A Multi-Center, Randomized, Subject/Evaluator Blind, Active-Controlled, Non-Inferiority Pivotal Clinical Study to Compare the Efficacy and Safety of Collabarrier® With Guardix-Sol for the Prevention of Postoperative Adhesion After Surgery for Disc Herniation or Spinal Stenosis

Official Title	A Multi-Center, Randomized, Subject/Evaluator Blind, Active-Controlled, Non-Inferiority Pivotal Clinical Study to Compare the Efficacy and Safety of Collabarrier® With Guardix-Sol for the Prevention of Postoperative Adhesion After Surgery for Disc Herniation or Spinal Stenosis
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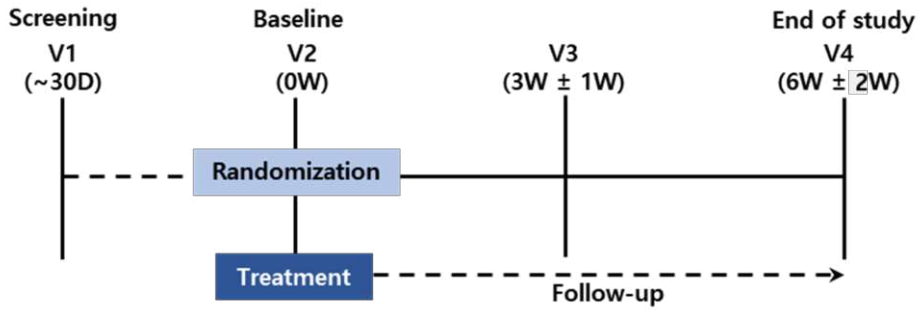
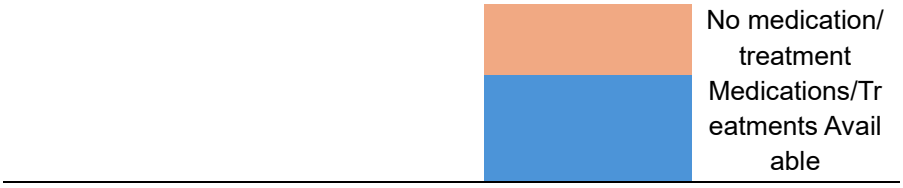
1. QUICK INFORMATION

1.1 Protocol Summary

<table>
<tr><td colspan="2">Official title</td><td>A Multicenter, Randomized, Subject/Rater-blinded, Active-controlled, Non-inferiority Confirmatory Trial to Compare the Anti-adhesion Efficacy and Safety of Collabarrier® and Guardix-sol After Surgery for Herniated Disc or Lumbar Canal Stenosis</td></tr>
<tr><td colspan="2">Clinical trial sponsors</td><td>Dalim Tissen Co., Ltd.</td></tr>
<tr><td colspan="2">Clinical Trial Sites and
Clinical Trial Director</td><td>Department of Neurosurgery, Eunpyeong St. Mary’s Hospital, College of Medicine, The Catholic University of Korea
Department of Neurosurgery, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea
Department of Neurosurgery, St. Vincent’s Hospital, College of Medicine, The Catholic University of Korea
Department of Neurosurgery, Asan Medical Center, Seoul
Department of Neurosurgery, Korea University Anam Hospital, Korea University College of Medicine, Seoul, Korea
Department of Neurosurgery, Ajou University Hospital</td></tr>
<tr><td colspan="2">Duration of the trial</td><td>Approximately 36 months from the date of approval of the clinical trial plan</td></tr>
<tr><td colspan="2">Clinical trial objectives</td><td>In order to prove that it is non-inferior by comparing the anti-adhesion effect and safety of postoperative adhesions caused by disc herniation or lumbar stenosis by comparing the investigational device Collabarrier® and the control device Guardix-sol.</td></tr>
<tr><td colspan="2">Clinical trial design</td><td>A Multicenter, Randomized, Subject/Evaluator-Blinded, Active-Controlled, Non-inferiority Confirmatory Trial</td></tr>
<tr><td rowspan="2">Subjects</td><td>Number of subjects</td><td>Total number of subjects: 69 (Initially, the target number of subjects was calculated to be 68 considering a dropout rate of 10%, but one additional person was enrolled during the recruitment process.)
<table>
<tr><th></th><th>Test group</th><th>Control group</th><th>Total
Number of subjects</th></tr>
<tr><td>Number of subjects</td><td>30</td><td>30</td><td>60</td></tr>
<tr><td>Number of subjects considered for dropout 10%</td><td>34</td><td>34</td><td>68</td></tr>
</table></td></tr>
<tr><td>Inclusion Criteria</td><td>1) Adult males and females 19 years of age or older
2) Diagnosed with herniated disc or lumbar canal stenosis by radiographic (MRI or CT) evidence of nerve root compression at one of the levels of the 3rd-4th lumbar intervertebral or 4th-5th lumbar vertebra or 5th lumbar vertebrae-1st sacral intervertebral
3) Those who are scheduled to undergo partial laminectomy or nucleus pulposus removal for the first time for the treatment of symptoms corresponding to the above 2 symptoms.
4) Those who meet at least one of the following conditions
A. Those who have had at least 4 weeks of prior conservative treatment in the 6 months prior to V1</td></tr>
</table>

		(e.g., use of physical therapy, anti-inflammatory drugs, muscle relaxants, etc.) B. Those who are suffering from unbearable pain and are judged by the investigator to require surgery for herniated discs or lumbar spinal stenosis C. Those who have significantly advanced neurological loss 5) Those who have voluntarily given written informed consent and are able to comply with the trial procedures and visit schedule
	Exclusion Criteria	1) Subjects who have a history of hypersensitivity to the main component and other components of this investigational device 2) Subjects who have a history of fragility fractures 3) Subjects who have previously had a fracture or ligament injury of the lumbar spine due to trauma 4) Subjects who require spinal surgery other than partial laminectomy or nucleus pulposus removal (osteophytectomy is allowed) to treat symptoms 5) Subjects with neurogenic bowel/bladder dysfunction 6) Subjects with uncontrolled excessive exudate at the application site, bleeding, acute edema, accompanied by symptoms of infection 7) Subjects with degenerative spinal disease (except for herniated disc or lumbar spinal stenosis) or scoliosis (Cobb's angle 15° or more) 8) Subjects who have lymphatic system diseases or blood clotting diseases or who are receiving blood clotting drugs 9) Subjects with uncontrolled diabetes that may affect the course of surgery or postoperatively, according to the judgment of the investigator 10) Subjects who have connective tissue disease or autoimmune disease or have received treatment for malignant tumors within 5 years 11) Subjects who have had previous spinal surgery in the area where surgery is scheduled 12) Subjects who have received epidural steroid treatment within 2 weeks before surgery, or who have taken oral steroid preparations within 10 days before surgery 13) Subjects who have undergone myelogram or lumbar puncture within 24 hours prior to screening 14) Subjects who are immunocompromised or have clinically significant abnormalities found in laboratory tests at the time of screening 15) Subjects who have had or currently have a medical illness such as clinically significant disorders of the cardiovascular, digestive, respiratory, endocrine, or central nervous system or psychiatric disorders that significantly affect this clinical trial 16) Subjects who have participated in other interventional clinical trials within 30 days prior to screening or require continued participation 17) Pregnant or lactating women 18) Subjects who cannot agree to use contraception from the date of signing the written informed consent form to the completion of the end visit in this clinical trial 19) Other cases where the investigator deems unsuitable for this clinical trial

Clinical Trials way	**Procedure**	If subjects who meet the inclusion/exclusion criteria and voluntarily sign the consent form for the clinical trial are enrolled in this clinical trial, they will be treated with an investigational device or a control device during surgery for herniated disc or lumbar spinal stenosis and before surgical site closure. In addition, the procedure will be performed by the same investigator at each clinical trial site to minimize the impact of the procedure method. At 3 and 6 weeks after the application of the investigational device, safety Evaluations will be conducted and 3 and 6 weeks, VAS Evaluation for back and leg pain and Oswestry Disability Index (ODI) Evaluation for functional disability will be performed. In addition, MRI imaging of the medical device application area will be performed at 6 weeks after the application of the investigational device. The MRI of the subjects will be randomly assigned a new assignment number for each photo regardless of the assignment group by an independent data manager, and then sent to the independent evaluator with the subject's information completely excluded. The independent evaluator will evaluate the MRI Scar score evaluation criteria presented in this clinical trial by applying the same to each photo.  Clinical trial model
	Investigational devices	Investigational device: Collabarrier® Control device: Guardix-sol
	Areas of application and How to apply	Before applying this investigational device, all cleaning solution will be aspirated and removed, and all hemostatic agents (e.g., pads, sponges) will be removed. After confirming complete hemostasis in the wound area, the plug on the front part of the syringe is removed, and a medical spreader or catheter is inserted. Then, apply the test device or control device completely to the lateral surface of the nerve root, dorsal side, and the outer surface of the dura mater. The device was applied in a layer filling the area from the dorsal aspect of the nerve root and dura mater to the dorsal surface of the posterior lamina within the range of lamina resection. The amount applied was determined at the investigator's discretion according to the patient's condition, surgical site, and extent, with a maximum of 5 mL.
	Prohibited Concomitant Medications/Treatments	

<table>
<tr><td></td><td></td><td>
<table>
<tr><th>drug</th><th>V1 ~ V2</th><th>V2 ~ V3</th><th>V3 ~
V4 2 weeks ag
o</th><th>2 weeks ago ~
V4</th></tr>
<tr><td>NSAIDs</td><td colspan="3">allowed</td><td>Not Allowed</td></tr>
<tr><td>Steroid injec
tions
(Epidural
Adrenal cort
ex
including ho
rmone infusi
ons)</td><td>Not allow
ed</td><td colspan="2">allowed</td><td>Not allowed</td></tr>
<tr><td>Oral
steroid</td><td>Not allow
ed</td><td colspan="2">allowed</td><td>Not allowed</td></tr>
<tr><td>Anticoagula
nts</td><td colspan="4">Not allowed</td></tr>
<tr><td>Antiplatelet
Drugs</td><td colspan="4">Not allowed</td></tr>
<tr><td>Fibrinolytic
agents</td><td colspan="4">Not allowed</td></tr>
<tr><td>Investigatio
nal
Medical Dev
ices
Other
Anti-adhesi
on agents</td><td colspan="4">Not allowed</td></tr>
</table>
* Among the prohibited drugs, anticoagulants, antiplatelet drugs, and Fibrino lytic agents are allowed as exceptions after discussion between the sponsor and the researcher.
</td></tr>
<tr><td></td><td>Dropout Criteria</td><td>1) If the following are found during surgery
A. If there must be other devices left at the surgical site that may interfere with the interpretation of the study results
B. If dural rupture and dural hole are found during surgery
C. Epidural fat placement
D. If you have a herniated disc and need surgery at more than one level
E. If you are applying a sealant or making other attempts to repair a fibro us annulus tear
F. If a tumor in the spine is found during surgery
G. Entering the dura mater during surgery
H. If spinal fusion is required
I. If the hemostatic agent must remain at the surgical site
, but if it is cleaned after stopping the bleeding, it will not be dropped o ut.
J. If antibiotic powder is injected into the surgical site
(antibiotic cleaning is only allowed before the application of the medica</td></tr>
</table>

		l device, not after application.) K. When the following products are applied to exposed nerve elements - Amniotic tissue or amniotic fluid - adhesive - steroid - Platelet-rich plasma fluid - Gel Foam - Allograft tissue - Fibrin Adhesive - Dural patch 2) The subject (or legal representative) voluntarily wishes to discontinue the trial. 3) Surgery that may affect safety and efficacy evaluation, or when using other drugs and procedures in conjunction with other drugs and procedures 4) If an adverse event occurs during follow-up observation that makes it difficult to continue the clinical trial 5) Subjects who are not able to continue to follow up on the treatment of this clinical trial due to loss of contact during this clinical trial 6) Inclusion/exclusion criteria non-conformity confirmed since enrollment in the trial 7) If the principal investigator deems it inappropriate as a subject (if he does not comply with the investigator's instructions, if it is judged that he or she can no longer participate in the clinical trial in terms of safety or ethics due to a change in the subject's condition, etc.);	
Evaluation Criteria	**Efficacy Evaluation**	Primary Efficacy Endpoint	Mean MRI Scar score between the test and control groups assessed by an independent evaluator at 6 weeks after the application of the investigational device
		Secondary Efficacy Endpoints	1) Mean score on the 100-mm Visual Analogue Scale (VAS) for back pain in the test and control groups as assessed by subjects at baseline and at 3 and 6 weeks 2) Mean score on the 100-mm Visual Analogue Scale (VAS) for leg pain in the test and control groups as assessed by subjects at baseline and at 3 and 6 weeks 3) Mean score on the Oswestry Disability Index (ODI) for the limitation of daily living in the test and control groups as assessed by subjects at baseline and at 3 and 6 weeks
	Safety Evaluation	1) Adverse Events 2) Laboratory tests, vital signs, physical examination	
Statistical analysis method	**Analysis target group**	The data obtained from the subjects through this clinical trial will be divided into the Safety Set, FA (Full Analysis) Set. Statistical analysis will be performed by dividing it into PP (Per Protocol) Sets. The main population of this trial will be the PP Set, the secondary evaluation group will be the FA Set, and the safety evaluation will be analyzed with the Safety Set.	

s	**Efficacy endpoints**	Primary efficacy variables	Descriptive statistics (number of observed subjects, mean, standard deviation, median, minimum, maximum) for MRI Scar score assessed by an independent Evaluator at 6 weeks for each dosing group are presented, and two-sided 95% confidence intervals are presented for the mean difference between dosing groups (test group-control group).
		Secondary efficacy variables	Descriptive statistics (number of observed subjects, mean, standard deviation, median, minimum, maximum) are presented for the following endpoints and analyzed by two sample t-test (Wilcoxon's rank sum test if the normality distribution assumption is not satisfied). 1) Mean score on the 100-mm Visual Analogue Scale (VAS) for back pain in the test and control groups as assessed by subjects at baseline and at 3 and 6 weeks 2) Mean score on the 100-mm Visual Analogue Scale (VAS) for leg pain in the test and control groups as assessed by subjects at baseline and at 3 and 6 weeks 3) Mean score on the Oswestry Disability Index (ODI) for the functional disability in the test and control groups as assessed by subjects at baseline and at 3 and 6 weeks
	Safety endpoints	1) Adverse Events The number of subjects, incidence, and number of occurrences of adverse events that occurred after the application of the investigational device are presented. Adverse events are standardized with System Organ Class (SOC) and Preferred Term (PT) according to the latest version of the Medical Dictionary for Regulatory Activities (MedDRA), and the number of subjects, incidence, and number of adverse events are presented. 2) Laboratory tests, vital signs, physical examination Laboratory tests, vital signs, and physical examination data will be analyzed by two sample t-tests (Wilcoxon's rank sum test if the normality distribution assumption is not satisfied) if the data is continuous, descriptive statistics (number of observed subjects, mean, standard deviation, median, minimum, maximum) will be presented. Comparison before and after application of the investigational device will be analyzed by paired t-test (Wilcoxon signed rank test if the normality distribution assumption is not satisfied). Categorical data will be presented with frequencies and percentages and analyzed by Pearson's chi-square test (Fisher's exact test if cells with an expected frequency of less than 5 exceed 20%). The comparison before and after the application of the investigational device will be analyzed by McNemar's test.	

		3) Concomitant medications Concomitant drugs are classified according to the latest version of the WHO -ATC (World Health Organization-Anatomical Therapeutic Chemical) Index, and the frequency, percentage, and number of drugs are presented.

1.2 Clinical trial Schedule

Visit ± Visit window	Screening1)	Surgery date2)	Follow-up	End of Clinical Trial	Un-scheduled Visit
	Before surgery Within 4 weeks	0 days	3 weeks postoperatively ± 1 week	6 weeks postoperatively ± 2 weeks	
	Visit 1	Visit 2	Visit 3	Visit 4	
Written informed consent3)	●				
Screening number assignment	●				
Demographic survey4)	●				
Concomitant medication/treatment5)	●	●	●	●	●
Medical history6)	●				
Body Measurement7)	●				
Physical examination8)	●	●	●	●	(●)
Laboratory Tests9)	●	●		●	(●)
Vital signs10)	●	●	●	●	(●)
Evaluation of Inclusion/Exclusion Criteria	●	●			
Randomization		●			
Surgery		●			
Investigational device Application		●			
MRI Scar score11)				●	(●)
100mm-VAS Evaluation (Waist)[12)]		●	●	●	(●)
100mm-VAS Evaluation (Legs)[12)]		●	●	●	(●)
ODI Evaluation12)		●	●	●	(●)
Adverse Event Evaluation		●	●	●	●

* (●) Marks are carried out as necessary according to the judgment of the examiner.

1) Screening tests will be performed within 30 days before surgery.
   The screening visit (V1) and surgery (V2) can be performed on the same day.
2) If the hospital stay is prolonged or severe treatment is required due to the occurrence of surgical complications, it is reported as an SAE.
3) Written informed consent must be obtained before clinical trial procedures are performed.
4) After obtaining written informed consent, demographic information (sex, age, and reproductive status) will be investigated.
5) Prior medications/treatments will be collected for medications administered preoperatively and treatments administered within 4 weeks from the time of V1, and as concomitant medications/treatments if ongoing treatment is required.
6) Medical history will include any illness or clinically significant medical condition experienced or ongoing within 12 months at the time of V1.
7) Collect height, weight.
8) It is collected under the following items: 'appearance', 'skin', 'head/neck', 'heart', 'abdomen', 'urinary/reproductive system', 'limbs', 'musculoskeletal system', 'nervous system', 'lymph nodes', and 'others'.
9) The investigator will investigate the following items from the subject's blood and urine at V1, V2, and V4, and if necessary, this test may also be performed at un-scheduled visits at the investigator's discretion. If there is

already a result within 4 weeks prior to V1, the result can be replaced with a screening test. Subjects who do not meet the screening test results for Inclusion/exclusion may be re-tested only once, in which case the re-test results will be used. If the V2 visit date is within 7 days of the V1 visit date, the V1 laboratory test results can be substituted for the V2 laboratory results.
In the case of pregnancy response testing, urine hCG pregnancy test (if not allowed, serum test is replaced) may be performed only for women of childbearing potential and may be performed at each visit point if necessary at the discretion of the investigator.

Hematological tests	white blood cell (WBC), WBC with differential (Lymphocyte, Monocyte, Eosinophil, Basophil, Segmented neutrophils), red blood cell (RBC), hemoglobin (Hb), hematocrit (Hct), platelet count (PLT)
Hematological Chemical Tests	alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine transaminase (ALT), Gamma Glutamyl Transpeptidase (GGT), total bilirubin, albumin, serum creatinine, blood urea nitrogen (BUN)
Urinalysis	Specific Gravity, Color, pH, Protein, Glucose, Bilirubin, Blood, WBC, Urine hCG pregnancy test (This test will be performed only for women of childbearing age before menopause, only at the screening visit (Visit 1), and if necessary, additionally performed at the last visit (Visit 4).)

10) Measurements of sitting systolic/diastolic blood pressure, pulse, and body temperature.
11) At 6 weeks after the application of the investigational device, subjects will come to the hospital for efficacy evaluation and undergo MRI imaging of the surgical site.
12) At the preoperative time point (baseline) and at 3 and 6 weeks after the application of the investigational device, subjects will come to the clinic for efficacy evaluation to undergo a 100-mm Visual Analogue Scale (VAS) Evaluation for back and leg pain and an Oswestry Disability Index (ODI) Evaluation for the limitation of daily living.

1.3 Abbreviation Definition

Abbreviation	Full Term
ADE	Adverse Device Effect
AE	Adverse Event
SAE	Serious adverse event
TEAE	Treatment Emergent Adverse Event
IRB	Institutional Review Board
KFDA	Korea Food and Drug Administration
CRO	Contracted Research Organization
CRF	Case Report Form
GCP	Good Clinical Practice
UV	Unscheduled visit
FBSS	Failed Back Surgery Syndrome
HAS	Sodium Hyaluronate
CMC	Sodium Carboxymethylcellulose
VAS	Visual Analogue Scale
ODI	Oswestry Disability Index
MRI	Magnetic Resonance Imaging
CS	Clinically Significant
NCS	Not Clinically Significant
IV	Intravenous
IN	Intramuscular
SC	Subcutaneous
AGO	Full Analysis
PP	Per-Protocol

2. TITLE OF THE TRIAL

A Multicenter, Randomized, Subject/Evaluator-Blinded, Active-Controlled, Non-inferiority Confirmatory Trial to Compare and Evaluate the Anti-adhesion Efficacy and Safety of Collabarrier® and Guardix-sol After Surgery for Herniated Disc or Lumbar Canal Stenosis

3. EXAMINERS AND TRIAL ADMINISTRATION ORGANIZATIONS

3.1 Name and location of the clinical trial site

No.	Testing Institution Name	location
01	The Catholic University of Korea Eunpyeong St. Mary's Hospital	1021 Tongil-ro, Eunpyeong-gu, Seoul
02	The Catholic University of Korea Seoul St. Mary's Hospital	222, Banpo-daero, Seocho-gu, Seoul
03	The Catholic University of Korea St. Vincent's Hospital	93, Jungbu-daero, Paldal-gu, Suwon-si, Gyeonggi-do
04	Asan Medical Center	88, Olympic-ro 43-gil, Songpa-gu, Seoul
05	Korea University School of Medicine Hospital (Anam Hospital)	73, Korea-daero, Seongbuk-gu, Seoul
06	Ajou University Hospital	164 World Cup-ro, Yeongtong-gu, Suwon-si, Gyeonggi-do

The head of the implementing institution shall equip the clinical trial room, facilities, and professional personnel necessary for the conduct of the clinical trial at each stage of the clinical trial,and make perfect preparations to properly conduct the clinical trial.

3.2 Name and title of the principal investigator, responsible person, and co-investigator of the clinical trial

ATTACHMENT 5. REFER TO THE NAMES AND TITLES OF CLINICAL TRIAL LEADERS, RESPONSIBLE PERSONS, AND CO-INVESTIGATORS

The Clinical Trial Coordinator and the principal investigator are responsible for all conduct of clinical trials at the site of the clinical trial. During the entire period of the clinical trial, the subject must be evaluated, and the efficacy and safety of the medical device are evaluated using appropriate personnel. The clinical trial manager is in charge of clinical trial-related work under the delegation and supervision of the principal investigator.

3.3 Name and title of the manager who manages the investigational device

ATTACHMENT 6. REFER TO THE NAME AND TITLE OF THE MANAGER WHO MANAGES THE INVESTIGATIONAL DEVICE

The person in charge of the investigational device is responsible for the receipt, storage, management, and return of the medical device used in clinical trials at the site of the site.

3.4 Clinical trial sponsor name and location

Client Name	Ceo	address
Dalim Tissen Co., Ltd.	Jung Jong-seop	31 Yeonhui-ro, Mapo-gu, Seoul, Yeonnam Building 3~5th floor

It has full responsibility for planning and conducting clinical trials.

3.5 Name and location of the clinical trial contract organization

Client Name	Ceo	address
Seoul CRO	Park Kwan-so	10, 4th-6th floor, Bongeunsa-ro 6-gil, Gangnam-gu, Seoul

Clinical trial protocols are prepared, modified, and monitored in accordance with KGCP.

4. PURPOSE AND BACKGROUND OF THE TRIAL

4.1 Purpose of the trial

In order to prove that it is non-inferior by comparing the anti-adhesion effect and safety of postoperative adhesions caused by disc herniation or lumbar stenosis by comparing the test device Collabarrier® and the control device Guardix-sol.

4.2 Background of the trial

1) Causes of postoperative adhesions

Adhesions that occur after surgery are caused by the body's internal action to supply oxygen and nutrients to the tissue damaged during surgery. Tissue hypodysphomania caused by surgery causes an inflammatory response, resulting in the generation of free radicals and active nitrogen. This inflammatory response affects the release of histamine, cytokines, and growth factors, the penetration of polymorphonuclear leukocytes into the tissue, and the fibroblasts in the tissue. This causes adhesions to form fibrous masses on the surface of the damaged tissue [1]. Such postoperative adhesions can lead to obstruction of the small intestine, It can lead to serious complications such as infertility and chronic pain. Despite the ongoing research to prevent adhesions that occur after surgery, many patients still suffer a lot from adhesions that occur after surgery.

2) Spine Surgery and the Need for Anti-Adhesion Agents

The normal healing process of tissue after spinal surgery refers to the migration of fibrocytes to the wound area and the replacement of epidural fibrous tissue with fat [2]. However, if fat cannot be moved to the epidural, the located fibrous tissue may directly compress the nerve tissue or affect the surrounding muscles or bones, causing functional impairment [3,4]. This epidural adhesion causes fibrous tissue to be deposited on the nerve roots around the surgical site, interfering with blood flow and causing nerve damage. In addition, it is known that it interferes with the mobility of the nerve roots themselves at the same time, causing further pain, and it is known that symptoms such as neuralgia, paresthesia, and numbness appear due to neurodegeneration [5~7]. The pain that occurs after surgery is known as surgical failure syndrome (FBSS), and it is estimated that the recurrent pain caused by the disease contributes to 60% of all symptoms [8].

In this way, patients who actually experience pain due to fibrous tissue at the surgical site are 3.2 times more likely to develop epidural scar tissue than those without tissue [4], and Hurme, Matti, et al reported an increase in fibrous tissue in 18 patients 5 years later out of 40 patients who underwent lumbar disc herniation surgery [9]. In addition, a retrospective prior study of 24,882 patients who underwent spinal surgery in Washington State between 1990 and 1993 found that 19% of patients who underwent spinal surgery in the 11 years after surgery were affected by pain or complications from surgery It has been shown that revision surgery is necessary[10], and according to 'Clancy, Ciara, Alison Quinn, and Fiona Wilson', 40% of patients who underwent postoperative laminectomy were diagnosed with surgical failure syndrome due to chronic pain after surgery [11]. Surgical failure syndrome can lead to complications such as spinal stenosis, dural rupture, and damage to nerve and muscle tissue [12], and surgical revision surgery caused by this increases patient pain and is not efficient in terms of time and cost, so it is necessary to prevent it in advance. Therefore, there have been attempts to apply anti-adhesion agents to the epidural space that was stranded during surgery, and currently polymer synthesis, Products using natural materials are being developed [13].

3) Description and Development Background of the Investigational Device (Collabarrier®)

Physical barrier materials used to prevent adhesion include Oxidized Regenerated Cellulose, Sodium Carboxylmethyl Cellulose (CMC), Dextran, and Sodium Hyaluronate (HA) made from polysaccharides derived from natural kite, and polyethylene glycol (PEG), Poloxamer, and Gore-tex are known as synthetic polymers. Currently, commercialized anti-adhesion agents include solution, In the case of anti-adhesion agents in the form of gels, films, or membranes, and in the form of solutions and gels, they are easy to apply and have the characteristics of high viscosity, but they have the disadvantage of flowing down from the wound by gravity or the process of absorption and expulsion in the body occurring rapidly, making it difficult to control the duration of the physical barrier to prevent adhesion. On the other hand, in the case of film and membrane anti-adhesion agents, they can be used on relatively large surgical sites, but depending on the characteristics of the product, there are disadvantages such as difficulty in suturing and fixing the wound area or handling it when applying internal organs, and it may not be accurately positioned on the wound site due to organ movement.

Referring to these points, Dalim Tissen Co., Ltd. has developed a gel-type anti-adhesion dressing material 'Collabarrier' with type 1 collagen as the main ingredient with the characteristics of hydrophilic, biocompatible, and biodegradable and confirmed whether it can prevent adhesions and its safety through all clinical trials, and has been approved for the purpose of reducing adhesions during thyroid, uterine cavity, and abdominal surgery as an anti-adhesion dressing material (Regulation No. 15-1572). In this study, we will observe the effectiveness and safety of the product by applying Collabarrier®, an anti-adhesion agent, to patients undergoing surgery for herniated discs or lumbar spinal stenosis. This product is expected to prevent or minimize epidural adhesions by preventing fibrous tissue that may occur during spinal surgery by forming a membrane that surrounds the dura mater and nerve roots, and the results of this study will provide patients with another treatment plan.

5. OVERVIEW OF INVESTIGATIONAL DEVICE AND CONTROL DEVICE

5.1 Investigational device

5.1.1 Name and Origin of Manufacture

1) Device Name: Collabarrier®
2) Item Name: Anti-Adhesion Barrier
3) Item Number: B07070.14
4) Classification Class: Grade 3
5) Manufacturer: Dalim Tissen Co., Ltd.
6) Main Ingredient: Type I Collagen

5.1.2 Shape and structure

1) Principle of action

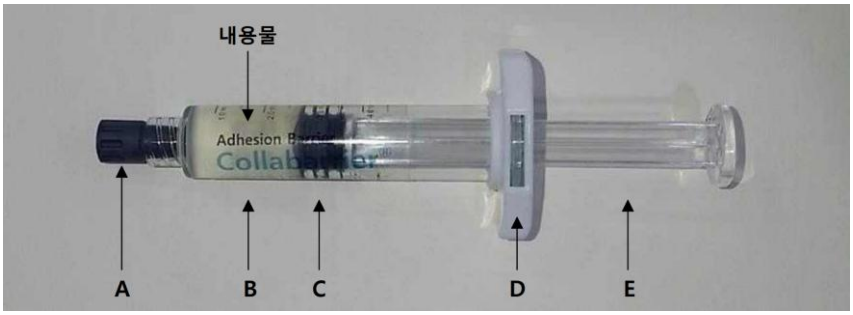
This product is a gel-like wound dressing used to reduce adhesions, and is mainly used when applied to the thyroid, uterine cavity, intra-abdominal cavity, and surgical site and surrounding tissues

after spinal surgery. When the product is applied to the application area, a physical barrier is formed to prevent adhesions between tissues. This product is bioabsorbed after about 7 days.

2) Appearance

1. Contents and syringes

- Exterior photo



- Appearance description

A. Contents: Collagen solution filled in syringe

i. Syringe:

A. Tip Cap: Latex material that protects the tip of the syringe and prevents the ingress of foreign objects

B. Barrel: A container for liquid, and the end of the barrel is screw-shaped so that it can be conne cted to the catheter

C. Plunger: Fixed to a rolling pin and pushing the contents to allow the contents to come out

D. Finger Grip: Helps you hold the syringe securely.

E. Plunger Rod: Pushes the suction to allow the contents to come out

2. Catheter

- Exterior photo

A. Catheter

B. Protective sheath for catheter

C. Upholstered

- Appearance description

It is a catheter that comes with the contents and syringe, and can be connected to the front of the syringe if necessary. Available on select models.

*This is a licensed product (universal catheter, No. 10-1220, model name: 14G-80).

5.1.3 Storage method and expiration date

- Storage method: 2~8 °C storage
- Shelf life: 2 years from the date of manufacture

5.1.4 How to use

1. Pre-use preparation

1) Since this product is supplied in a sterile state, it is confirmed that there is no damage to the packaging material and that the product has not expired.
2) Do not open the package until use and ensure that it remains sterile.
3) The packaging must be opened in a sterile place.
4) After checking the contents before use, do not use if you see damage to the container or loss of viscosity of the solution.
5) Fully explain the product to the patient and be sure to check the patient's condition.
6) It should be used by a medical professional.

2. How to use and how to operate

1) Before administering this product, all cleaning solution should be sucked out and removed, and all sponges filled to stop bleeding should be removed.
2) Check for complete hemostasis at the wound site.
3) The plug on the front of the syringe is removed, and a medical spreader or catheter is inserted.
4) It is administered so that it is completely applied to the application site.
5) Discard the solution left after use.

3. How to store and care after use

1) Discard products stored after opening even if not in use.

2) Since it is a disposable product, dispose of it after use.

5.1.5 Intended use

As an anti-adhesion dressing material, it mainly reduces adhesions during thyroid, uterine cavity, abdominal cavity, and spine surgery.

5.2 Control device

5.2.1 Name and Origin of Manufacture

1) Device Name: Guardix-sol

2) Item Name: Anti-Adhesion Barrier

3) Item license number: No. 05-102

4) Classification Class: Grade 3

5) Manufacturer: Genewell Co., Ltd.

6) Salesperson: Hanmi Pharmaceutical Co., Ltd.

7) Main Ingredients: HA(Sodium Hyaluronate), CMC(Sodium Carboxymethylcellulose)

5.2.2 Storage method and expiration date

- Storage method: Room temperature storage (1 ~ 30 °C, 33.8 ~ 86.0 °F)
- Shelf life: 24 months

5.2.3 How to use

1. Preparations before use

1) Be careful not to open the package until just before use.

2) When using, the packaging must be opened in a sterile place.

2. How to use

1) All cleaning solution is sucked up with an aspirator to remove it, and all packs and sponges filled to stop bleeding after surgery are removed.

2) Confirm that the wound has completely stopped bleeding.

3) Be sure to unwrap the product in a sterile place, remove the plug from the syringe, and turn the catheter to insert it.

※ If a medical spreader is used to spray this product, the medical spreader should be rotated and inserted instead of the catheter.

4) Administer enough so that it can be fully applied to the application site.

5) The remaining solution after administration is discarded.

5.2.4 Intended use

Mainly reduced adhesions during intraoperative surgery in the nasal sinuses, ophthalmology, breast, abdominal cavity, uterine cavity, spine and urology

6. PACKAGING AND LABELING OF INVESTIGATIONAL DEVICES

6.1 Packaging and Labeling

Investigational devices are supplied by the sponsor to the clinical trial medical device manager of the site of the clinical trial. The description of the label of a medical device for clinical trial use shall include the following items in accordance with Article 43, Paragraph 2 of the Enforcement Regulations of the Medical Device Act.

1) Labeling "Investigational"
2) Product and Model Name
3) Manufacturing number and date of manufacture (if there is an expiration date, it can be written as an expiration date.)
4) How to store (store)
5) The trade name of the manufacturer or importer (in the case of contract manufacturing or import, the name of the manufacturer and country are included)
6) "Not for use for any purpose other than clinical trial"

6.2 Management of Investigational devices

1. The management of medical devices used in clinical trials may be managed by the medical device manager delegated by the principal investigator under the responsibility of the principal investigator.
2. The clinical trial sponsor must distribute the medical device used in the clinical trial directly to the medical device manager, and must receive and keep the receipt certificate.
3. Medical device managers check the quality status of medical devices used in clinical trials and check whether they match the quantity on the packaging list and receipt.
4. The medical device manager shall store and manage the medical devices used in clinical trials to ensure that they are not used for purposes other than clinical trials.

5. The medical device manager shall make a record of receipt and payment of medical devices during the clinical trial, inventory, and use status, as well as the return and disposal of unused medical devices, to check the quantity and storage status of medical devices used in clinical trials, and take measures to ensure that clinical trials can proceed appropriately. The receipt record includes the date, quantity, and manufacturing number (or lot number).
6. The clinical trial sponsor shall collect the unused medical device upon suspension or termination of the clinical trial. At this time, the medical device manager shall return the unused medical device to the clinical trial sponsor after consulting with the principal investigator and keep the return certificate.

7. SUBJECT INCLUSION CRITERIA· EXCLUSION CRITERIA, NUMBER OF PERSONNEL, AND GROUNDS

7.1 Inclusion Criteria

1) Adult males and females 19 years of age or older
2) Diagnosed with a herniated disc or lumbar canal stenosis by radiographic (MRI or CT) evidence of nerve root compression at the level of the 3rd-4th lumbar intervertebral or the 4th-5th lumbar intervertebral or the 5th lumbar spine-1st sacral intervertebral
3) Those who are scheduled to undergo partial lamminectomy or nucleus pulposus removal for the first time for the treatment of symptoms corresponding to the above 2 symptoms.
4) Those who meet at least one of the following conditions
   A. Those who have had at least 4 weeks of prior conservative treatment in the 6 months prior to V1 (e.g., use of physioTreatments, anti-inflammatory drugs, muscle relaxants, etc.)
   B. Those who are suffering from unbearable pain and are judged by the investigator to require surgery for herniated discs or lumbar spinal stenosis
   C. Those who have significantly advanced neurological loss
5) Those who have voluntarily given written consent and are able to comply with the trial procedures and visit schedule

7.2 Exclusion Criteria

1) Subjects who have a history of hypersensitivity to the main component and other components of this investigational device
2) Those who have a history of fragile fractures
3) Those who have previously had a fracture or ligament injury of the lumbar spine due to trauma
4) Those who require spinal surgery other than partial laminectomy or nucleus pulposus removal (ost eophytomy is allowed) to treat symptoms
5) Those with neurogenic bowel/bladder dysfunction
6) Those with uncontrolled excessive exudate at the application site, bleeding, acute edema, accomp anied by symptoms of infection
7) Those with degenerative spinal disease (except for disc herniation or lumbar spinal stenosis) or sc oliosis (Cobb's angle 15° or more)
8) Those who have lymphatic system diseases or blood clotting diseases or who are receiving blood clotting drugs
9) Those with uncontrolled diabetes that may affect the course of surgery or postoperatively, accordin g to the judgment of the investigator
10) Those who have connective tissue disease or autoimmune disease or have received treatment for malignant tumors within 5 years
11) Those who have had previous spinal surgery in the area where surgery is scheduled
12) Those who have received epidural steroid treatment within 2 weeks before surgery, or who have ta ken oral steroid preparations within 10 days before surgery
13) Those who have undergone myelogram or lumbar puncture within 24 hours prior to screening
14) Subjects who are immunocompromised or have clinically significant abnormalities found in laborat ory tests at the time of screening
15) Those who have had or currently have a medical illness such as clinically significant disorders of t he cardiovascular, digestive, respiratory, endocrine, or central nervous system or psychiatric disor ders that significantly affect this clinical trial

16) Those who have participated in other interventional clinical trials within 30 days prior to screening or require continued participation
17) Pregnant or lactating women
18) Those who cannot agree to use contraception from the date of signing the written informed conse nt form to the completion of the end visit in this clinical trial
19) Other cases where the investigator deems unsuitable for this clinical trial

7.3 Target number of subjects

	Test group	Control group	Total number of subjects
Number of subjects	30	30	60
Number of subjects considered for dropout 10%	34	34	68

7.4 Rationale for calculating the number of subjects

This clinical trial is a clinical trial to prove non-inferiority by comparing the test device Collabarrier® and the control device Guardix-sol on the effectiveness and safety of preventing postoperative adhesions caused by disc herniation or lumbar stenosis, and the primary efficacy endpoint is the mean MRI Scar score assessed by an independent evaluator at 6 weeks after the application of the investigational device. Therefore, the hypothesis of this clinical trial was established as follows.

$$H_0: \mu_T - \mu_C \geq \delta \ \ vs. \ H_1: \mu_T - \mu_C < \delta$$

In order to determine the effectiveness of the control device Guardix-sol in preventing postoperative adhesions caused by disc herniation or lumbar stenosis, we tried to calculate the number of subjects using the results of previous studies, and the assumptions and data for this purpose are as follows.

[Comparison of MRI Scar score after surgery at 6 weeks between Guardix-sol and no treatment group [14]]

Efficacy criteria	Prior Treatments (Guardix-sol)			Placebo (no treatment)		
	N	Mean	SD	N	Mean	SD
Hanyang University Hospital Scar Score	15	0.80	0.414	14	2.14	0.535
Yeongdong Severance Hospital Scar Score	15	1.20	1.014	14	2.14	1.167
Total	30	1.00	0.774	28	2.14	0.908

(1) Assuming that the true mean difference between the test device and the control device (test device-control device) is 0
(2) The standard deviation of the MRI Scar score is assumed to be the same as the test group (Guardix-sol), and the standard deviation of the control group will be the joint standard deviation (=0.774) of the two standard deviation values obtained from the results of the previous study.
(3) The non-inferiority limit was set as follows.

As a result of reviewing the existing literature, it was confirmed that 0.57 was set as the non-inferiority limit value in a domestic clinical trial (Hong, 2013) [17] that compared the anti-adhesion effect between the test device BNCH-202 and the control device Guardix-sol in a non-inferiority manner, which is a level that preserves 50% of the effect of Guardix-sol in the difference between the MRI Scar score mean between the test group (the target group applying Guardix-sol, the control device of this clinical trial) and the control group (no treatment group) in the results of the previous study of Guardix-sol.

- Statistical non-inferiority limit

Based on the results of the previous study of Guardix-sol, the upper limit of the 95% confidence interval for the difference between the mean of the MRI Scar score between the test group (the target group with Guardix-sol, the control device of this clinical trial) and the control group (no treatment group) was considered, and 0.71 was calculated (Non-inferiority Clinical Trials to Establish Effectiveness, 2016). In this clinical trial, we intend to set 0.57 (δ>0), which is 80% of the statistically calculated non-inferiority limit of 0.71, as the non-inferiority tolerance limit, taking into account the clinical figures.

$$(1.00 - 2.14) + z_{\alpha/2}\sqrt{\frac{0.908^2}{28} + \frac{0.774^2}{30}} = -1.14 + 1.96 * 0.22 = -0.71$$

Based on the above assumptions, the minimum number of subjects required for a significance two-tailed test of 0.05 and a power of 80% was calculated using PASS 15, and a minimum of 30 subjects in each group is required, and 34 subjects in each group will be enrolled, for a total of 68 subjects, considering a dropout rate of 10%.

Non-Inferiority Tests for the Difference Between Two Means

Numeric Results for Non-Inferiority Test (H0: Diff ≥ NIM; H1: Diff < NIM)
Higher Means are Worse
Test Statistic: T-Test

Target Power	Current Power	N1	N2	N	BEFORE	D	S1	S2	Alpha
0.80	0.80086	30	30	60	0.6	0.0	0.8	0.8	0.025

References

Chow, S.C.; Shao, J.; Wang, H. 2003. Sample Size Calculations in Clinical Research. Marcel Dekker. New York.
Julious, Steven A. 2004. 'Tutorial in Biostatistics. Sample sizes for clinical trials with Normal data.' Statistics in Medicine, 23:1921-1986.

Report Definitions

Target Power is the desired power value (or values) entered in the procedure. Power is the probability of rejecting a false null hypothesis.
Actual Power is the power obtained in this scenario. Because N1 and N2 are discrete, this value is often (slightly) larger than the target power.
N1 and N2 are the number of items sampled from each population.
N is the total sample size, N1 + N2.
NIM is the magnitude of the margin of non-inferiority. Since higher means are worse, this value is positive and is the distance above the reference mean that is still considered non-inferior.
D is the mean difference at which the power is computed. D = Mean1 - Mean2, or Treatment Mean - Reference Mean.
S1 and S2 are the assumed population standard deviations for groups 1 and 2, respectively.
Alpha is the probability of rejecting a true null hypothesis.

Summary Statements

Group sample sizes of 30 and 30 achieve 80% power to detect non-inferiority using a one-sided, two-sample t-test. The margin of non-inferiority is 0.6. The true difference between the means is assumed to be 0.0. The significance level (alpha) of the test is 0.025. The data are drawn from populations with standard deviations of 0.8 and 0.8.

Dropout-Inflated Sample Size

	Sample Size			Dropout-Inflated Enrollment Sample Size			Expected Number of Dropouts		
Dropout Rate	**N1**	**N2**	**N**	**N1'**	**N2'**	**N'**	**D1**	**D2**	**D**
10%	30	30	60	34	34	68	4	4	8

Definitions

Dropout Rate (DR) is the percentage of subjects (or items) that are expected to be lost at random during the course of the study and for whom no response data will be collected (i.e. will be treated as "missing").

N1, N2, and N are the evaluable sample sizes at which power is computed. If N1 and N2 subjects are evaluated out of the N1' and N2' subjects that are enrolled in the study, the design will achieve the stated power.

N1', N2', and N' are the number of subjects that should be enrolled in the study in order to end up with N1, N2, and N evaluable subjects, based on the assumed dropout rate. After solving for N1 and N2, N1' and N2' are calculated by inflating N1 and N2 using the formulas N1' = N1 / (1 - DR) and N2' = N2 / (1 - DR), with N1' and N2' always rounded up. (See Julious, S.A. (2010) pages 52-53, or Chow, S.C., Shao, J., and Wang, H. (2008) pp. 39-40.)

D1, D2, and D are the expected number of dropouts. D1 = N1' - N1, D2 = N2' - N2, and D = D1 + D2.

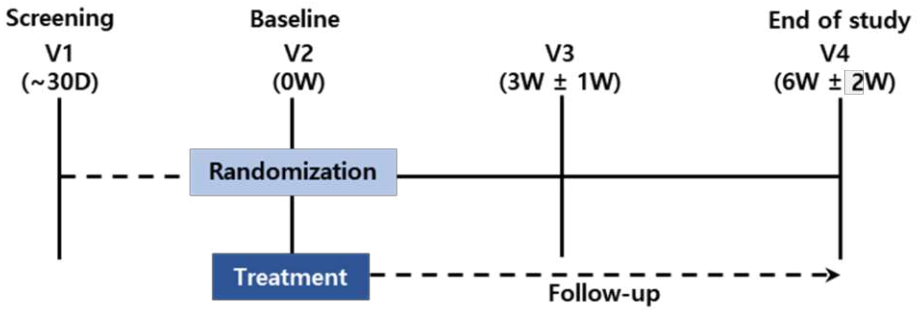
8. DURATION OF THE TRIAL

After obtaining approval from the Ministry of Food and Drug Safety and the Institutional Review Board (IRB), it is expected that the recruitment period of clinical trial subjects will take about 28 months and the follow-up period will be about 2 months , and after the clinical trial ends, it will take about 6 months for data processing, statistical analysis, preparation of results reports, and submission of IRB, which is expected to take about 36 months.

9. CLINICAL TRIAL METHODS

9.1 Clinical trial design

If subjects who meet the inclusion/exclusion criteria and voluntarily sign the consent form for the clinical trial are enrolled in this clinical trial, they will be treated with an investigational device or a control device during surgery for herniated disc or lumbar spinal stenosis and before surgical site closure. In addition, the procedure will be performed by the same investigator at each clinical trial site to minimize the impact of the procedure method. At 3 and 6 weeks after the application of the investigational device, subjects will be confirmed for safety, and 3 At 6 weeks, VAS Evaluation for back and leg pain and Oswestry Disability Index (ODI) Evaluation for limitation of daily life will be performed. In addition, MRI imaging of the medical device application area will be performed at 6 weeks after the application of the investigational device. The MRI of the subjects will be randomly assigned a new assignment number for each photo regardless of the assignment group by an independent data manager, and then sent to the independent evaluator with the subject's information completely excluded. The independent evaluator will evaluate the MRI Scar score evaluation criteria presented in this clinical trial by applying the same to each photo.



Clinical trial model

9.2 Randomization Method

The randomization table will be prepared by a statistician who is not directly related to this clinical trial using SAS® (Version 9.4 or higher, SAS institute, Cary, NC, USA) so that each group can be assigned in a 1:1 ratio by stratified block randomization method considering the site as a stratification factor. Subsequently, subjects who participate in the clinical trial and meet the Inclusion/exclusion criteria will be sequentially assigned to each application group according to the randomization number, and the randomization number will be used as the subject identification code during the clinical trial.

9.3 Subject Assignment

9.3.1 How to Assign Screening Numbers

For subjects who have given written consent to participate in this clinical trial, the investigator will assign a screening number as follows.

SX-NN

SX-NN	Description
S	Characters that mean screening
X	Institution Number Example) ◯◯ Hospital: 1, ●● Hospital: 2, ▲▲ Hospital: 3, ...
NN	Subject serial number (two-digit number assigned sequentially by site) Example) 01, 02, ... 01, …

9.3.2 How to assign randomization numbers

For subjects who meet the Inclusion/exclusion criteria through screening and are suitable for enrollment in this clinical trial, the randomization number will be given as follows.

RX-NN

RX-NN	Description
R	Letters that mean randomization
X	Institution Number Example) ◯◯ Hospital: 1, ●● Hospital: 2, ▲▲ Hospital: 3, ...
NN	Subject serial number (two-digit number assigned sequentially by site) Example) 01, 02, ... 01, …

9.4 Application method of investigational device

Before applying this investigational device, all cleaning solution will be sucked out and removed, and all hemostatic products such as pads and sponges filled for hemostasis will be removed. After confirming complete hemostasis in the wound area, the plug on the front part of the syringe is removed, and a medical spreader or catheter is inserted. Then, apply the test device or control device completely to the lateral surface of the nerve root, dorsal side, and the outer surface of the dura mater. The thickness of the medical device was applied from the dorsal side of the nerve root and dura mater to the dorsal surface of the posterior lamina in the range of the resection of the posterior lamina, and an appropriate amount was applied according to the patient's condition, surgical site, and extent under the judgment of the investigator, and a maximum of 5 ml was applied.

9.5 Trial Design Rationale

9.5.1 Basis for Inclusion of control device

Guardix-sol, which was selected as the control group, is an anti-adhesion dressing that is applied to the surgical site during surgery to provide temporary viscous/lubricating coding to the tissues around the surgery to reduce adhesions during surgery in the nasal sinuses, ophthalmology, breast, abdominal cavity, uterine cavity, spine, and urinary tract, and the main ingredients are Sodium Hyaluronate (HA) and Sodium Carboxymethylcellulose (CMC) [15]. HA is one of the main components of extracellular matrix found in various tissues such as connective tissue, skin, cartilage, hyaline, synovial fluid, etc., and is known as a substance that prevents adhesion by inhibiting the formation of fibrin by covering the tissue surface exposed during Surgery for its hydrophilic, non-immune, and viscoelastic properties. CMC is also water-soluble and has the characteristics of being able to act effectively as a physical barrier due to its long residual time in the body, as it is an ingredient that is used in various ways such as excipients, thickeners, lubricants, and stabilizers. The control device made of the two components has the characteristic of being naturally degraded in the body 2 weeks after surgery and absorbed and excreted within 1 month,and has been used as a control device in previous studies of anti-adhesion agents targeting spine surgery [16,17]. In addition, Hanmi Pharmaceutical's Gaddix is a product that is used universally as it occupies more than half of the domestic anti-adhesion agent market [18], so it was judged to be suitable for comparing the effectiveness and safety of this test device and evaluating its non-inferiority, so it was selected as a control device.

9.5.2 Blinding

This clinical trial was designed with subject and independent evaluator blinding. Since the two medical devices used in this clinical trial do not have an application and removal procedure in the subject's perceived situation, it is expected that a blinding design will be allowed, so this method was adopted. Since the investigator will know the treatment group assigned in advance by the application of the investigational device, blinding of the investigator is not allowed. However, this clinical trial is a controlled clinical trial, and in order to prevent bias in the primary efficacy endpoint, three radiology specialists were assigned as independent evaluators to maintain blinding during the evaluation of the primary endpoint. Attachment 7. Independent Evaluation Manual'.

The unique assignment code will be managed in a sealed state by the sponsor and the principal investigator of the clinical trial site, and the subject and investigator shall remain blinded to each subject's treatment arm assignment after the end of the study until the data management process is completed and the assignment code is released. If it is deemed necessary to release the subject's assignment code due to the occurrence of an emergency such as a serious adverse event, or if it is determined that it is absolutely necessary for the rights and safety of the subject, the blinding may be lifted according to the unblinding procedure.

9.6 Concomitant Treatments

9.6.1 Prohibited Concomitant Medications and Treatments

No Medication/Treatment Medications/Treatments Available

drug	V1 ~ V2	V2 ~ V3	V3 ~ V4 2 weeks ago	2 weeks ago ~ V4
NSAIDs	allowed			Not allowed
Steroid injections (epidural adrenal cortex including hormone infusions)	Not allowed	allowed		Not allowed
Oral steroids	Not allowed	allowed		Not allowed
Anticoagulants	Not allowed			
Antiplatelet Drugs	Not allowed			
Fibrinolytic Agents	Not allowed			
Investigational devices Other anti-adhesion agents	Not allowed			

* Among the prohibited drugs, anticoagulants, antiplatelet drugs, and fibrinolytics are allowed as exceptions after discussion between the sponsor and the researcher.

9.6.2 Permitted Concomitant Medications and Treatments

During the clinical trial, the following drugs are allowed:

1) Concomitant medications that the subject has been taking prior to participating in this clinical trial and that are considered not to affect the interpretation of the results of this clinical trial are allowed at the discretion of the investigator.

2) Drugs used for the purpose of temporary treatment of other diseases should be administered in combination with the doctor in charge.

3) Among the prohibited concomitant medications, anticoagulants, antiplatelet agents, and fibrinolytic agents used for purposes other than anticoagulation, antiplatelet, and fibrinolytic drugs are exceptionally allowed after discussion between the sponsor and the researcher.

When administering all concomitant drugs (including therapeutic drugs in the event of other diseases or adverse events), information about the drug (product name, purpose of administration, dosage, start date of administration, end date of administration, etc.) is recorded in detail in the CRF and medical record.

10. OBSERVATION ITEMS · CLINICAL EXAMINATION ITEMS AND OBSERVATION TEST METHODS

10.1 Observations

10.1.1 Primary Efficacy Evaluation

Mean MRI Scar score between the test and control groups assessed by an independent evaluator at 6 weeks after the application of the investigational device

10.1.2 Secondary Efficacy Evaluation

1) Mean score on the 100-mm Visual Analogue Scale (VAS) for back pain in the test and control groups as assessed by subjects at baseline and at 3 and 6 weeks
2) Mean score on the 100-mm Visual Analogue Scale (VAS) for leg pain in the test and control groups as assessed by subjects at baseline and at 3 and 6 weeks
3) Mean score on the Oswestry Disability Index (ODI) for the limitation of daily living in the test and control groups as assessed by subjects at baseline and at 3 and 6 weeks

10.1.3 Safety Evaluation

1) Adverse Events
2) Laboratory tests, vital signs, physical examination

10.2 Clinical trial timeline

Refer to '1.2 Clinical Trial Schedule Summary'.

10.3 Inspection items by visit

10.3.1 Visit 1(Screening Visit, -4W~)

At Visit 1, procedures will be carried out to ensure that the voluntarily consented trial participants are suitable as subjects.

- Written consent
- Screening number assignment
- Demographic Survey
- Medications/Treatments Review
- Medical history
- Body Instrumentation
- Physical
- Laboratory tests
- Pregnancy test (only for women of childbearing potential)
- Vital signs

- Evaluation of Inclusion/Exclusion Criteria

10.3.2 Visit 2(Surgery, OD)

If the clinical trial participation is finally suitable through Visit 2, they will be randomized at this visit and receive the investigational device.

- Medications/Treatment Review
- Physical
- Laboratory tests
- Vital signs
- Evaluation of Inclusion/Exclusion Criteria
- Randomization
- 100 mm-VAS Evaluation (Waist & Legs)
- ODI Evaluation
- surgery
- Investigational device Application
- Check for adverse events

10.3.3 Visit 3(Follow up, 3W±1W)

At 3 weeks after the application of the investigational device, subjects will visit the hospital and perform the following tests.

- Medications/Treatments Review
- Physical
- Vital signs
- 100 mm-VAS Evaluation (Waist & Legs)
- ODI Evaluation
- Check for adverse events

10.3.4 Visit 4(End Of Study, 6W±2W)

At 6 weeks after the application of the investigational device, subjects will visit the hospital for MRI scans, and the following tests will also be performed.

- Medications/Treatments Review
- Physical
- Laboratory tests
- Vital signs
- MRI imaging
- 100 mm-VAS Evaluation (Waist & Legs)
- ODI Evaluation
- Check for adverse events

10.3.5 Un-scheduled Visit

This is a visit that is conducted when additional irregular visits are required according to the investigator's judgment to confirm adverse events other than regular visits, and the schedule of regular

visits should not be changed due to such visits. Medications/Treatments Review and adverse event checks are performed, and physical examinations, laboratory tests, vital signs, MRI scans, and questionnaire evaluations (100 mm-VAS and ODI evaluations) may be performed if necessary.

10.4 Inspection method for each item

10.4.1 Obtaining written informed consent and granting a screening number

When the subject visits the institution for the first time to participate in this study, the investigator will explain to the subject about this study, answer the questions asked by the subject, and ask to participate in the study. If the subject agrees to participate in the study, a study number will be given according to '9.3 Subject Assignment'.

10.4.2 Demographic, drug/treatment, medical history

Demographic information (date of birth, gender, childbearing status) will be investigated at Visit 1.

In the case of prior drugs/treatments, drugs administered or being administered before the application of the investigational device within 4 weeks from the time of V1 will be investigated. The drug name (brand name or name name), purpose of administration, daily dose, unit, route of administration, and the start and end dates of administration are recorded, and information on the treatment performed before the application of the investigational device is also collected. At this time, it is judged whether the drug and treatment are continued, and if continuous prescription is required after the application of the investigational device, it is collected as a combination drug/treatment. In addition, information on the drugs administered after the application of the investigational device and the treatment performed will be collected.

Medical history will be examined at Visit 1. In the case of medical history, the presence or absence of past and current medical history, including diseases experienced or ongoing within 12 months or clinically significant medical conditions within 12 months at the time of V1, the time of occurrence (date of occurrence), whether it continues, and the opinion of the investigator will be recorded.

10.4.3 Body Instrumentation

At Visit 1, body measurements (height, weight) will be performed.

10.4.4 Physical

The investigator will comprehensively evaluate the subject's appearance, skin, head/neck, heart, abdomen, urinary/reproductive system, limbs, musculoskeletal system, nervous system, lymph nodes, and other items at each visit. Clinically significant abnormal results observed before the application of the investigational device will be recorded in the medical history, and clinically significant abnormal results observed after the application of the investigational device will be recorded as adverse events.

10.4.5 Laboratory tests

The investigator will investigate the following items from the subject's blood and urine at Visit 1, Visit 2, and Visit 4, and if necessary, this test may also be performed at the un-scheduled visit at the investigator's discretion. If the results are already available within 4 weeks prior to Visit 1, the results can be replaced with a screening test. Subjects who do not meet the screening test results for Inclusion/exclusion may be re-tested only once, in which case the re-test results will be used. If the V2 visit date is within 7 days of the V1 visit date, the V1 laboratory test results can be substituted for the V2 laboratory results. In the case of pregnancy response testing, urine hCG pregnancy test (if not allowed, serum test is replaced) may be performed only for women of childbearing potential and may be performed at each visit point if necessary at the discretion of the investigator.

Hematological tests	white blood cell (WBC), WBC with differential (Lymphocyte, Monocyte, Eosinophil, Basophil, NeutrophilSegment), red blood cell (RBC), hemoglobin (Hb), hematocrit (Hct), platelet count (PLT)
Hematological Chemical Tests	alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine transaminase (ALT), Gamma Glutamyl Transpeptidase (GGT), total bilirubin, albumin, serum creatinine, blood urea nitrogen (BUN)
Urinalysis	Specific Gravity, Color, pH, Protein, Glucose, Bilirubin, Blood, WBC, Urine hCG pregnancy test (This test will be performed only for women of childbearing age before menopause, only at the screening visit (Visit 1), and if necessary, additionally performed at the last visit (Visit 4).)

Laboratory test results are classified as normal and abnormal (NCS, CS), and if laboratory test results after application of the investigational device are judged to be clinically significant compared to before application, they are reported as adverse events and findings on abnormal values are recorded.

10.4.6 Vital signs

The investigator will measure the subject's seated systolic/diastolic blood pressure, pulse, and body temperature at each visit to investigate vital signs. All vital signs will be examined with the subject resting for at least 5 minutes. Clinically significant abnormal results observed before the application of the investigational device will be recorded in the medical history, and clinically significant abnormal results observed after the application of the investigational device will be recorded as adverse events.

10.4.7 Evaluation of Inclusion/Exclusion Criteria and Assignment of Randomization Numbers

Based on the observations and examination items at Visit 1 and Visit 2, the Inclusion/exclusion criteria for suitability to participate in this clinical trial will be confirmed. Only subjects who are finally confirmed at Visit 2 will be assigned a registration number according to '9.3 Subject Assignment'.

10.4.8 Surgery

The surgery specified in Visit 2 will be performed.

10.4.9 Investigational device Application

After surgery, the test device Collabarrier® or the control device Guardix-sol will be applied to the application area and the application amount will be collected.

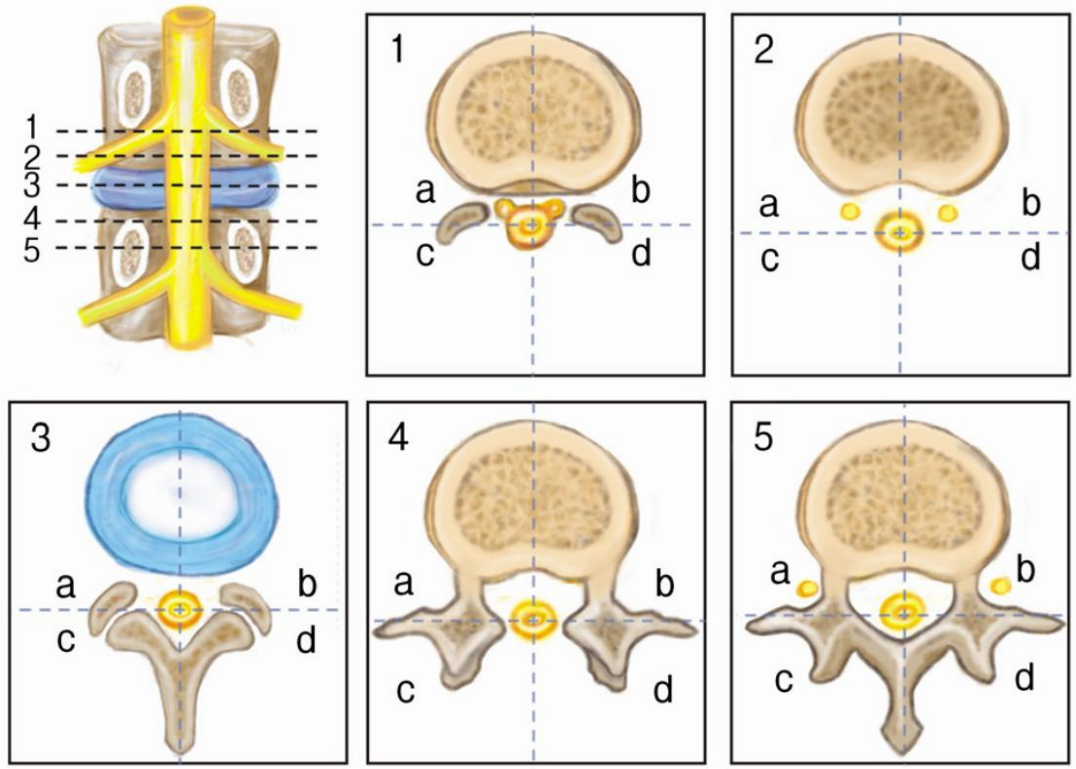
10.4.10 MRI Scar score

At 6 weeks after the application of the investigational device, the subject will present to the institution for MRI scans of the surgical site. The MRIs taken will be classified by subject, and when evaluated by an independent evaluator, the subject information from all photographs of the institution will be blinded to ensure that the blinding is maintained. The same imaging will be performed at all institutions by referring to the following information and pictures [16, 17].

A. Axial slice thickness: The slice thickness is taken at a distance of 3 ~ 4 mm from the sagittal plane centered on the intervertebral disc at the surgical site.

B. In an axial arrangement, each cross-section for the axial plane contiguous to the axial plane in five axes close to the center of the intervertebral disc is quadrant perpendicular to the thecal sac.

C. T1-weighted Gadolinum will be taken both non-enhanced before administration and enhanced images after administration.



This clinical trial is a multicenter clinical trial, and although the instruments used by each institution are different, the sequence is uniformly shot and the same is recorded, and the parameters of each device are adjusted to achieve the same image as allowed. The location recording of supradural fibrosis on MRI and the evaluation of adhesions will be made by an independent evaluator, and the degree of scar will be scored for 20 cross-sections with 5 MR images in 4 quadrants per subject. The largest score among the total 20 SCA scores evaluated will be selected to compare and evaluate the mean value of the scar score between the test group and the control group, and the score according to the degree of scar of the dura mater will be evaluated as 0 ~ 4 points, and the relevant details are shown in the table below.

score	Details
0	No / trace scar
1	> 0% and ≤ 25% of quadrant filled with scar
2	> 25% and ≤ 50% of quadrant filled with scar
3	> 50% and ≤ 75% of quadrant filled with scar
4	> 75% of quadrant filled with scar

The investigator creates a folder for each subject and keeps the photo file. In the created folder, the photographs are stored in the form shown in the table below, separating the subject's visit time and the test group and control group. If the investigator saves each photo in the form of an electronic file on an external hard drive or USB, the monitoring personnel of the clinical trial site can create a material receipt sheet and send it to the independent data manager. Photographs should be sent at least once a quarter, and may not be sent if there are no registered patients. Photographs should be sent in a compressed folder if necessary, and the folder name should be the same. For details related to the evaluation procedure of independent evaluators, please refer to 'Attachment 7: Independent Evaluation Manual'.

Subject RX-NN photo folder name	Protocol No_Subject Number
Example Photo Folder Name of Subject R1-001	DRT-04_R1-001
Photographic name for subject identificati on	Protocol No_Subject Number_Visit Date_ Placement Group
Example of test group photo name of V4 s ubject R1-001	DRT-04_ R1-001_V4_ Test Group

10.4.11 100 mm Visual Analogue Scale(VAS)

At the preoperative time point (baseline) and at 3 and 6 weeks after the application of the investigational device, subjects will come to the hospital for efficacy evaluation and undergo a 100 mm Visual Analogue Scale (VAS) Evaluation for back and leg pain. In the case of legs, VAS evaluation will be performed only on one of the two legs with severe pain. The 100 mm VAS marks the left end as no pain '0' and the right end as '100' for severe pain on a 100 mm parallel line. The subject draws a vertical line exactly on the parallel line and measures the mm from no pain (0) to the vertical line to

check the value. For details, refer to 'Annex 3. 100 mm Visual Analogue Scale (VAS) Evaluation Sheet'.

10.4.12 Oswestry Disability Index(ODI)

At the preoperative time point (baseline) and at 3 and 6 weeks after the application of the investigational device, subjects will come to the clinic for efficacy Evaluation and undergo an Oswestry Disability Index (ODI) Evaluation of the limitation of daily living. Subjects will be evaluated in 'Annex 4. The Oswestry Disability Index (ODI) questionnaire will be used to evaluate the 'Oswestry Disability Index (ODI)', and the scoring method of the questionnaire is as follows [19].

Oswestry Disability Index(ODI) Scoring Method
The maximum score for each section within the questionnaire is '5 points', and the total score for all 9 sections combined is '45 points'. In each section, if you check phrase 1, the score for that question ite m is '0 points', and if you check the last phrase (phrase 6), the score is '5 points'. Once all 9 sections a re completed, the score will be calculated as follows:
Calculations: [Total score / 5 × sections answered] × 100 = ____% Example (1): If all sections are checked and the total score is 16 [16 (Total Score) / 5 × 9] × 100 = 35.6% Example (2): If one section is missing or not applied, and the total score is 16 [16 (Total Score) / 5 × 8] × 100 = 40.0%

10.4.13 Adverse Case Investigation

Adverse events that occur after the application of an investigational device will be identified, and the investigator will be trained to voluntarily report any adverse events that occur. In addition, the investigator will check whether adverse events occur through interviews and medical examinations during regular visits during the clinical trial.

The investigator will observe and record the adverse events that appear after the application of the investigational device by examining the subject on each visit day, and record in detail the time of symptom onset, termination, severity, progress, action, outcome, severity, and causality of the adverse event.

Laboratory tests will also be reviewed, and abnormal results will be assessed for clinical significance. Clinically significant laboratory test abnormalities will be followed up until they return to acceptable values or can no longer be followed up (loss of follow-up or withdrawal of informed consent). However, if the principal investigator determines that the adverse event does not require further follow-up, the clinical trial may be terminated at the end visit (Visit 4).

11. PREDICTED SIDE EFFECTS AND PRECAUTIONS FOR USE

11.1 Investigational Device

1. Warnings (contraindications)
   1) Do not use on patients with contamination or infection at the surgical site.
   2) Do not use in patients with hypersensitivity to porcine-derived products.
   3) If you experience an allergic reaction or infection during the use of this product, do not use it and seek appropriate treatment according to your doctor's instructions.
   4) This product should not be used when excessive exudate, bleeding, acute edema, or symptoms of infection are not controlled.
   5) This product is prohibited for use other than medical use or use.
   6) In case of unexpected local and systemic allergic reactions, you should consult a doctor.
2. Precautions for use considering the characteristics of medical devices
   1) It is not studied and is prohibited for the following patients:
   ① Patients with coagulation diseases of lymphatic fluid or blood or patients who have received coagulants
   ② Patients with immunosuppressed or autoimmune diseases
   ③ Patients with severe hepatic or renal disease or who have undergone surgery involving opening of the gastrointestinal tract or urinary tract
   2) Patients who have received oral or parenteral hypoglycemic drugs for diabetes are not studied and are administered with caution.
   3) When this product is used in combination with other drugs such as anti-adhesion products and absorbent hemostatic agents, its safety and efficacy have not been confirmed in animal tests.
3. Adverse reactions (side effects) that may occur as a result of the use of medical devices
   1) The surgeon should inform the patient that the following symptoms may appear immediately after injection of this product or after a certain period of time, and report to the salesperson when these symptoms occur.
      - Infection, allergies, pain, inflammatory reactions, etc.
   2) If the above reactions persist or other side effects occur, consult a specialist immediately for treatment.
4. General Caution
   1) Depending on the storage method, it should be stored until use.
   2) Do not reuse for single use.
   3) Check sterile packaging and do not use products with torn or damaged packaging.
   4) Do not use products that have expired.
5. Use for pregnant, lactating, fertile women, newborns, infants, and children

1) Jaundice may occur, so it should not be used in late pregnancy, premature babies, primiparous babies, or newborns within the first month of life.

2) The safety of using foreign plants in pregnant, parturient or lactating women has not been established, so they should be used with caution and under the judgment of a doctor.

3) Since there has been no clinical application of this product to pregnant women, it is used when it is judged that there is a therapeutic benefit when applying this product to pregnant women.

6. Precautions for application

1) Do not administer by the IV, IM, and SC routes.

2) Do not re-sterilize.

3) Only products that have been sterilized must be used, and should not be used if the packaging has been opened.

4) This product is sterile, so once used, it is not reused.

5) Do not use sterile packaging that has been opened or damaged.

6) It should be used according to the usage method for safety.

7) If bleeding is severe, it is used after hemostatic treatment.

8) Check the product's usage period.

9) It is contraindicated for use in areas where safety and efficacy have not been clinically verified.

10) Do not use it in places where bacteria are infected, where the area to be treated is infected, or where the infection is in progress without a special prescription from a medical professional.

11) It is not used by anyone other than those who have received training or more than professional training or qualifications.

12) Do not mix with non-standard or unlicensed medical devices. If you experience allergic reactions or symptoms of infection while using the product, do not use it and receive appropriate treatment according to the instructions of a doctor or pharmacist.

7. When it is necessary to prevent safety accidents

1) When used outside the operating room or clean room, side effects such as fever and inflammatory reactions may occur due to infection caused by external contaminants, so it should be used under sterile conditions.

11.2 Control device

1. General Notes

1) This product is sterile, so make sure it remains sterile during the procedure and do not use it after the sterilization expiration date has passed.

2) Do not use the container if it shows signs of damage or moisture after checking the contents before use.

3) Before inserting this product into the surgical site, the surgeon should absorb and remove excess fluid from the injection site.

2. Precautions for handling

1) This product should be stored at room temperature before use.

2) This product is supplied sterile. Do not re-sterilize

3) This product is for one-time use and should not be reused.

3. Contraindications

1) Patients who are prohibited from receiving

① This product should not be used on patients who are currently infected or contaminated with the surgical site.

② Do not use this product in patients with hypersensitivity.

2) Careful dosing

① This product has not been studied in patients with lymphatic fluid or blood clotting disorders or patients who have received coagulants.

② This product has not been studied in patients who have received oral or parenteral hypoglycemic drugs for diabetes.

③ This product has not been studied in immunosuppressed patients or patients with autoimmune diseases.

④ This product has not been studied in patients with severe liver or kidney disease or in patients who have undergone surgery involving opening the gastrointestinal tract or urinary tract.

⑤ When this product is used in combination with other drugs such as anti-adhesion products and absorbable hemostatic agents, its safety and efficacy have not been confirmed in animal tests.

⑥ This product is not recommended for use during pregnancy. After using this product, it is recommended to avoid pregnancy until the end of the first menstrual cycle.

4. side effect

1) contagion

2) Allergic reactions

3) pain

4) Inflammatory response

12. CRITERIA FOR SUBJECT DISCONTINUATION OR DROPOUT

12.1 Discontinuation or Dropout of the Clinical Trial

If the following cases occur, all or part of the clinical trial sites will review the existence of the clinical trial based on the relevant clinical trial plan.

1) If the situation observed during the clinical trial is determined to be unreasonable for the clinical trial to continue, the principal investigator must request the clinical trial review board to stop the clinical trial, and may suspend the clinical trial according to the decision of the clinical trial review board.

2) If the subject is discontinued due to the occurrence of an adverse event/serious adverse event that makes it difficult to proceed with the clinical trial (if the investigator determines that the study should be stopped)

3) When a change in the clinical trial plan is required, but the site is unable to respond to it

4) When the head of the site gives an amendment order based on the opinion of the review committee of the site and the sponsor is unable to approve it,

5) If the director of the site orders the suspension of the clinical trial based on the opinion of the institution's review board that the clinical trial cannot be continued.

6) If the site has committed serious or continuous violations that are different from KGCP and this clinical trial agreement

In addition, if the sponsor decides to suspend or discontinue the clinical trial, he or she shall promptly notify the Clinical Trial Review Committee and the principal investigator in writing of the purpose and reason. However, if there is a separate notification regulation for suspension or suspension of clinical trials depending on the institution, it shall be followed.

If the principal investigator receives a notice from the sponsor regarding the suspension or suspension of the clinical trial, the principal investigator shall promptly notify the subject of the suspension or suspension of the clinical trial and ensure appropriate treatment and follow-up treatment.

12.2 Handling of Discontinuation

1) If the clinical trial is suspended, the principal investigator shall summarize and deliver the CRF of the subject to the time of suspension, the progress status and results of the clinical trial to the sponsor, and return all trial-related materials (CRF and investigational device, etc.) to the sponsor.

2) If the study is discontinued, the principal investigator shall notify the IRB in writing of the study suspension.

12.3 Subject dropouts

1) If the following are found during surgery

   A. If there must be other devices left at the surgical site that may interfere with the interpreta tion of the study results

B. If dural rupture and dural hole are found during surgery
C. Epidural fat placement
D. If you have a herniated disc and need surgery on more than one level
E. If you are applying a sealant or making other attempts to repair a fibrous annulus tear
F. If a tumor in the spine is found during surgery
G. Entering the dura mater during surgery
H. If spinal fusion is required
I. If the hemostatic agent must remain at the surgical site
, but if it is cleaned after stopping the bleeding, it will not be dropped out.
J. If antibiotic powder is injected into the surgical site
(antibiotic cleaning is only allowed before the application of the medical device, not after applicati

on.)

K. When the following products are applied to exposed nerve elements

- Amniotic tissue or amniotic fluid
- adhesive
- steroid
- Platelet-rich plasma fluid
- Gel Foam
- Allograft tissue
- Fibrin Adhesive
- Dural patch

2) The subject (or legal representative) voluntarily wishes to discontinue the trial.

3) Surgery that may affect safety and efficacy evaluation, or when using other drugs and procedures in conjunction with other drugs and procedures

4) If an adverse event occurs during follow-up observation that makes it difficult to continue the clinical trial

5) Subjects who are not able to continue to follow up on the treatment of this clinical trial due to loss of contact during this clinical trial

6) Inclusion/exclusion criteria non-conformity confirmed since enrollment in the trial

7) If the principal investigator deems it inappropriate as a subject (if he does not comply with the investigator's instructions, if it is judged that he or she can no longer participate in the clinical trial in terms of safety or ethics due to a change in the subject's condition, etc.);

12.4 Handling of dropouts

1) If the subject drops out midway, the reason for dropout and the data related to the clinical trial that was conducted before the dropout will be recorded and kept.

2) If the subject fails to come to the hospital during the test, the subject's health and wellness should be checked and the reason should be clarified.

3) Those who drop out will be included in the statistical processing of safety and efficacy evaluation unless there is a valid reason or basis.

4) The data obtained through clinical trials should have a dataset for safety analysis and efficacy analysis, and if there is a defect in the data, the appropriate correction method should be presented in the research protocol, and the analysis should be performed after calibration.

13. CRITERIA, EVALUATION METHODS, AND INTERPRETATION METHODS FOR EFFICACY EVALUATION (STATISTICAL ANALYSIS METHODS)

13.1 Definition of Analysis Group

The data obtained from the subjects through this clinical trial will be divided into the Safety Set, FA (Full Analysis) Set. Statistical analysis will be performed by dividing it into PP (Per Protocol) Sets. The main population of this trial will be the PP Set, the secondary evaluation group will be the FA Set, and the safety evaluation will be analyzed with the Safety Set.

Full Analysis Set (FA Set)

Subjects who have been applied to an investigational device at least once after randomization and who can obtain information about the results of the primary efficacy evaluation after baseline are eligible.

Per-Protocol Set (PP Set)

The PP Set is for subjects included in the FA Set who have completed the clinical trial according to the clinical trial protocol without any serious protocol violations, and subjects who fall under the following cases will be excluded from the PP Set.

1) Dropout
2) Violation of Inclusion/Exclusion Criteria
3) Taking prohibited drugs or using prohibited treatments (except for other purposes)
4) Other cases that may be considered serious violations of the plan

Safety Set

Subjects who have been applied to an investigational device at least once after randomization and whose safety-related data have been evaluated at least once will be included.

13.2 General principles

Continuous variables present the number of observed subjects, mean, standard deviation, median, minimum, and maximum values, while categorical variables present frequency and percentage. Unless otherwise specified, all tests will be two-tailed tests at the significance level of 5%. All p-values will be presented up to 4 decimal places, and if they are less than 0.05, they will be judged to be statistically significant. The missing values that occurred in this clinical trial will be reflected in the analysis as they are without correction.

13.3 Subject Basis Information

Demographic data and basic characteristics will be summarized for each administration group, and will be conducted for FA sets.

1) Demographic information and basic characteristics

Demographic data and basic characteristics are summarized by dosing group. Continuous variables present the number of observed subjects, mean, standard deviation, median, minimum, and maximum, while categorical variables present frequency and percentage. Comparisons between dosing groups will be analyzed by two sample t-test (Wilcoxon's rank sum test if the normality distribution assumption is not satisfied) for continuous variables and Pearson's chi-square test (Fisher's exact test if cells with an expected frequency of less than 5 exceed 20%).

2) Medical history and prior medications

Medical history will be standardized to System Organ Class (SOC) and Preferred Term (PT) according to the latest version of the Medical Dictionary for Regulatory Activities (MedDRA) for each administration group, and the frequency, percentage, and number of medical history will be presented. The prior drugs will be standardized into Anatomical main group (Level 1) and Therapeutic subgroup (Level 2) according to the latest version of the WHO-ATC (World Health Organization-Anatomical Therapeutic Chemical) Index (WHO-ATC) Index for each administration group, and the frequency and percentage of subjects and the number of drug cases will be presented.

13.4 Primary Efficacy Evaluation Methods

Descriptive statistics (number of observed subjects, mean, standard deviation, median, minimum, maximum) for MRI Scar score assessed by an independent Evaluator at 6 weeks for each administration group will be presented, and compared with two sample t-tests (Wilcoxon's rank sum test if normality distribution assumptions are not satisfied).For the mean difference between the administration groups (test group-control group), a two-sided 95% confidence interval is presented. At this time, the upper limit of the confidence interval is 0 for non-inferiority limit.If it is less than 57, it will be judged that the non-inferiority of the test group compared to the control group has been demonstrated.

13.5 Secondary Efficacy Evaluation Methods

1) Mean score on the 100-mm Visual Analogue Scale (VAS) for back pain in the test and control groups as assessed by subjects at baseline and at 3 and 6 weeks

   : Descriptive statistics (number of observed subjects, mean, standard deviation, median, minimum, maximum) of the 100-mm Visual Analogue Scale (VAS) for back pain assessed by subjects at baseline and at 3rd and 6th weeks for each administration group will be presented and analyzed with two sample t-tests (Wilcoxon's rank sum test if the normality distribution assumption is not satisfied).

2) Mean score on the 100-mm Visual Analogue Scale (VAS) for leg pain in the test and control groups as assessed by subjects at baseline and at 3 and 6 weeks

   : Descriptive statistics (number of observed subjects, mean, standard deviation, median, minimum, maximum) of the 100-mm Visual Analogue Scale (VAS) for leg pain assessed by subjects at baseline and 3 and 6 weeks for each administration group will be presented and analyzed by two sample t-tests (Wilcoxon's rank sum test if the normality distribution assumption is not satisfied).

3) Mean of the Oswestry Disability Index (ODI) for the limitation of daily living in the test and control groups as assessed by subjects at baseline and at 3 and 6 weeks

: Descriptive statistics (number of observed subjects, mean, standard deviation, median, minimum, maximum) of the Oswestry Disability Index (ODI) for the limitation of daily living assessed by subjects at baseline and at 3rd and 6th weeks for each administration group will be presented and analyzed by two sample t-test (Wilcoxon's rank sum test if the normality distribution assumption is not satisfied).

13.6 Safety Evaluation Methods

13.6.1 Adverse Events

The number of subjects, incidence, and number of occurrences are presented for adverse events (TEAEs), adverse medical device reactions (ADEs), and serious adverse events/adverse medical device reactions (Serious AEs/ADEs) that occurred after the application of the investigational device.

Adverse events, adverse medical device reactions, and serious adverse events are standardized with System Organ Class (SOC) and Preferred Term (PT) according to the latest version of the Medical Dictionary for Regulatory Activities (MedDRA), and the number of subjects, incidence, and number of adverse events are presented.

13.6.2 Laboratory tests, vital signs, physical examination

Laboratory tests, vital signs, and physical examination data will be analyzed with descriptive statistics (number of observed subjects, mean, standard deviation, median, minimum, maximum) if they are continuous data, and two sample t-tests (Wilcoxon's rank sum test if normality distribution assumptions are not satisfied). The comparison before and after the application of the investigational device will be analyzed by Paired t-test (Wilcoxon signed rank test if the normality distribution assumption is not satisfied).

Categorical data will be presented with frequencies and percentages and analyzed by Pearson's chi-square test (Fisher's exact test if cells with an expected frequency of less than 5 exceed 20%). The comparison before and after the application of the investigational device will be analyzed by McNemar's test.

13.6.3 Concomitant medications

Concomitant medications will be standardized based on the latest version of the WHO-ATC (World Health Organization – Anatomical Therapeutic Chemical) Index by Anatomical Main Group (Level 1) and Therapeutic Subgroup (Level 2), and the number of subjects, percentage, and number of medications will be presented for each treatment group.

14. EVALUATION CRITERIA, EVALUATION METHODS, AND REPORTING METHODS FOR SAFETY INCLUDING ADVERSE EVENTS

14.1 Definitions of safety-related terms

14.1.1 What is an adverse event (AE)?

"Adverse Event (AE)" means any unintended symptom (including symptoms, signs, abnormalities in laboratory test results, etc.), symptoms, or diseases that occur in a subject during a clinical trial and does not necessarily have a causal relationship with the investigational device.

14.1.2 Adverse Device Effect (ADE)

"Adverse Device Effect (ADE)" refers to any harmful and unintended reaction caused by an investigational device and a causal relationship with an investigational device cannot be denied.

14.1.3 Serious AE/Serious ADE

"Serious adverse events, adverse medical device reactions (SDEs)" refers to adverse events or adverse reactions to medical devices used in clinical trials that fall under any of the following:

1) In the event of death or danger to life
2) Need to be hospitalized or need to extend the length of hospitalization
3) Resulting in permanent or significant disability and functional decline
4) If the fetus has malformations or abnormalities

Significant medical events that are not immediately life-threatening and do not result in death or hospitalization, but that, based on appropriate medical judgment, require intervention to endanger the subject or prevent the consequences listed in the above definition, should also be considered serious adverse events or adverse medical device reactions. If the subject presents to the emergency department and the treatment time exceeds 24 hours, the admission criteria are considered to have been met, and if the subject is scheduled to be hospitalized before the application of the first investigational device, or in the case of cosmetic plastic surgery, it is not considered as an adverse event, serious adverse event, or adverse reaction to a medical device. Elective surgery in the absence of adverse events and subsequent hospitalization are also not considered serious adverse events or adverse medical device reactions. However, if hospitalization is not planned or is the result of an adverse event, it is considered a serious adverse event or adverse medical device reaction.

Even if it is not the situation listed above, if a situation occurs that is medically considered to have a significant impact on the safety and health status of the subject, the medical judgment of the doctor in charge and relevant experts will determine whether or not to consider it a serious adverse event and take appropriate measures accordingly.

14.1.4 Unexpected ADE

"Unexpected Adverse Device Event" refers to a difference in the aspect or degree of harm of an adverse medical device in light of available medical device-related information such as clinical trial data books or medical device accompanying documents.

14.2 Record of Adverse Events

From the time of application of the investigational device to the date of the last visit, undesirable and unintended symptoms (e.g., abnormalities in laboratory tests), symptoms, and diseases that occur in the subject will be recorded as adverse events. Symptoms, symptoms, or diseases that appeared before the application of the investigational device will only be considered as adverse events if they worsen after the application of the investigational device.

14.2.1 Record of Adverse Events

For all adverse events that occur immediately after the application of the investigational device, the investigator shall record the information in the CRF and medical record using the following guidelines and definitions when reporting the following adverse events.

1) Characteristics of adverse events

: It is preferable to describe a comprehensive diagnosis or syndrome rather than individual symptoms/symptoms. The investigator should report adverse events using standard medical terminology. CRF and supporting documents should be consistent.

2) Manifestation date (start date)

: The date of the start of the adverse event, the date of the test reported as abnormal for clinically significant abnormalities in the laboratory test value

3) Adverse event severity

: If an adverse event occurs, it shall be reported according to the following "Regulations on the Management of Safety Information on Adverse Events of Medical Devices" in accordance with Article 7 (Evaluation Criteria and Evaluation Methods for Adverse Events) Paragraph 1 [Appendix 3] criteria.

Mild	If it does not interfere with the normal daily life (function) of the user of the medi cal device, causes minimal inconvenience, and can be easily tolerated
Moderate	If it causes inconvenience that significantly interferes with the normal daily life (f unction) of the user of the medical device
Severe	If it makes it imallowed for the user of the medical device to live normally (functi on)

4) Actions for Investigational devices

: Measures regarding the application of an investigational or control medical device due to the occurrence of an adverse event shall be recorded in the CRF and medical record according to the following classifications.

A. Not applicable: Adverse events occurring during the non-application period of the investigational or comparator medical device (before and after the treatment period or in the case of single-application clinical trials)

B. Temporary discontinuation: Temporarily discontinued use of an investigational or comparative medical device due to this adverse event because the subject chooses to discontinue the application of the investigational or comparative medical device, or the investigator determines that discontinuation of the application of the investigational or comparative medical device is the best course of action considering the safety of the subject.

C. No change in dose: Investigational or comparator medical device application remains the same despite the presence of adverse events

D. Permanent discontinuation: If the subject chooses to discontinue the application of the investigational or comparative medical device, or if the investigator determines that discontinuation of the investigational or comparative medical device is the best course of action for the subject, and the application of the investigational or comparative medical device is permanently discontinued due to this adverse event

5) Other actions taken

: Regarding the treatment of adverse events, etc., select one of the following items and record it in the CRF and medical record.

A. None: No other action was taken for this adverse event.

B. Drug application: For this adverse event, a specific drug (prescription or over-the-counter drug) was applied or the existing drug dose was changed.

C. Hospitalization or prolonged hospital stay: This adverse event resulted in the subject being hospitalized or the length of hospital stay was prolonged.

D. Therapeutic or diagnostic procedures: Subjects have utilized other therapeutic means (e.g., ice, electric cushions, orthoses, plaster bandages, etc.) or underwent diagnostic procedures due to this adverse event (e.g., additional laboratory tests, x-rays, etc.).

E. guitar

6) Loss date (end date)

: Date of extinction of the adverse event. If the adverse event consists of multiple symptoms/symptoms, the duration of the adverse event is determined by the symptom/symptom with the longest duration.

7) result

: Changes in adverse events are judged based on the following criteria.

A. Recovered: The adverse event no longer exists. (Complete extinction)

B. Recovering: Subject's condition is improving or symptoms are still residual

C. Recovered but Aftereffects: Abnormal Damage has been restored, but residual effects still remain.

D. Non-recovery: If the subject's condition does not recover, and there is no change in symptoms (e.g., atrial fibrillation has become chronic)

E. Death: This adverse event caused the death of the subject or directly caused the death of the subject.

F. Undecidable

8) Evaluation of causal relationships with investigational devices

: In the event of an adverse event, the investigator shall evaluate whether it is related to the investigational device according to the following "Regulations on the Management of Safety Information on Adverse Events of Medical Devices" Article 7 (Evaluation Criteria and Evaluation Methods for Adverse Events) Paragraph 2 [Appendix 3], and the investigator's opinion shall be described. In this case, except for "not related", the rest of the evaluation items are evaluated as having an association with the investigational device.

Relevance Obvious (Definitely related)	The relationship between the occurrence of an adverse event and the use of the medical device is valid, and it is most likely explained by the use of the medical device more than any other reason, and the adverse event sy mptoms caused by the discontinuation of the use of the medical device di sappear, and the adverse event symptoms appear when reuse (performe d only when reuse is allowed), and the adverse event that occurs is consi stent with information already known about the medical device or the med ical device of the same class.
Relevant (Probably related)	There is evidence of the use of the medical device, the temporal sequenc e of the use of the medical device and the occurrence of the adverse eve nt is reasonable, it is explained more likely by the use of the medical devi ce than by other causes, and the symptoms of the adverse event caused by the discontinuation of the use of the medical device disappear
Doubtful relevance (Possibly related)	There is evidence that the medical device was used, the temporal sequen ce of the use of the medical device and the occurrence of the adverse ev ent is reasonable, it is determined that the use of the medical device is att ributable to the same level as other allowed causes, and the symptoms of the adverse event caused by the discontinuation of the use of the medical device disappear.
Less relevant (Probably not related)	There is evidence of the use of the medical device, there is a more likely cause for the adverse event, the symptoms of the adverse event caused by the discontinuation of the use of the medical device disappear or are a mbiguous, and the result of reuse of the medical device (performed only if reuse is allowed) does not show or is ambiguous
Not relevant (Definitely not related)	The medical device was not used, or the temporal sequence between the use of the medical device and the onset of the adverse event was not vali d, or there was another obvious cause for the adverse event.
Unassessable (Unknown)	If the information is insufficient or conflicting and cannot be judged, and it cannot be supplemented or verified.

14.2.2 What to do in the event of an adverse event

1) Adverse Case Training

The principal investigator shall educate the investigator and the subject or representative on all adverse events that may occur after the application of the investigational device and report all phenomena that appear after use.

In the event of an adverse event, it is managed so that the necessary examination and treatment can be received immediately from the attending doctor. In the event of a serious adverse event, the clinical trial of the subject shall be stopped and prompt and appropriate measures shall be taken in accordance with "17.3 Reporting of Serious Adverse Events".

2) Follow-up observation of abnormal cases

The investigator shall follow up the subject with an adverse event until the symptoms disappear and the condition stabilizes, and if requested by the sponsor, submit a report on the subsequent progression of the adverse event.

3) Treatment in case of worsening symptoms

: Criteria for subject discontinuation or dropout set forth in "12.1 Discontinuation or dropout of the clinical trial" (2) If the subject is discontinued due to the occurrence of adverse events or serious adverse events that make it difficult to proceed with the clinical trial, the application shall be stopped immediately and replaced with an appropriate treatment regimen to ensure the safety of the subject.

14.3 Reporting of adverse medical device reactions

14.3.1 Reporting Procedures for Major Adverse Events

Obligations of the Sponsor

1) The sponsor shall report all serious and unexpected adverse events to the investigator, the Director of the Ministry of Food and Drug Safety, and, if necessary, the review committee by the deadline according to the following categories.

   가. Causing death or threatening life: Within 7 days of the date the sponsor is reported or aware of the fact. In this case, the sponsor must additionally report detailed information about the adverse event within 8 days from the date of the initial report.

   나. requiring hospitalization or prolongation of hospital stay; irreversible or results in severe disability or functional decline; Causing congenital anomalies or abnormalities: within 15 days from the date the sponsor receives or becomes aware of the fact

2) If additional information regarding a serious adverse event, as described in item 1), becomes available, the sponsor shall continue to report such information until the adverse event is considered resolved (i.e., the adverse event has disappeared or no further follow-up is deemed necessary).

3) The sponsor must prepare and submit to the 'Medical Device Adverse Event Report', which is the [Attachment No. 1 form] of the 'Regulations on the Management of Safety Information on Adverse Effects of Medical Devices', in accordance with 1) to the Director of the Ministry of Food and Drug Safety.

Duties of the principal investigator

1) The principal investigator shall promptly report all serious adverse events (except those stipulated in the clinical trial protocol or other documents such as clinical trial protocols or clinical investigator data books that do not require immediate reporting) in writing within the period specified in the clinical trial protocol in accordance with the reporting method specified in the protocol.

   In the event of a serious adverse event, regardless of whether it is causally related to the application of the investigational device, the principal investigator or person in charge shall report to the monitor agent (or person in charge) designated by Dalim Tissen Co., Ltd. as described below within 24 hours. In addition, the institution shall report to the institution in accordance with the Institutional Review Board standards of the clinical trial site in which the serious adverse event occurred.
   of the subject's personal information, such as the subject's name, social security number, and address, in order to protect the confidentiality of the subject's personal information, and shall follow the instructions provided by the sponsor regarding the reporting of adverse events, if any.

2) The principal investigator shall report to the sponsor within the period specified in the protocol for adverse events or abnormalities in laboratory test results that are separately designated as important in relation to safety evaluation in the protocol in accordance with the reporting method specified in the protocol.

3) If a death is reported, the principal investigator must provide additional information to the sponsor and the review committee, such as an autopsy report (only if an autopsy was performed) and terminal medical reports.

14.3.2 What to do in the event of a serious adverse event

Follow-up should be followed until the serious adverse events have resolved, reached a stable state, or the investigator determines that they are no longer clinically significant. During the clinical trial, the principal investigator and the investigator must make every effort to ensure the safety of the subjects, and in the event of a serious adverse event, take prompt and appropriate measures to minimize adverse events.

15. INFORMED CONSENT FORM

In the conduct of this study, the investigator shall fully explain to the subjects the content of the study, the effects of the investigational device, and adverse events in advance, obtain the consent of the subjects, fill out the consent form, and write the date of consent acquisition in the CRF and medical records. (Refer to 'Attachment 1: Informed Consent and Written Consent Form')

16. COVENANT ON VICTIM COMPENSATION

'Annex 2. Regulations on Compensation for Victims'

17. MATTERS CONCERNING THE SUBJECT'S CARE AFTER THE TRIAL

Subjects who are dropped out of the clinical trial or have no response will be instructed to receive other appropriate treatments, and subjects who have been terminated from the clinical trial will be able to receive medical treatment at any time according to the doctor's advice in case of unexpected delayed adverse events. The compensation evaluation criteria for medical expenses, etc. incurred during medical treatment/treatment are 'Attachment 2. Regulations on Compensation for Victims'.

18. MEASURES FOR THE SAFETY PROTECTION OF SUBJECTS

18.1 Obligations for the safety protection of subjects

The obligations of clinical trial institutions, institutional review boards, principal investigators, investigators, sponsors, and monitoring personnel to protect the safety of subjects are as follows.

Clinical Trial Sites

The head of the clinical trial site shall be equipped with the necessary clinical trial rooms, facilities, and professional personnel to conduct the clinical trial, and shall be able to conduct the clinical trial appropriately, such as taking necessary measures in case of emergency.

Institutional Review Board

The Institutional Review Board shall be constituted in accordance with domestic laws/practices. The IRB must protect the rights, safety, and welfare of subjects, and if a subject in a vulnerable environment participates in a clinical trial, it must carefully review the validity of the reasons.

The Institutional Review Board shall take necessary measures to the principal investigator, such as ordering the suspension of part or all of the clinical trial, if the subject's consent to participate in the trial is not properly obtained in the performance of its duties, if the clinical trial is not conducted according to the clinical trial protocol, or if serious adverse events appear.

Examiner

The term "investigator" refers to the principal investigator and the person in charge of the exam. The investigator must conduct the clinical trial in accordance with the clinical trial protocol agreed with the sponsor and approved by the Institutional Review Board and the Director of the Ministry of Food and Drug Safety.

During or after the clinical trial, the investigator shall take measures to ensure that the subject receives appropriate medical treatment for all adverse events that occur in the clinical trial, including abnormalities in clinically meaningful laboratory test values, and shall inform the subject of the need for medical treatment for the subject's intercurrent illness that the investigator becomes aware of. In addition, according to paragraph 14.3.1. Procedures for Reporting Serious Adverse Events, the investigator has the obligation to recognize the adverse event and report to the principal investigator, and the principal investigator has the obligation to report the adverse event reported by the investigator to the sponsor.

The investigator accurately analyzes and understands the clinical trial plan and actively responds to the subject's problems.

Sponsor

It refers to individuals, companies, implementing institutions, and organizations that are responsible for the planning, management, and finance of clinical research. The clinical trial subject, test method,

and the format and content of the CRF must be made in accordance with the procedures of the clinical trial protocol.

The sponsor's inspection plan and procedures should be determined based on the importance of the trial, the number of subjects, the type and complexity of the trial, the degree of potential risk to the subject, and the problems in the conduct of the clinical trial that have already been identified.

18.2 Confidentiality

The identity of all subjects will be kept confidential and will be recorded and evaluated using the number (identification code) given during the trial. Inform the subject that all test materials are stored on a computer and are treated as strictly confidential. The signed informed consent form will be kept by the principal investigator or investigator.

Sponsors, monitors, and inspectors involved in this study may access the subject's records for the purpose of monitoring, checking, and managing the progress of this study. By signing this protocol, the investigator acknowledges that the sponsor or the monitor and inspector of the contract research organization may review or copy the relevant documents to verify the subject's medical records and CRF records in terms of domestic laws and ethics. Such information must be kept confidential, and facilities and management standards for confidential storage must be in place. On the other hand, all documents related to clinical trials, such as CRFs, are recorded and distinguished by the initials and identification codes of the subject's name, not the subject's name.

19. OTHER MATTERS NECESSARY FOR SAFE AND SCIENTIFIC CONDUCT OF CLINICAL TRIALS

19.1 Ethical conduct of clinical trials

This clinical trial will be conducted in compliance with and in accordance with relevant laws and regulations, such as the Declaration of Helsinki (Recommendations for Physicians on the occasion of biological research on the human body), the Enforcement Regulations of the Medical Device Act, and the Full Provision of the Regulations on Approval of Medical Device Clinical Trial Plans.

19.2 Clinical Trial Sites

The head of the clinical trial institution shall equip the clinical trial room, facilities, and professional personnel necessary for the implementation of the clinical trial at each stage of the clinical trial, and make perfect preparations to properly conduct the clinical trial.

19.3 Quality control and quality assurance of materials

19.3.1 monitoring

Clinical trial monitoring is handled by the sponsor or the institution entrusted by the sponsor. The monitor personnel will consult with the investigator regarding the actual conduct of the clinical trial and compliance with the protocol/GCP/ all applicable regulatory requirements.

The investigator will allow the monitor agent to regularly review all CRFs and corresponding supporting documents (e.g., medical, hospital, and clinical laboratory records of individual trial participants) at mutually convenient times during and after completion of the trial. Therefore, the monitor can directly view these recorded documents. Monitoring visits provide an opportunity to assess the progress of the trial, verify the accuracy and completeness of the CRF records, ensure compliance with all protocol requirements, applicable regulations, and investigator obligations, and resolve any discrepancies in the trial records.

19.3.2 Audit and Inspection

The investigator allows auditors to conduct audits of this clinical trial and inspections by the Ministry of Food and Drug Safety. The primary purpose of the inspection and survey is to determine whether the rights, safety, and welfare of the enrolled subject are being protected, or whether the enrolled subject (i.e., signing the consent form and going through the trial procedures) is suitable for the trial, as well as to ensure that all information that is valid for the evaluation of the investigational device is processed/reported in compliance with the planned preparation, protocol, SOPs of the institution and IRB, GCPs, and applicable regulatory requirements. The investigator will provide direct access to all clinical trial documents, evidence records, and evidence data. If the Ministry of Food and Drug Safety notifies the investigator of the intention to conduct a fact-finding investigation, the investigator must immediately notify the sponsor.

19.3.3 Data Management

The monitoring personnel shall ensure the concordance between the CRF and the evidence and the appropriateness of the case report description. In addition, the data manager checks the appropriateness of the CRF description, whether the description is accurately entered into the computer, and whether there are any logical contradictions on the computer.

If there are inconsistencies in the supporting data, inadequacy of the description, and ethical contradictions, the validity of the relevant items should be reviewed together with the data manager and the investigator, and the case record should be corrected if necessary. The client declares a data lock after confirming that there are no abnormalities in the CRF and the final data through the data manager and tester.

19.3.4 Quality Assurance for Data

The sponsor conducts inspections and guarantees the quality of the data.

19.4 Explanation of the clinical trial plan to the principal investigator and investigators

The sponsor shall explain the contents of the clinical trial plan to the principal investigator, investigator, clinical trial coordinator, and clinical trial medical device manager before initiating the clinical trial.

19.5 Agreement and compliance with clinical trial plans

The sponsor shall agree with the principal investigator on the contents of the clinical trial protocol and CRF and the compliance with the clinical trial plan. To ensure the above agreement, the principal investigator and the sponsor shall write the name and date on a separate signature page. The principal investigator and investigator shall conduct the clinical trial in accordance with the clinical trial protocol agreed with the sponsor and approved by the Clinical Trial Review Board and the Ministry of Food and Drug Safety.

19.6 Amendments to clinical trial protocols

If you want to obtain approval for a clinical trial or change the approved clinical trial to conduct it, you will obtain approval from the IRB of the relevant institution or the Ministry of Food and Drug Safety to change the clinical trial protocol for each stage of the clinical trial. In addition, the principal investigator must sign and date a separate agreement document to ensure consensus on the revised protocol or CRF, and proceed with the clinical trial in accordance with the approved protocol for the change. However, only in the following cases, a clinical trial may be conducted differently from the original clinical trial protocol before obtaining approval for the clinical trial change protocol.

1) If the immediate risk factor that has arisen in the subject needs to be eliminated
2) When it is necessary to change administrative procedures, such as changing the monitoring personnel, changing the test personnel, changing the emergency contact number, etc.

The principal investigator shall submit a document documenting the fact and reason for implementation and the change plan to the sponsor, the institution's Clinical Trial Review Board, and the Ministry of Food and Drug Safety as soon as allowed for changes that require the elimination of immediate risk factors that occur to the subject, and shall submit to the sponsor, the institution's Clinical Trial Review Board, and the Ministry of Food and Drug Safety for consensus and approval, respectively.

19.7 Termination of the trial

The end of this clinical trial shall be the date of the last visit of the last subject with the target number of cases. The principal investigator shall report the termination of the clinical trial to the clinical trial review board in writing after the application and observation of the medical device specified in the clinical trial plan for the final subject is completed.

19.8 Results Report & Publication

All data and results generated during this clinical trial period are owned by Dalim Tissen Co., Ltd., and the principal investigator and clinical trial manager shall prepare and publish a report on the content of the study for the results of the clinical trial conducted in accordance with this clinical trial protocol.

Authorship of the manuscript intended for submission to a medical journal will be determined in accordance with the principles outlined in the 'Uniform Requirements for Manuscripts Submitted to Biomedical Journals' established by the International Committee of Medical Journal Editors (ICMJE).

If the site is part of a multicenter clinical trial, the site and the site investigator must make a prior arrangement with Dalim Tissen Co., Ltd. prior to the scheduled announcement of the clinical trial results, and cannot publish or announce the results of the individual site in advance of the results of the multicenter clinical trial without the written consent of Dalim Tissen Co., Ltd.

As described below, the authors are ultimately responsible for their presentations and their decisions to submit them. In order to protect the intellectual property rights of Dalim Tissen Co., Ltd., all planned manuscripts, oral presentations, abstracts, and all clinical trial results/presentations based on clinical trials must be submitted to Dalim Tissen Co., Ltd. for review 30 days prior to the submission for publication or any form of presentation.

In the rare event that such an announcement affects the patent rights of all inventions entitled by DalimTissen Co., Ltd., DalimTissen Co., Ltd. protects its right to request an additional delay within 90 days of the scheduled announcement so that it can maintain its intellectual property rights.

19.9 Documentation Archive

A separate place for storing various materials and records related to the conduct of clinical trials should be prepared and secured to ensure good preservation. The storage period is in accordance with Article 24 of the Enforcement Regulations of the Medical Device Act (Standards for Conducting Clinical Trials, etc.), Paragraph 13.

1) Clinical trials for manufacturing, sale, and import product licenses (including modification permits): 3 years from the date of manufacturing, sale, and import product approval
2) Other clinical trial-related data: 3 years from the date of completion of the clinical trial

The sponsor must inform the investigator in writing about the need to preserve the data and the retention period, and if the sponsor determines that the data is no longer necessary, the sponsor must inform the principal investigator of this fact in writing.

19.10 Data provided by the sponsor to each clinical trial site

Investigational device, clinical trial protocol, CRF, major adverse event report, subject consent and written consent, investigational device receipt and payment record form, etc.

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