	61.3 ± 2
FMCY30	Gold	36	35.2 ± 2
FMCY45	Gold	70	49.3 ± 2
FMCY60	Gold	88	61.3 ± 2
FMCX30	Black	36	35.2 ± 2
FMCX45	Black	70	49.3 ± 2
FMCX60	Black	88	61.3 ± 2
FACC30	Gray	36	35.2 ± 2
FACC45	Gray	70	49.3 ± 2
FACC60	Gray	88	61.3 ± 2
FACW30	White	36	35.2 ± 2
FACW45	White	70	49.3 ± 2
FACW60	White	88	61.3 ± 2
FACT30	Brown	36	35.2 ± 2
FACT45	Brown	70	49.3 ± 2
FACT60	Brown	88	61.3 ± 2
FACB30	Blue	36	35.2 ± 2
FACB45	Blue	70	49.3 ± 2
FACB60	Blue	88	61.3 ± 2
FACG30	Green	36	35.2 ± 2
FACG45	Green	70	49.3 ± 2

Model/specification of reload	Reload color	Reload number	Anastomosis length (L2)
FACG60	Green	88	61.3 ± 2
FACP30	Purple	36	35.2 ± 2
FACP45	Purple	70	49.3 ± 2
FACP60	Purple	88	61.3 ± 2
FACY30	Gold	36	35.2 ± 2
FACY45	Gold	70	49.3 ± 2
FACY60	Gold	88	61.3 ± 2
FACX30	Black	36	35.2 ± 2
FACX45	Black	70	49.3 ± 2
FACX60	Black	88	61.3 ± 2
DMCC30	Gray	36	35.2 ± 2
DMCC45	Gray	70	49.3 ± 2
DMCC60	Gray	88	61.3 ± 2
DMCW30	White	36	35.2 ± 2
DMCW45	White	70	49.3 ± 2
DMCW60	White	88	61.3 ± 2
DMCT30	Brown	36	35.2 ± 2
DMCT45	Brown	70	49.3 ± 2
DMCT60	Brown	88	61.3 ± 2
DMCB30	Blue	36	35.2 ± 2
DMCB45	Blue	70	49.3 ± 2
DMCB60	Blue	88	61.3 ± 2
DMCG30	Green	36	35.2 ± 2
DMCG45	Green	70	49.3 ± 2
DMCG60	Green	88	61.3 ± 2
DMCP30	Purple	36	35.2 ± 2
DMCP45	Purple	70	49.3 ± 2
DMCP60	Purple	88	61.3 ± 2
DMCY30	Gold	36	35.2 ± 2
DMCY45	Gold	70	49.3 ± 2
DMCY60	Gold	88	61.3 ± 2
DMCX30	Black	36	35.2 ± 2
DMCX45	Black	70	49.3 ± 2
DMCX60	Black	88	61.3 ± 2
DACC30	Gray	36	35.2 ± 2

Model/specification of reload	Reload color	Reload number	Anastomosis length (L2)
DACC45	Gray	70	49.3 ± 2
DACC60	Gray	88	61.3 ± 2
DACW30	White	36	35.2 ± 2
DACW45	White	70	49.3 ± 2
DACW60	White	88	61.3 ± 2
DACT30	Brown	36	35.2 ± 2
DACT45	Brown	70	49.3 ± 2
DACT60	Brown	88	61.3 ± 2
DACB30	Blue	36	35.2 ± 2
DACB45	Blue	70	49.3 ± 2
DACB60	Blue	88	61.3 ± 2
DACG30	Green	36	35.2 ± 2
DACG45	Green	70	49.3 ± 2
DACG60	Green	88	61.3 ± 2
DACP30	Purple	36	35.2 ± 2
DACP45	Purple	70	49.3 ± 2
DACP60	Purple	88	61.3 ± 2
DACY30	Gold	36	35.2 ± 2
DACY45	Gold	70	49.3 ± 2
DACY60	Gold	88	61.3 ± 2
DACX30	Black	36	35.2 ± 2
DACX45	Black	70	49.3 ± 2
DACX60	Black	88	61.3 ± 2

5.2 Product Structural Composition

- Electric stapler consists of stapler body, arm rod, reload-resisting base, reload base, battery pack or power adapter.
- The cartridge component is composed of reload, reload-pushing piece and anastomotic nail, etc.

5.3 Product Performance

The main technical indicators of electric stapler include convenient replacement of stapler components, reliable positioning. In addition, the stapler is equipped with a safety protection device for empty staple cartridge to maintain its reliability. The product shall be sterile.

5.4 Trial Scope

The product is intended for patients planning to receive gastrointestinal tissue cutting and anastomosis.

6. Product Applicable Scope, Contraindications and Precautions

6.1 Applicable Scope

The Disposable Powered Articulating Endoscopic Linear Cutter Stapler is intended for transection, resection, and/or creation of anastomoses. The instrument has application in multiple open or minimally invasive general, gynecologic, urologic, thoracic, and pediatric surgical procedures. It can be used with staple line or tissue buttressing materials. The instrument may also be used for transection and resection of liver parenchyma (hepatic vasculature and biliary structures), pancreas, kidney and spleen.

6.2 Contraindications

- ■ Do not use the instruments on the aorta.
- ■ Do not use the instruments on ischemic or necrotic tissue.
- ■ Do not use any linear cutter on major vessels without making provision for proximal and distal control.
- ■ Tissue thickness should be carefully evaluated before firing any stapler. Refer to Reload Product Codes for tissue compression requirement (closed staple height) for each staple size. If tissue cannot comfortably compress to the closed stale height, or easily compresses to less than the closed staple height, the tissue is contraindicated as it may be too thick or too thin for the selected staple size.
- ◆ These instruments are not intended for use when surgical stapling is contraindicated.

6.3 Cautions

See the IFU for details.

6.4 Precautions

See the IFU for details.

6.5 Application Method

See the IFU for details.

7. Reference Medical Device-Related Information

7.1 Stapler Information

Product name	ECHELON Flex Powered Articulating Endoscopic Linear Cutters
Specification/model	PSE45A, PCE45A, PLE45A, PSE60A, PCE60A, PLE60A
Registration No.	GXZJ 20173226240
Structural	The product is a sterile device for single patient use, consisting of closing rod, red firing lock, firing handle, anvil release button, lithium battery pack, battery pack-releasing piece, hole cover plate for manual override maintenance, knife-reversing switch, knob,

composition	articulation fins, reload alignment slot, anvil jaw and reload jaw. The lithium battery pack must be installed prior to use. The product has been sterilized by irradiation. This product is provided for single use.
Applicable scope	The Disposable Powered Articulating Endoscopic Linear Cutter Stapler is intended for transection, resection, and/or creation of anastomoses. The instrument has application in multiple open or minimally invasive general, gynecologic, urologic, thoracic, and pediatric surgical procedures. It can be used with staple line or tissue buttressing materials. The instrument may also be used for transection and resection of liver parenchyma (hepatic vasculature and biliary structures), pancreas, kidney and spleen.
Manufacturer	Ethicon Endo-Surgery, LLC
Agent	Johnson & Johnson Medical (Shanghai) Ltd.

7.2 Reload Information

Product name 1	echelon 60 ENDOPATH STAPLER Endoscopic Linear Cutter Reloads
Specification/model 1	ECR60W
Registration No. 1	GXZJ 20153080094
Structural composition 1	The linear cutter stapler reload is composed of cartridge, anastomotic nail and reload-protecting board, in which the material of anastomotic nail is Ti3Al2.5V. The reload is sterilized by radiation and provided for single use.
Product name 2	ECHELON 45 ENDOPATH Stapler Endoscopic Linear Cutter and Reloads
Specification/model 2	ECR45M, EC45, SC45, ECLG45, ECR45W, ECR45B, ECR45D, ECR4 5G
Registration No. 2	GXZJ 20163654883
Structural composition 2	The product is composed of anvil, trigger, firing trigger, handle and cartridge component. The reload is sterilized by radiation and provided for single use.
Product name 3	ECHELON FLEX Articulating Linear Cutters and Reloads Articulating Endoscopic Linear Cutter Reloads
Specification/model 3	EC45A, SC45A, EC45AL, EC60A, SC60A, LONG60A, ECR60W, ECR 60B, ECR60D, ECR60G, ECR60T, ECR60M
Registration No. 3	GXZJ 20173656323

Structural composition 3	This product is composed of stapler and cartridge. Its components include cartridge, closing rod, firing rod, rotary knob, articulating piece, manual knife-reversing switch, trip count indicator, knife direction indicator, anvil release button, closing rod, and anvil. The stapler is made of stainless steel, and the anastomotic needle is made of titanium alloy (Tianium3A12.5V). The product is sterilized by radiation.
Applicable scope	It is used for transection, resection and/or anastomosis. It can be used in a variety of open or minimally invasive general, gynecologic, urologic, thoracic, and pediatric surgical procedures. It can be used with staple line or tissue buttressing materials. These devices can also be used for transection and resection of liver parenchyma tissues (hepatic vasculature and biliary structures), pancreas, kidney and spleen.
Manufacturer	Ethicon Endo-Surgery, LLC
Agent	Johnson & Johnson Medical (Shanghai) Ltd.

8. Overall Design

8.1 Test Design

8.1.1 Primary objective

To evaluate whether the primary effectiveness evaluation indicator "anastomosis success rate" of the Disposable Powered Articulating Endoscopic Linear Cutter Stapler manufactured by Fengh Company is non-inferior to the similar product manufactured by Johnson & Johnson Company in gastrointestinal tissue cutting and anastomosis.

8.1.2 Secondary objectives

To evaluate whether there are differences in the secondary evaluation indicators when the Disposable Powered Articulating Endoscopic Linear Cutter Stapler manufactured by Fengh Company is used in gastrointestinal tissue cutting and anastomosis compared with the similar product manufactured by Johnson & Johnson Company.

To evaluate whether there are differences in the safety evaluation indicators (e.g., incidence of AEs, incidence of SAEs, incidence of device defects) between the Disposable Powered Articulating Endoscopic Linear Cutter Stapler manufactured by Fengh Company and the similar product manufactured by Johnson & Johnson Company in gastrointestinal tissue cutting and anastomosis.

8.1.3 Selection of test method and reasons

This clinical trial is a "prospective, multi-center, stratified-block randomization, incomplete blinding, parallel

positive control, non-inferiority test".

(1) Prospective: A research method that tracks from the present to the future. Prospective studies can clarify the causal relationship; uniform diagnostic, detection, and evaluation criteria can be available for the obtained data, the data processing therefore is controllable.

(2) Multi-center: 5 clinical trial institutions were selected to conduct this clinical trial. The application of multi-center trial can allow to obtain more cases than those of single-center trial in the same time, the clinical trial time therefore can be shortened; since the multi-center trial is completed by different regions, different trial centers and many clinical researchers, the conclusion therefore is often widely representative.

(3) Stratified block randomization: This trial adopts the stratified block randomization method (with the study site as the stratification factor) and the randomization envelope to randomize the subjects who are screened successfully. The randomized-grouping time is when the subjects sign the ICF, which also meets the inclusion and exclusion criteria in the protocol at the same time. Randomized grouping ensures that, except for treatment factors, other non-treatment factors that may have confounding effect are kept consistent in each group as far as possible, so as to ensure the balance of baseline of each group; randomized-grouping allows each subject to have equal opportunity to be assigned to the test group or control group.

(4) Incomplete blinding: Since the investigational medical device and the control medical device are different in appearance, while the subjects are under anesthesia during the operation, the grouping arrangement can not be known. Therefore, the method of incomplete blinding is used, that is, the investigators knows the grouping result, while the subject does not know the grouping result. The blinding method can minimize the bias caused by "placebo effect" and investigator bias; for the less precise observation indicators, it can significantly reduce the bias; and make the evaluation of adverse reactions by investigators and subjects more objective.

(5) Parallel positive control: The investigational medical device has the mature application technology with many similar products that are marketed at home and abroad. It has been used in clinical practice for many years, with exact effect and predictable occurrence of adverse events. Therefore, parallel positive control is adopted in this clinical trial.

(6) Non-inferiority test: To evaluate whether the main effectiveness evaluation indicator "success rate of anastomosis" of the Disposable Powered Articulating Endoscopic Linear Cutter Stapler manufactured by Fengh Company is non-inferior to the similar product manufactured by Johnson & Johnson Company in gastrointestinal tissue cutting and anastomosis. It is expected that the test product is similar to the control product in performance. There is no significant difference in the expected results between the two groups

in the primary efficacy indicator of "success rate of anastomosis" during gastrointestinal tissue cutting and anastomosis. Therefore, the non-inferiority test is adopted.

8.1.4 Measures for reducing and avoiding bias

(1) Before the start of the study, the sponsor shall provide relevant training for the investigators participating in the study to ensure that the investigators fully understand the study process and are familiar with the operation of the study device; during the study, the investigators shall operate in strict accordance with the operating methods and procedures in the study protocol, and the clinical trial monitor shall do a good job in quality control and monitoring to ensure that the investigators operate and implement in strict accordance with the study protocol. The above measures shall be implemented throughout the implementation phase of the study to reduce errors or operational errors.

(2) Subjects shall be screened in strict accordance with the clinical diagnostic criteria, as well as the inclusion and exclusion criteria of the trial protocol to reduce selection bias.

(3) Total laparoscopic digestive tract reconstruction is difficult to operate, which should be carried out in centers with rich experience in laparoscopic surgery. In view of the learning curve of laparoscopic surgery, doctors can be more proficient based on at least 50 cases[2]. The operating surgeon of laparoscopic surgery is recommended to be experienced in at least 100 cases of open surgery as the operator and 50 cases of laparoscopic surgery as the primary assistant.

(4) When the clinical trial is completed, the data storage and collation shall be done well. When data problems are found, the data analyst shall check and confirm the data through the data clarification form to avoid recording errors.

8.1.5 Investigational medical device and control medical device or control diagnosis and treatment method

See the corresponding IFU for the diagnosis and treatment method with the investigational medical device and the reference medical device. In addition, subjects may use circular stapler or other types of staplers during the clinical trial. If these staplers are used, the investigators should truthfully record the model of these staplers and staple cartridge for reference.

When subjects experience adverse events related to the stapler, the investigators should truthfully judge the correlation between adverse events and the test device.

8.1.5.1 Information of circular stapler

Product name	ILS Curved and Straight Intraluminal Staplers
Specification/model	CDH21A, CDH25A, CDH29A, CDH33A, SDH21A, SDH25A, SDH29A, SDH33A

Registration No.	GXZJ 20152652249
Manufacturer	Ethicon Endo-Surgery, LLC
Structural composition	The product is composed of orange display area, trocar, reload, safety indicator window, adjusting knob, safety device, firing trigger, staple board, anti-trocar, anti-trocar protective cover, staple anvil head, knotting groove, locking spring leaf and staple anvil rod. The material of stapler is medical stainless steel, the material of knob is polycarboxylate, and the material of staple is titanium alloy. Radiation sterilization, single use.
Scope of application	This product is used for end-to-end, end-to-side and side-to-side anastomosis of the whole digestive tract.
Requirements for use	If the subjects in the test group or control group (only for the subjects at rectal site) need to use the circular stapler during the clinical trial, the investigators shall uniformly use the circular stapler (Johnson & Johnson brand, model CDH25A or CDH29A) uniformly provided by Fengh Company. For the using process, records shall be truthfully kept for reference.

8.1.6 Selection of Subjects

8.1.6.1 Clinical trial indications

At present, the Disposable Powered Articulating Endoscopic Linear Cutter Stapler can be used for "a variety of open or minimally invasive surgeries in general surgery, obstetrics and gynecology, urology, thoracic surgery and pediatrics. They can be used with suture or tissue staple supporting material. They also can be used for transection and excision of liver parenchyma (hepatic vascular system and bile duct structure), pancreas, kidney and spleen.

However, according to the *Guidelines for Technical Review of Endoscopic Stapler Registration*, "the surgical site and/or tissue type and thickness selected for clinical trial shall cover the intended clinical applicable scope of the product under application". Therefore, gastrointestinal surgery is selected for the clinical trial.

Therefore, the indication of this clinical trial is: "**gastrointestinal tissue cutting and anastomosis**".

8.1.6.2 Inclusion criteria

Subjects meeting all of the following conditions only can be included:

(1) Subjects are aged 18-70 years (inclusive), male or female;

(2) Subjects are scheduled to accept gastrointestinal tissue cutting and anastomosis;

(3) Subjects or their guardians are able to understand the purpose of the study, show adequate compliance with the trial protocol, and sign an ICF.

8.1.6.3 Exclusion criteria

Subjects meeting any of the following conditions can not be included:

(1) Subjects who are scheduled to receive gastrointestinal emergency surgery;

(2) Subjects with moderate malnutrition (BMI < 17 kg/m^2) and severe anemia (Hb < 60 g/L);

(3) Subjects with a BMI ≥ 28 kg/m^2;

(4) Subjects with platelet (PLT) < 60 × 10^9/L or international normalized ratio (INR) > 1.5;

(5) Subjects with a forced expiratory volume in one second (FEV1)/predicted value ≤ 50%, or a forced expiratory volume in one second (FEV1)/forced vital capacity (FCV) ≤ 60%;

(6) Subjects with ejection fraction ≤ 50%;

(7) Subjects with important organ failure or other serious diseases (e.g., the subject's aspartate aminotransferase (AST), alanine aminotransferase (ALT), or serum creatinine (Scr) is more than 3 times of the upper limit of normal before surgery; the subject's fasting blood glucose value before surgery is ≥ 10.0 mmol/L);

(8) Subjects who are pregnant or lactating women;

(9) Subjects who have participated in other drug or device clinical trials within 3 months prior to the trial;

(10) Other situations not suitable for inclusion judged by the investigators.

8.1.7 Study termination criteria

Study termination refers to that the clinical study has not been completed according to the protocol, and all clinical studies are stopped halfway. The purpose of terminating the clinical study is to protect the rights and interests of the subjects and ensure the quality of clinical study. Except for Item 6 below, the sponsor and the investigators shall jointly negotiate whether to terminate the trial:

(1) If serious safety problems occur during the clinical study, the clinical study should be terminated in a timely manner;

(2) If the product is found to have no clinical value during the clinical study, the clinical study shall be terminated;

(3) In the process of clinical study, it is found that the clinical study protocol has major errors and it is difficult to evaluate the product effect; or the protocol has serious deviation in the implementation, in which it is difficult to evaluate the product effect if the study is continuously to be conducted, , the clinical study shall be terminated;

(4) The sponsor requests to terminate the study (for reasons, e.g., financial, etc.);

(5) The clinical trial institutions and investigators fail to comply with the laws and regulations related to clinical trial and clinical trial protocol, and fail to make correction after being pointed out, resulting in

serious situations or failure to change.

(6) NMPA orders to terminate the clinical study for some reason(s).

After the study is terminated, the investigators should continue to provide appropriate treatment for the subjects from the perspective of protecting the rights and interests of the subjects, and inform the subjects of the treatment received during the trial and related treatment in detail. The subject data continues to be acceptable for evaluating the safety of the product.

The investigators should timely feed back the termination of the subject study to the sponsor.

8.1.8 Enrollment time

It is estimated that the first subject will be enrolled in June 2018. The total enrollment time is 6 months, and the trial end time for the last subject will be December 2018.

8.1.9 Expected duration of clinical trial and the reasons for determination

The expected enrollment time for the first subject is June 2018. The enrollment time for subjects is 6 months. The time for the last subject to complete the trial is December 2018. The time for statistical analysis and preparation of study summary report after the completion of clinical trial is 2 months, and the total clinical study period is 8 months.

8.1.10 Expected duration of participation of each subject

The expected screening period from signing the ICF to enrollment for each subject is 7 days, and the postoperative follow-up period is about 30 days. The total subject observation period is 37 days. If a subject experiences an adverse event during the clinical trial, the outcome of the adverse event needs to be observed.

8.1.11 Number of subjects required for clinical trial

The total sample size is 164. See Section 9.2 for details.

8.1.12 Drop-out criteria and treatment

(1) Definition of drop-out: All the subjects who have signed the ICF and passed screening to enter the clinical trial, no matter when or when they withdraw from the study, will be called drop-out cases as long as they have not completed the observation period specified in the protocol.

(2) Drop-out criteria:

a) The subject is unwilling or impossible to continue the clinical trial for any reason, and the clinical trial is terminated by putting forward a request for withdrawal from the clinical trial to the investigator;

b) The subject is lost to follow-up due to no treatment or examination although the subject does not

explicitly withdraw from the clinical trial;

c) If the subject experiences a serious adverse event (SAE), the investigator should withdraw the subject from the clinical trial;

d) Poor subject compliance.

For all the dropout cases, it is necessary to fill in the summary form of completion of clinical trial in the case report form and analyze the reasons for dropout. When a subject dropped out, the investigator should contact the subject as far as possible, ask the reason and record the last clinical symptom, and complete the evaluation items that could be completed. When withdrawing from the study due to adverse events, the investigator should take appropriate treatment measures according to the actual situation of the subject.

When a subject or his/her guardian actively requests to withdraw from the trial, the subject or his/her guardian should be asked that whether the subject's previous data can be continuously used in the clinical trial, and whether the results can be recorded in the original records. When no enquiry is performed, the data are available by default.

8.1.13 Supplementary procedures for subjects

During the clinical trial, if the number of subjects fails to meet the statistical requirements due to dropout for any reason, or the investigator considers it necessary to supplement subjects, the reasons shall be analyzed firstly, and then the investigator, sponsor and statistician shall discuss whether to supplement or not. After determining the number of supplemented cases, the information shall be submitted to relevant departments for review.

8.1.14 Study completion criteria

Study completion refers to that the clinical study has included sufficient subjects according to the requirements of clinical protocol and completed the treatment, observation and evaluation for all subjects, and the collected data can be used to evaluate the safety and effectiveness of the study product.

8.1.15 Effectiveness evaluation method

8.1.15.1 Main effectiveness evaluation indicators, method and time for evaluation, recording and analysis

(1) Success rate of anastomosis

Justification for selection: According to the *Guidelines for Technical Review of Endoscopic Stapler Registration* issued by NMPA (original CFDA) on March 13, 2017, the "success rate of anastomosis" is selected as the primary evaluation indicator for such products.

Evaluation time: During the surgery.

Evaluation site: Tissues receiving linear stapler for gastrointestinal anastomosis.

Evaluation method: The transection and anastomosis of lung tissues are performed during the operation. The device is withdrawn after successful triggering. The cutting staple line is carefully checked for integrity, air leakage and bleeding. Anastomosis is considered as successful if all anastomotic rings are intact without leakage or bleeding, otherwise it is considered as failure. If necessary, the gas injection method is used to inspect whether there is bubble overflow at anastomotic stoma. If there is no bubble overflow, it is recorded as successful anastomosis; if there is obvious bubble overflow, it is recorded as anastomosis failure.

Formula: Anastomosis success rate = number of subjects with successful anastomosis in each group/total number of subjects in this group × 100%

Precautions: During gastrointestinal tissue cutting and anastomosis, the subject may be converted into thoracotomy due to his complicated condition. At this time, the investigators need to determine whether the subject's conversion to thoracotomy is caused by the stapler. If it is caused by the stapler, it is judged as anastomosis failure. After gastrointestinal tissue anastomosis, the investigator may need to supplement the stitching treatment for anastomotic tissues. If the supplement is resulted from incomplete anastomosis ring, leakage and bleeding, it is considered as anastomosis failure.

8.1.15.2 Secondary effectiveness evaluation indicators, method and time for evaluation, recording and analysis

(1) Stapler-resulted conversion rate

Justification for selection: The need for conversion to thoracotomy due to failed anastomosis increases the risk to the subject. Therefore, the "stapler-resulted conversion rate" is selected as one of the effectiveness indicators of the product. At the same time, with reference to the *Guidelines for Technical Review of Endoscopic Stapler Registration* issued by NMPA (original CFDA) on March 13, 2017 , the "stapler-resulted conversion rate" is selected as an effectiveness evaluation indicator for such products.

Evaluation time: During the surgery.

Evaluation method: Indicators of conversion to laparotomy are ① bleeding difficult to control; ② invasion of adjacent organs or blood vessels resulting in difficulty in surgery; ③ patients difficulty in tolerating pneumoperitoneum during surgery; ④ accidental injury of other organs during surgery, which are difficult for treatment; ⑤ severe intraoperative adhesions found during surgery. If the conversion to laparotomy is caused by the stapler, it should be recorded truthfully.

Formula: Stapler-resulted conversion rate = number of eligible subjects in each group/total number of subjects in this group × 100%

(2) Number of stitches repaired with staple line

Justification for selection: When the stapler is used for gastrointestinal tissue anastomosis, the situation that

the staple line needs to be repaired may occur. When the number of repair needles becomes larger, it may increase the risk to the subject. Therefore, the "number of stitches repaired with staple line" is selected as one of the indicators to evaluate the effectiveness of the product. At the same time, with reference to the *Guidelines for Technical Review of Endoscopic Stapler Registration* issued by NMPA (original CFDA) on March 13, 2017 , the "number of stitches repaired with staple line" is selected as an effectiveness evaluation indicator for such products.

Evaluation time: During the surgery.

Evaluation method: The number of staple line repair needles of each subject during operation is recorded.

Precautions: Anastomotic repair is required when the anastomotic ring is incomplete, leaking and bleeding. Anastomotic repair may also be necessary when there is a dehiscence of the staple line during surgery. Sometimes the investigators may perform anastomotic repair in order to strengthen the anastomotic site. Therefore, the reasons for repair should be recorded.

(3) Operation time

Justification for selection: The main purpose of stapler is to reduce the surgeon's operation intensity and save operation time. Therefore, the operation time is selected as one of the indicators to evaluate the product performance. Meanwhile, with reference to the *Guidelines for Technical Review of Endoscopic Stapler Registration* issued by NMPA (original CFDA) on March 13, 2017, the "operation time" is selected as the secondary evaluation indicator for such products.

Evaluation time: During the surgery.

Evaluation method: The investigators record the time taken from thoracotomy to chest closure to the nearest minute.

(4) Anastomosis time

Justification for selection: The main purpose of stapler is to reduce the surgeon's operation intensity and save operation time. Therefore, the stapling time is selected as one of the indicators to evaluate the product performance. Meanwhile, with reference to the *Guidelines for Technical Review of Endoscopic Stapler Registration* issued by NMPA (original CFDA) on March 13, 2017, the "anastomosis time" is selected as the secondary evaluation indicator for such products.

Evaluation time: During the surgery.

Evaluation method: The investigators record the time taken for the subject to perform the transection from the completion of mobilization of gastrointestinal tissues (the first operation site) to the completion of anastomosis of gastrointestinal tissues. The time is accurate to minutes.

(5) Anastomotic healing time

Justification for selection: Anastomotic healing is an important indicator for effectiveness and safety

evaluation of such products. Therefore, the anastomosis time is selected as one of the indicators to evaluate the product performance. Meanwhile, with reference to the *Guidelines for Technical Review of Endoscopic Stapler Registration* issued by NMPA (original CFDA) on March 13, 2017, eventually, the "anastomotic healing time" is used as a secondary indicator for evaluation.

Evaluation time: After surgery.

Evaluation method: The recovery of borborygmus and smooth eating and defecation are considered as anastomotic healing. Only when the subjects meet these three criteria, it can be judged as the anastomotic healing, and the latest time observed shall be the basis for evaluation. The time is accurate to day.

(6) Time of first flatus

Justification for selection: After gastrointestinal surgery, anus exhaust indicates the gradual recovery of intestinal function and the gradual healing of anastomotic stoma, which is one of the markers for the gradual recovery of patients undergoing gastrointestinal surgery. Meanwhile, with reference to the *Guidelines for Technical Review of Endoscopic Stapler Registration* issued by NMPA (original CFDA) on March 13, 2017, the "time of first flatus" is selected as a secondary evaluation indicator for such products.

Evaluation time: After successful operation to before discharge.

Evaluation method: After the surgery, the investigators instructed the subjects to pay attention to the time of first anus exhaust. The subjects fed back to the physician after feeling the first flatus. The time is accurate to day.

(7) Time of first bowel movement

Justification for selection: After gastrointestinal surgery, the intestinal function gradually recovers. When the patients can recover spontaneous defecation, it indicates that the anastomotic stoma gradually heals, which is one of the markers for the gradual recovery of patients undergoing gastrointestinal surgery. Meanwhile, with reference to the *Guidelines for Technical Review of Endoscopic Stapler Registration* issued by NMPA (original CFDA) on March 13, 2017, the "time of first bowel movement" is selected as a secondary evaluation indicator for such products.

Evaluation time: After successful operation to before discharge.

Evaluation method: The investigators observed the time for subjects to recover spontaneous defecation for the first time after operation. The time is accurate to day.

(8) Time of eating semi-liquid food

Justification for selection: After gastrointestinal surgery, the intestinal function gradually recovers when the patients eat semi-liquid food, which indicates that anastomotic stoma gradually heals, which is one of the markers for patients undergoing gastrointestinal surgery. Meanwhile, with reference to the *Guidelines for Technical Review of Endoscopic Stapler Registration* issued by NMPA (original CFDA) on March 13, 2017,

the "time of eating semi-liquid food" is selected as a secondary evaluation indicator for such products.

Evaluation time: After successful operation to before discharge.

Evaluation method: The investigators determine whether the subject can eat semi-liquid food according to his/her recovery, and record the time of eating semi-liquid food. The time is accurate to day.

8.1.16 Safety evaluation method

(1) Incidence of anastomotic stoma dehiscence

Justification for selection: When stapler is used for intestinal anastomosis, it is necessary to select appropriate reload. Dehiscence of the anastomotic stoma may increase the risk to the subject. Therefore, the "incidence of anastomotic stoma dehiscence" is selected as one of the safety indicators of the product under evaluation. At the same time, with reference to the *Guidelines for Technical Review of Endoscopic Stapler Registration* issued by NMPA (original CFDA) on March 13, 2017, the "incidence of anastomotic stoma dehiscence" is selected as a safety evaluation indicator for such products.

Evaluation time: During the surgery.

Evaluation method: Anastomotic stoma dehiscence due to "staple popping" during surgery is recorded.

Formula: Incidence rate of anastomotic stoma dehiscence = number of eligible subjects in each group/total number of subjects in the group × 100%

(2) Incidence of anastomotic stoma bleeding

Justification for Selection: Anastomotic stoma bleeding is a common complication in gastrointestinal anastomosis procedures, which will increase the risk to subjects. Therefore, "the incidence of anastomotic stoma bleeding" is selected as one of the indicators to evaluate the product safety. Meanwhile, with reference to the *Guidelines for Technical Review of Endoscopic Stapler Registration* issued by NMPA (original CFDA) on March 13, 2017, the "incidence rate of anastomotic stoma bleeding" is selected as a safety evaluation indicator for such products.

Evaluation time: from the end of surgery to the end of follow-up.

Evaluation method: Alimentary tract bleeding occurs after operation, and is confirmed as the anastomotic stoma source by observing digestive cavity decompression tube and intraperitoneal drainage tube, endoscope and angiography. If the source is not identified, it is then called gastrointestinal bleeding.

Formula: Incidence rate of anastomotic stoma bleeding = number of eligible subjects in each group/total number of subjects in the group × 100%

(3) Incidence of anastomotic leakage

Justification for selection: Anastomotic leakage is a common complication of gastrointestinal anastomosis, which will increase the risk to subjects. Therefore, the "incidence of anastomotic leakage" is selected as one of the safety indicators for product evaluation. At the same time, with reference to the *Guidelines for*

Technical Review of Endoscopic Stapler Registration issued by China Food and Drug Administration on March 13, 2017, the "incidence of anastomotic leakage" is selected as a safety evaluation indicator for such products.

Evaluation time: From the end of surgery to the end of follow-up.

Evaluation method: Patients with at least one of the following items are considered as anastomotic leakage: A. imaging examination, such as gastrointestinal radiography, confirms anastomotic leakage; B. fecal substances appearing in the abdominal drainage tube or incision, in which other sources of intestinal tract can be excluded; C. reoperation exploration confirms anastomotic leakage; D. abdominopelvic abscess beside the anastomosis. Anastomotic leakage is divided into 3 grades according to the severity: Grade A: no special treatment is required; Grade B: active treatment is required, but no reoperation is required; Grade C: reoperation is required.

Formula: Incidence of anastomotic leakage = eligible subjects in each group/total number of subjects in this group × 100%

Precautions: Necessary records should be kept for the treatment of anastomotic leakage.

(4) Incidence of anastomotic stricture

Justification for Selection: Anastomotic stricture is a common complication of gastrointestinal anastomosis, which will increase risks to subjects. Therefore, "the incidence of anastomotic stricture" is selected as one of the indicators to evaluate the product safety.

Evaluation time: From the end of surgery to the end of follow-up.

Evaluation method: The clinician judges whether the subject has an anastomotic stricture based on the symptoms, signs, endoscopy, angiography, etc.

Formula: Incidence rate of anastomotic stricture = eligible subjects in each group/total number of subjects in the group × 100%

(5) Incidence of anastomotic stricture infection

Justification for Selection: Anastomotic stricture infection is a common complication of gastrointestinal anastomosis, which will increase risks to subjects. Therefore, "the incidence of anastomotic stricture infection" is selected as one of the indicators to evaluate the product safety.

Evaluation time: from the end of surgery to the end of follow-up.

Evaluation method: The clinician judges whether the subject has a staple line infection based on the symptoms, signs, endoscopy, angiography, etc.

Formula: Incidence rate of anastomotic stricture infection = eligible subjects in each group/total number of subjects in the group × 100%

(6) Incidence of SAE (serious adverse event)

Evaluation time: During the whole clinical trial process.

Evaluation method: Serious adverse event refers to an event occurs in the process of clinical trials, which results in death or serious deterioration of health, including fatal disease or injury, permanent damage to the body structure or function, requiring hospitalization or prolonging the hospitalization, requiring medical or surgical intervention to avoid the permanent damage to the body structure or function; results in fetal distress, fetal death or congenital abnormality, congenital defect, etc.

Formula: SAE incidence = number of subjects with SAE in this group/number of all subjects in this group × 100%.

Precautions: The adverse events related to the anastomotic stoma during clinical trial shall be considered as serious adverse events. Since "anastomotic stoma repair" may be associated with "anastomotic stoma dehiscence", the “anastomotic stoma repair "is not repeatedly considered a serious adverse event.

(7) Incidence of AE (adverse event)

Evaluation time: During the whole clinical trial process.

Formula: Incidence of adverse events = number of subjects with adverse events in this group/number of all subjects in this group × 100%.

Definition: An adverse event is any untoward medical occurrence in a clinical investigation, whether or not related to the device. It is necessary to analyze the postoperative vital signs and laboratory tests (blood routine, biochemical indicators, etc.).

(8) Incidence of device defects

Measurement time: During the whole process of clinical trial.

Calculation formula: Incidence of device defect = number of device defects/total number of devices × 100%.

Precautions: A test device defect that occurs during the course of a clinical trial. "Staple pop" due to human factors (e.g., incorrect reload selection) is not a defect of the device.

8.1.17 Operational performance evaluation

(1) Stapler operating performance evaluation

Measurement time: During the stapler operation process.

Evaluation method: ① Whether the single-handed operation of stapler is smooth; ② whether the stapler can fire normally; ③ whether the back-off is smooth after the completion of anastomosis, whether there is tissue entrapment, whether there is resistance; ④ whether the stapler can fire continuously for many times is reliable; ⑤ whether the stapler can completely cut off the tissue; ⑥ whether the battery supply is stable; ⑦ whether the electric cutting is smooth.

8.2 Test Process

8.2.1 Test Flow Chart

Visit Time / Visit Item	Visit 1 Before surgery (Day -7 ~ 0)	Visit 2 During surgery (Day 0)	Visit 3 After surgery (Day 7 ± 2 days)	Visit 4 After surgery (Day 30 ± 5 days)
Informed consent	▲			
Subject screening	▲			
Demographic data	▲			
History of present illness	▲			
Past medical history	▲			
Vital signs	▲	▲	▲	▲
Blood routine	▲		▲	
Coagulation routine	▲		▲	
Blood biochemistry	▲		▲	
Cardiac examination	▲		▲	▲
Pulmonary function test	▲			
Arterial blood gas analysis	▲			
Preoperative imaging	▲			
Blood pregnancy test[1]	▲			
Randomization		▲		
Intraoperative observation record		▲		
Use of device		▲		
Postoperative imaging[2]			▲	
Postoperative follow-up observation			▲	▲
Concomitant medication	▲	▲	▲	▲
Adverse events	▲	▲	▲	▲
Device defect		▲		

1 Only for women of childbearing potential.

2 In case of anastomotic leakage and bleeding, the investigators may perform relevant examinations for the subjects according to actual needs.

8.2.2 Enrollment

The investigators screened the subjects according to the inclusion and exclusion criteria after obtaining their informed consent; before the day of conducting gastrointestinal tissue cutting and anastomosis, the subjects were randomly divided into the test group and the control group according to the random assignment instructions.

8.2.3 Randomization

The trial was stratified by clinical trial institutes with the randomization method of stratified blocks. The seed number and block length were determined with SAS9.1 statistical software programming. The subjects were divided into the test group and the control group in a ratio of 1:1. The random grouping arrangement of at least 164 subjects was generated, and the corresponding sequentially numbered, opaque and sealed randomization envelopes were made. The randomization envelopes were kept and allocated by relevant personnel who were not involved in the screening and treatment of subjects and authorized by the investigator.

The random number is a 4-digit sequential number consisting of "center number" and "serial number" (which is generally the “center digit occupied + sample size digit occupied”). The first digit is the number of the clinical trial institution, and the last 3 digits are the "serial number" assigned by randomization. When the serial number is less than 3 digits, add “0” to make up 3 digits. If the randomization number "1001" is the first randomization number of the clinical trial institute with the institute number of 01, it corresponds to the first subject randomized at the institute.

When a subject was determined to be enrolled, the investigators or other authorized designee requested randomization assignment from the randomization envelope manager. The randomization envelope keeper took out the randomization envelope in the order of random number, filled in the screening number and initials of the subject to be assigned to the designated place on the back of the envelope, and signed the name and date to complete the allocation. The investigators or other authorized designee then intervened based on the results of the randomization assignment (i.e., test groups).

8.2.4 Blinding method

The investigators could not be blinded due to the difference in appearance between the test device and the control device, this trial therefore adopted an incomplete blinding method, and the subjects were not informed of the randomization results (i.e., the subjects did not know their own treatment assignment).

8.2.5 Inspection items

8.2.5.1 Medical history and vital signs

(1) Demographic data: gender, date of birth;

(2) History of present illness: admission time, surgical site [3];

(3) Past medical history: allergy history, dysfunction history of vital organs (heart, lung, liver and kidney), surgery history, and previous medication history [4] (within 1 month);

(4) Vital signs: height, weight, blood pressure, pulse, temperature, respiration, BMI [5];

8.2.5.2 Laboratory examinations

(1) Blood routine: hemoglobin (Hgb), red blood cell count (RBC), white blood cell count (WBC), neutrophil count (NEUT), neutrophil ratio (NEUT%), platelet count (PLT);

(2) Coagulation blood routine: prothrombin time (PT), activated partial thromboplastin time (APTT), international normalized ratio (INR);

(3) Cardiac examination: ECG, cardiac ejection fraction;

(4) Fasting blood glucose [6];

(5) Fecal examination: occult blood test;

(6) Cardiac ultrasonography: cardiac ejection fraction;

(7) Pulmonary function test: forced expiratory volume in one second (FEV1)/predicted value, forced expiratory volume in one second (FEV1)/forced vital capacity (FVC);

(8) Blood pregnancy test: applicable to women of childbearing age (18 ~ 50 years old);

8.2.5.3 Preoperative imaging [7]

(1) CT examination: tumor stage, whether there is liver metastasis, whether there is pelvic metastasis, whether there is lung metastasis;

8.2.5.4 Post-operative imaging [8]

(1) Angiography: whether there is anastomotic bleeding;

(2) Upper gastrointestinal radiography: whether there is anastomotic leakage and stricture;

3 The data can be completed after the end of surgery.

4 Mainly record drugs that affect healing (e.g., antineoplastic agents, corticosteroids) or coagulation.

5 Body mass index (BMI) = weight (kg) ÷ height2 (m2)

6 Combined with clinical practice, the subjects enrolled in this trial are all hospitalized patients who will receive routine blood biochemical examination (including blood glucose item), and the blood glucose value in the blood biochemical results of hospitalized patients after blood collection in the morning is generally fasting blood glucose value; if the subject does not have fasting blood glucose value, the blood glucose value (≤10.0 mmol/L) is also used for screening confirmation; this is acceptable to be the fasting blood glucose data in the screening period. The investigators may choose to do this according to the subject's condition.

7 If the subject is a non-tumor patient, such examination may not be performed, and the CRF should be completed as "Not Applicable".

8 In case of anastomotic leakage, stricture and bleeding, the investigators may decide whether the subject will receive angiography, upper gastrointestinal radiography and gastrointestinal endoscopy according to actual needs. If relevant examination is not required, the CRF should be completed as "Not Applicable".

(3) Gastrointestinal endoscopic examination: whether there is anastomotic leakage and stricture;

(4) Abdominal CT: whether there is abdominal effusion and the amount of abdominal effusion;

8.2.5.5 Other tests:

(1) Intraoperative observation items: name of operation, start time of operation, end time of operation, start time of anastomosis, end time of anastomosis and intraoperative blood loss;

(2) Observation of the study product[9]: whether the digestive tract is successfully transected and stapled, whether the cutting anastomosis ring/staple line is complete, whether there is leakage of cutting anastomosis ring/staple line, whether there is bleeding of cutting anastomosis ring/staple line, whether there is bubble overflow at the anastomotic stoma[10], whether there are indicators of conversion to laparotomy[11], number of needles for anastomotic repair[11], whether there is anastomotic dehiscence[11], whether there are other complications[11], whether the staple line or tissue buttressing materials are used, and the operating performance of stapler;

(3) Device use[12]: model and specification of electric stapler, model of cartridge, use condition[13], cutting and stapling tissues[14], device defects;

(4) Postoperative follow-up observation: first anus exhaust time, semi-liquid feeding time, first defecation time, bowel sound recovery time, whether there is anastomotic bleeding[15], whether there is anastomotic leakage[15], whether there is anastomotic stenosis[15], whether there are other complications[15], whether there is abdominal effusion and the abdominal effusion volume;

(5) Routine observation items: adverse events, concomitant medication, protocol deviations.

8.2.6 Device using specification

According to the results of random allocation, the investigators apply the study medical device to the subjects who enter the test group, and the control medical device to the subjects who enter the control group. If a subject requires the use of a circular stapler during the trial, the brand and model of the circular stapler shall be recorded.

9 Only the conditions related to the use of test product and control product are recorded here. However, during the trial, subjects may use circular stapler or other staplers. If adverse events related to the stapler also occur, the occurrence shall be truthfully recorded in the adverse events.

10 It is necessary to use gas injection method for inspection. If relevant examination is not required, the CRF should be completed as "Not Applicable".

11 If yes, please specify the reason and whether it is related to the stapler.

12 The model and amount used in the clinical trial shall be truthfully recorded. Meanwhile, whether the subject uses the brand and model of circular stapler shall also be collected.

13 Investigators faithfully record whether each reload is used laparoscopically or laparotomically.

14 The tissues cut and anastomosed by each cartridge, such as stomach, duodenum, jejunum, ileum, appendix, ascending colon, transverse colon, descending colon, sigmoid colon and rectum, etc. are recorded.

15 If corresponding symptoms occur, the reasons for confirming the event should also be briefly described, so as to facilitate the review. In addition, generally anastomotic bleeding is judged by the presence or absence of persistent fresh bleeding from the gastric tube, and the diagnosis is confirmed by gastroscopy or second surgical exploration.

8.2.7 Visit schedule

Subjects should receive 4 visits before the end of the study: before surgery (Day -7 ~ 0), during surgery (Day 0), on Day 7 ± 2 after surgery, and on Day 30 ± 5 after surgery.

8.2.7.1 1st visit 1/before surgery (Day -7 ~ 0)

(1) The ICF form shall be signed;
(2) Screening subjects according to the inclusion and exclusion criteria;
(3) Recording demographic data, current medical history and past medical history are recorded;
(4) Examining vital signs;
(5) Performing preoperative imaging examination[16] (CT examination);
(6) Performing laboratory examinations[17] (blood routine, coagulation routine, blood biochemistry, fasting blood glucose, occult blood test, cardiac ultrasound, pulmonary function, blood pregnancy test) ;
(7) Recording concomitant and concomitant medications;
(8) Recording protocol deviations;

8.2.7.2 2nd visit 2/during surgery (Day 0)

(1) Examining vital signs;
(2) Intraoperative observation records (intraoperative observation, observation of investigational product, use of device);
(3) Randomization;
(4) Use of device;
(5) Recording concomitant medication/treatment;
(6) Monitoring of adverse events and serious adverse events;
(7) Recording device defects;
(8) Recording protocol deviations;

8.2.7.3 3rd visit 3/after surgery (Day 7 ± 2 days)

(1) Examining vital signs;
(2) Conducting laboratory examinations (blood routine, coagulation routine, blood biochemistry, occult blood test);
(3) Conducting postoperative imaging examinations (angiography 8, upper gastrointestinal radiography 8, gastrointestinal endoscopy 8, postoperative abdominal CT) ;
(4) Postoperative follow-up observation;

16 For imaging examination, reports/results within 1 month prior to surgery in our hospital my be accepted.

17 For laboratory examination, reports/results at within 7 days prior to surgery in our hospital may be accepted.

(5) Postoperative follow-up observation;

(6) Recording concomitant and combined medications;

(7) Recording adverse events and serious adverse events;

(8) Recording protocol deviations;

8.2.7.4 4th visit/after surgery (Day 30 ± 5 days)

(1) Examine vital signs;

(2) Occult blood test;

(3) Conducting postoperative imaging examinations (angiography, upper gastrointestinal radiography, gastrointestinal endoscopy) 8;

(4) Postoperative follow-up observation (anastomotic healing time, whether there is anastomotic bleeding, whether there is anastomotic leakage, whether there is stricture and other complications);

(5) Recording concomitant and combined medications;

(6) Monitoring adverse events and serious adverse events;

(7) Recording protocol deviations;

8.2.8 Concomitant medication/treatment management

If a subject takes medication or therapeutic measures that caused the AE for various reasons during the study, such situation shall be recorded in the case report form (CRF) by investigators for reference.

(1) Prohibited therapies: Products with similar efficacy to the study medical device and the control device are prohibited for use by all subjects during the clinical trial.

(2) Allowable treatment: The treatment with other drugs or therapeutic measures required due to underlying diseases, concomitant diseases or adverse events should be recorded in the original medical records in detail, including the name, dosage, usage of the drug and the name, usage and frequency of the therapeutic measures.

(3) The generic name, type, dose, frequency, route of administration and days of administration of other drugs used by the subjects as well as the name, method and frequency of treatment should be recorded in detail. The information is used to evaluate the possible bias on clinical trial results.

8.2.9 Case report form completion

Case Report Form (CRF) is a document designed according to the clinical protocol to record the data of each subject during the trial. The correct completion of case report form will help to make a correct judgment on the trial results. Each investigator should complete the case report form carefully and pay attention to the following points:

(1) Required fields on the CRF must not be left blank;

(2) When completing the CRF, be sure to make the unit of test results consistent with the unit filled in;

(3) All data on the CRF should be derived from original documents and be consistent with the original documents;

(4) The investigator should complete and sign the CRF within 2 weeks after each subject completes relevant examinations, which is for overall monitoring by the clinical research associate;

(5) If there is any uncertainty in the filling process, please communicate with the sponsor in a timely manner.

8.3 Monitoring Plan

The sponsor shall, in accordance with the requirements of *Good Clinical Practice for Medical Devices*, select the qualified monitor to perform monitoring responsibilities for all the participating institutions. The monitoring frequency of each participating institution will be adjusted according to the speed of subject recruitment and subject number in each institution participating in the study. The monitor will complete the following responsibilities:

(1) Confirming that the clinical trial institution has been equipped with appropriate conditions before the trial, including qualified staffing and training, complete laboratory equipment, good working condition, expected to have a sufficient number of subjects, and investigators familiar with the trial requirements;

(2) Monitoring whether the clinical trial institutions and investigators abide by relevant regulations, this specification and clinical trial protocol before, during and after the trial;

(3) Confirming that each subject has signed the ICF before participating in the clinical trial, and that the inclusion of subjects as well as the progress of the trial are well known; monitoring and recording the failure follow up, non-conducted trial, non-conducted examination by the investigators, and whether the errors and omissions are corrected; for the revised ICF, confirming that the clinical trial process is not completed and the affected subjects have re-signed the ICF;

(4) Confirming that all the CRFs are correctly filled in and consistent with the original data; that all the errors or omissions have been corrected or explained, which have been signed and dated by the investigators; and that the disease type, total number of cases and gender, age and therapeutic effect in each trial have been confirmed and recorded;

(5) Confirming that the subject withdrawing from the clinical trial or non-compliant with the requirements set forth in the ICF is recorded and discussed with the investigators;

(6) Confirming that all adverse events, complications and other device defects are recorded, and serious adverse events and device defects that may cause serious adverse events are reported and recorded within the specified time;

(7) Monitoring the supply, use, maintenance, transportation, reception, storage, distribution, processing and recovery of investigational medical device samples;

(8) Supervising the regular maintenance and calibration of relevant equipment during the clinical trial;

(9) Ensuring that all the documents related to the clinical trial received by the investigators are of the latest version;

(10) Submitting a written report to the sponsor after each monitoring, which shall include the name of the monitor, date of monitoring, time of monitoring, place of monitoring, content of monitoring, name of the investigator, completion status of the project, existing problems, conclusions, and corrections to errors and omissions, etc.

9. Statistical Considerations

9.1 Statistical Design, Methods and Analysis Procedure

This study is a prospective, multi-center, stratified block randomization, incomplete blinding, parallel positive control and non-inferiority test. All statistical analysis methods are detailed in the statistical analysis plan. The first draft of the statistical analysis plan will be formed after the trial protocol and case report forms are finalized and will be finalized before database lock.

9.2 Sample Size Calculation

9.2.1 Total sample size

164 subjects are planned to be enrolled in this clinical trial. The sample size determination process is as follows:

This clinical study is a parallel positive control clinical validation design. The "anastomosis success rate" is adopted as the basis for sample size estimation. Based on literature review [3-11], the success rate of anastomosis is up to 100% when the similar devices are used for total laparoscopic distal gastrectomy for gastric cancer. According to relevant literatures and considering clinical practice, when such products are used for anastomosis from esophageal site to gastrointestinal site, the "success rate of anastomosis" can reach 97%. Therefore, the "anastomosis success rate" of this clinical trial is determined to be 97% with a clinical non-inferiority margin of 10%. The parameters are set as follows: $\alpha = 0.025$ (one-sided), $\beta = 0.2$, $\delta = 10\%$, and the ratio of test control group is 1:1. The estimation formula of sample size for non-inferiority clinical validation is adopted, and the sample size required in each group is at least 65 cases. The calculation formula [12] and correction formula [13] are as follows:

$$n_A = \frac{(\pi_A(1-\pi_A)+\pi_B(1-\pi_B))(Z_{1-\beta}+Z_{1-\alpha})^2}{((\pi_A-\pi_B)-d)^2}$$

$$n_B = \frac{n_3\left\{1+[1+4/(\delta n_A)]^{\frac{1}{2}}\right\}^2}{4}$$

Considering that the number of subjects who may drop out or be lost to follow-up during clinical validation is about 20%, the sample size of each group is expanded to 82 cases, and the total sample size required for the two groups is 164 cases.

9.2.2 Number of cases for clinical trial of each disease and reasons for determination

The investigational product is mainly used for the cutting and anastomosis of gastrointestinal tissues, other diseases therefore are not involved in this clinical trial.

9.2.3 Minimum and maximum number of subjects in each clinical trial institution and reason

A total of 164 subjects are planned to be enrolled in this clinical trial, and a total of 5 clinical trial institutions are planned to participate in this trial. In the trial, the sample balance in each site should be maintained as far as possible. In combination with the total sample size and the number of participating clinical trial institutions, considering different number of disease sources in each center and possible difficulties in individual centers, each clinical trial institution should recruit at least 16 subjects but no more than 60 subjects.

9.3 Significance Level and Power of Clinical Trial

Significance level α (one-sided) = 0.025 with 80% power.

9.4 Expected Dropout Rate

A 20% dropout rate is expected during sample size estimation.

This drop-out rate refers to the proportion of subjects who finally can not be included in the primary analysis. Drop-out subjects refer to those confirmed by the principal investigator with serious protocol violation (affecting the main evaluation/efficacy evaluation). The following conditions may be included, but not limited to: the subject violates the inclusion and exclusion criteria; the subject does not receive any examination/treatment with the study device; the subject receives the concomitant medication/device prohibited by the protocol; the data of main evaluation indicators are missing; the subject fails to obtain any data after randomization; the subject fails to complete the follow-up visit according to the regulations.

9.5 Qualification/Disqualification Criteria for Clinical Trial Results

The non-inferiority hypothesis is tenable if the lower limit of 95% confidence interval of the difference in the primary effectiveness evaluation indicator between the test group and the control group is greater than the non-inferiority critical value (-10%).

The secondary effectiveness evaluation indicators and safety evaluation indicators are tested by difference test, and the significance level is set at 0.05. If the test result of the difference in any secondary evaluation indicator and safety evaluation indicator between the test group and the control group is $p > 0.05$, then there is no significant difference in this indicator between the test group and the control group.

9.6 Criteria and Reasons for Terminating Trial Based on Statistical Reasons

No interim analysis will be performed for this study, therefore, no standard for terminating the trial for statistical reasons is developed.

9.7 Statistical Methods of Data, Together with Processing Methods of Missing, Unused or Wrong Data and Unreasonable Data

9.7.1 Statistical method for data

Statistical analysis is performed using the SAS 9.1 software.

Statistical description on all data, including demographic data, baseline data, all efficacy indicators and all safety data shall be performed. Measurement data will be statistically described using mean, standard deviation, minimum, maximum, median, 25^{th} percentile and 75^{th} percentile; enumeration data will be statistically described using frequency and percentage.

The primary effectiveness evaluation indicator (anastomosis success rate) is evaluated by the confidence interval method.

The secondary evaluation indicators are evaluated by the difference test. Measurement data are compared using two independent samples t-test or Wilcoxon rank sum test. Enumeration data are compared using Pearson's X^2 test or Fisher's exact test.

The safety evaluation indicators are evaluated by the difference test. Enumeration data are compared using Pearson's X^2 test or Fisher's exact test. The adverse events and device defects occur in this trial shall be shown in list.

The stapler operational performance is evaluated by the difference test. Enumeration data are compared using Pearson's X^2 test or Fisher's exact test.

The central effect is considered in the analysis process. The general linear model is used for measurement data, and CMH or logistic regression is used for enumeration data.

9.7.2 Missing, unused, or incorrect data (including dropouts and withdrawals) and unreasonable data

All missing, unused or incorrect data (including dropouts and withdrawals) and unreasonable data will be discussed and finally determined by the investigators and biostatistician in the data review stage. The basic statistical principles for the processing of these data are as follows:

(1) The details of each drop-out case shall be described, and the drop-out between the test group and the control group shall be compared using Pearson X^2 test or Fisher exact test;
(2) Missing data at baseline shall not be estimated;
(3) Missing values of main evaluation indicator (success rate of anastomosis) shall not be estimated;

(4) Missing values of secondary evaluation indicators shall not be estimated;

(5) Missing values for operational performance evaluation shall not estimated;

(6) The wrong and unreasonable data shall be regarded as missing values;

(7) Missing values for all safety measures shall be estimated using the worst case;

(8) Sensitivity analysis shall be performed on the safety data set for all the safety evaluation indicators after treatment.

(9) Missing data shall be statistically analyzed in the table.

9.8 Procedures for Reporting Deviations from Original Statistical Plan

In general, only the statistical analysis contents pre-specified in the statistical analysis plan can be presented in the clinical trial report of this trial. The increased need for statistical analysis due to various indeterminate reasons will be considered exploratory only.

9.9 Selection Criteria and Reasons for Subjects Included in Analysis

(1) Full analysis set (FAS): According to the basic principles of intention to treat analysis, all the subjects who have received at least one treatment with the investigational medical device and had at least one post-baseline observation data are included in the FAS. The FAS will be used as the primary population for baseline data (and efficacy evaluation) in this study.

(2) Per-protocol set (PPS): It refers to the subjects in the FAS who do not seriously deviate from the trial protocol, have good compliance and have no missing primary efficacy indicators. The PPS will be used as the primary population for efficacy analysis in this study.

(3) Safety set (SS): All subjects who have received at least one treatment with the investigational medical device and had at least one safety evaluation. The SS will be used as the primary population for safety analysis in this study.

9.10 Exclusion of Special Information During Hypothesis Validation and Reasons

Not applicable.

10. Data Management

10.1 Database Design

The CRF designer is responsible to annotate the final version of the blank CRF and describe in detail the necessary elements (e.g., variable name, length, type, range of the database variable, etc.).

The database designer determines the requirements for database establishment and database structure according to CRF and annotated CRF, and designs the database.

The database must be thoroughly tested to ensure that the contents and structure of the database are consistent with those of the CRF and annotated CRF, that the specified data are appropriately entered into the

database, and that the entered data points are correctly exported into the corresponding database variables.

The database can be officially released for use only after it is approved.

10.2 Data Receipt and Data Entry

Data may be received by mail, courier with tracking for confidentiality, hand delivery by the monitor, web entry, or other electronic means. When the paper CRF data is received, it shall be recorded in the data receiving record form. After the completion of data receiving, the CRF shall be scanned and backed up; the data received via network or other electronic means shall be stored in the corresponding documents and records to confirm the data source.

Data entry can be double-entered by blind verification (two persons independently enter the data, and the inconsistency is resolved at the second entry), and double-entered by interactive verification (the second entry resolves the inconsistency between the two entries, and pays attention to the value of the first entry), manual review of single entry and other forms.

Prior to data entry, the data manager shall train the entry clerk or investigators on system operation or matters specific to this study.

After the completion of data entry, the database data shall be checked with original data to ensure that the database data are consistent with original data.

10.3 Management of Data Verification and Query

Data verification includes manual inspection of data, and computer verification designed for identification error, invalid data range, data integrity, protocol violation and consistency inspection. Data administrator shall complete relevant procedures of preparing and approving the Data Verification Plan before the first data receipt to determine the data verification content. Programmer will program and test the verification procedure according to the finalized Data Verification Plan.

Based on the results of manual inspection and computer verification, the data administrator will resolve the doubtful data in the form of data query form, data processing agreement and self-evident correction, and update the database according to the answers or descriptions in relevant documents.

10.4 Database Lock and Data Archiving

The clinical trial database must be closed and locked to ensure the consistency and integrity of the data results, data analysis and data submitted to the official authorities.

When all data have been received and all data cleaning has been completed, all queries have been answered, all unanswered questions have been explained, the data review report has been confirmed, the division of statistical analysis dataset has been clarified, and the data quality control has been completed (the database quality is up to standard), the data administrator shall apply for database locking to the project team members.

After being jointly confirmed by the investigators, the sponsor and project team members, the data editing authority of the database will be taken back to lock the database. After the database is locked, the data administrator shall transfer the data to the statistical analysis department in a timely manner. If data correction is required, the review and approval of Database Unlock Application Form shall be completed, and the database shall be unlock, so that corresponding personnel can enter the database to correct the data.

The data administrator shall establish the Data Management Project Folder, and shall be responsible for archiving the data or record files when they meet the conditions for archiving. Upon completion of the study, the data administrator will revoke the database access of relevant personnel, create a copy of the database, and archive the study documents and data management documents.

11. Feasibility Analysis

11.1 Probability Analysis of Success

(1) According to the relevant clinical trials, it shows that such product is safe and reliable; and such product has been used in clinical practice for many years, and its safety and reliability have been verified.

(2) The company producing the study medical device has rich experience. The product quality is reliable and meets the requirements of clinical trials; the device has passed the product registration inspection designated by NMPA (original CFDA).

(3) The clinical institutions undertaking this trial have complete instruments, equipment and technical resources.

(4) The investigators are excellent academic leaders in related disciplines in China, all of whom are physicians at or above the deputy director level, have rich clinical trial experience, have received GCP and relevant training, and can carry out treatment in strict accordance with the clinical trial protocol.

11.2 Probability Analysis of Failure

(1) Too many subjects withdrawing from the trial due to SAE;

(2) Too many subjects lost to follow-up;

(3) The IFU and label information of test product can not effectively instruct the operator;

(4) Unskilled operation of investigators.

11.3 Conclusion

In conclusion, this product can be used for the anastomosis of gastrointestinal tissues to benefit relevant patients. This study has great feasibility and high possibility of success.

12. Quality Control of Clinical Trial

12.1 Quality Assurance

12.1.1 Definition

Quality assurance is defined as planned and systematic activities. These activities are established to ensure that the study, generation, citation (recording) and reporting of data are conducted in compliance with *Good Clinical Practice* (GCP) and applicable regulatory requirements.

12.1.2 Audit

Audit refers to a systematic independent inspection of clinical trial-related activities and documents organized by the sponsor to determine whether the implementation of such activities and the recording, analysis and reporting of data comply with the clinical trial protocol, standard operating procedures, GCP and relevant applicable management requirements.

12.1.3 Inspection

Inspection refers to the activities of the food and drug regulatory authority in reviewing and supervising relevant documents, facilities, records and other aspects of a clinical trial.

12.1.4 Clinical trial monitoring

The sponsor shall be responsible for comprehensively tracking and monitoring the implementation of clinical trial, ensuring that the trial is conducted in compliance with GCP and relevant regulations, and is in compliance with the trial protocol. NMPA (original CFDA) may also inspect the clinical trial during or after the trial is completed, and promptly notify the sponsor if investigators receive such notification.

The monitor will make periodic visits to the conduct and completion of the trial. Monitors will check the completeness of case records, the accuracy of case report form content, verify trial data, check the investigator's compliance with the trial protocol and the GCP, and ensure the accuracy of distribution, storage and counting of the study device.

12.2 Quality Control

12.2.1 Definition

Quality control is defined as operational techniques and activities performed under a quality assurance system, such as monitoring, which is intended for verifying that the study-related activities meets the requirements.

Quality control should be applied to each stage of data processing to ensure that all data are credible and correctly processed.

12.2.2 Study monitoring

The authorized and qualified monitor will visit the clinical trial centers regularly according to the monitoring plan to verify the source data, the investigator's compliance with the protocol and regulations, and to assist the investigators.

12.2.3 Laboratory quality control

Each clinical trial center laboratory should establish unified standards for experimental test indicators, standard operating procedures and quality control procedures. Each experimental test item must adopt the national legal unit of measurement, and the test report items must be complete (including date, test item, test result and normal range), and relevant personnel should sign the report. Special inspection items must be specially assigned to be tested.

12.2.4 Quality control for other inspections

Each clinical trial center should establish unified evaluation criteria, standard operating procedures and quality control procedures for the evaluation of vital signs and damage. Each clinical trial center should evaluate the subject's condition according to the unified standard and standard operating procedures.

12.2.5 Qualification of study personnel

The investigators participating in the clinical trial must have the professional expertise, qualification and ability of clinical trials, and pass the qualification review. The personnel requirements shall be relatively fixed.

12.2.6 Study staff training before study initiation

The sponsor is responsible for the training of study personnel before the start of the trial to help the clinical study personnel get a full understanding and understanding of the overall situation of the trial, protocol, CRF, etc.

13. Ethical Issues and Informed Consent of Clinical Trial

13.1 Ethical Considerations

This clinical trial must be carried out in accordance with the *Declaration of Helsinki*, relevant medical device clinical trial regulations and laws in China. The study protocol must be approved by the Ethics Committee (EC) of the clinical trial institute before the study is initiated.

Before each subject is enrolled in the study, the study physician is responsible for explaining the contents of the trial to the subject in a verbal or written language understandable to the subject and carefully answering

the subject's questions. Each subject must be given a written subject informed consent prior to enrollment. It is the responsibility of the study physician to obtain informed consent prior to each subject entering the study and to retain it in the study file.

This study is conducted based on the *Declaration of Helsinki*, *Good Manufacturing Practice* (GMP) for medical devices, *International Conference on Harmonisation Good Clinical Practice* (ICH-GCP), applicable laws and regulations in the People's Republic of China.

Based on ethical considerations, in accordance with ICH-GCP , relevant laws and regulations applicable within the territory of the People's Republic of China, the design and implementation of this study put the safety of subjects first on the requirements that the study medical device must be tested firstly when used under clinical conditions. Therefore, in this pre-clinical study, the biological safety of the materials used is tested firstly, and the purpose is to minimize the potential risks in the use of the materials. In order to fundamentally elucidate safety issues, various criteria for this study are also identified.

13.2 Approval of Study Protocol

Before the clinical trial, the investigators should submit the study protocol, informed consent form and other relevant documents to the medical ethics committee of the hospital where the study site is responsible for. The clinical trial can only be initiated after obtaining the approval of the Ethics Committee. Any amendment to the study protocol must be approved by the Ethics Committee before implementation. Serious adverse events during the clinical trial should be reported to the Ethics Committee in written form in a timely manner.

13.3 Informed Consent Process and Informed Consent Form Text

Before each subject is enrolled in this study, the investigators are responsible for introducing the contents and description of the informed consent form to him/her or his/her guardian completely and comprehensively in written form.

The informed consent form should be written in a language understandable to the subject or his/her guardian. The informed consent form shall contain no content that may cause the subject to give up his/her legal rights and interests, and that exempt the clinical trial institution, the investigators, the sponsor or his/her agent from taking the responsibilities.

Each subject must be given a written subject informed consent prior to enrollment. It is the responsibility of the investigators to obtain informed consent before each subject enters the study and to retain it in the study file.

For an incapacitated subject, if the Ethics Committee agrees in principle and the investigators believe that the subject's participation in the clinical trial is in his/her own interests, he/she can also enter the clinical trial, but his/her guardian should sign and date it before the trial.

When the subject or his/her guardian is unable to read, a witness shall be present during the process of

informed consent. After the informed consent form is explained in detail, the witness reads the informed consent form, which shall be consistent with the oral informed consent. After the subject or his/her guardian gives oral consent, the witness signs and dates the informed consent form, and the signature of the witness shall be on the same day as that of the investigator.

See the Informed Consent Form for details.

13.4 Personal Data and Data Protection

(1) All data obtained in clinical trials are subject to data protection. The investigators should not disclose the subject's name and other personal data (excluding date of birth/age and gender).

(2) The CRFs and other documents transmitted to the sponsor will not contain names, but only the study code of the subject.

(3) Similarly, the data used for statistical evaluation can only be performed under the study code of the subject. Only the investigator can identify the subject's name and other personal information through the study code.

(4) During the study, if the subject name needs to be identified for medical reasons, all relevant personnel are obligated to keep it confidential.

14. Provisions for Reporting Adverse Events and Device Defects

14.1 Adverse Event

14.1.1 Definition of adverse events

Adverse event (AE): refers to any adverse medical event occurring in the clinical trial process, no matter whether it is related to the investigational medical device or not.

14.1.2 Adverse event grading

(1) Mild: Symptoms inquired.

(2) Medium: Symptoms that are actively described but can be tolerated.

(3) Severe: Intolerable symptoms with objective manifestations.

14.1.3 Reporting and handling of adverse events

All the adverse events and serious adverse events observed in the clinical trial should be clearly filled in the adverse event column of case report form. The duration of adverse event (i.e., the date of occurrence and disappearance of adverse event), severity, relationship with the clinical trial, and corresponding treatment and other handling measures should be recorded. Subjects occurring such event shall be followed up to end of the trial or the adverse event outcome.

14.1.4 Correlation between adverse event and product

The correlation between all adverse events and study interventions must be judged by the investigators. The investigators then assessed based on temporal relationship and clinical experience. The followings are the evaluation criteria and judgment results of correlation:

① The adverse event occurs within a reasonable time after the application of the device;

② The adverse event can not be explained by other reasons;

③ The adverse event id relieved or disappeared after the the device is not applied;

④ The adverse event reappears after reapplication of the device.

Table 3. Correlation evaluation table

Standard / Results	①	②	③	④
Definitely related	+	+	+	+
Probably related	+	+	+	?
Possibly related	+	-	?	?
Unlikely related	-	-	?	?
Unrelated	-	-	-	-
"+" indicates conformity, "-" indicates non-conformity, "?" Indicates unable to judge				

14.1.5 Handing protocol of adverse events that may occur in this clinical trial

(1) Anastomotic bleeding: It is related to the factors of anastomotic leakage. The bleeding is generally the technical factor. The prevention is mainly to avoid the tension at the anastomotic stoma and the fat drop left at the cutting site.

(2) Anastomotic leakage: The incidence of anastomotic leakage is reported to be 4% to 15% in the literature. It may be caused by the stapler, or related to the patient's condition or the doctor's operation;

(3) Anastomotic stricture: It is one of the most common complications, mostly occurring after 1 month after surgery.

(4) Major incisional bleeding: Drop in hemoglobin ≥ 20g/l resulting in ≥ 1 transfusion.

(5) Minor incision bleeding: Bleeding that does not meet the criteria for "severe bleeding".

(6) Incision site infection: Infection at the incision site due to improper nursing, resulting in prolonged incision healing time, prolonged suture removal time, or unplanned antibiotic therapy.

(7) Delayed healing of incision: The incision in contact with suture has delayed healing time.

(8) Anemia and hypoproteinemia: Symptoms caused by tumor deterioration in patients with gastric cancer;

(9) Tumor recurrence or metastasis: Symptoms caused by further tumor deterioration in patients with gastric cancer;

(10) Gastrointestinal discomfort symptoms: Common symptoms of gastrointestinal diseases, such as nausea, belching, constipation, diarrhea, acid reflux, abdominal pain, etc.

14.1.6 Handing of adverse events that may occur in this clinical trial

The above are foreseeable adverse events of this study. The investigators may treat adverse events according to clinical diagnosis and treatment regulations as needed and record them faithfully.

14.2 Serious Adverse Event

14.2.1 Definition of serious adverse event

Serious adverse event refers to events occur in the process of clinical trial that causes death or serious deterioration of health, including

(1) Fatal disease or injury;
(2) Permanent damage to the body structure or body function;
(3) Requiring hospitalization or prolonging the hospitalization
(4) Requiring medical or surgical intervention to avoid the permanent damage to the body structure or body function;
(5) Any event that results in fetal distress, fetal death, or a congenital anomaly or birth defect.

14.2.2 Handling of serious adverse events

(1) In case of any serious adverse event in the clinical trial, the investigators should immediately take appropriate therapeutic measures for the subjects, report to the management department of medical device clinical trial of the clinical trial institution in written form, and notify the sponsor in written form.
(2) The management department of medical device clinical trial shall submit a written report to corresponding ethics committee, food and drug regulatory authority, and health commission authority of the local province, autonomous region or municipality directly under the central government where the clinical trial institution is located within 24 hours.
(3) For death-typed events, the clinical trial institutions and investigators should provide all required data to the ethics committee and the sponsor.
(4) For serious adverse events and device defects that may cause serious adverse events, the sponsor shall report to the filed food and drug regulatory authority and the health commission authority at the same level within 5 working days after being informed, notify other clinical trial institutions and investigators participating in the trial, and timely notify the ethics committee of the clinical trial institution through its medical device clinical trial management department.

14.3 Reporting and Handling of Device Defects

Device defects refer to unreasonable risks that may endanger human health and life safety under normal use of a medical device during a clinical trial, such as labeling errors, quality problems and failures, etc.

Possible device defects: identification error, product quality problem; design defect; damage of disinfection package, etc.

All device defects are documented on the Device Defect Record form, and device defects that could have led to serious adverse events shall be reported and documented within 5 working days.

15. Device Management

15.1 Study Device Management

Clinical trial institutions shall establish a strict registration system for the distribution of study devices. The sponsor shall assign a special person to directly deliver the study medical devices and control medical devices to each clinical trial institution. Clinical trial institutions and the sponsor shall establish perfect device receiving formalities, and the records shall include the date, quantity, batch number and expiry date. Each clinical trial institution uses a special *Record Form for Use of Medical Devices in Clinical Trials* to register the name of the subject, date of use, and signature of the device administrator, etc.

15.2 Device Packaging

The external package and number of study medical devices shall be unified, and the number, name, specification, course of treatment, production date, shelf life and the words "for clinical study only" shall be indicated on the package.

15.3 Recovery of Remaining Device

Upon termination of the trial, the sponsor will collect all unused study medical devices and control medical devices, and the sponsor is responsible for destroying the unused medical devices. All supplies must be accounted for at the end of the study.

16. Deviations from Clinical Trial Protocol and Provision for Amendments to Clinical Trial Protocol

16.1 Deviations from Clinical Trial Protocol

16.1.1 Definition of protocol deviation

Deviation refers to a situation where the requirements of the clinical trial protocol are not followed intentionally or unintentionally.

16.1.2 Deviation control measures

16.1.2.1 Sponsor

(1) The protocol shall be clearly described, and possible protocol deviations shall be considered. The protocol shall be designed in a way to minimize the occurrence of protocol deviations, and possible protocol deviations shall be simply and clearly identified and confirmed.

(2) In the investigator meeting and monitor training of the study project, the implementation details of the protocol, and the reporting and monitoring of protocol deviations should be given intensive training.

(3) There is a special protocol deviation control group that regularly reviews the protocol deviation records to identify potential trends and system errors; the correction of protocol deviation should be implemented. If it is necessary to immediately amend the protocol or study plan, the study project should be suspended in time, and the study can be continued after the protocol is amended and the retraining is completed.

16.1.2.2 Investigators

(1) At the project evaluation stage before the start of the study, the study protocol shall be read carefully, and the enforceability of the protocol in the institution shall be fully discussed with the sponsor.

(2) The investigators are responsible to explain the importance of compliance with the protocol to the subject at the time of informed consent.

(3) The investigators shall comply with the protocol approved by the Ethics Committee. In addition, the occurrence of protocol deviation should be recorded and explained immediately when he/she recognizes it.

16.1.3 Retraining

In the following cases, the investigators must receive re-training, and may receive multiple trainings if necessary.

(1) There are deviations in the understanding of the protocol;

(2) There are new investigators participating in the trial;

(3) The study plan changes;

(4) The investigators are reminded of the protocol details.

16.1.4 Protocol deviation report

In case of any deviation from the clinical trial protocol that affects the rights, safety and health of the subjects or the scientificity of the clinical trial, including the requested deviation and the reported deviation; the investigators should timely report to the management department for medical device clinical trial of the clinical trial institution, and timely notify the sponsor and the Ethics Committee to determine whether the

trial can continue to be conducted.

In order to protect the rights, safety and health of subjects, where the deviation occurs in an emergency can not be reported in a timely manner, it shall be reported in written form as soon as possible afterwards in accordance with relevant regulations.

During the clinical trial, in case of revising the clinical trial protocol, informed consent form and other documents, requesting for deviation and resuming the suspended clinical trial, the implementation can only be continued after obtaining the written approval from the Ethics Committee.

The investigators should strictly follow the clinical trial protocol. Without the approval of the sponsor and the Ethics Committee, or failing to obtain the approval from NMPA (original CFDA) as required, the investigators should not deviate from the protocol or materially change the protocol. However, in the event of an emergency that requires immediate removal, such as when the subject is at an immediate risk, a written report may be made afterwards.

16.2 Amendments to Clinical Trial Protocol

Medical device study protocol should be based on the primary principle of protecting the rights, safety and health of the subjects to the maximum extent. It should be jointly designed and formulated by the medical institution responsible for the clinical trial and the sponsor, and should not be implemented until recognized by the Ethics Committee; if the investigators have any revision to the study protocol, informed consent form and case report form during the study, the clinical trial should not be continued until approved by the Ethics Committee.

17. Direct Accessed Source Data/Source Documents

The authorized monitor has the right to access and verify the source data/documents of the subjects, so as to judge whether the investigators conduct the clinical trial according to the requirements of the protocol, and whether the source data/documents are timely recorded in the subject medical records. The monitor should confirm that the source data/documents are traceable and verifiable. Meanwhile, the data filled in the CRF should correspond to the source data/documents.

When any personnel participating in the clinical trial question the clinical trial data, the investigators shall timely provide the source data/source documents for verification by relevant personnel and carefully reply to the relevant queries.

Source data/documents should be properly kept in accordance with the requirements of relevant laws and regulations. Prior to destruction, it shall be signed and confirmed by the sponsor, and comply with relevant laws and regulations.

18. Finance and Insurance

The sponsor of this clinical trial is responsible for providing the investigational medical device and control

medical device required by this clinical trial, and providing the inspection item cost required by this clinical trial. The sponsor shall bear the treatment cost and corresponding economic compensation for the subjects who suffer from injury or death related to the clinical trial, except for the damage caused by the faults of medical institutions and their medical staff in the diagnosis and treatment.

The specific requirements for finance and insurance are detailed in the relevant agreements.

Medical accidents refer to accidents in which medical institutions and their medical staff violate the laws, trial protocols and guidelines for medical and health management in medical activities, and negligence results in personal damage to patients.

19. Contents Covered in Clinical Trial Report

The clinical trial report shall be prepared in accordance with relevant requirements of GCP and with reference to *Template for Clinical Trial Report of Medical Devices*, including but not limited to:

(1) General information;
(2) Abstract;
(3) Introduction;
(4) Clinical trial purpose;
(5) Clinical trial method;
(6) Clinical trial content;
(7) General clinical data;
(8) Investigational medical device and control medical device or control diagnosis and treatment method;
(9) Statistical analysis method and evaluation method adopted;
(10) Clinical evaluation criteria;
(11) Organizational structure of clinical trial;
(12) Ethical statement;
(13) Clinical trial results;
(14) Adverse events identified in clinical trials and handling situations;
(15) Analysis and discussion of clinical trial results, especially indications, applicable scope, contraindications and precautions;
(16) Clinical trial conclusion;
(17) Existing problems and suggestions for improvement;
(18) List of trial personnel;
(19) Other situations requiring explanation.

20. Confidentiality

The investigators must strictly keep confidential the study results, protocol and other data, and can not release

them by themselves unless authorized by the sponsor in written form. If referenced, a written authorization must also be obtained from the sponsor in advance.

All personal information of subjects is confidential. Besides relevant study personnel, only the sponsor, ethics committee members and relevant national/local food and drug administration personnel related to this study project can be allowed to access such information. The investigators and sponsor should keep the personal information of the subjects confidential.

21. Agreement on Publication of Study Results

The sponsor and investigators shall agree with the final study report.

The results of the study may be made publicly available as scientific literature and the results may be submitted to authorities. This clause is intended to protect trade secret materials.

All information about the study medical device (e.g., patent application, previously undisclosed manufacturing process provided to the investigators by the sponsor, basic scientific data, etc.) is considered confidential and its ownership belongs to the sponsor. The investigators may not use it for other purposes without the written permission of the sponsor.

Prior to publication or presentation of the results of this study, the investigators allow the sponsor to review the manuscript and comment within 30 days to confirm that the confidential information is not disclosed, and to supplement the relevant information. According to the generally accepted principles of scientific cooperation, the investigators should discuss the manuscript with the relevant personnel of the sponsor and reach a consensus before the manuscript is published.

22. Responsibilities Assumed by Each Party

22.1 Responsibilities of Sponsor

(1) The sponsor is responsible for initiating, applying for, organizing and monitoring the clinical trial, and is responsible for the authenticity and reliability of the clinical trial.

(2) The sponsor is responsible for organizing the development and revision of the investigator's brochure, clinical trial protocol, informed consent form, case report form, relevant standard operating procedures and other relevant documents, and organizing the training necessary for the clinical trial.

(3) Before signing the clinical trial agreement with the clinical trial institution, the sponsor shall provide the clinical trial institution and investigators with the latest investigator's brochure and other relevant documents for them to decide whether they can undertake the clinical trial.

(4) The sponsor shall not exaggerate the publicity of the mechanism and efficacy of the study medical device in organizing the development of clinical trial protocol.

(5) During the clinical trial, when the sponsor obtains important information affecting the clinical trial, the investigator's brochure and relevant documents shall be revised in a timely manner, and submitted to the

ethics committee for review and approval through the medical device clinical trial management department of the clinical trial institution.

(6) The sponsor shall reach a written agreement with the clinical trial institution and the investigators on the detailed rules related to the clinical trial.

(7) The sponsor is responsible for the safety of the study medical device in the clinical trial.

(8) Where the sponsor decides to suspend or terminate the clinical trial, it shall notify the management department of medical device clinical trial of all the clinical trial institutions within 5 days, and explain the reasons in written form.

(9) The sponsor shall ensure that all investigators conducting clinical trials strictly follow the clinical trial protocol, and timely point out and correct the clinical trial institutions and investigators who fail to comply with relevant laws and regulations, this Practice and clinical trial protocol; if the situation is serious or does not change continuously, the trial shall be terminated and reported to the food and drug regulatory authority of the provinces, autonomous regions and municipalities directly under the central government where the clinical trial institutions are located, as well as NMPA (original CFDA).

(10) The sponsor shall bear the treatment cost and corresponding economic compensation for the subjects who suffer from injury or death related to the clinical trial, except for the damage caused by the faults of medical institution and its medical staff in the diagnosis and treatment.

(11) The sponsor should bear the responsibility of monitoring and verifying the clinical trial.

(12) For serious adverse events and device defects that may cause serious adverse events, the sponsor shall report to the food and drug regulatory authority which files the trial, as well as the health commission at the same level within 5 working days after being informed. The sponsor shall notify other clinical trial institutions and investigators participating in the trial, and timely notify the Ethics Committee of the clinical trial institution through its medical device clinical trial management department.

(13) The sponsor shall ensure that the clinical data in the electronic clinical database or remote electronic clinical data system are controlled and authentic, and form complete validation documents.

(14) The sponsor shall ensure that the CRFs are rigorously and rationally designed, so that the coordinating investigators can obtain all data from the clinical trial institutions of each sub-site.

22.2 Responsibilities of Clinical Trial Institution and Investigators

(1) Before accepting a clinical trial, the clinical trial institution should evaluate relevant resources according to the characteristics of the study medical device to determine whether to accept the clinical trial.

(2) The clinical trial institution should properly keep the clinical trial records and basic documents according to the agreement with the sponsor.

(3) The investigators responsible for the clinical trial should have the corresponding qualification.

(4) Before a clinical trial, the management department for clinical trial of medical device of the clinical trial institution should cooperate with the sponsor in submitting an application to the Ethics Committee and submitting the relevant documents as required.

(5) The investigators should ensure that relevant staff participating in the trial are familiar with the principles, applicable scope, product performance, operation methods, installation requirements and technical indicators of the study medical device; understand the pre-clinical study data and safety data of the study medical device; and master the prevention and emergency treatment methods of possible risks in the clinical trial.

(6) The investigators should ensure that the study medical device is only used for the subjects of the clinical trial, and should not charge any fee.

(7) The investigators should strictly follow the clinical trial protocol. Without the approval of the sponsor and the ethics committee, or failing to obtain the approval from NMPA (original CDFA) as required, the investigators should not deviate from the protocol or materially change the protocol. However, in the event of an emergency that requires immediate removal, such as when the subject is at an immediate risk, a written report may be made afterwards.

(8) The investigator is responsible for recruiting the subject and communicating with the subject or his/her guardian.

(9) The investigators or other personnel involved in the trial should not coerce or induce the subject to participate in the trial in other improper ways.

(10) When the investigators find unexpected adverse events of the study medical device during the clinical trial, they should modify the relevant contents of the informed consent form with the sponsor. After reporting to the Ethics Committee for review and approval according to the relevant working procedures, the affected subjects or their guardians should re-sign and confirm the revised informed consent form.

(11) The investigators shall be responsible for making medical decisions related to the clinical trial. In case of any adverse event related to the clinical trial, the clinical trial institution and the investigators shall ensure to provide adequate and timely treatment, as well as processing for the subjects.

(12) In case of any serious adverse event in the clinical trial, the investigators should immediately take appropriate therapeutic measures for the subjects, report to the management department of medical device clinical trial of the clinical trial institution in written form, and notify the sponsor in written form.

(13) The investigators should record all adverse events occur and device defects found during the clinical trial, work with the sponsor to analyze the causes of the events, form a written analysis report, propose the comments on continuing, suspending or terminating the trial, and report to the Ethics Committee by the management department for clinical trial of medical device of the clinical trial institution for review.

(14) The investigators should ensure that the clinical trial data are accurately, completely, clearly and timely recorded in the CRF.

(15) The clinical trial institution and investigators shall ensure that the data, documents and records generated from the clinical trial are authentic, accurate, clear and safe.

(16) The clinical trial institution and investigators should accept the monitoring and verification by the sponsor, as well as the supervision by the Ethics Committee; and provide all required records related to the trial.

(17) When the clinical trial institution and investigators need to suspend or terminate the clinical trial when they find that the risks outweigh the possible benefits, or the results are enough to judge the safety and effectiveness of the study medical device, they should inform the subjects and ensure that the subjects receive appropriate treatment and follow-up, report according to the provisions, and provide a detailed written explanation.

(18) The clinical trial institution and investigators shall report to the food and drug regulatory authority of the province, autonomous region or municipality directly under the central government where the sponsor li located if the sponsor violates relevant regulations or requirements to change the trial data and conclusions.

(19) At the end of the clinical trial, the investigators should ensure the completion of various records and reports, and timely deliver the required clinical data to the clinical trial institution as required.

(20) The investigators should provide relevant training for the authorized personnel, and form the corresponding documents.

Note: See the "Clinical Trial Contract" and other relevant documents for the responsibilities assumed by specific parties.

23. References

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24. Supplementary Provisions

Meanings of the academic terms involved in this study protocol:

Medical device clinical trial institution: it refers to the medical institution undertaking medical device clinical trial recognized by NMPA (original CFDA) and NHFPC. Unless otherwise specified, "clinical trial institution" in this protocol refers to "medical device clinical trial institution".

Investigational/study medical device: it refers to the medical device to be applied for registration whose safety and effectiveness are confirmed or verified in the clinical trial.

Sponsor: it refers to the institution or organization initiating, managing and providing financial support for the clinical trial.

Investigator: it refers to the person responsible for conducting the clinical trial in the clinical trial institution. If a trial is conducted by a team of individuals at a clinical trial institution, the investigator is the responsible

leader of that team, also known as the principal investigator.

Ethics Committee: it refers to an independent institution set by the clinical trial institution to review the scientificity and ethicality of the medical device clinical trial project.

Management department of medical device clinical trial: it refers to the division or department set within a clinical trial institution to be responsible for the organization management and quality control of the medical device clinical trial.

Multi-center clinical trial: it refers to the clinical trial conducted in more than three (including three) clinical trial institutions in accordance with the same clinical trial protocol.

Subject: it refers to an individual recruited for the clinical trial of a medical device.

Informed consent: it refers to the process that the subject voluntarily participates in the clinical trial after being informed of all aspects of the clinical trial, as evidenced by the signed and dated informed consent form.

Informed consent form: it refers to the supporting document for the subject voluntary participation in the clinical trial.

Monitoring: it refers to the activities that the sponsor designates special personnel to evaluate and investigate the clinical trial institution and investigator; verify, record and report the data during the clinical trial so as to ensure that the clinical trial carried out can comply with the clinical trial protocol, standard operating procedures, *Good Clinical Practice* for medical devices and relevant applicable regulatory requirements.

Monitor: it refers to the special personnel assigned by the sponsor to monitor the medical device clinical trial project.

Audit: it refers to a systematic and independent inspection of clinical trial-related activities and documents organized by the sponsor to determine whether the implementation of such activities, recording, analysis and reporting of data comply with the clinical trial protocol, standard operating procedures, *Good Clinical Practice* for medical devices and relevant applicable regulatory requirements.

Auditor: it refers to the personnel entrusted by the sponsor to audit the medical device clinical trial project.

Inspection: it refers to supervision and management activities conducted by regulatory authorities on relevant documents, facilities, records and other aspects of clinical trials

Inspector: it refers to the personnel assigned by regulatory authorities to inspect the medical device clinical trial project.

Deviation: it refers to the situation where the requirements of the clinical trial protocol are not followed intentionally or unintentionally.

Case report form: it refers to the document designed in accordance with the clinical trial protocol to record

all the information and data of each subject obtained during the trial.

Endpoint: it refers to an indicator used to assess a clinical trial hypothesis.

Source data: it refers to all information in original records and their approved copies of clinical findings, observations and other activities in a clinical trial that can be used for reconstruction and evaluation of the clinical trial.

Source document: it refers to the printed, visible or electronic documents containing source data.

Adverse event: it refers to any adverse medical event occurring in the clinical trial process, no matter whether it is related to the investigational medical device or not.

Serious adverse event: it refers to any adverse event that results in death or serious deterioration in the health of the subject during the clinical trial, including a life-threatening illness or injury, a permanent impairment of a body structure or a body function, in-patient hospitalization or prolongation of existing hospitalization, medical or surgical intervention to prevent permanent impairment of a body structure or a body function; results in fetal distress, fetal death, or a congenital abnormality or birth defect, etc.

Device defect: it refers to unreasonable risks that may endanger human health and life safety under normal use of a medical device during a clinical trial, such as labeling errors, quality problems and failures, etc.

Standard operating procedure: it refers to the standard and detailed written procedure proposed to effectively implement and complete each work in the clinical trial.

Clinical data: it refers to the safety and performance information obtained from the relevant literature or clinical application of the medical device.

Investigator Statement

I agree that:

1. This clinical trial should be conducted in strict accordance with the *Declaration of Helsinki*, current laws and regulations of China, and the requirements of the study protocol.
2. All required data shall be recorded accurately on the case report form (CRF), and the clinical trial report shall be completed on time.
3. The investigational medical device is only used for this clinical trial. The receipt and use of the investigational medical device will be completely and accurately recorded during the clinical trial, and the records will be kept.
4. The monitor, inspector and regulatory authority authorized or dispatched by the sponsor will be allowed to monitor, verify and inspect the clinical trial.
5. The terms of clinical trial contract/agreement signed by all parties shall be strictly performed.

I have read the clinical trial protocol, including the above statement, and I agree all contents above.

Comments of sponsor

Agree.

Fengh Medical Co., Ltd.
★
3202811906439

Signature (seal): Zhang Xinghua

Date: 2019.01.25

Comments of investigator

Agree.

Signature: Ni Qing

Date: 2019.01.31

Affiliated Hospital of Yangzhou University
★
National Drug Clinical Trial Institute
3210000006278

Comments of medical device clinical trial institution

Agree.

Signature (seal):

Date: 2021.07.01