Novapak Prospective Observational Clinical Trial
Clinical Investigation Plan Version A
24-Oct-2022
NCT05747014

Medtronic

Clinical Investigation Plan

Clinical Investigation Plan/Study Title	Novapak Prospective Observational Clinical Trial
Clinical Investigation Plan Identifier	Novapak
Study Product Name	Novapak Nasal Sinus Packing and Stent
Sponsor/Local Sponsor	Medtronic ENT 6734 Southpoint Drive North Jacksonville, FL 32216 **Canada (Local Sponsor):** Medtronic Canada ULC 99 Hereford Street Brampton, ON, L6Y 0R3 Canada 1-905-460-3800
Document Version	A
Version Date	October 24, 2022
Document Reference Number	MDT22031

Confidentiality Statement

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1. Glossary

Term	Definition
ADE	Adverse Device Effect
AE	Adverse Event
ASADE	Anticipated Serious Adverse Device Effect
BIPP	Bismuth iodoform paraffin paste
CEC	Clinical Event Committee
CFR	Code of Federal Regulation
CIP	Clinical Investigation Plan
CRO	Clinical Research Organization
CRS	Chronic rhinosinusitis
CRF	Case Report Form
CTA	Clinical Trial Agreement
CV	Curriculum Vitae
DD	Device Deficiency
DMC	Data Monitoring Committee
DoH	Declaration of Helsinki
DTL	Delegated Task List
eCRF	Electronic Case Report Form
EC/IRB/REB/Ethics Board	Ethics Committee
ENT	Ear, nose, and throat
ESS	Endoscopic sinus surgery
FAL	Foreseeable Adverse Event List

Term	Definition
FD	Financial Disclosure
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act
FEDS	Functional endoscopic dilation sinus surgery
FESS	Functional endoscopic sinus surgery
GCP	Good Clinical Practice
HCL	Hydrochloric acid
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator Brochure
IC	Informed Consent
ICH	International Conference of Harmonization
IRB	Institutional Review Board
IFU	Instructions For Use
MDD	Medical Device Directive
MedDRA	Medical Dictionary for Regulatory Activities
MHLW	Ministry of Health, Labour, and Welfare
MN	Minnesota
MW	Molecular weight
NP	Nasal polyposis or Nasal polyps
NSR	Non-Significant Risk
OR	Operating room
PETG	Polyethylene terephthalate glycol
PHI	Protected Health Information

Term	Definition
QoL	Quality of Life
RA	Regulatory Authority
REB	Research Ethics Board
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SBS	Solid Bleached Sulfate
SC	Steering Committee
SNOT-22	Sino-Nasal Outcome Test-22
SR	Significant Risk
SID	Subject Identification
UAE	Unavoidable Adverse Event
US	United States
USP Grade	United States Pharmacopeial Convention Standard

Device Trademarks

Novapak™ is a trademark of Medtronic Xomed, Jacksonville, FL, USA.

2. Synopsis

Title	Novapak Prospective Observational Clinical Trial
Clinical Study Type	Prospective, Observational, Case-Series, Post-Market, Clinical Trial
Product Name	Novapak Nasal Sinus Packing and Stent CS3600 and CS3900
Sponsor	Medtronic ENT 6743 Southpoint Drive North; MS SS-54 Jacksonville, FL 32216 All funding for this study will be the responsibility of this sponsor.
Local Sponsor	Medtronic Canada ULC 99 Hereford Street Brampton, ON, L6Y 0R3 Canada 1-905-460-3800
Indication under investigation	The Novapak Nasal Sinus Packing and Stent is intended for use in patients undergoing nasal/sinus surgery as a space-occupying stent to: • Separate tissue or structures compromised by surgical trauma. • Separate and prevent adhesions between mucosal surfaces in the nasal cavity. • Control minimal bleeding following surgery or trauma by tamponade effect, blood absorption, and platelet aggregation. • Act as an adjunct to aid in the natural healing process. Novapak Nasal Sinus Packing and Stent is indicated for use as a nasal packing to treat epistaxis. This study will be conducted in accordance with these indications.
Investigation Purpose	Obtain clinical data on the safety and effectiveness of the Novapak device under use as intended in the device indications.
Product Status	This study will be conducted in geographies where the Novapak device is commercially released.
Primary Objective(s) and/or Endpoint(s)s	The primary objective is to assess the safety of the Novapak Nasal Sinus Packing and Stent device used as indicated post-operatively in patients undergoing nasal/sinus surgery by: • Collecting all AEs directly attributed to the device and/or those that cannot be determined; and calculating a point estimate and confidence interval • Collecting all AEs and calculating an overall rate and safety profile for the device
Secondary Objective(s) and/or Endpoint(s)	The secondary objectives are to confirm device effectiveness during the procedure, 2 weeks and 1-month post treatment.

<table>
<tr><td>Study Design</td><td>Prospective, observational, multi-site, non-controlled, non-randomized, case-series, with a 2 week and 1-month follow-up in adults undergoing nasal/sinus surgery with Novapak Nasal Sinus Packing and Stent device used as indicated post-operatively</td></tr>
<tr><td>Sample Size</td><td>This study will include a minimum of 75 subjects.</td></tr>
<tr><td>Inclusion/Exclusion Criteria</td><td>Inclusion Criteria
1. Subject is at least 18 years of age.
2. Subject undergoing nasal/sinus surgery with the intended need for nasal sinus packing (i.e., Novapak).
3. After being informed of the nature of the study; the subject understands, agrees to its provisions, is willing to participate and provide written consent.
4. Mentally stable and able to follow the instructions for self-assessment/questionnaire completion.
Exclusion Criteria
1. Subject has a shellfish allergy.
2. Subject has known bleeding disorder or prescribed anticoagulants.
3. Subject has craniofacial abnormalities that may interfere with access to the sinuses.
4. Subject is immunocompromised (e.g., taking immunosuppressive medication).
5. Subject is participating in another investigational device, biologic, or drug study and has not completed the primary endpoint(s) or if there is a potential for clinical interference beyond the primary endpoint.</td></tr>
<tr><td>Study Procedures and Assessments</td><td>
<table>
<tr><td>Visit</td><td>Procedure</td><td>Data Collection</td></tr>
<tr><td>Pre-Surgery</td><td>Inform subject about the study requirements
Ask shellfish allergy questions
Schedule surgery</td><td>Consent document signed
SNOT-22 (subject)</td></tr>
<tr><td rowspan="2">Surgical Procedure (Day 0)</td><td>Endoscopic exam</td><td>Lund- Mackay Scores
Lund-Kennedy Scores (baseline)</td></tr>
<tr><td>Functional Endoscopic Sinus Surgery
Other interventions if bleeding more than minimal</td><td>Procedural Details
Boezaart Surgical Field Grading Scale[77] (pre-packing)
Boezaart Surgical Field Grading Scale[77] (post-packing)</td></tr>
</table>
</td></tr>
</table>

			Collect Adverse Events and/or device deficiencies Question: Bleeding controlled post packing?
	Day 1, 2, 3…	Daily Irrigations	Subject records volume / date Subject records any Adverse Events
	Day 14 (-2, +5)	Office Visit Endoscopic exam Observe for residual product (remove) Debride Adhesions (if necessary) Review Subject Irrigations Records	SNOT-22 (subject) Lund-Kennedy Scores Question: residual product? Score Adhesions (Valentine method[44]) Question: Bleeding controlled? Collect Adverse Events and/or device deficiencies
	Day 30 (-2, +12)	Office Visit Endoscopic exam Debride Adhesions (if necessary)	SNOT-22 (subject) Lund-Kennedy Scores Score Adhesions (Valentine method[44]) Collect Adverse Events and/or device deficiencies
Safety Assessments	Collect all AE observations and characterize those that are device related.		
Statistics	1. All continuous variables summarized as the number of subjects, means, standard deviations, medians, minimums, maximums, and interquartile ranges. 2. Categorical variables will be summarized as frequencies and percentages. 3. Analyses of the primary and secondary endpoints will be descriptive.		

3. Introduction

3.1 Background

Chronic rhinosinusitis (CRS) affects millions of people each year,[1,2] a condition defined as symptoms lasting for more than 12 weeks without complete resolution and with or without nasal polyps. Symptoms include inflammation of the nose and the paranasal sinuses with either nasal discharge or nasal blockage, obstruction, or congestion, with or without facial pain and/or pressure with or without reduction or loss of smell.[3] In most cases, medical management is sufficient to relieve the symptoms, and if that should fail, surgical procedures are well-established. Approximately 250,000 sinus procedures are performed each year in the US to relieve acute rhinosinusitis (ARS) or CRS, most commonly known as functional endoscopic sinus surgery (FESS).[1-3]

Dressing and packing devices in the ear, nose, and throat (ENT) and other procedures such as FESS are commonly used to absorb fluids during or after surgery, to improve and maintain hemostasis, to allow wounds to heal postoperatively, and/or when local measures have proven unsuccessful in controlling minor or severe epistaxis (bleeding). Dressings and packing products are some of the most common products used in surgeries. These types of dressing and packing products are placed in the affected area by physicians until sufficient pressure exists to tamponade the bleeding.[4-11] The use of chitosan as a packing material has revealed several favorable biological properties (i.e., biocompatibility, biodegradability, low toxicity, and mucoadhesiveness), thus making this polymer a promising substrate for biomaterial medical devices. The general safety of chitosan has been found quite satisfactory in recent review articles.[11-23]

Other efficacious and well-tolerated options are gauze, synthetic sponge packs, and balloon packing, which are the most conservative approaches to controlling any kind of bleeding. Some products such as gauze or sponges can be coated with an antibiotic or a product such as bismuth iodoform paraffin paste (BIPP) to prevent infection.[8-10,24-26] Variances in the devices (i.e. size, shape, attachment of a string) have been made to allow for convenient access to certain parts of the anatomy. For example, standard gauze or sponges are used to treat bleeding in the anterior nasal area; however, epistaxis originating in the posterior nasal source would indicate the need for long ties attached to the gauze pack or sponges for easy removal. An alternative device to posterior packing is a balloon catheter which can be inserted into the nasopharynx via the nostrils and inflated with sterile water.[27,28] Over time, the balloon deflates and the volume drops, therefore it can remain in the cavity for up to 72 hours. Most gauze and sponges used in patients with CRS or other procedures are removed within 48 hours, depending on the extent of the bleeding.[5,6,24,29,30]

No consensus has been established about nasal splint or nasal packing choices and intranasal stay of nasal splints after surgery.[31] Researchers have observed no difference in pain and the perception of nasal fullness or complications such as synechia, infection, hematoma, or perforations when nasal splints remained in place for 3, 5, or 7 days.[31-33] Some data have suggested superior performance of

bioabsorbable (dissolvable) packs compared with non-absorbable packs with respect to patient comfort. For hemostasis and wound healing, variation in performance metrics makes interstudy comparison difficult.[34-36] Weber (2001 and 2009) and Zhao (2013) confirm that <3 days of intranasal stay of nasal packing is non-influential on the surgical outcome and non-functional for prevention of adhesions. [32,33,37] In order for wound healing to take place, a minimum of 5 to 7 days and up to 2 weeks with appropriate changing of dressing is recommended in other studies.[38-40]

Medtronic Xomed has developed a nasal sinus stenting / packing material for use in post-sinus surgery, including ESS. Many new biomaterials have been developed to control hemostasis, reduce adhesion formation, and improve healing. Several biomaterials are used for post-surgical nasal packing in the field of otorhinolaryngology including those that contain chitosan.[41-44] Chitosan is a kind of natural polysaccharide that is widely exploited for biomedical applications due to its good biocompatibility, low immunogenicity and specific biological activities.[45] Chitosan is derived from the shells of crustaceans (e.g., crab, shrimp), and has demonstrated biocompatibility and high biodegradability, including being easily excreted in the urine.[12,14,21,42,43,45-47] Used for post-surgical nasal packing in the field of otorhinolaryngology, chitosan has been developed to control hemostasis and reduce adhesion formation and improve healing.[12,15-18,20-22,41-43] Chitosan-based in situ gelling systems have already gained much attention as smart biomaterials in the development of several biomedical applications, such as for drug delivery systems and regeneration medicine.[14,21,23,45,48]

Products made from chitosan have shown good hemostatic control and improved healing in animal and human studies. [28,41,42,44,49-54] Absorbable dressings for ENT surgery made with chitosan are Hemopore® Hemostatic Bioresorbable Nasal Dressing (Stryker Neuro Spine ENT, Kalamazoo, MI, USA), PosiSep™ and PosiSep™ X Intranasal Splints (Hemostasis, LLC, Saint Paul, MN, USA), and XeroGel® (Entellus Medical™, Plymouth, MN, USA). Other non-chitosan-derived absorbable nasal dressings are MeroGel® Nasal Dressing and Sinus Stent (Anika Therapeutics, Inc., Bedford, MA, USA; Medtronic Xomed, Jacksonville, FL, USA), MeroPak® Bioresorbable Nasal Packing and Sinus Stent (Medtronic Xomed, Jacksonville, FL, USA), Nasastent® (Arthrocare Corporation, Austin, TX, USA), Surgicel® Original Absorbable Hemostat, Ethicon US, LLC, a J&J company, Cincinnati, OH, USA), Oxycel (Woundcare, Worcester, England), Stammberger Sinu-Foam® (Arthrocare ENT Corporation, Austin, TX, USA and Remscheid, Germany) Surgi shield (D. med, Seoul, South Korea), and NasoPore® (Stryker Neuro Spine ENT, Kalamazoo, MI, USA). It is important to note that in the literature, the term absorbable has been typically used interchangeably with the term dissolvable though most of these dressings do not absorb into local tissue.

3.2 Purpose

Medtronic, Inc. is sponsoring the Novapak Nasal Sinus Packing and Stent Study, a prospective, observational, multi-site, non-controlled, non-randomized, case-series, investigational, clinical study. The purpose of this study is to assess the safety of the Novapak Nasal Sinus Packing and Stent device

used as indicated post-operatively in patients undergoing nasal/sinus surgery. In addition, this study will observe some key measures of device effectiveness from the physician and subject perspective.

The Novapak Nasal Sinus Packing and Stent study is being conducted as a non-significant risk post-market investigational study in the US and Canada in accordance with Canadian local regulations and ISO 14155:2020 in support of EU MDR regulatory submission for a CE Mark.

4. Objectives and/or Endpoints

4.1 Objectives

The study is being conducted to support the safety profile of the Novapak Nasal Sinus Packing and Stent device used as indicated post-operatively in patients undergoing nasal/sinus surgery.

4.1.1 Primary Objective(s)

The primary objectives of this study are to assess the safety profile of the Novapak Nasal Sinus Packing and Stent device used as indicated post-operatively in patients undergoing nasal/sinus surgery.

4.1.1.1 Primary Study Endpoint(s)

The study endpoints for safety will be:

1) the statistical analysis of designated primary safety endpoint AEs that are directly attributable to the device and/or for which direct cause cannot be determined
2) the rate of all AEs as defined below. Refer to **Section 13** for more details regarding endpoint analysis. The data resulting from this study will be summarized in a final report generated by the Study Sponsor.

4.1.1.1.1 Primary Device Safety Endpoints

The primary safety endpoint is an assessment of all AEs that are directly attributable to the device and/or for which cause cannot be determined, and that meet the definition of designated primary safety endpoint AEs (see section 11.4) that will be used to determine the point estimate and its confidence interval. This endpoint will be analyzed by calculating the point estimate with a confidence interval of its rate. All AEs will be collected for each subject from time of treatment until their study completion. Study completion for each subject is the time point at which the 30-day follow-up visit is completed, outstanding AE follow-up (if any) has been concluded, and a Study Exit CRF has been completed. For subjects who withdrew or were lost to follow-up, study completion will be the date of withdrawal or the date the subject meets the definition of lost to follow-up. Refer to **Section 13** for how missing data will be handled.

4.1.1.1.2 Secondary Safety Endpoint

The secondary safety endpoint is the tabulation of all AEs (both device related AEs used in the primary safety endpoint and all other AEs) for the overall AE rate to establish a safety profile for use of the

Novapak device. All AEs will be collected for each subject from time of treatment until their study completion. Study completion for each subject is the time-point at which the 30-day follow-up visit is completed, outstanding AE follow-up (if any) has been concluded, and a Study Exit CRF has been completed. For subjects who withdrew or were lost to follow-up, study completion will be the date of withdrawal or the date the subject meets the definition of lost to follow-up. Refer to **Section 13** for how missing data will be handled.

4.1.2 Secondary Objective(s)

The secondary objectives of this study will gather data to support the effectiveness of Novapak's inherent features and claims of performance:

Adhesions – Sinus packing devices act as a space occupying stent to prevent raw tissues from contact and forming unwanted, obstructive tissue connections known as synechia or adhesions. This study will collect the number of adhesions observed by endoscopic examination as well as a grade of the adhesions based on the percentage of vertical height of the middle turbinate taken up by the adhesion. This data will be compared to historical data related to adhesions post sinus surgery.

Control of bleeding – Sinus packing devices control bleeding by absorption and pressure on the bleeding surfaces known as the tamponade effect. Chitosan a component of Novapak also has hemostatic properties. This study will collect data related to post-operative bleeding. Since bleeding can be different for each subject and based on the extent of tissue trauma; a baseline observation immediately post-surgery using the Boezaart Surgical Field Grading Scale will be collected. After the packing is applied the surgical field will be graded again. In addition, any residual bleeding will be observed and noted at the subject visits.

Aid in healing – Novapak acts as an adjunct to aid in the natural healing process by providing a moist environment for the tissues during the proliferation phase of wound healing. In addition, the chitosan component within Novapak has hemostatic properties and is antibacterial to reduce unwanted microbial action which could lead to inflammation. The physician will grade the sinuses before surgery and then at each subject visit using the Lund-Kennedy scoring system. In addition, the subjects will provide sinus health responses to the SNOT-22 questionnaire prior to surgery and again at each subject visit.

Novapak is a dissolvable sinus packing device that under normal use with daily irrigation will be eliminated from the sinuses without the need for removal from the physician. An observation of residual Novapak will be done by the physician at each subject visit. These observations will be compared to the subject's compliance to daily irrigation.

5. Study Design

Prospective, observational, multi-site, non-controlled, non-randomized, case-series, with adult subjects undergoing nasal/sinus surgery and using Novapak Nasal Sinus Packing and Stent device used as indicated post-operatively with 14-day and 30-day follow-up visits. The study is expected to be conducted at up to 5 study sites located in the US and/or Canada. A minimum of 75 subjects will be enrolled in the study and one device is expected to be used per subject. Study sites that enroll faster than others will be allowed to do so in order to maintain an adequate enrollment rate; however, there is a site maximum enrollment of 60% (45 subjects) of the total enrollment. No known factors have been foreseen that may compromise the outcome of the clinical study or interpretation of the results.

5.1 Duration

The expected total study duration is approximately 9 months, based upon the following assumptions: 5 months for subject enrollment, 1 month for last subject follow-up, and 3 months for data cleaning, analysis, and final report distribution. The duration of individual subject participation will vary based on timing of study site enrollment procedures, review of eligibility criteria, and scheduling sinus surgery; however, at a minimum, participation of an individual subject will be at least 1 month.

Site activation and initiation activities may take approximately 3 months prior to any subject enrollment but this may vary per site.

5.2 Rationale

This study is being conducted to support the safety and treatment effectiveness profile of the Medtronic Novapak Nasal Sinus Packing and Stent device as a post-surgical space-occupying stent for use in patients undergoing nasal/sinus surgery. The data from this study will support the claims stated in the product labeling related to adhesion prevention, control of minimal bleeding and acting as adjunct to aid in the natural healing process.

The single-arm prospective design was chosen as the best option for obtaining the desired data. We rejected designs that use an inappropriate control device that is either non-dissolving, dissolves at a different rate or consistency, or a no treatment arm without packing.

5.3 Study Oversight

The study will utilize our internal ENT Medical Director, to advise on the scientific content of the study and provide input for the execution.

6. Product Description

6.1 General

The Medtronic Novapak device is a single-use, nasal packing and stent for use following sinus surgery to prevent adhesions, control mild bleeding, and provide a level of antibacterial effectiveness. Novapak is

composed of formulated chitosan and cellulose ingredients that is lyophilized (freeze dried under vacuum) in a sponge form. The sponge can be compressed for insertion into anatomy and can be cut to size.

The Novapak Nasal Sinus Packing and Stent device will be used within intended use as described in the IFU (document M977497A001 C) product labeling which is cleared under US FDA 510k regulations (K202623) and as per Health Canada License 103651 for Canada.

The device is sterile, single-use, with duration of use at 7-14 days with adequate irrigation within a single surgery. No long-term use of the device is considered or indicated.

Shelf-life is determined by the packaging materials and the materials of the device(s) and components within the device(s). The device and packaging are expected to be stable over extended periods of time.

The Chitosan HCL material is derived from the exoskeleton (shell) of shellfish specifically from snow crab (Chinoecetes opilio). The shells are deproteinized, decalcified and deacetylated; the final product Chitosan HCL is deemed non-viable.

The Novapak sponge is intended for use in patients undergoing nasal/sinus surgery as a space occupying packing and is intended for single use for 7-14 days with adequate irrigation. Novapak is also an invasive non-implantable device (**Table 1**).

Table 1: Materials in Contact with Tissues and/or Body Fluids

Device	Use	Invasive/ Non-invasive	Implantable/ Non-implantable	Duration of use	Contact with Body	Body Contact	Materials
CS3600 Novapak, standard	Single use / dissolvable	Invasive	Non-implantable	7-14 days with adequate irrigation	Yes	Nasal cavity	Chitosan HCL; Cellulose – sponge scaffolding
CS3900 Novapak, firm	Single use / dissolvable	Invasive	Non-implantable	7-14 days with adequate irrigation	Yes	Nasal cavity	Chitosan HCL; Cellulose – sponge scaffolding

Novapak hydrates with sterile saline and forms a gel. The sponge dissolves within the nasal cavity with daily irrigation and natural mucus flow over several days. Residence time is typically 7-14 days with adequate irrigation. Alternately, the dressing may be removed through gentle aspiration at the discretion of the physician. Figure 1 depicts the Novapak Sponge (8 cm long by 1.8 cm wide and 1.3 cm tall).

Figure 1: Novapak Sponge (photo of 2 sponges)

Class of Device: Class I sterile (US FDA); Class II (Canada); Class III sterile (EU MDR)
Device Identifier: 20643169662241 (for CFN CS3600-10), 20643169662227 (for CFN CS3600-2), 20643169662258 (for CFN CS3900-10), 20643169662234(for CFN CS3900-2)
Device CFNs: Novapak Standard (CS3600); Novapak Firm (CS3900)
Device or therapy or technology group the device belongs to: ENT Tissue Health

The study will be conducted using the products/components described in the table below. Instructions for use of the devices used in this study are provided in their respective manuals or IB. As a fully commercially released medical device, Novapak has undergone required verification and validation testing as well as biocompatibility testing in accordance with ISO 10993-1:2018.

Table 2: System Product / Component Information

Model Number (CFN)	Component (Manufacturer)	Investigational or Market-released
CS3600	Novapak Standard	Market released
CS3900	Novapak Firm	Market released

6.2 Dosage Form and Route of Administration

The Novapak Nasal Sinus Packing and Stent is applied to the internal nasal passages by direct insertion through the nasal opening. It may be compressed and or folded to a thin sheet and trimmed before insertion to fit an individual anatomy. It will absorb body fluids in the immediate area of insertion and should be hydrated with sterile surgical irrigation fluid (i.e., Saline) to fully form the sponge.

6.3 Manufacturer

The following table contains the manufacturer details.

Table 3: Manufacturer Contact Details

Name of the Device	Medtronic Novapak Nasal Sinus Packing and Stent
Legal Manufacturer	Medtronic ENT 6743 Southpoint Dr. North Jacksonville, FL 32216 USA

6.4 Packaging

The primary packaging for each Novapak Nasal Sinus Packing and Stent device consists of a thermoformed PETG tray sealed to a non-porous foil lid. These sealed tray assemblies are packaged and sold in SBS paperboard cartons in packs of two or ten devices for both the standard and firm device formulation. A SBS paperboard insert is used to organize and protect the trays within the sales unit carton. Each sealed tray and sales unit carton is labeled with a paper-based adhesive label printed with resin-based black ink. Each sales unit carton includes a paper instruction for use (IFU) document and is sealed closed with a blank, paper-based adhesive label.

Study product is available commercially and as such, current labeling for the study product and reference/technical manual(s) where clinical indications and contraindications for use and any cautions and warnings can be found in the Instructions for Use provided with the devices.

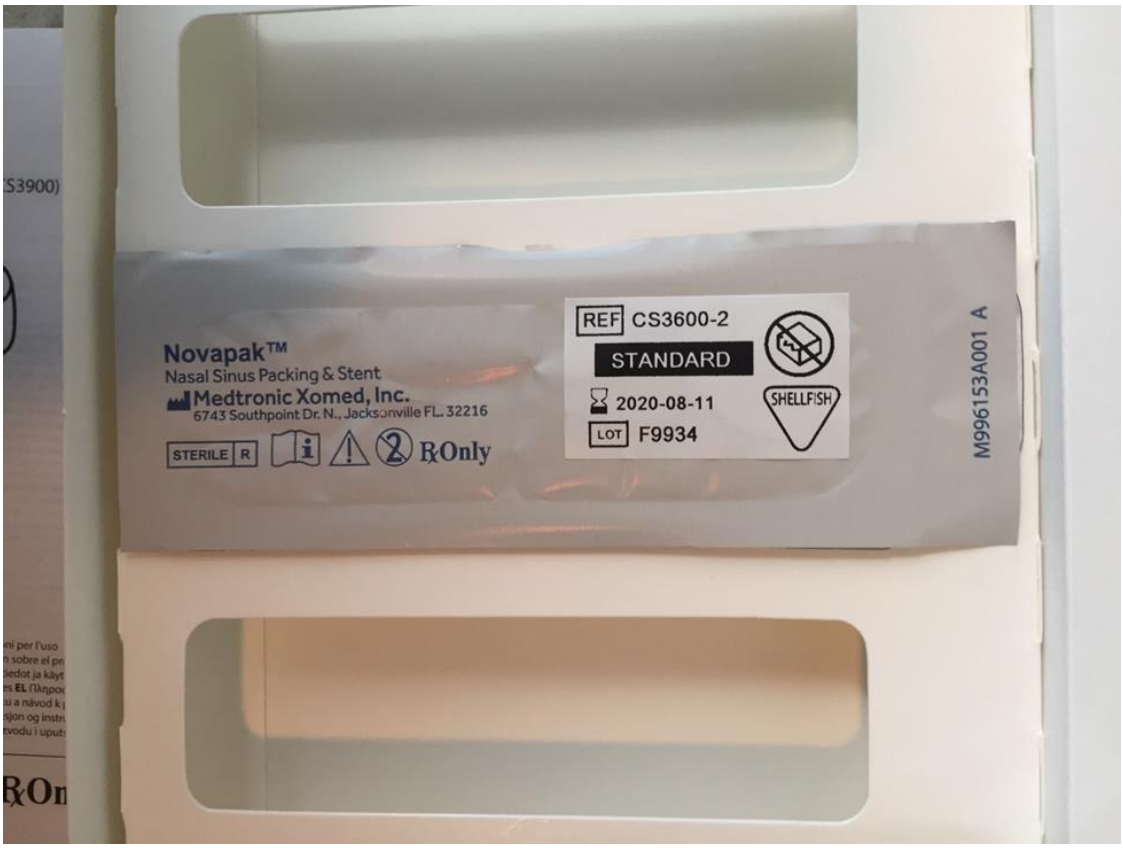

Figure 2 Example of Product Inner Label

6.5 Intended Population

The Medtronic Novapak nasal packing and stent is indicated for use in adults following sinus surgery to prevent adhesions, control mild bleeding, and provide a level of antibacterial effectiveness.

6.6 Equipment

The following equipment must be available at each study site to support study activities:

- Nasal Endoscope (used for physician examination of the subject sinus tissues)

No monitoring, maintenance or calibration is required for a nasal endoscope.

The Novapak Nasal Sinus Packing and Stent device is commercially available; therefore, devices used in this study will be taken from the stock shelves of each individual site. In this study, the devices are being used according to their cleared indications. Disposition management of all device inventories by investigational sites will be in accordance with their respective operating policies, this protocol and applicable regulatory agency regulations.

6.7 Product Use

The Medtronic Novapak Cellulose/Chitosan stent (sponge) is provided as a dry sponge which can be compressed to fit into anatomy and can be hydrated (before or after insertion) with saline. The stent shall degrade and dissolve away within 1-2 weeks (CS3600 ~1 week, CS3900 ~2 weeks) via bio-erosion into a gel. Novapak sponge (CS3600 & CS3900) is manufactured using a lipolyzed process. Packaged product is sterilized via E-Beam. Medtronic Xomed Jacksonville facility controls inventory storage, and release.

The Novapak material provides stenting of the middle meatus of the nasal cavity by physically separating the tissue surfaces (See anatomy in Figure 3) and preventing adhesion formation. The Novapak material controls minimal bleeding and oozing of the debrided mucosal surfaces via tamponade effect, blood absorption and platelet aggregation as a result of material application. The hemostatic properties are a known characteristic of chitosan materials.[12,28,44,54-65] The Novapak material provides a moist environment which aids in the healing process post-surgery. In addition, Novapak has demonstrated a level of antibacterial effectiveness during in vitro testing.[14,42,66-72] The main component in Novapak is Chitosan HCL, which is a cationic biopolymer with inherent properties that make it antimicrobial. The gel forms an antibacterial barrier at the wound site, thus preventing both bacterial growth on the device and the penetration of microbes.[73] The method of elimination of the Novapak material is via hydrolysis during irrigation, and is expelled from the body via swallowing and ingestion or through the nares.

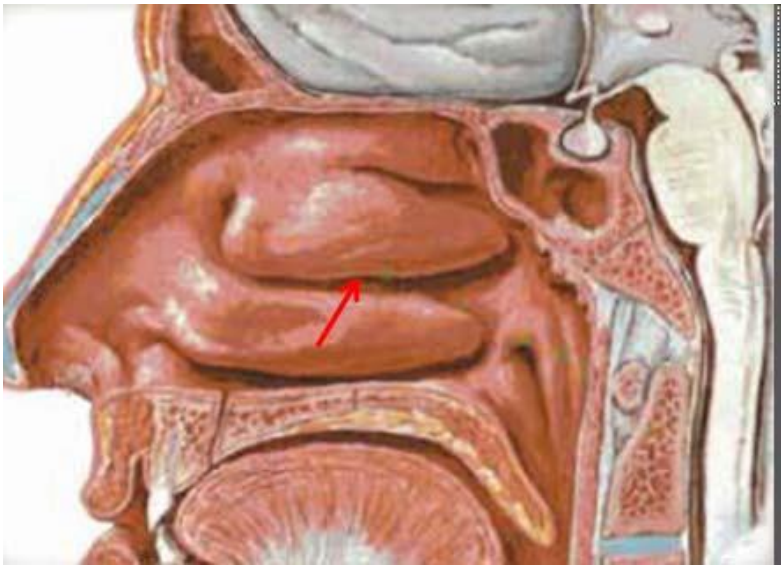

Figure 3: Anatomy of Application Site

6.8 Product Training Materials

This device is intended for use by healthcare practitioners trained in the treatment described in the indications for use. No specific device use training is required or expected for the healthcare practitioners participating in this study.

6.9 Product Storage

Since Novapak is a commercially released product, it is the responsibility of the investigator to correctly handle, and store, products maintained at the study site according to the IFU.

6.10 Product Return

No product will be returned to Medtronic.

6.11 Product Accountability

Product delivery:

Commercially available product supply will be managed in a manner consistent with other market-released products.

Product receipt and tracking:

All products used in this study will be market released in the geographies they are used. If there are additional local requirements related to the Novapak Nasal Sinus Packing and Stent device beyond what is collected by Medtronic on the eCRF, this is the Investigator's responsibility and should be recorded in the subject's medical records, but will not be collected by Medtronic (e.g., national registration card number, identification code linked to names and contact information, log of all subjects enrolled in the study, lot or batch number).

7. Study Site Requirements

7.1 Investigator/Investigation Site Selection

All investigators managing the subject's sinus and upper airway health must be qualified practitioners and experienced in the diagnosis and treatment of subjects with sinus disease. All ENT physicians must be experienced and/or trained in the handling of Medtronic Novapak.

The role of the principal investigator is to implement and manage the day-to-day conduct of the clinical investigation as well as ensure data integrity and the rights, safety and well-being of the subjects involved in the clinical investigation.

The principal investigator shall:

- Be qualified by education, training, and experience to assume responsibility for the proper conduct of the clinical investigation

- Be experienced in the field of otorhinolaryngology, sinus surgery and the application nasal sinus packing and stenting (e.g., use of Medtronic Novapak)
- Disclose potential conflicts of interest, including financial, that interfere with the conduct of the clinical investigation or interpretation of results
- Be able to demonstrate that the proposed investigational study site:
  - Has an adequate pool of eligible subjects within the recruitment period
  - Has one or more qualified investigators, a qualified investigational study site team and adequate facilities for the foreseen duration of the clinical investigation

Study site personnel training will be completed and documented prior to participation in this study.

7.2 Study Site Activation

During the activation process (prior to subject enrollment), Medtronic will train study site personnel on the clinical investigation plan, informed consent, and on data collection and reporting tools. If new members join the study site team, they will receive training on the applicable study requirements relevant to their role before contributing to the study.

Prior to performing study related activities, all regulatory requirements shall be fulfilled, including, but not limited to the following:

- IRB/REB approval (and voting list, as required by local law) of the current version of the CIP and IC.
- RA approval or notification (as required per local law)
- Fully executed CTA
- Financial disclosure (if applicable)
- CV of investigators and key members of the investigation study site team (as required). The signature on the CV must be dated within 3 years prior to the date of activation of the study site.
- Documentation of delegated tasks
- Documentation of study training.

Additional requirements imposed by local regulations, the IRB/REB and RA shall be followed, if appropriate.

In addition, all participating study site staff must be trained on the current version of the CIP as well as on the applicable study requirements depending on their role and must be delegated by the principal investigator to perform study related activities.

Medtronic will provide each study site with documentation of study site/investigator readiness; this letter must be received prior to performing study related activities.

7.3 Role of the Sponsor Representatives

In addition to performing monitoring and auditing activities, sponsor representatives may provide support at the study site as required for the study under supervision of the Principal Investigator, including:

- Provide study training relevant and pertinent to the involvement of personnel conducting study activities and investigator responsibilities
- Technical support at the site visits under the supervision of a study investigator, but no data entry, shall be performed by Medtronic personnel or their representatives at study sites

Sponsor representatives that provide study support will be documented on the site's Sponsor Technical Support list.

8. Selection of Subjects

8.1 Study Population

A sample size was selected that is adequate to assess the safety and treatment effectiveness of the Medtronic Novapak Nasal Sinus Packing and Stent device. The sample size is not based on a formal power calculation; however, results from no fewer than 75 subjects and one device used per subject are expected to provide sufficient evidence that the Medtronic Novapak does not introduce new complications or increase severity or likelihood of occurrence of existing complications in this population. It is anticipated that there may be subjects who will not receive nasal packing for any reason after enrollment (including withdrawal prior to treatment). Based on literature, it is expected that an average of one sinus per subject will be treated. Thus, if all 75 subjects have one sinus treated, data will be collected for approximately 75 sinuses. Note: all sinuses requiring treatment will be treated, 75 sinuses are the minimum number required for the protocol, but additional sinus data is likely.

In relationship to this unilateral or bilateral treatment, the number of devices used could be one or two per subject. Therefore, total product used in this study would be a minimum of 70 if a single device is used, to approximately 150 if two devices are used per subject. Note: Physicians are free to modify the size and shape of the device to fit in a unique individual anatomy.

8.2 Subject Enrollment

Enrollment of the subject will occur after the subject is screened for eligibility, informed of the study requirements and the subject signs the informed consent.

When a subject and the principal investigator or authorized designee, as required, have personally signed and dated the IC, the subject is considered a subject enrolled in the study. The date the subject signed the IC and data protection authorization if applicable must be documented in the subject's medical records.

Subjects will be recruited from the practices and clinics of the participating Study Investigators or from other non-investigator Otolaryngologist or Rhinologist physician referrals. Potential subjects will have

the need to undergo nasal/sinus surgery using a space-occupying stent. Subjects may continue their medical therapy regimen (antibiotics, steroids, nasal sprays, etc) per their treating physician.

All subjects will be screened for study eligibility. A qualified member of the investigational site's research team will review the inclusion and exclusion criteria to screen each subject.

There will be no minimum number of subjects enrolled at a site, no site will enroll greater than 60% (45 subjects) of the total enrollment goal. This numerical goal is to ensure a diversity of experience and surgical techniques throughout the study, while allowing flexibly of enrollment based on eligible populations of subjects.

Subjects will be considered enrolled into the study when they have:

- Been informed of the study design, objectives, risks and benefits
- Met the eligibility criteria
- Confirmed interest in participation by signing a written Informed Consent and Research Authorization Form

8.3 Inclusion Criteria

- Subject is at least 18 years of age.
- Subject has the need to undergo nasal/sinus surgery with the intended need for nasal sinus packing (i.e., Novapak).
- After being informed of the nature of the study; the subject understands, agrees to its provisions, is willing to participate and provide written consent.
- Mentally stable and able to follow the instructions for self-assessment/questionnaire completion.

8.4 Exclusion Criteria

- Subject has a shellfish allergy.
- Subject has known bleeding disorder or prescribed anticoagulants.
- Subject has craniofacial abnormalities that may interfere with access to the sinuses.
- Subject is immunocompromised (e.g., taking immunosuppressive medication).
- Subject is participating in another investigational device, biologic, or drug study and has not completed the primary endpoint(s) or if there is a potential for clinical interference beyond the primary endpoint.

9. Study Procedures

The subjects will encounter the following procedures during their participation in the study:

- Lund-MacKay Scores (pre-surgical history)
- Lund-Kennedy Score (pre-surgery, 14, 30)
- SNOT-22 questionnaire (pre-surgery, 14, 30)

- Endoscopic Exams (day 0, 14, 30)
- Functional Endoscopic Sinus Surgery (day 0)
- Insertion of the Novapak device in the nasal cavity (day 0)
- Post – Surgical Daily saline irrigations (day 1 through day 14 + longer if prescribed by physician)
- Debridement of adhesions at day 14 and/or day 30 (if necessary)
- Removal of residual product at day 14 (if necessary)

A patient needing sinus surgery with the use of dissolvable packing would encounter all or most of these procedures during the course of treatment.

9.1 Schedule of Events

Table 4: Planned Visits, Procedural Events and Data Collection

Visit	Procedure	Data Collection
Pre-Surgery	Inform subject about the study requirements Ask shellfish allergy questions Schedule Surgery	Consent document signed SNOT-22 (subject)
Day 0	Endoscopic exam	Lund-MacKay Scores Lund-Kennedy Scores (baseline)
	Functional Endoscopic Sinus Surgery Other interventions if bleeding more than minimal	Procedural Details Boezaart Surgical Field Grading Scale (pre-packing) Boezaart Surgical Field Grading Scale (post-packing) Question: Bleeding controlled post packing? Collect Adverse Events and/or Device Deficiencies
Day 1, 2, 3…	Daily Irrigations	Subject records volume / date Subject records any Adverse Events
Day 14 (-2, +5)	Office Visit Endoscopic exam Observe for residual product (remove) Debride Adhesions (if necessary) Review Subject Irrigations Records	SNOT-22 (subject) Lund-Kennedy Scores Question: residual product? Score Adhesions (Valentine method) Question: Bleeding controlled? Collect Adverse Events and/or Device Deficiencies
Day 30 (-2, +12)	Office Visit Endoscopic exam Debride Adhesions (if necessary)	SNOT-22 (subject) Lund-Kennedy Scores

	Review Subject Irrigations Records	Score Adhesions (Valentine method) Collect Adverse Events and/or Device Deficiencies

9.2 Data Collection

Please refer to the Case Report Form Instructions for details regarding directions on completing CRFs, allowable data on CRFs, and source document requirements**. Table 5** shows the schedule on which CRFs are to be completed by designated investigational personnel.

Table 5: Schedule for Completion of CRFs

CRF	Phase of Protocol			
	Enrollment/ Screening	Procedure	Follow Up	Other
Screening/Baseline	X			
Application		X		
Visit 1 / Visit 2			X	
Adverse Event		X*	X*	X*
Device Deficiencies		X*	X*	X*
Study Exit	X*	X*	X*	X*
Protocol Deviation Form	X*	X*	X*	X*

*Adverse Events, Device Deficiencies, Protocol Deviations, and Study Exit CRFs should be completed at any time point in which the corresponding events occur.

9.3 Scheduled Follow-up Visit Windows

After receiving notice of successful implantation/device application, Medtronic will provide the target dates and windows for each subject's visits to the study site if applicable. Should a subject miss a visit or the visit fall outside the pre-specified window, a study deviation must be reported, and the original follow-up schedule maintained for subsequent visits.

Data analyses include follow-up visits, regardless of whether the visit occurs within the window. Therefore, a late visit is preferred over a missed visit but must be accompanied by a deviation report. Follow-up visit windows are listed in **Table 6** and are based on days post-implant.

Table 6: Data collection and study procedure requirements at subject visits

Study Follow-up Visit	Window (Calculated days post-surgery)		
	Window Start (days post-surgery)	Target (days post-surgery)	Window End (days post-surgery)
1. Day 14 (-2, +5)	12	14	19
2. Day 30 (-2, +12)	28	30	42

9.4 Subject Screening

All subjects that are considered for the study should be screened based on the inclusion/exclusion criteria. The reason for non-eligibility, as determined by the Investigator should also be recorded on appropriate eligibility eCRF. The screening information serves as a method for Medtronic to assess selection bias in the trial and other reasons for subject rejection (e.g., subject with a known shellfish allergy). Additional shellfish allergy criteria questions have been added to determine the potential subjects' eligibility based on their previous exposure risk to shellfish and other organisms containing the tropomyosin protein. If the potential subject is completely naïve to shellfish allergic status the site primary investigator will assess the risk based on responses to screening questions and may either include, exclude or test the subject for shellfish allergy potential.

9.5 Prior and Concomitant Medications/Therapies

Subjects that are immunocompromised and/or are taking immunosuppressive medication are not eligible for this study. There are no other medication/therapy restrictions in the study unless they are investigational and may confound the study results, in which case, prior approval would be needed from Medtronic.

9.6 Subject Consent

Informed consent is defined as a legally effective documented confirmation of a subject's (or their legally authorized/designated representative or guardian) voluntary agreement to participate in a particular study after information has been given and explained to the subject on all aspects of the study that are relevant to the subject's decision to participate. This process includes obtaining an IC form (and where required, a/an Authorization to Use and Disclose Personal Health Information/Research Authorization/other privacy language as required by law) that has been approved by Medtronic and the study IRB/REB (specific study site or central IRB/REB where authorized) and signed and dated by the subject (or their legally authorized/designated representative or guardian). A subject may only consent after information has been given and explained to the subject on all aspects of the clinical investigation that are relevant to the subject's decision to participate. IC may be given by the legally

authorized/designated representative only if a subject is unable to make the decision to participate in a clinical investigation. In such cases, the subject shall also be informed about the clinical investigation within his/her ability to understand.

The template IC will be provided under separate cover. Prior to enrolling subjects, the IC site (and where required the Authorization to Use and Disclose Personal Health Information/Research Authorization/other privacy language as required by law) must be approved by Medtronic and the IRB/REB. The document(s) must be controlled (i.e. versioned and dated) to ensure it is clear which version(s) were approved by the IRB/REB. Any adaptation of the sample IC must be reviewed and approved by Medtronic and the IRB/REB reviewing the application prior to enrolling subjects.

The investigator must notify the subject (or their legally-authorized/designated representative or guardian) of any significant new findings about the study that become available during the course of the study which are pertinent to the safety and well-being of the subject, as this could impact a subject's willingness to participate in the study. If relevant, consent may be requested from subjects to confirm their continued participation.

Prior to initiation of any study-specific procedures, IC must be obtained from the subject (or their legally authorized/designated representative or guardian). Likewise, privacy or health information protection regulation may require subjects to sign additional forms to authorize study sites to submit subject information to the study sponsor. The IC process must be conducted by the principal investigator or an authorized designee, and the IC Form (and where required, Authorization to Use and Disclose Personal Health Information/Research Authorization/other privacy language as required by law) must be given to the subject (or their legally authorized/designated representative or guardian) in a language he/she is able to read and understand. The process of IC must be conducted without using coercion or undue improper influence on or inducement of the subject to participate by the investigator or other study site personnel. The IC process shall not waive or appear to waive subject's legal right. The language used shall be as non-technical as possible and must be understandable to the subject and the impartial witness, where applicable.

The subject must have ample time and opportunity to read and understand the IC form, to inquire about details of the study, and to decide whether or not to participate in the study. All questions about the study should be answered to the satisfaction of the subject.

When the subject decides to participate in the study, the IC must be signed and personally dated by the subject and investigator or authorized designee, as required by the IC, and ensured by the principal investigator or his/her authorized designee.

A copy of the IC (and where required, the Authorization to Use and Disclose Personal Health Information/Research Authorization/other privacy language), signed and dated as required by law, must be provided to the subject and his/her authorized designee.

If the IC is obtained the same day the subject begins participating in study-related procedures, it must be documented in the subject's case history that consent was obtained prior to participation in any study-related procedures. It is best practice for the IC process to be documented in the subject's case history, regardless of circumstance.

In the event the subject or legally designated representative cannot read and/or write, the IC process shall be obtained through a supervised oral process. An independent and impartial witness must be present during this process. The IC and any other information must be read aloud to the prospective subject or his/her legally designated representative. Whenever possible, either the subject or his/her legally designated representative shall sign and personally date the informed consent form. The witness signs and personally dates the IC attesting that the information was accurately explained and that informed consent was freely given.

The original of the signed IC must be filed in the hospital/clinical chart and/or with the subject's study documents.

The IC (and where required, Authorization to Use and Disclose Personal Health Information/Research Authorization/other privacy language as required by law) must be available for monitoring and auditing.

9.7 Enrollment

A subject is considered enrolled when the consent process has been finalized. The date the subject (or the subject's authorized/designated representative or guardian) signed the IC and Data Protection Authorization, as required by law, must be documented in the subject's medical records. A log of all subjects enrolled in the study should be maintained. Once consent is obtained, report adverse events/deaths, device deficiencies, study deviations and subject exits as they occur.

After completion of study-related training, designated study personnel may conduct a preliminary assessment of subjects for enrollment into the study. The potential study candidate will be interviewed for their interest in the study and willingness to comply with the study protocol. If the potential study subject is interested and willing to comply, they will be asked to sign the Informed Consent and Research Authorization Form. Upon signing, study personnel will confirm eligibility based on study inclusion and exclusion criteria and will collect baseline information such as:

- Demographics – including date of birth, age, gender, ethnicity
- Medical history including previous interventions and disease state

Subjects who do not meet the eligibility criteria or decline study participation will be considered screen failures. Screen-failed subjects, including reason for exclusion, will be documented on the Screening and Enrollment Log.

9.8 Surgical Procedure

On the day of the Sinus Surgical Procedure the subject should be scheduled giving enough time for study procedures and data collection prior to surgical procedures.

The following information is required to be collected at the surgical procedure visit:

- Lund-MacKay Scores (pre-surgical history)
- Subject completes the baseline SNOT-22 questionnaire
- Physician conducts Endoscopic Examination pre-surgery and grades the sinuses using Lund Kennedy Scores
- Surgical Information: Date of surgery, the surgical location (left, right or both nasal cavities), type of surgery (e.g. turbinectomy, septoplasty, FESS, etc.)
- Collect any Adverse Events and/or device deficiencies
- Physician grades bleeding post-surgery and before packing is inserted using the Boezaart Surgical Field Grading Scale
- Physician grades bleeding post-surgery and after packing is inserted using the Boezaart Surgical Field Grading Scale
- The type of Novapak used and lot number(s)

Subjects may be treated with the Novapak device unilaterally or bilaterally, the number of devices used could be one or two per subject. Therefore, total product used in this study would be a minimum of 75 if a single device is used, to approximately 150 if two devices are used per subject. Note: Physicians are free to modify the size and shape of the device to fit in a unique individual anatomy.

9.9 Scheduled Follow-up Visits

Scheduled visits will occur at day 14 and day 30 post-surgical procedure.

The following information is required to be collected at follow-up visits:

Day 14 visit

- Subject turns in daily irrigations log
- Subject completes the visit SNOT-22 questionnaire
- Collect any Adverse Events and/or device deficiencies
- Physician conducts Endoscopic Examination and grades the sinuses using Lund Kennedy Scores
- Physician conducts adhesion scores and grades the sinuses using the method of Valentine
- Physician debrided adhesions (if necessary)
- Physician removes residual Novapak product if present in the sinuses
- Physician notes any bleeding observed at this examination

Day 30 visit

- Subject completes the visit SNOT-22 questionnaire

- Collect any Adverse Events and/or device deficiencies
- Physician conducts Endoscopic Examination and grades the sinuses using Lund Kennedy Scores
- Physician conducts adhesion scores and grades the sinuses using the method of Valentine
- Physician debrided adhesions (if necessary)

9.10 Unscheduled Follow-up Visits

If a subject returns to the Investigator outside the scheduled follow-up visit window, the Investigator will evaluate the subject according to existing standard of care methods. The reason for the unscheduled follow-up visit will be recorded on the Follow-Up eCRF. Adverse events that present at the time of the visit will also be recorded on the Adverse Event eCRF. Device Deficiencies that present at the time of the visit will also be recorded on the Device Deficiencies eCRF.

Upon the follow-up assessment, the designated study personnel will record the following information:

- Date of Visit
- Reason for unscheduled visit
- Observations from standard of care medical evaluation
- Adverse Events and/or device deficiencies, if applicable

9.11 SNOT-22 Questionnaires

The Sino-Nasal Outcome Test (SNOT-22) is a standardized questionnaire given to assess the subject's severity of symptoms related to their nasal sinuses. The questionnaire will be administered to each subject prior to surgery and then again at day 14 and day 30 visits. A progression in improvement of the scores would indicate that the surgical procedure was successful and the packing material did not hinder this improvement.

9.12 Irrigation Compliance

In order for the Novapak to perform effectively and to fully dissolve as intended the subjects must irrigate their sinuses daily with a saline solution. The subjects will be given a sinus rinse kit with instructions. The kit includes a plastic bottle and packets of Sodium Chloride & Sodium Bicarbonate (USP Grade) which the subjects will make the saline solution using distilled water.

The subjects will log the total daily volume and date of each irrigation. The site coordinator will collect this log at day 14 and inspect for completeness. The number of days where irrigation was done and volume will be recorded.

9.13 Assessment of Efficacy

The following parameters will be used to assess the effectiveness of the Novapak device used according to device indications:

Adhesions – in order to show that Novapak acts a nasal stent to separate tissue or structures compromised by surgical trauma and separate and prevent adhesions between mucosal surfaces in the nasal cavity the study physician will count the number of adhesions present and grade the sinuses using the ordinal scale method published by Valentine 2010.

Control of bleeding – in order to show that Novapak controls minimal bleeding the study physician will grade the bleeding post-surgery and prior to packing using the Boezaart Surgical Field Grading Scale. After inserting the Novapak product with irrigation to hydrate the product the bleeding will be graded again using the same scale.
During the day 14 visit the physician will be asked if any bleeding is observed during the exam and prior to any debridement procedure.

Progression of healing – The Lund Kennedy endoscopic grading system will be used to show that Novapak acts as an adjunct to aid in the natural healing process. The physician will perform an endoscopic exam prior to surgery (to establish a baseline), at day 14 and day 30 visits (to show progressive healing).

Residual Novapak – Novapak dissolves naturally with daily irrigation. Any residual Novapak in the nasal cavity will be recorded at the 14 day visit and compared to the subject compliance to the daily irrigation log.

9.14 Assessment of Safety

AE information is collected in this study. See Section 11 for further information on the collection of AEs and safety information.

9.15 Recording Data

Data entered must be traceable to source documents. Source documentation is defined as the first time data appear, and may include original documents, data, and records (e.g., hospital records, clinical and office charts, procedure reports, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, X-rays, subject files, device data and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the study).

In general, eCRFs (or paper copies) may not serve as source documents. An exception may be the completed SNOT-22 Questionnaires and endoscopic grading worksheets. Source documentation for data elements not routinely captured in medical records may vary from study site to study site; the study site may use source document worksheets if identified as source documents.

The investigator must ensure the availability of source documents from which the information on the eCRFs was derived. The type and location of source documents should be documented. Where printouts of electronic medical records, are provided as source documents, or where copies of source documents are retained as source documents, those should be certified. Certification must contain (1) the signature of the individual making the copy, (2) the date the copy was made and (3) a statement attesting to the accuracy and completeness of the copy.

The source documents must be made available for monitoring, safety data review or auditing by Medtronic's representative or representatives of the competent authorities and other applicable regulatory agencies.

The CRF may be considered source for the following data collection elements:

- Enrollment Notification
  - Study site assigned subject reference
- Baseline
  - Administrative information
- AE eCRF
  - Date study site became aware of event
  - Relatedness of adverse event
- DD eCRF
  - Date study site became aware of event
- Deviations
  - Reason for deviation
- Device Disposition Log

9.16 Deviation Handling

A study deviation is defined as an event within a study that did not occur according to the CIP or the CTA.

Prior approval by Medtronic is expected in situations where the investigator anticipates, contemplates, or makes a conscious decision to deviate. Prior approval is not required when a deviation is necessary to protect the safety, rights or well-being of a subject in an emergency or in unforeseen situations beyond the investigator's control (e.g. subject failure to attend scheduled follow-up visits, inadvertent loss of data due to computer malfunction, inability to perform required procedures due to subject illness).

For medically justifiable conditions which preempt a subject's ability to complete a study-required procedure, it may be permitted to report only one deviation which will apply to all visits going forward. This may also apply for other unforeseen situations (e.g. the subject permanently refuses to complete a study required procedure and the data will not contribute to the primary end point analysis). However, prior approval from Medtronic is required for such situations.

All study deviations must be reported on the CRF regardless of whether medically justifiable, pre-approved by Medtronic, an inadvertent occurrence, or taken to protect the subject in an emergency. Multiple deviations of the same type at the same visit may be reported on one case report form.

In the event the deviation involves a failure to obtain a subject's consent or is made to protect the life or physical well-being of a subject in an emergency, the deviation must be reported to the IRB/REB as well as Medtronic within five (5) working days. Reporting of all other study deviations should comply with IRB/REB policies and/or local laws and must be reported to Medtronic as soon as possible upon the study site becoming aware of the deviation. Reporting of deviations must comply with IRB/REB policies,

local laws, and/or RA requirements. Refer to Investigator Reports, Section 15.9.1 for geography-specific deviation reporting requirements and timeframes for reporting to Medtronic and/or RAs.

Medtronic is responsible for analyzing deviations, assessing their significance, and identifying any additional corrective and/or preventive actions (e.g. amend the CIP, conduct additional training, terminate the investigation). Repetitive or serious investigator compliance issues may result in initiation of a corrective action plan with the investigator and study site, and in some cases, may necessitate suspending enrollment until the problem is resolved or ultimately terminating the investigator's participation in the study. Medtronic will provide study site-specific reports to investigators summarizing information on deviations that occurred at the investigational study site as needed.

Examples of study deviations include but are not limited to:

- Failure to obtain proper IC
- Failure to collect required study data
- Inclusion/exclusion criteria not met
- Visit conducted outside of scheduled visit window
- Device not used per labeling

9.17 Subject Exit, Withdrawal or Discontinuation

Should a subject withdraw or be lost to follow-up, the designated study personnel will complete the Study Exit CRF, including:

- Date of Study Exit
- Subject status (i.e., reason for withdrawal)

At any time between enrollment and study completion, study personnel may complete the Study Exit CRF. The number (minimum 2) and type of attempts to contact subject (email, text, call, etc.) prior to Lost to Follow-up designation should be documented in the subject's medical record.

9.17.1 Study Exit

A study exit eCRF is required for all subjects. Prior to exiting a subject from the study, it is recommended to follow the subject until all ongoing system and/or procedure related AEs are resolved or unresolved with no further actions planned. Following exit, subjects will continue to receive standard medical care. Upon exiting from the study, no further study data will be collected or study visits will occur for the subject. All data available through the time of the subject's exit will be used for analysis.

Subjects are urged to remain in the study as long as possible but may be exited from the study for any of the following situations:

- Study completed
- Subject lost to follow-up

- Subject death
- Subject did not meet inclusion/exclusion criteria
- Investigator chose not to use the Novapak Nasal Sinus Packing and Stent device
- Subject did not provide consent (or data use protection authorization where required)
- Subject chooses to withdraw (e.g., consent withdrawal, relocation to another geographic location)
- Investigator deems withdrawal necessary (e.g., medically justified, inclusion/exclusion criteria not met, failure of subject to maintain adequate study compliance)

The following information is required to be collected at study exit:

- Date of Study Exit
- Reason for exit (subject status)
  - AE related
  - Covid related

If discontinuation is because of safety or lack of effectiveness, the subject shall be asked to be followed for collecting safety data outside the clinical investigation.

9.17.2 Study Completed

At the completion of the 30-day follow-up visit, subjects will be exited from the study. The 30-day follow-up visit and exit visit should be combined, and both a 30-day Subject Visit CRF and a Study Exit eCRF need to be completed.

9.17.3 Lost to Follow-up

A subject is considered to be lost to follow-up if at least two attempts to contact the subject are unsuccessful. The method of attempt (e.g., one letter and one phone record, or two letters) must be documented in the subject's medical record. In addition, regulation set forth by the governing IRB/REB must be followed.

9.17.4 Subject Chooses to Exit (i.e. Revokes Consent)

A subject can withdraw from the study at any time. If the subject wishes to exit from the study (i.e. the subject revokes consent), the study site is required to document the reason for exit on the Study Exit CRF. In addition, study sites shall follow the regulations set forth by the governing IRB/RCB. If possible, the following data should be collected prior to subject withdrawal:

- Date of study exit
- Reason for exit

9.17.5 Investigator Withdraws Subject

No subjects should be withdrawn by investigators unless compelling medical justification is present. It is recommended investigators discuss any withdrawals with the study team prior to withdrawing subjects.

Early removal of Novapak (within the first 7 days of application) alone may not be a reason for subject withdrawal. If an Investigator Withdrawal is necessary, the following data should be collected prior to subject withdrawal if possible:

- Date of study exit
- Reason for subject withdrawal

10. Risks and Benefits

10.1 Potential Risks

Medtronic follows rigorous Quality Assurance and Control procedures throughout the life of a product, from the business analysis phase through development, market release, and post-market surveillance. The risk analysis process for the Novapak Study, is being performed in accordance with ISO 14971 and will ensure that the level of risk is acceptable prior to starting the study.

There are no incremental risks introduced to the subject as a result of participation in this study.

There are inherent risks for nasal sinus surgery as well as any surgery where removal, cutting and modification of tissues are required. These risks include:

- Mild Bleeding
- Adhesions, tissue synechia
- Fatigue
- Infection
- Moderate Pain
- Inflammation and swelling
- Nasal Congestion
- Mild to moderate headaches
- Facial pressure

Nasal sinus packing in general has tried to address these surgical complications but may result in risks that are specific to the use of packing, as follows:

- Bleeding – present if packing is inadequate or bleeding is excessive– may require post-operative controls (e.g., suturing, cautery, more packing)
- Adhesions – present if packing is inadequate to separate tissue compromised due to surgical trauma – requires post-operative debridement of tissues which may lead to bleeding.
- Scarring - This risk is where the tissue heals abnormally

- Infection – due to introduction of bacterial during the surgery and/or if sterility is breached - packing could encourage bacterial growth if design controls are not in place to control bacterial growth.
- Toxic Shock Syndrome –defined as “A severe illness caused by infection with staphylococcus aureus and characterized by high fever of sudden onset, vomiting, diarrhea, and myalgia, followed by hypotension and in severe cases, shock; a sunburn like rash with peeling of the skin, especially of the palms and soles, occurs during the acute phase.”
- Respiratory Obstruction – physical obstruction of the breathing pathway – This harm may occur from stent migration and cause difficulty breathing (i.e., hypoxia, dyspnea)
- Aspiration of the packing – causes respiratory obstruction with tachypnea can lead to aspiration pneumonia, urgent medical intervention may be necessary
- Pneumonia - If the stent were aspirated, pneumonia may occur. The patient may be treated with IV medication.
- Potential toxicity reactions – components of the packing could lead to a toxicity reaction due to a non-biocompatibility reaction occurring, but the reaction would not be expected to go beyond an inflammatory response. (i.e., redness, swelling, etc.)
- Potential allergic hypersensitivity reactions – components of the packing could lead to an allergic hypersensitivity reaction - A patient may experience edema and difficulty breathing with IV medications used as medical intervention.
- Foreign Body Reaction - Potential tissue interactions with packing components, fragments, or surface texture. In addition to an inflammatory response, it usually includes the formation of a foreign body granuloma, or encapsulation around a foreign object. Medical intervention may be taken to remove the product.
- Inflammation - This harm includes local irritation from the product. This risk may require Oral medication to reduce inflammatory response.
- Fever - A medium-low grade fever may develop. This risk may require Oral medication to reduce inflammatory response.
- Device Fragments in Patient – If a device fragments migration of pieces of the stent could result in possible medical intervention needed
- Pain – during post-operative removal of non-dissolving packing devices most patients have reported some mild temporary pain.
- Decreased Therapeutic Response – The packing may not perform as expected and not control the risks as intended. It would not result in surgical correction but may require a minor medical intervention.

The use of the Novapak Nasal Sinus Packing and Stent may involve the risks listed above for all packing type devices, with the exception of pain upon removal, since it dissolves away with irrigation. There may be other discomforts and risks related to the Novapak Nasal Sinus Packing and Stent device and/or this study that are not foreseen at this time.

These are the current risks of Novapak seen in the field based on reports to our complaint system: (number of reported events as of June 24, 2022)

- Irritation – potential shellfish hypersensitivity (1)
- Post-operative bleeding requiring secondary controls (3)
- Post-operative device migration to oral cavity (1)
- Post-operative edema and pain (2)

10.2 Risk Minimization

The potential risks associated with the Novapak device were identified and have been successfully mitigated. Any potential risks associated with this study are further minimized by selecting qualified investigators and training study personnel on the CIP.

In addition, investigators will be actively involved in the nasal sinus surgery and follow-up of the subjects using the Novapak device.

Risks will be minimized by careful assessment of each subject prior to, during and after surgery, and during and after application of the Novapak Nasal Sinus Packing and Stent device. Prior to surgery, each subject will be screened for shellfish allergy to mitigate the risk of a hypersensitivity reaction to the chitosan component of the device. It is recommended subjects undergo a complete physical evaluation.

Medtronic has further minimized the possibility of risks by: performing required laboratory and pre-clinical testing prior to the Novapak study, implementing quality control measures into production processes, providing guidelines for subject selection and evaluation, and providing adequate instructions and labeling.

After surgery, subjects in the Novapak Study will be followed at regular intervals to monitor the condition of the nasal sinus healing process. At each protocol required follow-up, the investigator must assess any adverse events.

Table 7: Potential risks and risk minimization

Potential risk	Risk Minimization
Hypersensitivity	Screening for shellfish allergy
Infection	Design controls – device component has an antimicrobial effect

10.3 Potential Benefits

The Novapak Device is used for nasal packing to prevent bleeding after sinus surgery and may offer no benefit. The potential benefits of having the Novapak Nasal Sinus Packing and Stent device include control of minimal bleeding, prevent post-surgical adhesions by acting as a space occupying stent which separates tissues compromised by surgical trauma, aid in the natural healing process, eliminate the need for packing removal by dissolving away with irrigation. These potential benefits aid the patient as well as the physician by providing a tool to manage common post-surgical effects (i.e. bleeding,

adhesions and removal of packing). Additionally, information collected from this study may assist in the design of new products/therapies and/or IFU.

10.4 Risk-Benefit Rationale

The use of the Novapak device does not appear to add unreasonable risks to the common technique of nasal packing post nasal sinus surgery. Benefits of nasal packing with the Novapak device (Section 10.3) when used by a trained physician greatly outweigh any risks associated with this therapy (Section 10.1).

10.5 Risk Determination

The Novapak device is commercially available in the US and Canada. The device was cleared for use under US FDA 510(k) number K202623 on December 08, 2020, and this study is therefore exempt per US FDA 21 CFR 812. The device is licensed for use in Canada under license number 103651 issued September 25, 2019.

11. Adverse Events and Device Deficiencies

This section describes how Adverse Events and Device Deficiencies will be handled in this study.

11.1 Adverse Events

AE definitions are provided in **Table 9**. All AE information will be collected throughout the study duration, starting during sinus surgical procedure and treatment with the Novapak device and concluding with the 30-day visit and/or study exit (whichever occurs first).

Reporting of these events to Medtronic will occur on an AE eCRF. Each event must be reported separately. Documented pre-existing conditions are not considered AEs unless the nature or severity of the condition has worsened.

In all geographies, UAEs occurring post-surgery need not be reported unless the adverse event worsens or is present outside the stated timeframe post-surgery.

Table 8: Post-Surgery Unavoidable Adverse Events

Event Description	Timeframe – days after surgical procedure
Sudden visual changes or ocular swelling	1
Fever higher than 101°F	1
Anesthesia related complications	2
Medication related complications	2
Mild bleeding (bloody discharge)	5
Constant clear watery discharge	7
Facial pressure	7
Fatigue	7
Inflammation and swelling	7

Mild to moderate headaches	7
Moderate pain	7
Numbness of the Teeth or Palate	7
Nasal congestion	10

For AEs that require immediate reporting (see **Table 11**), initial reporting may be done by email or phone, or on the eCRF completing as much information as possible. The completed AE eCRF must be submitted to Medtronic as soon as possible.

Any medication/treatment associated with the treatment of an AE must be reported.

Subject deaths are also required to be reported. Refer to Section 11.6 for Subject Death collection and reporting requirements.

11.2 Device Deficiency

The DD definition is provided in **Table 9**. DD information will be collected throughout the study and reported to Medtronic. Note that DD that result in an AE to the subject should be captured as an AE only.

DD that did not lead to an AE but could have led to a SADE (i.e., if suitable action had not been taken, if intervention had not been made, or if the circumstances had been less fortunate) require immediate reporting (see **Table 11**).

11.3 Processing Updates and Resolution

For any changes in status of a previously reported adverse event or DD (i.e. change in actions taken, change in outcome, change in relatedness), information needs to be updated on, or added to the original AE or DD eCRF. All AEs must be followed until the AE has been resolved, is unresolved with no further actions planned, the subject dies or exits the study, or until study closure, whichever occurs first.

At the time of study completion, all collected adverse events that are unresolved must be reviewed and an update to the original AE must be reported.

11.4 Definitions/Classifications

Where the definition indicates “device”, it refers to only the device under investigation used in the study.

Table 9: Adverse Event and Device Deficiency Definitions

General	
Adverse Event	An untoward medical occurrence, unintended disease or injury, or untoward clinical signs in subjects, users or other

	persons, whether or not related to the investigational medical device and whether anticipated or unanticipated. NOTE: This definition includes events related to the investigational medical device. NOTE: This definition includes events related to the procedures involved. NOTE: for users or other persons, this definition is restricted to events related to the use of investigational medical devices.
Adverse Device Effect (ADE)	Adverse event related to the use of an investigational medical device. NOTE: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation or any malfunction of the investigational medical device. NOTE: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance. NOTE: Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labeling.
Relatedness - Procedure	An event that occurs as a result of the nasal sinus surgical procedure(s). This includes events involving devices used in the surgical procedure that are not the study device being assessed.
Relatedness - Device	An event that occurs as a result of application or use of the study device being assessed.
Relationship – Not Related	The relationship to the device or procedures can be excluded when:

	• the event is not a known complication or side effect of the procedures, study device or product category the device belongs to or of similar devices • the event has no temporal relationship with the use of the study device or the procedures • the event does not follow a known response pattern to the study device (if the response pattern is previously known) and is biologically implausible • the discontinuation of study device application or the reduction of the level of activation/exposure - when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the event • the event involves a body-site, or an organ not expected to be affected by the device or procedure • the event can be attributed to another cause (e.g. an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors) • harms to the subject are not clearly due to use error In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the seriousness of the event.
Relationship - Possible	The relationship with the procedure or use of the study device is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible.
Relationship - Probable	The relationship with the procedure or use of the study device seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.

Relationship - Causal	The event is associated with the study device or with procedures beyond reasonable doubt when:
	• the event is a known complication or side effect of the procedure, study device, or product category the device belongs to or of similar devices
	• the event has a temporal relationship with the study device use/application or procedures
	• the event involves a body-site or organ that
	  ○ the study device or procedures are applied to
	  ○ the study device or procedures have an effect on
	• the event follows a known response pattern to the study device (if the response pattern is previously known)
	• the discontinuation of the study device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the event (when clinically feasible)
	• other possible causes (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out
	• harm to the subject is due to error in use
	In order to establish the causal relationship, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the seriousness of the event.

Serious Adverse Event (SAE)	Adverse event that led to any of the following: a) Death, b) Serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following: 1) a life-threatening illness or injury, or 2) a permanent impairment of a body structure or a body function including chronic diseases, or 3) in-patient or prolonged hospitalization, or 4) medical or surgical intervention to prevent life-threatening illness or injury or permanent

	impairment to a body structure or a body function, c) Fetal distress, fetal death, a congenital abnormality, or birth defect including physical or mental impairment. NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Serious Health Threat	A signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons NOTE: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.
Unavoidable Adverse Event (UAE)	An adverse event that is an expected, known complication or side effect occurring after a surgical procedure.

11.5 Reporting of Adverse Events

11.5.1 Adverse Event and Device Deficiency Classification

All AE and DD will be reviewed by a Medtronic representative. AEs will be classified according to the definitions provided.

Upon receipt of AE at Medtronic, a Medtronic representative will review the AE/DD for completeness and accuracy and when necessary, will request clarification and/or additional information from the Investigator. Medtronic will utilize Medical Dictionary for Regulatory Activities (MedDRA), to assign a MedDRA term for each AE based on the information provided by the investigator.

Regulatory reporting of AEs and DDs will be completed according to local regulatory requirements. Refer to **Table 11** for a list of required investigator and Medtronic reporting requirements and timeframes. It is the responsibility of both to abide by any additional AE reporting requirements stipulated by the IRB/REB responsible for oversight of the study.

Appendix A contains the FAL, which is a list of AEs related to the device or procedure that have been observed in previous studies and may be experienced by subjects. This list may help to assess if an AE is unanticipated in nature.

For emergency contact regarding a SAE and/or SADE, contact a study representative immediately (refer to the study contact list provided in the study site's study documents binder/investigator site file or refer to the Sponsor contact information provided on the title page).

AEs will be classified according to the standard definitions as outlined below:

Table 10: Adverse Event Classification Responsibilities

What is classified?	Who classifies?	Classification Parameters
Relatedness	Investigator	Device and/or Procedure. • Relationship: not related, possible, probable, causal
	Sponsor	Device and/or Procedure. • Relationship: not related, possible, probable, causal
Seriousness	Investigator	SAE, DD with SADE potential
	Sponsor	SAE, DD with SADE potential
Diagnosis	Investigator	Based on presenting signs and symptoms and other supporting data
	Sponsor	MedDRA term assigned based on the data provided by Investigator

11.5.2 Adverse Event and Device Deficiency Reporting Requirements

Regulatory reporting of AEs and DDs will be recorded and reported according to local regulatory requirements. It is the responsibility of the Investigator and the sponsor to abide by the AE reporting requirements stipulated by local law and the study site's IRB/REB.

Sponsor shall fully record all of the following: (a) any adverse event of a type identified in the CIP as being critical to the evaluation of the results of that clinical investigation, (b) any serious adverse event, (c) any device deficiency that might have led to a serious adverse event if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate, (d) any new findings related to any event referred to in previous points and (e) any additional CIP procedure relatedness.

All reporting shall include the date of the adverse event, treatment, resolution, assessment of seriousness and the relationship to the investigational device and the related procedure.

Table 11: AE and DD Reporting Requirements

SAEs	
Investigator shall submit to:	
Medtronic	**All geographies:** Report to the sponsor, without unjustified delay, all serious adverse events.
RA	**All geographies:** Submit to RA per local reporting requirement.
IRB/REB	**All geographies:** Submit to IRB/REB per local reporting requirement.
Sponsor shall submit to:	
RA	**All geographies:** Submit to RA per local reporting requirement.
IRB/REB	**All geographies:** Submit to IRB/REB per local reporting requirement.
ADEs	
Investigator shall submit to:	
Medtronic	**All geographies:** Submit in a timely manner after the investigator first learns of the effect.
RA	**All geographies:** Submit to RA per local reporting requirement.
IRB/REB	**All geographies:** Submit to IRB/REB per local reporting requirement.
Sponsor shall submit to:	
RA	**All geographies:** Submit to RA per local reporting requirement.
IRB/REB	**All geographies:** Submit to IRB/REB per local reporting requirement.
SADEs	
Investigator shall submit to:	
Medtronic	**All geographies:** Immediately after the investigator learns of the event or of new information in relation to an already reported event.
RA	**All geographies:** Submit to RA per local reporting requirement
IRB/REB	**All geographies:** Submit to IRB/REB per local reporting requirement.
Sponsor shall submit to:	
RA	**All geographies:** Submit to RA per local reporting requirement.
IRB/REB	**All geographies:** Submit to IRB/REB per local reporting requirement.
Investigators	**All geographies:** Submit per local reporting requirement.
All other reportable AEs	
Investigator shall submit to:	
Medtronic	**All geographies:** Submit in a timely manner after the investigator first learns of the event.
RA	**All geographies:** Submit to RA per local reporting requirement.
IRB/REB	**All geographies:** Submit to IRB/REB per local reporting requirement.

DDs with SADE potential	
Investigator shall submit to:	
Medtronic	**All other geographies:** Submit or report as required per local reporting requirements.
RA	**All geographies:** Submit to RA per local reporting requirement.
IRB/REB	**All geographies:** Submit to IRB/REB per local reporting requirement.
Sponsor shall submit to:	
RA	**All geographies:** Submit to RA per local reporting requirement.
IRB/REB	**All geographies:** Submit to IRB/REB per local reporting requirement.
All other Device Deficiencies	
Investigator shall submit to:	
Medtronic	**All geographies:** Submit in a timely manner after the investigator first learns of the deficiency.
RA	**All geographies:** Submit to RA per local reporting requirement.
IRB/REB	**All geographies:** Submit to IRB/REB per local reporting requirement.

11.6 Subject Death

All subject deaths must be reported by the investigator to Medtronic on a single AE form (AE with outcome of fatal) as soon as possible after the investigator first learns of the death.

A copy of the death certificate, if available and allowed by state/local law, should be sent to the Medtronic clinical study team. When a death occurs in a hospital, a copy of the death summary report and all relevant hospital records, if available should be sent to the Medtronic clinical study team. If an autopsy is conducted, a copy of the autopsy report should also be sent to the Medtronic clinical study team if available and allowed by state/local law. When the death occurs at a remote study site, it is the investigative study site's responsibility to attempt retrieval of information about the death. Additionally, device disposition information should be updated.

In summary, the following data will be collected:

- Date of death
- Detailed description of death
- Cause of death
- Relatedness to device and/or procedure
- Device disposition information
- Death summary/hospital records (if available and allowed by state/local law)
- Autopsy report (if available and allowed by state/local law)
- Death certificate (if available and allowed by state/local law)

11.6.1 Death Classification and Reporting

Sufficient information will be required in order to properly classify the subject's death. The Medtronic Representative will review any reported deaths in the study subjects and obtain documentation regarding the primary cause of death and classification of death. Regulatory reporting of Subject Deaths will be completed according to local regulatory requirements.

11.7 Product Complaint Reporting

It is the responsibility of the investigator to report all product complaint(s) associated with a medical device distributed by Medtronic, regardless whether they are related to intended use, misuse or abuse of the product. Reporting must be done immediately and via the regular channels for market-released products. The reporting of product complaints by the clinical team must be done according to the local Standard Operating Procedures. Medtronic will notify the RAs (e.g. CA) as applicable for the following incidents immediately upon learning of them and is not limited to AEs and DDs only:

- Any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labeling or instructions for use which led or might have led to the death or serious deterioration in the state of health of a patient, user, or other person.
- Any technical or medical reason resulting in withdrawal of a device from the market by the manufacturer.

12. Data Review Committees

12.1 Clinical Events Committee Review

CEC is not needed for this study. This decision was made based on the following criteria: fast enrollment in this trial makes a CEC impractical, and there are no additional benefits of a CEC reviewing the data.

12.2 Data Monitoring Committee

DMC is not needed for this study. This decision was made based on the following criteria: fast enrollment in this trial makes a DMC impractical, and there are no additional benefits of a DMC reviewing the data.

13. Statistical Design and Methods

The following section describes the statistical design and methods for the Novapak study in general.

13.1 General Aspects of Analysis

Novapak Nasal Sinus Packing and Stent Study is a prospective, non-randomized, non-blinded, multi-site, investigational, clinical study.

The statistical analyses will be performed by Medtronic employed statisticians. The study population is defined as all eligible patients who signed the Patient Informed Consent Form.

All data collected from enrolled subjects will be utilized in the analyses as appropriate. Analyses of the primary and secondary endpoints will be descriptive.

All continuous variables will be summarized as the number of subjects, means, standard deviations, medians, minimums, maximums, and interquartile ranges. Categorical variables will be summarized as frequencies and percentages.

Any deviations from the original statistical plan will be summarized in the Clinical Study Report(s) (CSRs), along with the justification for the deviations.

No statistical techniques will be used to impute missing data for continuous or categorical outcomes. If a subject's data are missing for any reason, that subject will not be included in that portion of the analysis. The number of subjects included in each analysis will be reported so that the reader can assess the potential impact of missing data.

13.2 Interim Analysis

No interim analyses are planned for this study.

13.3 Primary Objective(s)

The primary objective is to assess the safety of the Novapak Sinus Packing and Stent device for use in patients undergoing nasal/sinus surgery:

- Collect all AEs directly attributed to the device and/or those that cannot be determined
- Collect all AEs and establish an overall rate and safety profile for the device

13.4 Secondary Objective(s)

The secondary objectives are to confirm device effectiveness during the procedure, 2 weeks and 1-month post treatment.

13.5 Sample Size Determination

As this is not a powered hypothesis-driven study, the sample size of a minimum of 75 subjects was selected that is adequate to assess the safety and treatment effectiveness of the Medtronic Novapak Nasal Sinus Packing and Stent device, not determined by statistical methods.

13.6 Minimization of Bias

The study methods include the following measures to minimize potential sources of bias:

- A qualified member of the investigational site's research team will review the inclusion and exclusion criteria to screen each subject to confirm subject eligibility.
- All sites will follow a standardized protocol for acquisition of endpoint data.

14. Ethics

14.1 Statement(s) of Compliance

This study will be conducted in compliance with international ethical and scientific quality standards, known as GCP. GCP includes review and approval by an independent IRB/REB before initiating a study, continuing review of an ongoing study by an IRB/REB, and obtaining and documenting the freely given informed consent of a subject before initiating the study.

The Novapak Study was designed to reflect the GCP principles outlined in ISO 14155:2020 and other international clinical requirements outlined below. These include the protection of the rights, safety and well-being of human subjects, controls to ensure the scientific conduct and credibility of the clinical investigation and the definition of responsibilities of the sponsor and investigators. In accordance with ISO 14155:2020, the sponsor shall avoid improper influence on, or inducement of, the subject, monitor, any investigator(s) or other parties participating in, or contributing to, the clinical investigation. All investigators shall avoid improper influence on or inducement of the subject, sponsor, monitor, other investigator(s) or other parties participating in or contributing to the clinical investigation. AE and DD handling in the Novapak Study is ISO 14155:2020 compliant for all participating geographies.

The principles of the Declaration of Helsinki (DoH) have been implemented through the IC process, IRB/REB approval, study training, clinical trial registration, pre-clinical testing, risk-benefit assessment and publication policy.

Ultimately, all study sites in all geographies will follow and comply with:

- Principles of DoH
- 21 CFR Part 11 (Electronic Records, Electronic Signatures)
- 21 CFR Part 54 (Financial Disclosure by Clinical Investigators)
- The CTA
- The procedures described within this CIP
- Local IRB/REB Requirements

In addition to the regulatory requirements outlined above, the study will be conducted according to federal, national and local laws, regulations, standards, and requirements of the countries/geographies where the study is being conducted. These include but are not limited to:

- In the United States, the study will be conducted in compliance with 21 CFR Parts:
  - 50: Protection of Human Subjects
  - 54: Financial Disclosure by Clinical Investigators
  - 56: IRBs
  - 803: Complaint reporting
- In Canada, in compliance with Canada Medical Device Regulation 1998 SOR/98-292

The study will be publicly registered prior to subject enrollment in accordance with the 2007 FDAAA and DoH on http://clinicaltrials.gov (PL 110-85, section 810(a)). In addition, the study may be registered in local regulatory databases where required by local law.

Approval of the CIP and CIP amendments is required from the following groups prior to any study procedures at a study site:

- Medtronic
- Principal Investigators (where required by local law/regulations)
- Geography-specific regulatory authorities (if regulatory approval is required)
- An independent medical IRB/REB

15. Study Administration

15.1 Monitoring

It is the responsibility of Medtronic to ensure proper monitoring of this study. Trained Medtronic personnel or delegates appointed by Medtronic may perform study monitoring at the study site, or remotely in order to ensure that the study is conducted in accordance with the CIP, the CTA, and the applicable regulatory and local requirements. Medtronic, or delegates, must therefore be allowed direct access to the subjects' case histories (clinic and hospital records, and other source data/documentation) upon request as per the IC, Research Authorization (where applicable) and CTA. The principal investigator should also be available during monitoring visits.

Monitoring visits may be conducted at the start, during and at the closure of the clinical study in accordance with Medtronic SOPs and the Monitoring Plan. At minimum, it will be verified whether signed and dated ICFs have been obtained from each participant at the point of enrollment and that AEs discussed in Section 11 were reported via completion of the AE eCRFs.

15.2 Data Management

Data will be collected using an electronic data management system for studies. CRF data will be stored in a secure, password-protected database hosted in a cloud service which is owned and validated by a third party. Data will be reviewed using programmed and manual data checks. Data queries will be made available to study sites for resolution. Study management reports may be generated to monitor data quality and study progress. At the end of the study, the data will be frozen and will be retained by Medtronic in accordance with applicable regulations.

All records and other information about subjects participating in this study will be treated as confidential. Data will be transferred and processed by Medtronic or a third party designated by

Medtronic in a key coded form, unless it's impossible to pseudonymize for instance, where the subject's name cannot be removed from the data carrier.

Procedures in the CIP require source documentation. Source documentation will be maintained at the study site. Source documents, which may include worksheets, subject medical records, and laboratory reports, must be created and maintained by the investigational study site team.

The investigator will clearly mark clinical records to indicate that the subject is enrolled in this clinical investigation.

The data reported on the CRFs shall be derived from source documents and be consistent with these source documents, and any discrepancies shall be explained in writing. Refer to the Case Report Form Instructions for CRFs and data collection elements that may be considered source.

15.3 Direct Access to Source Data/Documents

Medtronic may conduct audits at participating study sites. The purpose of an audit is to verify the performance of the monitoring process and the study conduct, independently of the personnel directly involved in the study. RAs, such as the FDA, may also perform inspections at participating study sites. The investigator and/or institution shall permit Medtronic, IRB/REBs and RAs direct access to source data and documents during monitoring, audits and regulatory inspections.

15.4 Confidentiality

All information and data sent to parties involved in study conduct concerning subjects or their participation in this study will be considered confidential. Study sites will assign a unique SID to each subject. Records of the subject/SID relationship will be maintained by the study site. The SID number is to be recorded on all study documents to link them to the subject's medical records at the study site. Confidentiality of data will be observed by all parties involved at all times throughout the clinical investigation. All data shall be secured against unauthorized access. The privacy of each subject and confidentiality of his/her information shall be preserved in reports and when publishing any data. In the US, "Protected Health Information" (PHI) will be maintained in compliance with the HIPAA of 1996. To maintain confidentiality, the subject's name or any other PHI should not be recorded on any study document other than the IC. This scenario will be covered in the IC. In the event a subject's name/PHI is included for any reason, it will be blinded as applicable. In the event of inability to blind the identification (e.g., digital media), it will be handled in a confidential manner by the authorized personnel. Data relating to the study might be made available to third parties (for example in case of an audit performed by RA), provided the data are treated as confidential and that the subject's privacy is guaranteed. No identifiable subject information will be published.

15.5 Clinical Trial Agreement

Medtronic contracts with participating institutions/investigators through a Clinical Trial Agreement that defines the scope and responsibilities and associated compensation related to carrying out the obligations under a clinical study sponsored by Medtronic.

Investigators that have a vested financial interest in Medtronic or the commercial sales and use of the study device will not be eligible for participation in this clinical trial. Medtronic will control this potential bias through the investigator / site selection process.

15.6 Liability/Warranty/Insurance Information

15.6.1 Warranty

Warranty information is provided in the product packaging for the commercially released device and additional copies are available upon request.

15.6.2 Insurance (Canada)

Medtronic of Canada ULC is a wholly owned subsidiary of Medtronic, which as the parent company of such entity maintains appropriate general liability insurance coverage as required under applicable laws and regulations and will comply with applicable local law and custom concerning specific insurance coverage. If required, a General Liability insurance statement/certificate will be provided to the REB.

15.6.3 Insurance (US)

Medtronic Xomed Ltd. is a wholly owned subsidiary of Medtronic, which as the parent company of such entity maintains appropriate clinical trial liability insurance coverage as required under applicable laws and regulations and will comply with applicable local law and custom concerning specific insurance coverage. If required, a Clinical Trial insurance statement/certificate will be provided to the IRB.

15.6.4 Subject Compensation

Reasonable provisions for subject time and effort will be compensated where required and/or approved by the governing IRB/REB. The amounts and events/tasks compensated will be detailed in the site-specific Clinical Trial Agreement.

15.7 CIP Amendments

Any revisions or amendments to the CIP or IC document, along with a statement of justification for the changes, will be submitted to all investigational sites and governing IRB/REBs, according to applicable regulations. Approval by IRB/REBs (where applicable) must be obtained prior to implementing a CIP revision at the study site.

15.8 Record Retention

All study-related documents must be retained for a period of at least 2 years after study closure (or longer if required by local law). Medtronic will inform the investigator/study site when these documents are no longer required to be retained.

No study document or image will be destroyed without prior written agreement between Medtronic and the investigator. The investigator should take measures to prevent accidental or premature destruction of documents. Should the investigator wish to assign the study records to another party or move them to another location, advance written notice must be given to Medtronic.

Medtronic will retain the study records according to Medtronic corporate policy and record retention schedule.

15.8.1 Investigator Records

The investigator is responsible for the preparation and retention of the records cited below. All of the below records, with the exception of case history records and case report forms, should be kept in the Investigator Site File (i.e., the study binder provided to the investigator) or Subject Study Binder. CRFs must be maintained and signed electronically within the electronic data capture system during the study. The following records are subject to inspection and must be retained for a period of two years (or longer as local law or hospital administration requires) after the date on which the investigation is terminated.

- All correspondence between the IRB/REB, sponsor, monitor, RA and the investigator that pertains to the investigation, including required reports.
- Subject's case history records, including:
  - Signed and dated IC (In U.S. and Canada, signed by subject).
  - Observations of AEs/ DDs
  - Medical history
  - Surgery and follow-up data
  - Documentation of the dates and rationale for any deviation from the protocol
- List of investigation study sites
- Subject screening information
- Normal value(s)/range(s) for clinical laboratory test(s)
- Lab report(s)
- Device use information containing model (CFN) and serial/lot numbers, subject IDs of the subjects receiving device, receive date by subject.
- All approved versions of the CIP, IC
- Signed and dated CTA
- CV of principal investigators and key members of investigation study site team (as required by applicable regulations.
- Documentation of delegated tasks
- IRB/REB approval documentation. Written information that the investigator or other study staff, when member of the IRB/REB, did not participate in the approval process. Approval documentation must include the IRB/REBs composition, where required per local law.
- Study training records for study site staff.

- Any other records that local regulatory agencies require to be maintained
- Final Study Report including the statistical analysis

15.8.2 Sponsor Records

Medtronic shall maintain the following accurate, complete, and current records:

- All correspondence which pertains to the investigation
- Signed Investigator Agreements, Financial Disclosure (if applicable) and current CV of principal investigator and key members of the investigation study site team (as required by local law), delegated task list
- All signed and dated case report forms submitted by investigator, including reports of AEs, and DDs
- All approved IC templates, and other information provided to the subjects and advertisements, including translations
- Copies of all IRB/REB approval letters and relevant IRB/REB correspondence and IRB/REB voting list/roster/letter of assurance
- Names of the institutions in which the study will be conducted
- Names/contact addresses of monitors
- Monitoring visit reports
- Statistical analyses and underlying supporting data
- Final report of the study
- The CIP, and study related reports, and revisions
- Study training records for study site personnel and Medtronic personnel involved in the study
- Any other records that local regulatory agencies require to be maintained.

Medtronic records and reports will be maintained in a password-protected document management system, and paper documents (where applicable) will be stored in stored in secured file cabinets at Medtronic during the course of this study.

After closure of the study Medtronic will archive records and reports indefinitely.

15.9 Reporting Requirements

15.9.1 Investigator Reports

The investigator is responsible for the preparation (review and signature) and submission to the sponsor of all case report forms, adverse events and device deficiencies, deaths, and any deviations from the clinical investigation plan. If any action is taken by an IRB/REB with respect to this study, copies of all pertinent documentation must be forwarded to Medtronic in a timely manner. Reports are subject to inspection and to the retention requirements as described above for investigator records.

Safety data investigator reporting requirements are listed in **Section 11**. The investigator shall prepare and submit in a complete, accurate and timely manner the reports listed in this section.

Table 12: Investigator Reports Applicable for All Geographies per Medtronic Requirements

Report	Submit to	Description/Constraints
Withdrawal of IRB/REB approval	Sponsor and Relevant Authorities	The investigator must report a withdrawal of approval by the reviewing IRB/REB of the investigator's part of the investigation within 5 working days.
Study Deviations	Sponsor and IRB/REB	Any deviation from the clinical investigational plan shall be recorded together with the explanation of the deviation. Notice of deviations from the CIP to protect the life or physical well-being of a subject in an emergency shall be given as soon as possible, but no later than 5 working days after the emergency occurred. Except in such emergency, prior approval is required for changes in the plan or deviations.
Final Report	IRBs/REBs and Relevant Authorities	This report must be submitted within 3 months of study completion or termination.

Table 13: Additional Investigator reports applicable to the United States per FDA regulations

Report	Submit to	Description/Constraints
Withdrawal of IRB approval (either suspension or termination)	Sponsor	The investigator must report a withdrawal of approval by the reviewing IRB of the investigator's part of the investigation within 5 working days. (21 CFR 812.150(a)(2))
Study deviations	Sponsor and IRB	Notice of deviations from the CIP to protect the life or physical wellbeing of a subject in an emergency shall be given as soon as possible, but no later than 5 working days after the emergency occurred. Except in such emergency, prior approval is required for changes in the plan or deviations. If the deviation may affect the scientific soundness of the plan or the rights, safety and welfare of the subjects, the deviation must be approved by Medtronic, the IRB, and the FDA/applicable RA. If the deviation does not affect these issues then only Medtronic must approve it. (21 CFR 812.150(a)(4))
Failure to obtain IC prior to investigational device use	Sponsor and IRBs	If an investigator uses a device without obtaining IC, the investigator shall report such use within 5 working days after device use. (21 CFR 812.150(a)(5))
Progress report	Sponsor and IRB	The investigator must submit this report to the sponsor and IRB at regular intervals, but in no event less than yearly intervals. (21 CFR 812.150 (a)(3)).
Final report	Sponsor IRBs Relevant Authorities	This report must be submitted within 3 months of study completion or termination of the investigation or completion or termination of the investigator's part of the investigation. (21 CFR 812.150(a)(6))
Other	IRB and FDA	An investigator shall, upon request by a reviewing IRB, FDA or any other RA, provide accurate, complete, and current information about any aspect of the investigation. (21 CFR 812.150(a)(7))

15.9.2 Sponsor Reports

Medtronic shall prepare and submit the following complete, accurate, and timely reports listed in the tables below (by geography). In addition to the reports listed below, Medtronic shall, upon request of the reviewing IRB/REB, provide accurate, complete and current information about any aspect of the investigation. Medtronic reporting requirements for safety data are listed in **Section 11.5**.

Table 14: Sponsor reports for Canada

Report	Submit to	Description/Constraints
Premature termination or suspension of the clinical investigation	Investigators, REB, Relevant authorities, and Head of the Institution	Provide prompt notification of termination or suspension and reason(s).
Recall and device disposition	Investigators, Head of Institution, REB, relevant authorities, and FDA	Notification within 30 working days and will include the reasons for any request that an investigator return, repair, or otherwise dispose of any devices.
Study deviation	Investigators	Ensure that all deviations from the CIP are reviewed with the appropriate clinical investigator(s), are reported on the CRFs and the final report of the clinical investigation. Study site specific study deviations will be submitted to investigators periodically.

Table 15: Sponsor reports for the United States

Report	Submit to	Description/Constraints
Withdrawal of IRB approval	Investigators, IRB, and relevant authorities	Notification within five working days. (21 CFR 812.150(b)(2))

Report	Submit to	Description/Constraints
Recall and device disposition	Investigators, Head of Institution, IRB, and relevant authorities	Notification within 30 working days and will include the reasons for any request that an investigator return, repair, or otherwise dispose of any devices. (21 CFR 812.150(b)(6))
Final report	Investigators, IRB	A final report will be provided to investigators, and IRBs within six months after completion or termination of this clinical study. (21 CFR 812.150(b)(7))
Study deviation	Investigators	Ensure that all deviations from the CIP are reviewed with the appropriate clinical investigator(s), are reported on the CRFs and the final report of the clinical investigation. Study site specific study deviations will be submitted to investigators periodically.
Other	IRB	Accurate, complete, and current information about any aspect of the investigation. (21 CFR 812.150(b)(10))
Premature termination or suspension of clinical study	IRB, Investigators, and regulatory authorities, where applicable	Medtronic will provide prompt notification of termination or suspension and reason(s) to investigator and where required to IRB and RAs.

15.10 Publication and Use of Information

Publications from the Novapak Study will be handled according to Standard Operating Procedures and as indicated in the CTA.

15.10.1 Publication Committee

Medtronic may form the Novapak Study Publication Committee from study investigators. Medtronic personnel may serve as members of the committee. This committee will manage study publications with the goal of publishing findings from the data. The Publication Committee will develop the final Publication Plan as a separate document.

The Publication Committee's role is to: 1) manage elements addressed in the publication plan, 2) develop the final Publication Plan under separate cover, 3) execute the Publication Plan, 4) oversee the publication of primary, secondary and ancillary study results, 5) review and prioritize publication proposals, 6) provide input on publication content, and 7) determine authorship. In addition, the committee will apply and reinforce the authorship guidelines set forth in the Publication Plan.

Membership in the Publication Committee does not guarantee authorship. The committee will meet at regular intervals, at least yearly, as needed.

15.10.2 Management of Primary, Secondary, and Ancillary Publications

The Publication Committee reviews, prioritizes, and manages all publications including primary, secondary and ancillary publications. Primary and secondary publications are those that address analyses of any or all primary objectives or secondary objectives, respectively, as specified in the CIP.

An ancillary publication is any publication that does not address the study objectives identified in the CIP. They include publications proposed and developed by other Medtronic departments or entities, clinicians participating in this study, and clinicians not participating in this study. The committee will work with Medtronic to ensure that requests do not present conflicts with other proposals, are not duplicative, and to determine which ancillary publication proposals, if any, will be supported.

The committee may decide that no publications, including abstracts, will be published prior to the end of the study or with individual study site data. Requests for publications on study objectives utilizing subset data (e.g., regional) will be evaluated for scientific validity and the ability of Medtronic to provide resources.

15.10.3 Criteria for Determining Authorship

Publications will adhere to authorship criteria defined by the International Committee of Medical Journal Editors (ICMJE, Uniform requirements for manuscripts submitted to biomedical journals, www.icmje.org). Individual authorship criteria defined by the target journal or conference will be followed when it differs from ICMJE criteria.

Authors, including Medtronic personnel, must at a minimum meet all of the conditions below:

- Substantial contributions to conception and design of the work, or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Decisions regarding authorship and contributor-ship will be made by the committee. The selected authors will be responsible for drafting the publication. All selected authors must fulfill the authorship conditions stated above to be listed as authors, and all contributors who fulfill the conditions must be listed as authors.

All investigators not listed as co-authors will be acknowledged as the “Medtronic Novapak Study Investigators” and will be individually listed according to the guidelines of the applicable scientific

journal when possible and affiliation. Any other contributors will be acknowledged by name with their specific contribution indicated.

15.10.4 Transparency

Transparency of clinical study results will be maintained by the following means:

- A final report, describing the results of all objectives and analysis, will be distributed to all investigators, ECs and CAs of participating countries when required by local law
- Registering and posting the study results on a publicly accessible database (e.g., ClinicalTrials.gov) based on the posting rules stipulated
- Submitting for publication the primary study results after the study ends
- Disclosing conflicts of interest (e.g., financial) of the co-authors of publications according to the policies set forth by the corresponding journals and conferences
- Making an individual study sites study data accessible to the corresponding investigator after the completion of the study, if requested

15.11 Suspension or Early Termination

The following sections are requirements for suspension or early termination of the whole investigation or one or more sites.

15.11.1 Planned Study Closure

Study Closure is a process initiated by distribution of a study closure letter. Study closure is defined as closure of a study that occurs when Medtronic and/or regulatory requirements have been satisfied per the CIP and/or by a decision by Medtronic or RA), whichever occurs first. The study closure process is complete upon distribution of the Final Report or after final payments, whichever occurs last. Ongoing EC oversight is required until the overall study closure process is complete. Refer to **Section 9.17** for additional information regarding study exit procedures.

15.11.2 Early Termination or Suspension

Early Termination is the closure of a study that occurs prior to meeting defined endpoints. This is possible for the whole study or a single study site. Suspension is a temporary postponement of study activities related to enrollment and distribution of the product. This is possible for the whole study or a single study site.

15.11.2.1 Study-wide termination or suspension

Possible reasons for considering study-wide suspension or termination of the study include but are not limited to:

- AEs associated with the system or product under investigation which might endanger the safety or welfare of the subject
- Observed/suspected performance different from the product's design intent
- Decision by Medtronic or RA (where the study is operating under RA)

- Technical issues during the manufacturing process

15.11.2.2 Investigator/study site termination or suspension

Possible reasons for investigator or study site termination or suspension include but are not limited to:

- Failure to obtain initial IRB/REB approval or annual renewal of the study
- Persistent non-compliance to the clinical investigation (e.g. failure to adhere to inclusion/exclusion criteria, failure to follow subjects per scheduled follow-ups)
- Lack of enrollment
- Noncompliance to regulations and the terms of the CTA (e.g. failure to submit data in a timely manner, failure to follow-up on data queries and monitoring observations in a timely manner, etc.)
- IRB/REB suspension of the study site
- Fraud or fraudulent misconduct is discovered (as defined by local law and regulations)
- Investigator request (e.g. no longer able to support the study)

15.11.3 Procedures for Termination or Suspension

15.11.3.1 Medtronic-initiated and regulatory authority-initiated

- Medtronic will promptly inform the clinical investigators of the termination or suspension and the reasons and inform the RAs where required
- In the case of study termination or suspension for reasons other than a temporary IRB/REB approval lapse, the investigator will promptly inform the IRB/REB
- In the case of study termination, the investigator must inform the subjects and may inform the personal physician of the subjects to ensure appropriate care and follow-up is provided
- In the case of a study suspension, subject enrollment must stop until the suspension is lifted by Medtronic
- In the case of a study suspension, enrolled subjects should continue to be followed out of consideration of their safety, rights and welfare

15.11.3.2 Investigator-initiated

- The investigator will inform Medtronic and provide a detailed written explanation of the termination or suspension
- The investigator will promptly inform the institution (where required per regulatory requirements)
- The investigator will promptly inform the IRB/REB
- The investigator will promptly inform the regulatory authorities
- The investigator will promptly inform the subjects and/or the personal physician of the subjects to ensure appropriate care and follow-up is provided
- In the case of a study suspension, subjects enrolled should continue to be followed out of consideration of their safety, rights and welfare

15.11.3.3 Ethics Committee-initiated

- The investigator will inform Medtronic and provide a detailed written explanation of the termination or suspension within 5 business days

- Subject enrollment must stop until the suspension is lifted
- Subjects already enrolled should continue to be followed in accordance with IRB/REB policy or its determination that an overriding safety concern or ethical issue is involved
- The investigator will inform his/her institution (where required per local requirements)
- The investigator will promptly inform the subjects, or legally-authorized designees or guardians and/or the personal physician of the subjects, with the rationale for the study termination or suspension
- The investigator will promptly inform the RA

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17. Appendices

Appendix A – Foreseeable AE List

18. Version History

The table below contains a history of the current CIP.

Version	Summary of changes	Justification of changes	Potential impact of the change on performance, effectiveness, or safety or other endpoints	Identification of the affected study documents	Author(s)/Title
A	• Not Applicable, New Document	N/A	N/A	N/A	David Hodge, Clinical Research Program Manager

Appendix A – Foreseeable AE List

The information provided in this section pertains to foreseeable adverse events that may be observed in the Novapak Study and may collectively assist in identifying those events for a given device or therapy that are unexpected in nature. The foreseeable adverse events information consists of three parts: 1) observed adverse device effect(s) in similar Medtronic studies, 2) adverse events reported in published literature, and 3) additional foreseeable adverse events. An evaluation of potentially anticipated events, adverse device effects observed in previous clinical studies, and reported events in literature may be used in combination with device labeling, current event reporting information, and other published data to assess for an unexpected occurrence.

The use of Novapak Nasal Sinus Packing and Stent device involves application after surgery, therefore, standard adverse events associated with a surgical procedure may be experienced (e.g. anesthesia complications, injury, infections, bleeding, exacerbation of pre-existing conditions, healing

complications, etc.). However, the focus of this section is to address in more detail, those events that are foreseeable due to the use, performance, and/or presence of the device under investigation.

Potential risks associated with the use of the Novapak Nasal Sinus Packing and Stent device, as well as risk minimization are discussed within Section 10. Treatment required for procedure and/or device related adverse events may include medication, device removal, or other surgical and medical remedies.

The remainder of this section provides examples of adverse event data from previous Medtronic clinical studies and literature. Evaluation of potentially anticipated events may involve data in this section as well as a thorough review of all available information (e.g. labeling, current event reporting, published data, etc.).

Risks and Complications of Sinus Surgery

Normal Expected Complications

- mild bleeding
- inflammation and swelling
- nasal congestion
- moderate pain
- fatigue
- mild to moderate headaches
- facial pressure

Complications that may occur

- Bleeding / Hemorrhaging
- Adhesions of Tissues
- Scaring of Tissues
- Infections
- Nasal Crusting or Dryness
- Loss of Smell or Taste
- Cerebral Spinal Fluid Leak
- Empty Nose Syndrome
- Damage to the Ocular Orbit
- Numbness of the Teeth or Palate
- Septal Perforation
- Return of Symptoms / Obstruction
- Anesthesia Related Risks

Risks Associated with Nasal Packing

Nasal sinus packing in general has tried to address these surgical complications but may result in risks that are specific to the use of packing, as follows:

- Bleeding – present if packing is inadequate or bleeding is excessive– may require post-operative controls (e.g., suturing, cautery, more packing)
- Adhesions – present if packing is inadequate to separate tissue compromised due to surgical trauma – requires post-operative debridement of tissues which may lead to bleeding.
- Scarring - This risk is where the tissue heals abnormally
- Infection – due to introduction of bacterial during the surgery and/or if sterility is breached - packing could encourage bacterial growth if design controls are not in place to control bacterial growth.
- Toxic Shock Syndrome –defined as “A severe illness caused by infection with staphylococcus aureus and characterized by high fever of sudden onset, vomiting, diarrhea, and myalgia, followed by hypotension and in severe cases, shock; a sunburn like rash with peeling of the skin, especially of the palms and soles, occurs during the acute phase.”
- Respiratory Obstruction – physical obstruction of the breathing pathway – This harm may occur from stent migration and cause difficulty breathing (i.e., hypoxia, dyspnea)
- Aspiration of the packing – causes respiratory obstruction with tachypnea can lead to aspiration pneumonia, urgent medical intervention may be necessary
- Pneumonia - If the stent were aspirated, pneumonia may occur. The patient may be treated with IV medication.
- Potential toxicity reactions – components of the packing could lead to a toxicity reaction due to a non-biocompatibility reaction occurring, but the reaction would not be expected to go beyond an inflammatory response. (i.e., redness, swelling, etc.)
- Potential allergic hypersensitivity reactions – components of the packing could lead to an allergic hypersensitivity reaction - A patient may experience edema and difficulty breathing with IV medications used as medical intervention.
- Foreign Body Reaction - Potential tissue interactions with packing components, fragments, or surface texture. In addition to an inflammatory response, it usually includes the formation of a foreign body granuloma, or encapsulation around a foreign object. Medical intervention may be taken to remove the product.
- Inflammation - This harm includes local irritation from the product. This risk may require Oral medication to reduce inflammatory response.
- Fever - A medium-low grade fever may develop. This risk may require Oral medication to reduce inflammatory response.
- Device Fragments in Patient – If a device fragments migration of pieces of the stent could result in possible medical intervention needed
- Pain – during post-operative removal of non-dissolving packing devices most patients have reported some mild temporary pain.

- Decreased Therapeutic Response – The packing may not perform as expected and not control the risks as intended. It would not result in surgical correction but may require a minor medical intervention.

Current Reported Patient Injury Complaints Related to Novapak Device

The use of the Novapak Nasal Sinus Packing and Stent may involve the risks listed above for all packing type devices, with the exception of pain upon removal, since it dissolves away with irrigation. There may be other discomforts and risks related to the Novapak Nasal Sinus Packing and Stent device and/or this study that are not foreseen at this time.

These are the current risks of Novapak seen in the field based on reports to our complaint system: (number of reported events as of June 24, 2022)

- Irritation – potential shellfish hypersensitivity (1)
- Post-operative bleeding requiring secondary controls (3)
- Post-operative device migration to oral cavity (1)
- Post-operative edema and pain (2)

Observed Adverse Device Effect in Previous Clinical Studies

There have been no previous clinical studies with the use of Novapak Nasal Sinus Packing and Stent device.