CLINICAL STUDY PROTOCOL

1 TITLE PAGE

Study Title	The EXPAND Study: A Clinical Evaluation of PROPEL® Contour Placement Following In-Office Frontal Sinus Balloon Dilation
Protocol Number	P500-1220
ClinicalTrials.gov ID	NCT04858802
Study Devices	PROPEL Contour Sinus Implant (mometasone furoate, 370 mcg) VenSure™ Nav Balloon Device Cube Navigation System
Study Design	Post-market, randomized, intra-patient controlled, blinded, multicenter trial
Sponsor's Name and Address	Intersect ENT, Inc. 1555 Adams Drive Menlo Park, CA 94025 USA Tel: +1 650-641-2100 Fax: +1 650-641-2053
National Principal Investigator	Boris Karanfilov, MD Ohio Sinus Institute 5378 Avery Road Dublin, Ohio 43016 Tel: +1 614-771-9871 bk@ohiosinus.com
Data Management and Study Monitoring	Intersect ENT, Inc.
Biostatistics and Data Analysis	Intersect ENT, Inc.

This study will be conducted under the guidance of the International Council on Harmonization (ICH) E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1) March 2018 (abbreviated as ICH E6(R2)); FDA's Good Clinical Practice (GCP) regulations for medical devices; ISO's Clinical investigation of medical devices for human subjects - Good clinical practice (ISO 14155:2020) and other applicable local and federal regulations.

The study-related COVID-19 contingency measures to assure the safety of study subjects, maintain compliance with GCP, and minimize risks to study integrity for the duration of the COVID-19 pandemic are detailed in Section **21.**

CONFIDENTIALITY STATEMENT

2 REVISION HISTORY

Revision	Revision Date	Reason for Revision
1.0	26-FEB-2021	Initial Release
2.0	18-MAR-2021	• Updated study devices in protocol summary for alignment. • Clarified primary efficacy endpoint measurement. • Modified inclusion criteria regarding successful in-office balloon dilation of bilateral FSO. • Modified eligibility criteria and added baseline procedure to allow for optional maxillary/sphenoid sinus dilation with a commercially available balloon sinuplasty device, if clinically necessary, prior to dilating the frontal sinuses. • Added exclusion criteria to align with contraindications noted in Cube Navigation System IFU. • Removed endoscopic confirmation of bilateral frontal stenosis from schedule of assessments. • Aligned concomitant medications noted in Protocol Summary and Concomitant Medication sections. • Added AE severity guidelines. • Clarified potential risks section.
3.0	30-APR-2021	• Realigned Sec 11.3 to defer to Core Laboratory Imaging Guidelines and removed Volume Evaluation from title of Sec 11.3 • Realigned Sec 11.4 to defer to Core Laboratory Reading Guidelines which specifies the sinus areas for evaluation, including the Contour area to measure the Primary Endpoint • Removed Appendix 2: Cone Beam CT Imaging Parameters • Included Disposable Inflation Device in applicable sections • Added “Device” after VenSure Nav Balloon throughout the document • Changed “patient” to “subject” throughout document • Changed Day 1 to Day 0 for Baseline/Procedure in Sec 5.0 Study Flow Diagram • Sec 3.0 Terms: Replaced ISO 14155:2011 definition of “Use Error” with updated definition and notes from ISO 14155:2020 • Sec 3.0 Terms: Removed ‘compatible accessory device’ from the 21 CFR 803 definition of “Device Malfunction” because it is not applicable in this study. • Sec 4.0 Aligned Study Title with Objective, added “in-office” and “bilateral” to Objective • Sec 10.4 subparagraph Bilateral Balloon Dilation of the FSO removed “includes guidewires” as they are not included in IFU • Phrase “Primary endpoint will be released after all eligible subjects have completed Day 45 CT scan.” Moved from Sec 9.2.1 to Statistics Sec 16.6 Intent-to-Treat (ITT) Population
4.0	03-SEP-2021	• Updated study title • Added ClinicalTrials.gov identifier • Updated study design includes increased number of study centers from 15 to 20, changed Day 90 phone visit to in-person visit and added

		patient symptom questionnaires (SNOT-22, RSI and CRS side-specific symptoms) at baseline and follow-up visit, requirement for endoscopic evaluation and video recording prior to the baseline procedure and at each follow-up visit • Updated Schedule of Assessments Study and Flow Diagram to reflect on the updated study design • Removed redundant and non-applicable eligibility criteria • Updated primary and secondary endpoints • Clarified investigator's standard protocol used for nasal endoscopy and procedures may be used; examples of anesthesia removed • Updated optional in-office baseline procedures allowed • Removed restriction that medically necessary maxillary and sphenoid sinus dilation must use a separate commercially available device • Added that CT scan may need to be redone if it does not meet the Cube Navigation System Requirements • Sec. 13 Clarified the acquisition and measurements of CT scans • Clarified training process • Sec. 17 Added indeterminate as a relationship classification for AEs and AE expectedness section • Sec. 18 Indicated that the detailed analysis plan for primary /secondary endpoints will be described in the statistically analysis plan • Added Sec. 21 with COVID-19 Contingency Measures • Made minor clarifications, edits and editorial changes throughout
5.0	20-MAY-2022	• Sec. 3 added FSOT abbreviation • Sec. 4 added FSOT definition • Sec. 5 and 9.2 replaced FSO maximum diameter with FSO minimum diameter, added FSOT volume to secondary endpoints, and specified frontal score for Lund-Mackay and Zinreich's modified Lund-Mackay • Sec 5 and 9.3 moved health-economic measures and patient satisfaction from secondary endpoints to exploratory endpoints • Sec. 9.1 and 13.2 updated wording of the primary efficacy endpoint to align with CP-00038 • Sec. 12.5 made optional assessments at unscheduled visits • Sec. 18.6 updated definition of PTE population and added examples of major procedural protocol deviations • Added CP-00038 Radiographic Evaluation Protocol for P500-1220 (The EXPAND Study) to references • Made minor clarifications, edits and editorial changes throughout

TABLE OF CONTENTS

3 LIST OF ABBREVIATIONS

Abbreviation	Expansion
ADE	adverse device effect
AE	adverse event
ASADE	anticipated serious adverse device effect
CFR	Code of Federal Regulations
CIP	clinical investigational plan
COPD	chronic obstructive pulmonary disease
CRF	case report form
CRS	chronic rhinosinusitis
CSP	clinical study protocol
CSR	clinical study report
CT	computed tomography
EDC	electronic data capture
e.g.	'exempli gratia' in Latin, meaning 'for example'
ESS	endoscopic sinus surgery
et al	'et alia' in Latin, meaning 'and others'
FDA	Food and Drug Administration
FSO	frontal sinus ostium/ostia
FSOT	frontal sinus outflow tract
GCP	good clinical practice
ICF	informed consent form
ICH	International Council on Harmonization
i.e.	'id est' in Latin, meaning 'that is'
IFU	instructions for use
INCS	intranasal corticosteroids
IRB	institutional review board
ITT	intent-to-treat
MF	mometasone furoate
OS	frontal sinus outflow narrowest diameter
PTE	per-treatment-evaluable
RSI	Rhinosinusitis Symptom Inventory
SADE	serious adverse device effect
SAE	serious adverse event
SBD	sinus balloon dilation
SOP	standard operating procedure
UADE	unanticipated adverse device effect
USADE	unanticipated serious adverse device effect

4 DEFINITIONS OF TERMS

Term	Definition
Adhesion/scarring grading scale for the ethmoid sinus	Adhesion/scarring severity in the ethmoid sinus graded on a 5-point scale as follows: • 0: None • 1: Small but non-obstructing (no separation required) • 2: Obstructing, but easily separated • 3: Dense and obstructing, separation difficult • 4: Severe: complete adhesion of the middle turbinate to the lateral nasal wall
Adhesion/scarring grading scale for the frontal sinus ostium/ostia (FSO)	Adhesion/scarring in the FSO assessed on a 4-point scale as follows: • 0: No visible granulation/scarring in the FSO • 1: Minimal amount of granulation, scarring or contraction observed but not obstructing the FSO (intervention not warranted) • 2: Moderate amount of obstructive granulation, scarring or contraction present in the FSO (intervention is warranted) • 3: Significant amount of scarring or contraction causing obstruction of the FSO requiring intervention (likely to compromise patency if not removed)
Adverse device effect (ADE)	Adverse event related to the use of an investigational medical device. 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. This definition also includes any event resulting from use error or from intentional misuse of the investigational medical device. If a comparator medical device is used in the investigation, this definition also applies to ADEs of the comparator device. [ISO 14155:2020]
Adverse event (AE)	Any untoward medical occurrence, unintended disease or injury, or untoward clinical sign(s) (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated. This definition includes events related to the procedures involved. This definition also includes events related to the investigational medical device or any comparator device. For users or other persons, this definition is restricted to events related to the use of investigational medical devices or comparators. [ISO 14155:2020]
Baseline	Information and values collected during Screening and before initiation of the study treatment.
Baseline procedure	In-office, bilateral frontal sinus balloon dilation.
Case report form (CRF)	A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject. [ISO 14155:2020]
Chronic rhinosinusitis (CRS)	Per the 2021 "International Consensus Statement on Allergy and Rhinology" definition, patient must have ≥ 12 weeks of: Two or more of the following symptoms: • Nasal discharge (anterior/posterior)

	• Nasal blockage/obstruction/congestion • Reduction/loss of smell • Facial pressure/pain And one or more of the following findings: • Evidence of inflammation on paranasal sinus examination or computed tomography • Evidence of purulence coming from paranasal sinuses or ostiomeatal complex
CRS side-specific symptom questionnaire	Allows to evaluate each of the following 5 cardinal symptoms of CRS on the left and right side: • Facial pain/pressure • Facial congestion/fullness • Nasal obstruction/blockage • Discolored or pus nasal discharge or post-nasal drip • Decreased sense of smell Each side is scored individually on a 6-point scale as follows: • 0: Absent • 1: Very mild • 2: Mild • 3: Moderate • 4: Severe • 5: Very severe
Clinical Investigational Plan (CIP) or Clinical Study Protocol (CSP)	Document that states the rationale, objectives, design and pre-specified analysis, methodology, organization, monitoring, conduct and record-keeping of the clinical investigation [ISO 14155:2020]
Device deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance. Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling. This definition also includes device deficiencies related to the investigational medical device or the comparator. [ISO 14155:2020]
Device malfunction	For an investigational medical device: Failure to perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical investigation plan (CIP), or Investigators' Brochure (IB). [ISO 14155:2020] Failure to meet its performance specifications or otherwise perform as intended. The intended performance of a device refers to the intended use for which the device is labeled or marketed. [21 CFR 803]
Enrolled	Subjects are considered enrolled upon signing the IRB-approved informed consent form.
Frontal sinus ostia/ostium (FSO)	Refers to the natural frontal sinus openings
Frontal sinus outflow tract (FSOT)	Refers to the region of the frontal sinus surrounding the FSO, bordered superiorly by the frontal infundibulum and inferiorly by the frontal recess
Implant delivery success	Successful access and deployment of the PROPEL Contour Sinus Implant into the FSO. Delivery is considered successful if the procedure concludes with correct implant placement on the intended side, even if a second attempt to place the implant is necessary. An attempted deployment

	occurs when the investigator introduces the delivery system into the subject's nostril with the intent of placing an implant. The proportion of successful deployments is defined as a fraction where the numerator is the number of successful deployments and the denominator is the number of sinuses in which a deployment was attempted.
Inflammation score	For the purpose of the endoscopic scoring method in this study, the term inflammation is a global descriptor that includes erythema, edema and/or polypoid changes. The inflammation present in the frontal recess/FSO is estimated visually based on the endoscopic examination on a scale ranging from 0 (no visible inflammation) to 100 (severe inflammation) involving extensive erythema, or polyposis
Institutional Review Board (IRB)	An independent body whose responsibility it is to review clinical investigations in order to protect the rights, safety and well-being of human subjects participating in a clinical investigation. The primary purpose of such review is to assure the protection of the rights, safety, and welfare of human subjects. The IRB should be established, operated, and function in conformance with 21 CFR 56.
Intent-to-treat (ITT) population	Consists of all randomized subjects and sinuses in whom the study implant in the target sinus was attempted. An attempt occurs when the physician introduces the delivery system into the subject's nostril with the intent of implant placement.
Lund-Mackay CT Staging System	Assigns a value of 0 if the sinus is totally patent, 1 if it is partial opacified or 2 if it is completely opacified to each of the frontal, anterior ethmoid, posterior ethmoid, maxillary, and sphenoid sinus. The ostiomeatal complex (OMC) is scored either 0 or 2. The maximum score for each side is thus 12, with a total score determined out of 24.
Patient satisfaction questionnaire	Question to patient on how satisfied is he/she with the PROPEL Contour for treatment of CRS and whether he/she would recommend the PROPEL Contour to a family member or a friend
Per-treatment-evaluable (PTE) population	Consists of all randomized subjects and sinuses that have received the assigned study implant in the target sinus, who have no major procedural protocol deviations and for whom follow-up data are available.
Polyp grading scale for the ethmoid sinus	Polyps originating from the ethmoid sinus assessed endoscopically and graded on an 8-point scale as follows: • 0: No visible sinonasal polyps • 1: Small amount of sinonasal polyps confined in middle meatus • 1.5: Small amount of sinonasal polyps confined in middle meatus with expanded amount of polypoid edema obstructing ≥ 25% of the ethmoid sinus cavity • 2: Expanded amount of sinonasal polyps confined in middle meatus • 2.5: Expanded amount of sinonasal polyps confined in middle meatus with expanded amount of polypoid edema obstructing ≥ 50% of the ethmoid sinus cavity • 3: Sinonasal polyps extending beyond middle meatus but not totally obstructing the nasal cavity

	• 3.5: Sinonasal polyps extending beyond middle meatus with expanded amount of polypoid edema obstructing ≥ 75% of the ethmoid sinus cavity • 4: Sinonasal polyps completely obstructing the nasal cavity
Polypoid edema in the FSO	Polypoid edema in the frontal recess/FSO is assessed on a 4-point scale as follows: • 0: Normal mucosa, no visible polyps/mucosal edema • 1: Minimal amount of polyps/mucosal edema • 2: Moderate amount of polyps/polypoid edema • 3: Expanded amount of polyps/polypoid edema
Rhinosinusitis Symptom Inventory (RSI)	RSI is administered using a paper (reflective) questionnaire to assess the CRS symptoms: 5 key symptoms (facial pain/pressure, facial congestion/ fullness, nasal obstruction/blockage, nasal discharge or post-nasal drip, decreased sense of smell), 7 other symptoms (headache, halitosis, dental pain, cough, ear symptoms, fevers, and fatigue) on a 6-point scale of 0 to 5, as follows: • 0: Absent • 1: Very mild • 2: Mild • 3: Moderate • 4: Severe • 5: Very severe The individual symptom scores were used to calculate 4 domain scores as follows: • Nasal: sum of scores for nasal obstruction, rhinorrhea, sense of smell • Facial: sum of scores for facial pain/pressure, facial congestion/ fullness, and headache • Oropharyngeal: sum of scores for halitosis, dental pain, cough, and ear symptoms • Systemic: sum of scores for fevers, and fatigue In addition, the RSI catalogs medication use (topical nasal corticosteroids, prescription antihistamines, and oral antibiotics), physician visits, and workdays missed due to CRS.
Safety population	Consists of all subjects and sinuses exposed to PROPEL Contour Sinus Implant. This population will be used for all summaries of adverse events. Any subjects enrolled in the study who are not exposed to the PROPEL Contour Sinus Implant will be summarized separately.
Serious adverse device effect (SADE)	An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event. If the nature, incidence, severity or outcome of a SADE has been identified in the device's risk analysis report, it is considered an anticipated SADE (or ASADE)
Serious adverse event (SAE)	Adverse events are considered "serious" if, in the view of either the investigator or sponsor, they result in any the following outcomes: • Death; or • A life-threatening illness or injury; or • Permanent impairment of a body structure or a body function; or

	• Inpatient hospitalization or prolongation of existing hospitalization; or • Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function; or • Fetal distress, fetal death, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Planned hospitalization for a pre-existing condition, or a procedure required by the CIP/CSP, without serious deterioration in health, is not considered a serious adverse event. [ISO 14155:2020]
Sino-Nasal Outcome Test (SNOT-22)	Validated, disease-specific, symptom-scoring instrument consisting of 22 questions, each scored by patient on a 6-point scale as follows: • 0: No problem • 1: Very mild problem • 2: Mild or slight problem • 3: Moderate problem • 4: Severe problem • 5: Problem as bad as it can be The maximum total score for all symptoms is equal to 110.
Source data	All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial.
Source documents	Original documents, data, and records. Printed, optical, or electronic documents containing source data.
Subject	An individual who participates in a clinical investigation
Unanticipated adverse device effect (UADE)	Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. [21 CFR 812] A UADE is comparable to an unexpected serious adverse device effect (USADE) as defined in ISO 14155:2020 (see definition below), although it doesn't include an "S" for serious in the FDA's acronym. NOTE: The occurrence of a diagnostic or elective surgical procedure for a pre-existing condition, unless the condition becomes more severe or increases in frequency because of the device, would not be considered an adverse device effect (ADE).
Unanticipated serious adverse device effect (USADE)	Any serious adverse device effect (SADE) which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report. [ISO 14155:2020; 21 CFR 812]

	If the nature, incidence, severity or outcome of a SADE has been identified in the device's risk analysis report, it is considered an anticipated SADE (or ASADE).
Use error	User action or lack of user action while using the medical device that leads to a different result than that intended by the manufacturer or expected by the user. Use error includes the inability of the user to complete a task. Use errors can result from a mismatch between the characteristics of the user, user interface, task or use environment. Users might be aware or unaware that a use error has occurred. An unexpected physiological response of the patient is not by itself considered a use error. A malfunction of a medical device that causes an unexpected result is not considered a use error. [ISO 14155:2020]
Zinreich's Modified Lund-Mackay Staging System	Each sinus is assigned a score based on the percentage of opacification from mucosal thickening as follows: • 0: 0% • 1: 1% to 25% • 2: 26% to 50% • 3: 51% to 75% • 4: 76% to 99% • 5: 100% or completely occluded The ostiomeatal complex (OMC) is given a score of 0 if it is completely patent, 1 if it is partially obstructed, or 2 if it is completely obstructed. Similar to the Lund-Mackay system, each side is graded, and their sum is the total score out of maximum of 54.

5 PROTOCOL SUMMARY

Study Title	The EXPAND Study: A Clinical Evaluation of PROPEL™ Contour Placement Following In-Office Frontal Sinus Balloon Dilation
Objective	To evaluate the efficacy of PROPEL Contour placement following an in-office frontal sinus balloon dilation (SBD) in patients with chronic rhinosinusitis (CRS)
Study Devices	PROPEL Contour (mometasone furoate, 370 mcg) VenSure™ Nav Balloon Device Cube Navigation System
Study Design	Post-market, randomized, intra-patient controlled, blinded, multicenter trial
Subject Enrollment	80 randomized subjects at up to 20 US study centers
Treatment Assignment	After successful in-office bilateral frontal SBD using the VenSure Nav Balloon Device and Cube Navigation System, subjects will be randomized to receive 1 PROPEL Contour on 1 side (the treatment group) and nothing on the contralateral side (the control group).
Primary Efficacy Endpoint	Side-to-side difference in FSO patency at Day 45 based on cross-sectional area of FSO by CT measurements performed by an independent, blinded reviewer

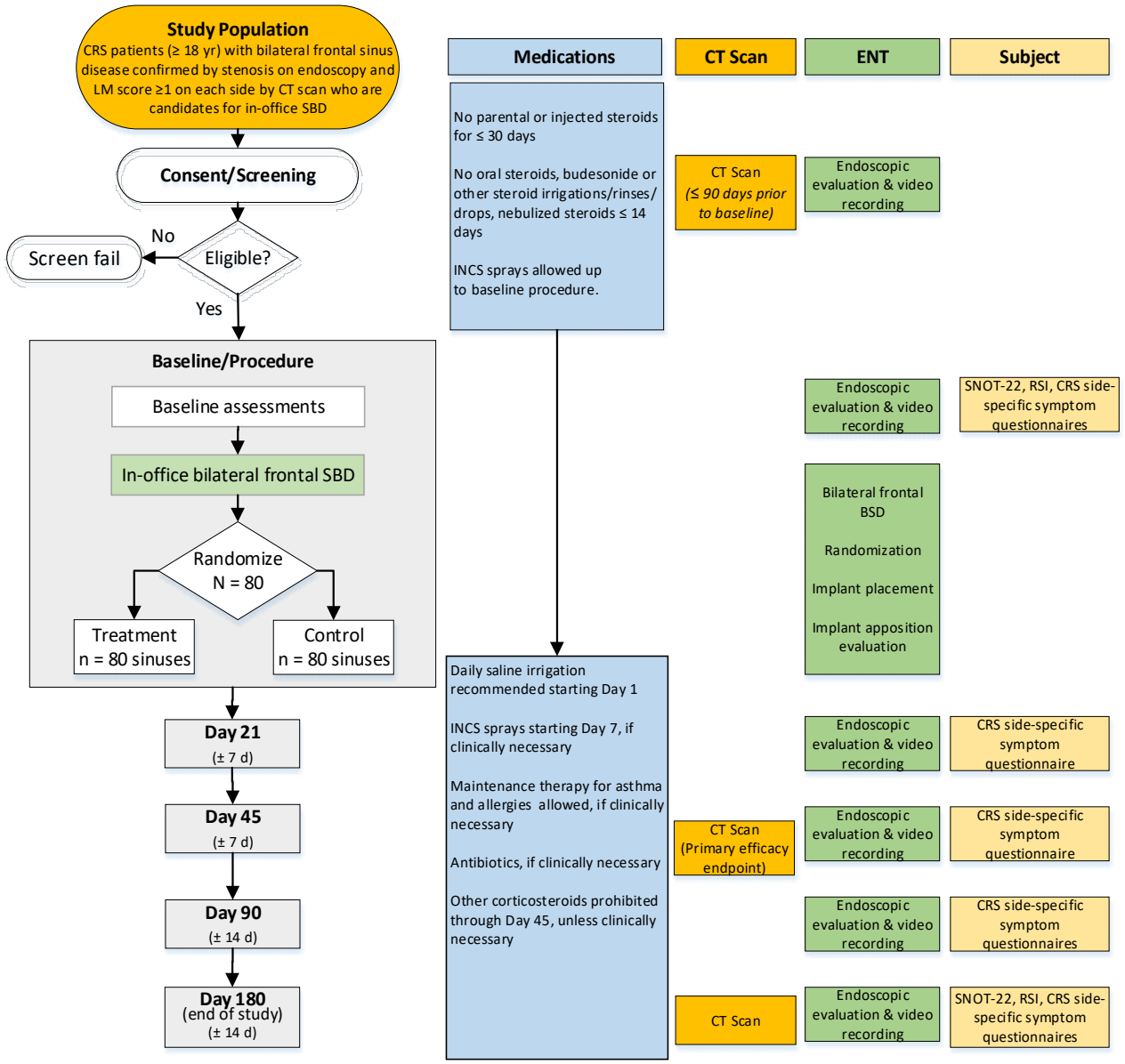
Secondary Endpoints	• CT grading by an independent, blinded reviewer (Day 45, 180):
	  ○ Cross-sectional area of FSO (Day 180 only)
	  ○ FSO minimum diameter
	  ○ FSOT volume
	  ○ Zinreich's modified Lund-Mackay score for the frontal sinus
	  ○ Lund-Mackay score for the frontal sinus
	• CT grading by clinical investigators (Day 45, 180):
	  ○ Lund-Mackay score for the frontal sinus
	• Endoscopic grading by clinical investigators (Day 21, 45, 90, 180):
	  ○ Adhesion/scarring grade in the frontal recess/FSO and ethmoid sinus
	  ○ Inflammation score in the frontal recess/FSO
	  ○ Polypoid edema in the frontal recess/FSO
	  ○ Polyp grade in the ethmoid sinus
	• Need for post-operative intervention as determined by clinical investigators per endoscopy (Day 21, 45, 90, 180)
	• Patient-reported outcomes:
	  ○ CRS side-specific symptom score (Day 21, 45, 90, 180)
	  ○ SNOT-22 score (Day 180)
	  ○ RSI score (Day 180)
	• Implant delivery success

Exploratory Endpoints	• Patient satisfaction (Day 90, 180) • Health-economic measures
Safety Measures	All adverse events and device deficiencies from enrollment through Day 180 (end of study) will be tabulated.
Study Population	Patients (≥ 18 years of age) with confirmed diagnosis of CRS who are candidates for in-office frontal SBD because they present with bilateral stenosis of the FSO and in whom placement of PROPEL Contour is feasible and medically appropriate.
Key Inclusion Criteria	• Patient is 18 years of age or older. • Patient has confirmed diagnosis of CRS per International Consensus Statement on Allergy and Rhinology: Rhinosinusitis 2021 (ICAR:RS) guidelines. ○ Patient must have ≥ 12 weeks of ≥ 2 of the following symptoms:

	▪ nasal obstruction or congestion ▪ nasal discharge (rhinorrhea or post-nasal drip) ▪ facial pain/pressure ▪ reduction/loss of smell ○ And ≥ 1 of the following findings: ▪ Evidence of inflammation on paranasal sinus examination or CT; or ▪ Evidence of purulence coming from paranasal sinuses or ostiomeatal complex. • In the opinion of the investigator, treatment with the PROPEL Contour Sinus Implant as an adjunct to frontal SBD with a 6 mm balloon is technically feasible and clinically indicated in FSO. • Female patients of reproductive age and potential must not be pregnant or nursing, and patient agrees to avoid becoming pregnant during their participation in the study. • Patient has bilateral disease in the frontal sinus (Lund-Mackay score ≥ 1 on each side) on CT scan performed within 90 days prior to the baseline. • Confirmation of bilateral FSO access with navigation assistance • A successfully completed in-office bilateral balloon dilation of the FSO with no complication on either side that, in the opinion of the investigator is amenable for PROPEL Contour Sinus Implant placement in both FSO.
Key Exclusion Criteria	• Patient has structural obstruction that precludes endoscopic visualization of one or both FSOs prior to implant placement. • Patient had prior Draf III surgery. • Patient had prior sinus surgery or endoscopic sinus surgery (ESS) ≤ 30 days from the baseline procedure or the mucosa has not healed yet. • Patient had prior frontal SBD or ESS with corticosteroid containing stents, packing materials or implants (e.g., PROPEL, PROPEL Mini, PROPEL Contour) within approximately 1 year prior to the baseline procedure. • Patient had prior frontal SBD without corticosteroid containing stents, packing materials or implants, or prior balloon dilation in other sinuses with corticosteroid containing stents, packing materials or implants, < 30 days from the baseline procedure. • Expanded amount of ethmoid sinonasal polyps extending beyond the middle meatus (grade > 2) unless reduced 30 days prior to the baseline procedure • Patient has oral-steroid dependent condition such as chronic obstructive pulmonary disease (COPD) or other conditions. • Known history of allergy or intolerance to corticosteroids or mometasone furoate • Patient has used parenteral or injected steroids (e.g., Kenalog) within 30 days prior to the baseline procedure. • Patient has used oral steroids, budesonide or other sinus steroid irrigations/rinses or drops, nebulized steroids administered nasally within 14 days prior to baseline procedure.
Treatment Strategy	• At the end of a successful in-office bilateral frontal BSD, the left or right FSO is randomly assigned to receive 1 PROPEL Contour. • No hemostatic packing materials of any kind are placed within the left or right FSO unless medically necessary.

	• Packing such as the Merocel may be placed in the nasal or ethmoid cavity, if necessary. No use of steroid soaked packing materials is permitted. • Other than implantation of one PROPEL Contour Sinus Implant on 1 frontal sinus side of the patient at the baseline procedure, no steroid-containing intranasal splints, spacers or corticosteroid-eluting sinus implants (PROPEL, PROPEL Mini, PROPEL Contour, SINUVA) in any sinuses are allowed. • It is preferred that the PROPEL Contour Sinus Implant in the FSO be left in place for at least 30 days but can be removed at clinical investigator discretion.
Prior and Concomitant Medications	• Allowed *prior* to and *post*-baseline procedure: o INCS sprays prior to and post, starting after 7 days o Orally inhaled steroids for control of asthma o Stable regimens of leukotriene inhibitors and/or immunotherapy for allergies • Not allowed *prior* to the baseline procedure: o A 30-day restriction for use of parenteral and injected steroids (e.g., Kenalog) o A 14-day restriction for use of oral steroids, budesonide and/or any other sinus steroid irrigations/rinses or drops, nebulized steroids administered nasally o A 45-day restriction for biologics for CRS treatment (such as Dupixent) • Allowed *post*-baseline procedure: o Daily use of saline sprays/rinses/irrigations in both sinuses starting on Day 1 o Antibiotics if infection is suspected o INCS sprays (excluding Xhance) in one or both sinuses starting after 7 days as clinically necessary. • Not allowed *post*-baseline procedure: o Other corticosteroids (e.g., oral, parenteral, injections, budesonide or other sinus steroid irrigations/rinses or drops, breath powered Xhance, nebulized steroids administered nasally or other drug eluting stents) through Day 45, unless clinically necessary, to ensure unbiased assessment of the primary endpoint o Biologics for CRS (such as Dupixent)
Subject Follow-Up	Subjects are required to complete **4** follow-up visits at Day 21, 45, 90 and 180 (end of study). Note: Day 45 CT should be obtained after suctioning and clearing mucous of the FSO and any implant debris to prevent unblinding. Investigators will confirm that no implant remnants are visible on the Day 45 CT scan before submitting it for blinded review.
Duration of Study	For a given subject: approximately **182** days = screening visit (1 day) + baseline/procedure (1 day) + follow-up (180 days). Overall: Approximately 15 months = 9-month enrollment phase + 6-month follow-up.

6 STUDY FLOW DIAGRAM



Abbreviations: CRS, chronic rhinosinusitis; CT, computed tomography; d, day; FSO, frontal sinus ostia/ostium; LM, Lund-Mackay; RSI, Rhinosinusitis Symptom Inventory; SBD, sinus balloon dilation; SNOT, Sino-Nasal Outcome Test.

7 SCHEDULE OF ASSESSMENTS

Assessments	**Screening**	**Baseline/ Procedure** (≤ 30 d from consent date)	**Day 21** (± 7 d)	**Day 45** (primary endpoint) (± 7 d)	**Day 90** (± 14 d)	**Day 180** (end of study) (± 14 d)
Informed consent	X					
Medical/surgical history	X					
CT scan[1]	X			X		X
Endoscopic evaluation & video recording	X[2]	X[2]	X	X	X	X
SNOT-22 questionnaire		X[3]				X
RSI questionnaire		X[3]				X
CRS side-specific symptom questionnaire		X[3]	X	X	X	X
In-office bilateral frontal SBD		X				
Randomization		X				
PROPEL Contour placement in FSO[4]		X				
Patient satisfaction questionnaire					X	X
Adverse event reporting	X	X	X	X	X	X
Device deficiency reporting		X	X	X	X	X
Concomitant medications	X	X	X	X	X	X

Abbreviations: CT, computed tomography; d, day; FSO, frontal sinus ostia/ostium; RSI, Rhinosinusitis Symptom Inventory; SBD, sinus balloon dilation; SNOT, Sino-Nasal Outcome Test.

[1] Screening CT must be performed ≤ 90 days prior to the baseline procedure to confirm the diagnosis of CRS. The follow-up CT at Day 45 and 180 shall be performed after endoscopic evaluation and debridement to ensure no implant remnants are present on the scan. All CTs should be uploaded for centralized blinded review.

[2] Screening endoscopic evaluation can be done at the baseline. Baseline values are entered into EDC.

[3] Complete endoscopic evaluation, SNOT-22, RSI and CRS side-specific symptom questionnaires prior to the baseline procedure. Assess implant apposition after the baseline procedure.

[4] Treatment side only.

8 BACKGROUND INFORMATION

8.1 Literature Review

Endoscopic sinus surgery (ESS) is recommended for patients with chronic rhinosinusitis (CRS) who have failed appropriate medical therapy (Orlandi 2021). While ESS has been demonstrated to be effective in reducing patient-reported symptoms in the short term, longer-term success rates have been reported in the range of 76% to 98% (Naidoo 2012, Ramadan 1999). Meanwhile, a relatively large number of patients continue to be symptomatic or experience recurrent symptoms or revision surgery within 1-2 years. Causes of surgical failure are numerous and include lateralization of the middle turbinate, adhesion formation between the middle turbinate and lateral nasal wall, ostial stenosis, persisting or recurrent mucosal edema, and polyposis. The same post-operative failure mechanisms within the ethmoid sinus apply to the frontal recess and frontal sinus ostia. These include formation of scarring, adhesions, synechiae, recurrent inflammation, and polyposis (Chandra 2004).

Many surgeons consider the postoperative treatment regimen to be as important as the surgery itself (Bugten 2006). There is strong evidence that postoperative endoscopic examination of the sinonasal cavity provides prognostic information concerning the potential for future episodes of sinusitis and that patients whose cavities became normal post-operatively are less likely to require revision (Kennedy 2000). Meticulous post-operative care following ESS involves several follow-up visits over the ensuing months. Maintenance of the surgical result is accomplished by routine endoscopic examination, meticulous cleaning of the cavity using saline rinses, debridement or other manipulations to remove adhesions, and adjustments in pharmacotherapy. Formation of adhesions, scarring, synechiae, middle turbinate lateralization, ostial stenosis and edema are major concerns often addressed by use of sinus stents and injectable gels. To address these post-operative issues, Intersect ENT (Menlo Park, CA) developed the PROPEL, PROPEL Mini and PROPEL Contour Sinus Implants.

The PROPEL Contour Sinus Implant was approved on 23 February 2017 for placement in maxillary and frontal sinuses following sinus surgery in CRS patients to maintain patency of the sinus ostia. Positive data from the PROPEL Contour Sinus Implant cohort of the PROGRESS study, a prospective, randomized, blinded, multi-center trial of 80 patients designed to assess the safety and efficacy of the implant when placed in the frontal sinuses following surgery (Luong 2018, Singh 2019), and a non-randomized, open-label EXCEED study in 15 patients for frontal and maxillary ostia, supported the approval. The study met its primary efficacy endpoint, demonstrating a statistically significant 65% relative reduction in the need for post-operative interventions, such as the need for additional surgical procedures or the need for oral steroid prescription, compared to surgery alone. The study utilized an intra-patient control design to assess the safety and efficacy of the PROPEL Contour Sinus Implant when placed following surgery performed in operating room on one sinus side compared to surgery alone on the contralateral side. The study results showed that placement of the PROPEL Contour Sinus Implant in the FSO

maintained sinus patency by reducing inflammation, scarring and polypoid edema. The study also confirmed that implant placement in the FSO poses negligible safety risks.

8.2 PROPEL Contour Sinus Implant

8.2.1 Description

A summary description of the PROPEL Contour Sinus Implant (**Figure 1**) is provided below. For more detailed delivery system and implant information, refer to the Instructions for Use (IFU). The PROPEL Contour Sinus Implant (part # 70033) is designed to accommodate the size and variability of the human sinus anatomy. The implant is intended to be inserted by a physician under endoscopic visualization and once positioned, is designed to be self-retaining against the mucosal surface in the area of the frontal recess/FSO.

The PROPEL Contour Sinus Implant is fabricated from a bioabsorbable monofilament polymer material commonly used in a variety of medical products, including dissolvable sutures. The implant is designed with an hour-glass shape to aid in anchoring / apposition to the tissue with the following dimensions: waist diameter = 15.5 mm (nominal), outer diameter = 27.0 mm (nominal), and height = 8.0 mm (nominal).

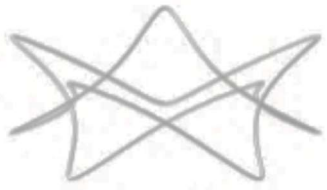


Figure 1: PROPEL Contour Sinus Implant

8.2.2 Intended Use

The PROPEL Contour Sinus Implant is intended for use in patients ≥ 18 years of age to maintain patency of the frontal and maxillary sinus ostia following sinus surgery and locally deliver steroids to the sinus mucosa. The PROPEL Contour Sinus Implant separates/dilates mucosal tissues prevents obstruction by adhesions/scarring and reduces edema. The implant reduces the need for post-operative intervention such as surgical adhesion lysis and/or use of oral steroids.

9 STUDY OBJECTIVE AND ENDPOINTS

The objective of the EXPAND study is to evaluate the efficacy of PROPEL Contour placement in the FSO following in-office bilateral frontal SBD in patients with CRS.

9.1 Primary Efficacy Endpoint

Side-to-side difference in FSO patency at Day 45 based on cross-sectional area of FSO using CT measurements performed by an independent, blinded reviewer.

9.2 Secondary Endpoints

- CT grading by an independent, blinded reviewer (Day 45, 180):
  - Cross-sectional area of FSO (Day 180 only)
  - FSO minimum diameter
  - FSOT volume
  - Zinreich's modified Lund-Mackay score for the frontal sinus
  - Lund-Mackay score for the frontal sinus
- CT grading by clinical investigators (Day 45, 180):
  - Lund-Mackay score for the frontal sinus
- Need for post-operative intervention as determined by clinical investigators based on endoscopic evaluation (Day 21, 45, 90, 180):
  - Repeat frontal SBD warranted or performed for restenosis/occlusion in the frontal recess/FSO; or
  - Surgical intervention warranted or performed to debride obstructive adhesions/scarring or for restenosis/occlusion in the frontal recess/FSO; or
  - Oral steroids warranted or prescribed to resolve recurrent edema in the frontal recess/FSO
- Endoscopic grading by clinical investigators (Day 21, 45, 90, 180):
  - Adhesion/scarring grade in the frontal recess/FSO and ethmoid sinus
  - Inflammation score in the frontal recess/FSO
  - Polypoid edema in the frontal recess/FSO
  - Polyp grade in the ethmoid sinus
- Patient-reported outcomes:
  - CRS side-specific symptom score (Day 21, 45, 90, 180)
  - SNOT-22 score (Day 180)
  - RSI score (Day 180)
- Implant delivery success rate by clinical investigators

9.3 Exploratory Endpoints

- Patient satisfaction (Day 90, 180)
- Health-economic measures to determine health-care resource utilization (see Section **9.5**)

9.4 Safety Measures

All adverse events (AEs) for each subject from the time the subject gives informed consent through Day 180 will be recorded in the electronic data capture (EDC) system and monitored. Each AE will be evaluated by the clinical investigators for their seriousness and relationship to the study devices. Where possible and if applicable, AEs will be localized to a sinus location.

Safety will be determined by assessment of, adverse device effects (ADE), serious adverse events (SAEs), unanticipated adverse device effect (UADE) and unanticipated serious adverse device effect (USADE) from enrollment through Day 180 post-procedure (Section **4**). All events will be separated between those attributed to PROPEL Contour Sinus Implant, those attributed to Cube Navigation System, VenSure™ Nav Balloon Device, Inflation device, Balloon Dilation Procedure, Implant Placement Procedure, and those that are a mix or indistinguishable.

9.5 Health-Economic Measures

Usage of the following interventions will be tracked and the first occurrence of each will be reported through Day 180:

- Treatment with antibiotics
- Use of intranasal corticosteroid (INCS) sprays starting after Day 7
- Use of other corticosteroids (e.g., oral, parenteral, injections, budesonide or other sinus steroid irrigations/rinses or drops, breath powered steroid delivery [e.g. XHANCE™, fluticasone proprionate], nebulized steroids administered nasally, or other drug eluting stents)
- Regimens of leukotriene inhibitors and/or immunotherapy for allergies
- Post-operative surgical interventions:
    - Post-operative debridement will be tracked separately but is within the expected post dilation outcome.
    - Use of post-operative intervention is a composite endpoint that includes:
        i. Device procedure reintervention including repeat balloon dilation or repeat implant placement will be tracked, and /or
        ii. Oral steroid intervention warranted to resolve recurrent inflammation or edema in the frontal recess/FSO. The sinus type (frontal) and side warranting surgical intervention is noted on the endoscopic assessment CRF.

- Hospitalizations
- ENT-related office visits

10 STUDY DESIGN

This is a post-market, randomized, intra-patient controlled, blinded, multicenter trial enrolling 80 randomized subjects from up to 20 US sites. No single site should enroll more than 16 subjects (20% of the total enrollment) for this study. Study subjects will be randomized following a successful in-office bilateral frontal BSD to receive one PROPEL Contour Sinus Implant on one FSO side (treatment), while the contralateral side serves as a control (see Section **6**). Subjects are expected to return for 4 follow-up visits at Day 21, 45, 90 and 180 (end of study). Endoscopic evaluation will be conducted at each visit, and CT scan will be repeated at Day 45 and 180 (see Section **7**).

11 STUDY POPULATION

Patients (≥ 18 years of age) with confirmed diagnosis of CRS who are candidates for in-office frontal SBD because they present with bilateral stenosis of the FSO and in whom placement of the PROPEL Contour is feasible and medically appropriate as determined by clinical investigator.

11.1 Inclusion Criteria

Subjects are eligible for the study if they meet *all* the following criteria:

General inclusion criteria

a. Patient has provided written informed consent using a form approved by the reviewing IRB.

b. Patient is 18 years of age or older.

c. Patient is willing and able to comply with protocol requirements.

d. Patient has confirmed diagnosis of CRS per International Consensus Statement on Allergy and Rhinology: Rhinosinusitis 2021 (ICAR:RS) guidelines.

Patient must have ≥ 12 weeks of:

Two or more of the following symptoms:

- nasal obstruction or congestion
- nasal discharge (rhinorrhea or post-nasal drip)
- facial pain/pressure
- reduction/loss of smell

And one or more of the following findings:

- Evidence of inflammation on paranasal sinus examination or CT

- Evidence of purulence coming from paranasal sinuses or ostiomeatal complex

e. In the opinion of the investigator, treatment with the PROPEL Contour Sinus Implant as an adjunct to frontal BSD with a 6 mm balloon is technically feasible and clinically indicated in both FSO.

f. Female patients of reproductive age and potential must not be pregnant or nursing, and patient agrees to avoid becoming pregnant during their participation in the study.

CT Imaging inclusion criteria

g. Patient has bilateral disease in the frontal sinus (Lund-Mackay score ≥1 on each side) on CT scan performed ≤ 90 days prior to the baseline procedure.

Intraprocedural inclusion criteria

h. Patient is able to tolerate topical/local anesthesia.

i. Confirmation of bilateral FSO access with navigation assistance

j. A successfully completed in-office bilateral balloon dilation of the FSO with no complication on either side that, in the opinion of the investigator is amenable for PROPEL Contour Sinus Implant placement in both FSO.

11.2 Exclusion Criteria

Subjects are eligible for the study if they meet *none* of the following criteria:

General exclusion criteria

a. Patient has structural obstruction that precludes endoscopic visualization of one or both FSOs prior to implant placement.

b. Patient had prior Draf III surgery.

c. Patient had prior sinus surgery or ESS ≤ 30 days from the baseline procedure or the mucosa has not healed from prior sinus surgery or ESS.

d. Patient had prior frontal SBD or ESS with corticosteroid containing stents, packing materials or implants (e.g., PROPEL, PROPEL Mini or PROPEL Contour) within approximately 1 year prior to the baseline procedure.

e. Patient had prior frontal SBD without corticosteroid containing stents, packing materials or implants, or prior balloon dilation in other sinuses with corticosteroid containing stents, packing materials or implants, ≤ 30 days prior to the baseline procedure.

f. Expanded amount of ethmoid sinonasal polyps extending beyond the middle meatus (grade > 2) unless reduced ≥ 30 days prior to the baseline procedure.

g. Patient has oral-steroid dependent condition such as chronic obstructive pulmonary disease (COPD) or other conditions.

h. Known history of allergy or intolerance to corticosteroids or mometasone furoate.

i. Patients with a known hypersensitivity to lactide, glycolide or caprolactone copolymers.

j. Patients with electronic devices in direct connection to the brain or the nervous system such as implantable neurostimulators (e.g., deep brain stimulation), programmable CSF shunts.

k. Patients with monopolar pacemakers (older designs, with lower resistance to interference) or ICD's (implantable cardioverter defibrillator).

l. Patients with implantable, body worn devices such as insulin pumps.

m. Patient has clinical evidence of acute bacterial sinusitis (e.g., acute increase of purulent discharge, fever).

n. Patient has clinical evidence or suspicion of invasive fungal sinusitis (e.g., bone erosion on CT scan, necrotic sinus tissue).

o. Patient has an active viral illness (e.g., COVID-19, flu, shingles).

p. Patient has active bacterial infection other than in the sinuses requiring oral antibiotics, unless resolved prior to baseline procedure.

q. Patient has clinical evidence of disease or condition that is likely to compromise survival or ability to complete follow-up assessments through Day 180 (end of study).

r. Patient has used parenteral or injected steroids (e.g., Kenalog) ≤ 30 days prior to the baseline procedure.

s. Patient has used oral steroids, budesonide or other sinus steroid irrigations/rinses or drops, nebulized steroids administered nasally ≤ 14 days prior to the baseline procedure.

t. Patient is currently participating in another clinical trial.

Intraprocedural exclusion criteria:

u. Patient fails the field mapping check during the pre-baseline procedure navigation assessment.

v. Other than implantation of one PROPEL Contour on one frontal sinus side of the subject at the baseline procedure, use of corticosteroid-eluting sinus implants (PROPEL, PROPEL Mini, PROPEL Contour, SINUVA®) or other steroid soaked packing materials in any sinuses.

11.3 Subject Withdrawal

Study subject may be withdrawn or terminated for the following reasons:

- Subject death
- Concomitant disease or any pre-existing disease or condition that precludes subject's participation
- Subject voluntarily chooses not to participate further in the study.

- Subject's non-compliance with study procedures
- Lost to follow-up: the subject has missed a study visit and three documented attempts to contact the subject are unsuccessful. A subject who misses a study visit should be contacted by site personnel to determine the reason for the missed visit, which should be documented in the subject's study records. Note: A subject who misses a study visit but attends a subsequent visit will no longer be considered lost to follow-up, and their previous missed visits will become 'missed visits'.
- In the clinical investigator's opinion, a significant safety concern arises that requires subject discontinuation.
- In the clinical investigator's opinion, it is not in the best interest of the subject to continue study participation.
- In the sponsor's or IRB's opinion, it is not in the best interest of subject to continue the study.

If a subject decides to withdraw from the study, clinical investigator should follow patients with ongoing AEs till resolution according to the standard of care. Data collected up to the point of subject withdrawal or termination will be maintained in the study database and included in analyses as appropriate. All enrolled subjects, including those withdrawn or lost to follow-up, will be accounted for and documented.

12 SUBJECT TREATMENT AND STUDY PROCEDURES

12.1 Pre-screening

During the pre-screening phase, the investigator or designee performs an initial evaluation of potential candidates for study eligibility. This initial pre-screening phase may include review of existing patient information (e.g., CT scans, previously performed diagnostic measures, laboratory studies, medical history, physical examination).

12.2 Informed Consent, Enrollment and Screening

If the patient appears to be a potential candidate for the study based on existing information, written informed consent will be obtained. No protocol required testing will be performed solely for the purposes of this study prior to obtaining written informed consent.

Clinical investigators or designees will approach the patient to obtain written informed consent. The background of the proposed study, the dilation procedure, implantation, the follow-up schedule and all potential risks and benefits will be carefully explained to each patient. The clinical investigator or designee obtaining the informed consent shall be in compliance with ICF regulations:

Each patient must sign and date the ICF approved by an appropriate Institutional Review Board (IRB). Patients are considered enrolled in the study upon signing the IRB-approved ICF. Enrolled

subjects will be assigned unique identifying codes by the Electronic Data Capture (EDC) system and entered into the study database. Upon enrollment, subjects will have a screening assessment.

The screening assessment will include:

- Review of CT scan (must be performed ≤ 90 days prior to baseline procedure; see Section **13**)
- Endoscopic evaluation with grading and video recording; and
- Female subjects of childbearing potential must confirm their nursing status, undergo pregnancy test to confirm they are not pregnant.

If the screening visit occurs on the same day as the baseline/procedure visit, all assessments will be recorded in the baseline visit forms (see Section **7**). All subjects who do not pass the screening assessment, including successfully completed in-office bilateral balloon dilation of the FSO with no complication and amenable for PROPEL Contour placement will be considered as screen failures and will be terminated from the study. The reason for ineligibility will be recorded in the EDC system.

12.3 Baseline/Procedure

Subjects should undergo the baseline procedure within approximately 30 days from signing the ICF. Final eligibility requirements will be assessed at the baseline visit. Subjects will undergo a baseline endoscopic examination, including grading prior to any surgical procedure(s). Video endoscopy capture is required, pictures are optional. Subjects will also undergo baseline assessments such as SNOT-22, RSI, and CRS side-specific symptom questionnaires before any surgical procedures.

- Female subjects of childbearing potential will need to confirm not pregnant or nursing prior to the baseline procedure per site standards.
- Subject preparation for baseline procedure
- Subjects will be prepared for the baseline procedure per standard investigator protocol used for nasal endoscopy and procedures.
- The anesthesia period should be as long as necessary to ensure complete numbness of the subject's septum and middle turbinate. Once properly anesthetized, subjects will undergo the baseline procedure.

12.3.1 Bilateral Frontal SBD

Confirm bilateral FSO access and complete bilateral in-office dilation per the Cube Navigation System, VenSure™ Nav Balloon Device, and Inflation Device IFUs. If the eligibility CT Scan does not meet the Cube Navigation System requirements, the CT Scan may need to be re-done.

Subjects may be asked to take off their mask (just like earrings, glasses, etc.,) for the few seconds during which the CT scan is captured to maximize accuracy with the navigation system.

Prior to implant placement:

- Confirm successful bilateral frontal SBD with an opening amendable for PROPEL Contour placement on each side.
- Evaluate final subject eligibility by confirming that the subject's anatomy and overall condition is appropriate for PROPEL Contour placement.

12.3.2 Optional In-office Procedures

If clinically necessary, in-office sinus surgical procedures (e.g., inferior turbinate reduction, concha bullosa treatment) may be performed according to standard of care at the baseline visit prior to randomization. Traditional surgical septoplasty for inferior septal deviation such as bone spur on maxillary crest may be performed. Packing such as Merocel may be placed in the nasal or ethmoid cavity, if necessary. These procedures should be performed bilaterally on each side of the sinuses.

If clinically necessary, bilateral dilation of the maxillary or sphenoid sinuses may be performed using the study devices (i.e., Cube Navigation System, VenSure Nav Balloon Device) after completing bilateral frontal BSD of the FSO. Alternatively, the investigator may use a commercially available balloon dilation device to dilate the maxillary, sphenoid sinuses or eustachian tubes.

Septoplasty ballooning and ethmoidectomy (anterior, posterior, total) are not permitted at the baseline visit prior to randomization. Polypectomy of nasal polyps extending beyond the middle meatus (grade >2) is not permitted. Draf I, Draf II a/b, Draf III or any other procedures involving cutting to the frontal sinuses are not permitted. No use of steroid soaked packing materials is permitted.

12.3.3 Randomization

Subjects meeting final eligibility and undergoing the successful completion of bilateral frontal BSD will be randomized using the envelop method to receive 1 PROPEL Contour on the treatment side.

12.3.4 Implant Placement

PROPEL Contour is provided by sponsor and must be placed by trained PIs according to the IFU. No hemostatic packing materials of any kind should be placed within the implants unless medically necessary. Packing such as the Merocel tampon may be placed in the nasal or ethmoid cavity, if necessary. No other packing materials or interventions containing steroids of any kind should be placed in any other sinus.

- Record video and perform endoscopy of post-procedure anatomy, including adequate view of the frontal sinus recess implant deployment and final implant placement; and
- Record the implant apposition on the CRF.

The study treatment phase begins upon introduction of the PROPEL Contour Sinus Implant delivery system into the study subject after successful bilateral balloon dilation of the FSO.

The PROPEL Contour Sinus Implant delivery system should be disposed per standard institutional practices for biohazard waste.

If the sinus implant, implant delivery system, VenSure Nav Balloon Device, Inflation Device, or other components are associated with a device-related AE, deficiency, malfunction or failure, the impacted device or its parts should be returned to sponsor for evaluation, if possible. For the return of biohazard product, sponsor must be contacted prior to product return for handling instructions.

12.4 Follow-Up

The follow-up period begins immediately post-treatment (once the study implant is placed in the subject in the clinical investigator's office).

At each follow-up visit, the subject will undergo endoscopic evaluation with grading and video recording at Day 21, 45, 90 and 180 (end of study). After suctioning, endoscopic grading is performed and recorded on the endoscopic assessment CRFs. Suctioning and clearing mucous/stent debris of the FSO should be completed prior to Day 45 CT scan. It is preferred that the PROPEL Contour Sinus Implant be left in place for 30 days but can be removed at investigator discretion.

An overview of the assessments to be performed at each follow-up interval along with required timing is provided in Section **7**.

A CT scan is repeated at Day 45 (primary endpoint) and again at Day 180. The acquisition and measurements by the centralized imaging core lab are detailed in Section **13**.

12.5 Unscheduled Visits

Subjects may come in for additional unscheduled office visits if necessary. Circumstances that may warrant additional visits include but are not limited to:

- Worsening of sinus symptoms, and/or
- Sinus-related adverse events requiring medical evaluation.

The assessment at an unscheduled visit may consist of:

- Endoscopic evaluation with grading and video recording; and.
- SNOT-22, RSI and site-specific symptom questionnaires.

13 CT SCAN AND PRODUCT ACCOUNTABILITY

13.1 Image Acquisition

The screening CT scan must be performed ≤ 90 days prior to the baseline procedure to confirm the diagnosis of CRS after a period of appropriate medical therapy and prior to making a recommendation for BSD. The follow-up CT at Day 45 and 180 shall be performed after endoscopic evaluation and debridement to ensure no implant remnants are present on the scan to ensure blinded review.

The subject needs to be in seated position with the chin in a chin rest for imaging to occur. The cone-beam CT scan window must encompass the frontal, ethmoid, maxillary and sphenoid sinuses and OMC on both sides in the axial, coronal and sagittal planes.

13.2 Centralized Blinded Review

The primary efficacy endpoint requires precise measurements of the FSO using reconstructed cone beam images in the axial, coronal and sagittal planes. The image reconstructions and measurements of CT-related endpoints will be performed by board-certified independent radiologists at the centralized imaging core lab in accordance with the standardized protocol (see CP-00038). The reviewers will be blinded to treatment assignment and have no access to any symptomatic or endoscopic outcomes.

13.3 Product Accountability

An appropriate number of EXPAND study devices including Inflation Device will be provided to the study sites. The sites maintain the EXPAND study devices in a locked, secure location. Only clinical investigators participating in the study will have access to the EXPAND study devices. Dispensing of EXPAND study devices will be documented by authorized personnel. Each batch of the PROPEL Contour Sinus Implant, VenSure Nav Balloon Device and Inflation Device will be tracked by the unique device identifier.

EXPAND study devices including the unique device identifier received by the clinical site will be logged in by the site personnel on inventory logs and/or the EDC system. Final reconciliation will be completed at each site before or during site closure. Any unused inventory and Cube Navigation System will be returned to the sponsor at the direction of the sponsor or at the close of the study. At the end of the study, overall study final device reconciliation will be completed internally by the sponsor.

14 PRIOR AND CONCOMITANT MEDICATIONS

The following medication is allowed *prior* to and *post*-baseline procedure:

- INCS sprays prior to and post, starting after 7 days
- Orally inhaled steroids for control of asthma; and

- Stable regimens of leukotriene inhibitors and/or immunotherapy for allergies

The following medication is *not* allowed *prior* to the baseline procedure:

- A 30-day restriction for use of parenteral and injected steroids (e.g., Kenalog)
- A 14-day restriction for use of oral steroids, budesonide and/or any other sinus steroid irrigations/rinses or drops, nebulized steroids administered nasally; and
- A 45-day restriction for biologics for CRS treatment (such as Dupixent).

The following medication is allowed *post*-baseline procedure:

- Daily use of saline sprays/rinses/irrigations in both sinuses from Day 1
- Antibiotics if infection is suspected at any time during the study; and
- INCS sprays (excluding Xhance) in one or both sinuses starting after 7 days as clinically necessary.

The following medication not allowed *post*-baseline procedure:

- Other corticosteroids (e.g., oral, parenteral, injections, budesonide or other sinus steroid irrigations/rinses or drops, breath powered Xhance, nebulized steroids administered nasally or other drug eluting stents) through Day 45, unless clinically necessary, to ensure unbiased assessment of the primary endpoint; and
- Biologics for CRS treatment (e.g., Dupixent).

15 MEDICAL AND SURGICAL INTERVENTIONS

Subsections below describe the rescue treatments consisting of medical and surgical interventions that will be allowed during the study follow-up based upon subject's symptomatic and endoscopic outcomes.

15.1 Medical Intervention

During study follow-up, INCS sprays (excluding Xhance) will be allowed starting after Day 7 visit, if clinically necessary.

Other corticosteroids (e.g., oral, parenteral, injections, budesonide or other sinus steroid irrigations/rinses or drops, breath powered Xhance, nebulized steroids administered nasally or other drug eluting stents) are not allowed through Day 45, unless there is a clinically significant increase or persistence in frontal sinus inflammation, coupled with subject complaint of sinusitis symptoms that cause subject to request medical intervention.

15.2 Surgical Intervention

Surgical intervention (e.g., repeat balloon dilation or sinus surgery, in-office polypectomy) may be required in cases where a clinically significant increase or persistence in frontal sinus

inflammation occurs, coupled with complaints of sinusitis symptoms that cause subject to prefer a surgical intervention (e.g., sinus surgery).

All medical and surgical interventions will be noted on the concomitant medication and follow up CRFs.

16 ASSESSMENT OF SAFETY

16.1 Specification of Safety Parameters

Adverse events (AE) for each subject from the time the subject gives written informed consent (enrollment) through Day 180 (end of study) will be recorded in the EDC system and monitored. Each AE will be evaluated by clinical investigators in terms of severity (i.e., mild, moderate, severe) as well as strength of relationship (i.e., not related, unlikely related, probably related, definitely related, indeterminate) to the study drug (mometasone furoate), study devices, and procedures (BSD, implant placement). Each AE will be reviewed by sponsor in accordance with sponsor's SOP. The study sponsor is responsible for ensuring that all AEs are appropriately recorded, adjudicated and, when applicable, reported to the government(s), ethics committee(s) and other study centers per applicable regulations.

Subjects with CRS experience a persisting set of symptoms associated with the disease and may continue to present with a wide range of symptoms during the recovery process after in-office balloon dilation. These may include symptoms such as pain and discomfort, headache, decreased sense of smell, crusting, epistaxis, and other symptoms. Patients healing appropriately after in-office procedure may suffer from acute infections and/or inflammatory exacerbations unrelated to the procedure due to the natural course of their CRS. Therefore, clinical investigators will evaluate the occurrence of AEs excluding usual post-operative recovery signs and symptoms experienced by study subjects, unless corroborated by objective findings and/or requiring specific medical or therapeutic interventions (e.g., antibiotics, repeat ESS).

Note: The need for medical or surgical intervention in the FSO post-dilation that is captured on the endoscopic assessment CRF will not be considered as an AE. Likewise, other endoscopic findings such as inflammation, adhesion/scarring, and edema of the FSO will not be considered as AEs.

16.2 Classification of AEs

16.2.1 AE severity

Each AE will be categorized in terms of their severity as defined in table below.

Severity	Definition
Mild	Events, signs or symptoms that are easily tolerated by the subject, or are clinical or diagnostic observations of the investigator
Moderate	Events, signs or symptoms that cause discomfort and interfere with normal functioning. Local or noninvasive intervention may be indicated
Severe	Events, signs or symptoms that disable the subject, are medically significant, lead to hospitalization or prolongation of hospitalization

16.2.2 AE causality

The relationship of each AE to the study drug (i.e., mometasone furoate), study devices (i.e., PROPEL® Contour Sinus Implant, VenSure™ Nav Balloon Device, Cube Navigation System), and procedures (i.e., frontal BSD, implant placement) will be evaluated by PIs and categorized as defined in table below.

Strength of Relationship	Definition
Definitely	Clear-cut temporal association, and no other possible cause
Probably	Clear-cut temporal association, and a potential alternative etiology are not apparent
Unlikely	Does not follow a reasonable temporal association; or causal relationship with the drug, devices or procedures involved in the research is unlikely but cannot be completely ruled out
Not-related	AE is completely independent of study product administration; and/or evidence exists that the event is definitely related to another etiology
Indeterminate	Information gathered about the AE is not sufficient to arrive at a definite conclusion about causal relationship

Any AE that is determined by a participating investigator to be related (definitely or probably related) to the study drug, study device, or procedure will be categorized as device related. All AEs will be attributed separately to each device (i.e., PROPEL Contour Sinus Implant, VenSure™ Nav Balloon Device, Cube Navigation System), each study procedure (i.e., inflation device, BSD, implant placement), and any other in-office baseline procedures, as well as those that are a mix or indistinguishable.

For device-related AE (anticipated or unexpected/unanticipated), the sponsor may request source documentation to confirm the relationship of the AE to the study devices and may review such AE with an independent otolaryngologist, as needed.

16.2.3 AE expectedness

It is sponsor's responsibility to evaluate expectedness of each device-related AE in accordance with sponsor's SOP. Expectedness is categorized as defined in table below.

Expectedness	Definition
Expected	AE is consistent with the risk information described in the ICF, IFU and clinical study protocol (see Section **17**)
Unanticipated or Unexpected	AE is considered UADE or USADE if it is not consistent with the risk information described in the ICF, IFU and clinical study protocol (see Section **17**).

16.3 AE Adjudication

AEs are reviewed by sponsor on a regular, ongoing basis in accordance with the sponsor's SOP. The following is reviewed for each AE:

- Need for clarification or additional information from the site
- Appropriateness of classifications for severity, causality and expectedness
- If the AE is unanticipated, determination as to whether it poses unreasonable risk of harm to study subjects if it were to reoccur; and
- Requirements for reporting to the FDA and site IRB based on the nature of the event.

Outputs of reviews are filed by sponsor, and action items are tracked to resolution. If the investigator and sponsor do not agree on the seriousness or causality of an event, the event will be reviewed by an independent adjudicator, who is a qualified medical expert. The adjudicator is blinded to treatment assignment and will have access to the following:

- AE information reported in the EDC system
- A list of potential risks associated
- Information provided by investigators, including clinical notes, laboratory results, concomitant medications, and medical/surgical history; and
- Clinical outcome measures reported in the EDC system.

The independent adjudicator may request further information if this is required to complete AE review. The adjudicator will confirm their determination of seriousness and causality of the event. The adjudicator's decision is considered as final and is recorded in the EDC system and used in all analyses.

16.4 Guidelines for AE Reporting

All AEs, regardless of seriousness or relationship to the study devices, will be recorded in the EDC system and will include event description, date of onset, investigator's assessment of severity, relationship to study devices, and date of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed through end of the study.

Any pre-existing medical condition that is present at the time of screening will not be reported as an AE. The occurrence of diagnostic or elective surgical procedures for a pre-existing condition will not be recorded as an AE, unless the condition become more severe or results in an AE.

Whenever possible, diagnosis or single syndrome should be reported instead of symptoms. The investigator should specify the date of onset, severity, action taken with respect to the study device(s), corrective treatment/therapy given, additional investigations performed, outcome, and his/her opinion as to whether there is a reasonable possibility that the AE was caused by the study device(s).

The investigator should take appropriate measures to follow all AEs until resolution or until progression has been stabilized, or until study exit, to ensure the safety of the subjects. If the AE continues beyond the last planned visit per protocol and/or the subject withdraws from the study, clinical investigators should follow the subjects according to standard of care.

If a subject decides to withdraw from the study, clinical investigator should follow patients with ongoing AEs till resolution according to the standard of care.

An investigator will submit to the sponsor a report of AEs occurring during this investigation as defined in the table below.

Type of Report	**Submission Schedule**
Device-related AE	Verbal report or initial entry into the AE CRF within 24 hours from assessment followed by written report within 10 working days
Subject Death	Verbal report within 24 hours followed by a written report within 2 working days
SAE/SADE/UADE/USADE	Verbal report within 24 hours followed by a written report within 5 working days

The investigator will report the above to the reviewing IRB per the IRB's guidelines. The study sponsor will be responsible for reporting safety events to the Food and Drug Administration (FDA) as required per 21 CFR 812 and 21 CFR 803.

All SAEs (SAE/SADE/UADE/USADE) will be followed until satisfactory resolution; until the investigator deems the event to be chronic or the adherence to be stable or until the subject exits the study. Other supporting documentation of the event may be requested by the sponsor and should be provided as soon as possible.

All device deficiencies including malfunctions, use errors, and inadequate labeling, will be reported to appropriate regulatory bodies and Institutional Review Boards (IRBs) as applicable.

17 RISK/BENEFIT ASSESSMENT

A risk/benefit analysis has been performed and a summary of the results is provided below.

17.1 Potential Risks

Risks associated with balloon dilation of the sinuses, as well as the placement and use of the PROPEL Contour Sinus Implant in the FSO are anticipated to be similar to those experienced by subjects who undergo balloon dilation of the sinuses as well as placement of other sinus stents.

Consequently, the risks potentially associated with the use of the sinus balloons may include but are not limited to the following:

- Epistaxis
- Cerebrospinal fluid leak
- Pneumocephalus
- Damage of the orbital wall or other ocular structures
- Impaired or loss of vision
- Impaired tearing
- Periorbital cellulitis/edema
- Infection
- Facial/nasal pain
- Facial/nasal discomfort
- Headache

Accordingly, the risks potentially associated with the placement of the PROPEL Contour Sinus Implant are:

- Special care should be taken to avoid bending, twisting or damaging the implant.
- The implant is not designed to be modified by the physician.
- The implant is not intended to be compressed and loaded into the delivery system more than two times.
- The implant must be placed under endoscopic visualization.
- The implant exhibits no antimicrobial properties.
- Foreign body reaction may occur as is possible with most surgical adjuncts.
- In rare instances, the physiochemical condition associated with sinus surgery, both with and without sinus implants or packing, may present a risk of toxic shock syndrome (TSS).
- Pediatric Use: The safety and effectiveness of the implant in pediatric patients have not been established.

- Pregnancy and Nursing Females: The safety and effectiveness of the implant in pregnant or nursing females have not been established.

Risks or side effects associated with the intranasal use of intranasal mometasone furoate (study drug):

- Nasal irritation
- Hypersensitivity reaction
- Intranasal bleeding
- Localized infection (bacterial, fungal colonization or viral) in the nose or pharynx
- Nasal burning
- Nasal dryness
- Susceptibility to secondary infections due to bacteria, fungi or viruses
- Glaucoma or elevation of intraocular pressure
- Cataracts or change in lens opacities
- Headache
- Pharyngitis

General side effects associated with steroids:

- Alteration of the HPA axis including growth suppression
- Immunosuppression
- Hypersensitivity reactions
- Headache
- Epistaxis
- Coughing
- Vomiting
- Candidiasis
- Glaucoma/elevation in intraocular pressure
- Cataracts or change in lens opacities
- Arthralgia
- Myalgia

Inhaled and intranasal mometasone furoate is generally well tolerated in clinical trials and any adverse effects are mild and generally of short duration with similar in incidence to placebo. The proportion of subjects discontinuing as a result of adverse events related to treatment is very low and generally <2-5% in most trials (Davies 1997, Drouin 1996, Graft 1996, Hebert 1996, Mandl 1997, McCormack 2006, Nayak 2002, Schenkel 2003).

Intranasal glucocorticoids may occasionally cause local adverse effects, such as a mild sensation of nasal irritation, crusting, dryness and usually minor epistaxis, however these are transient and do not worsen during long-term treatment (Mygind 2006). Local mycotic infections and septal perforations with prolonged use of nasal corticosteroids are extremely rare and have not been reported for mometasone furoate (Kyrmizakis 2000, Van Cauwenberge 2005, Vogt 1979). These findings may be related to the more rapid clearance of the topical corticosteroid by the ciliated nasal epithelium. The material used to make the implant has been used extensively in the manufacture of suture materials and other implantable medical devices and is not expected to present any new risks.

There are potential risks associated with CT scans with limited and medically acceptable dose of radiation. The radiation exposure from CT scan during this study is considered small and is not likely to affect subjects or subjects' sinus condition.

17.2 Minimization of Anticipated Risks

Risks associated with the PROPEL Contour Sinus Implant are minimized due to:

- The use of medical grade materials that have a long history of use and have been characterized and tested to assure biocompatibility.
- Incorporation of a very low dose (370 mcg) of mometasone furoate, the average daily release of which is below currently FDA approved intranasal doses for allergic rhinitis and nasal polyps.
- Pre-clinical evaluation including bench testing, analytical testing and animal studies.
- Prior clinical testing.
- Instructions for Use that details appropriate implant preparation and placement.
- Routine subject follow-up that includes direct endoscopic visualization of the implant and sinus tissue.
- In addition, risks will be minimized by including investigators experienced in performing sinus surgery and nasal endoscopy.

17.3 Potential Risks to Study Subject Confidentiality

In all clinical studies, confidentiality of protected health information may be breached due to study-related activities beyond those of routine clinical care. This risk will be minimized by not

collecting personally identifying information on CRFs or other study related documentation to be provided to the study sponsor. Any subject's personal identifying information from any documentation will be redacted by the site prior to being sent to Sponsor.

17.4 Potential Benefits of Study Participation

There may be no direct benefits of study participation. However, study subjects will undergo an enhanced level of clinical scrutiny compared to routine clinical care, which may provide some indirect health benefits.

The PROPEL Contour Sinus Implant is intended for use in patients ≥ 18 years of age to maintain patency of the frontal and maxillary sinus ostia following sinus surgery and locally deliver steroids to the sinus mucosa. The PROPEL Contour Sinus Implant separates/dilates mucosal tissues, prevents obstruction by adhesions/scarring, and reduces edema. The implant reduces the need for post-operative intervention such as surgical adhesion lysis and/or use of oral steroids. Addition of mometasone furoate is intended to minimize post-surgical inflammation, potentially reducing the frequency of adhesion formation and enhancing the wound healing process. Subjects may benefit from these actions. Because the implant is bioabsorbable, subjects may be able to avoid use of other sinus stents that require removal, which can be uncomfortable.

17.5 Risk/Benefit Conclusion

Based upon the Risk/Benefit Analysis performed by Sponsor, the benefits associated with the sinus implant are expected to outweigh the potential risks to the subject, and the anticipated possible risks remain reasonable and acceptable.

18 STATISTICAL CONSIDERATIONS

A detailed Statistical Analysis Plan (SAP) will be prepared prior to the primary analysis through Day 45. Following is a description of the study sampling plan and a summary of the intended analyses.

18.1 Randomization

The ratio of left to right sinus assignments will be 1:1. Following bilateral frontal BSD, eligible subjects will receive 1 PROPEL Contour (treatment) on 1 side, and no implant (control) on the contralateral side. Randomization will be stratified by site and will follow a blocked scheme, with blocks of varying sizes, and will be performed using the envelope method. The randomization scheme will be generated by an independent statistician.

18.2 Analysis of Primary Efficacy Endpoint

The detailed hypothesis, data analysis plan for the primary efficacy endpoint, as well as the sample size justification will be provided in the SAP.

18.3 Analysis of Key Secondary Efficacy Endpoints

To support potential device labeling claims, a subset of secondary endpoints at Day 45 will be identified and analyzed using appropriate methods for controlling for family-wise type error rate (FWER). This will be detailed in the SAP that will be prepared prior to the primary analysis.

18.4 Analysis of Secondary and Exploratory Endpoints

Secondary endpoints identified in Section **9.2** and health-economic measures identified in Section **9.5** will be analyzed as detailed in the SAP.

18.5 Safety Measures

The incidence of all AEs through Day 180 (end of study) will be reported.

18.6 Analysis Populations

The analysis of the primary and key secondary endpoints at Day 45 will be conducted on the intent-to-treat (ITT) population. The secondary endpoint analyses will be performed on the ITT and per-treatment evaluable (PTE) populations through Day 180 as applicable. The exploratory endpoint analysis will be performed on the PTE population. The safety will be evaluated on the safety population. All analysis populations are defined below:

- *ITT Population*. All randomized subjects and sinuses in whom SBD followed by placement of PROPEL Contour in the target sinus was attempted. An attempt occurs when the physician introduces the delivery system into the subject's nostril with the intent of implant placement. Subjects' sinuses are analyzed in the treatment group to which they are randomized. This is the main analysis population for the primary and key secondary efficacy endpoints.
- *PTE Population*. All randomized subjects who have received PROPEL Contour in the target sinus, who have no major procedural protocol deviations (e.g., underwent study-related procedures prior to informed consent, received treatment other than assigned by randomization), and for whom follow-up data are available. This population will be used for the secondary and exploratory endpoints.
- *Safety Population*. All subjects and sinuses exposed to PROPEL Contour. This population will be used for all summaries of AEs. Any subjects enrolled in the study who are not exposed to PROPEL Contour will be summarized separately.

18.7 Interim Analysis

No interim analysis will be planned for this study.

19 STUDY MANAGEMENT

As the study sponsor, Intersect ENT has the overall responsibility for the conduct of the study and will ensure that the study is conducted under ISO14155 and 21 CFR Parts 11, 50, 54, 56 and 812.

Personnel who participate in the conduct of this clinical trial will be qualified by education and experience as applicable prior to performing their tasks.

19.1 Ethical Considerations

The rights, safety and well-being of human subjects, which are the most important considerations and shall prevail over interests of science and society. These principles shall be understood, observed, and applied at every step in the clinical investigation. 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. The rights, safety and well-being of clinical investigational participants shall be protected in accordance with the ethical principles based in the Declaration of Helsinki (Rickham 1964).

Written informed consent shall be obtained in writing from the subject and the process shall be documented before any procedure specific to the clinical investigation is applied to the subject. All local competent authority, Institutional Review Board (IRB) and local requirements will be followed. IRB approval will be documented and obtained prior to study start at the applicable site.

It is expected that all parties will share in the responsibility for ethical conduct in accordance with their respective roles in the investigation.

19.2 Sponsor Responsibilities

Intersect ENT, as the study sponsor, has the overall responsibility for the conduct of the study and will ensure that the study is conducted under the guidance of International Council on Harmonization (ICH) Good Clinical Practice (GCP) (E6), Clinical investigation of medical devices for human subjects – Good clinical practice (ISO 14155) and other applicable local and federal (e.g., 21 CFR Parts 11, 50, 54, 56, and 812) regulations, including the archiving of essential documents. A list of the names, locations, and chairpersons of all IRBs (including actions taken by each IRB on the protocol) that have been or will be asked to review the protocol will be kept on file. Qualified personnel who participate in the conduct of this clinical trial will be qualified by education and/or experience and trained to perform their tasks. Intersect ENT will not use, in any capacity, the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this clinical study.

19.3 Blinding

The independent reviewer of CT images will be blinded to treatment assignment. Subjects, treating investigators and clinical research coordinators will be unblinded, as they will be attending the placement procedure.

19.4 Training

Sponsor personnel or designee will provide all clinical investigators performing procedures with training on use of the PROPEL Contour Sinus Implant, VenSure Nav Balloon Device, Inflation Device and Cube Navigation System prior to their participation in the clinical study. The study center staff involved will undergo training at site initiation (or separately) which will include:

- Study protocol
- Consenting procedures and Human Subjects Protection
- Instructions for use
- Investigator responsibilities, including reporting requirements
- Monitoring and auditing
- EDC system
- Electronic recordkeeping
- Endoscopic assessments
- EXPAND study devices accountability procedures
- Protection of subject confidentiality

CRF completion guidelines, CT imaging acquisition guidelines, and Imaging Site User Manual will be provided to sites. Applicable site staff will be trained to uploading CT imaging to Core Laboratory portal prior to commencing such activity.

New members of the investigation site team may be added from time to time at new or existing sites. New personnel should only start their assignment after receiving adequate training in the clinical investigation requirements and this training shall be documented. The names, initials, signatures, functions, and designated authorizations of new site personnel shall be documented.

19.5 Protocol Deviations

Any deviation from the requirements outlined in this protocol will be considered a protocol deviation. A protocol deviation that may affect the scientific soundness of the protocol or the rights, safety, or welfare of the subjects should be reported to the sponsor and the Institutional Review Board (IRB) as soon as possible. Other deviations are those that occur in direct association with a specific study subject. These include, but are not limited to, deviations from the informed consent process, inclusion/exclusion criteria, protocol-specified procedures and assessments, and EXPAND study device handling and usage. All efforts should be made to avoid any protocol deviation.

19.6 Monitor Responsibilities

Study site monitoring will be performed by trained and qualified personnel from Sponsor or their designee. A list of monitors will be maintained by Sponsor and will be available upon request. Study sites will be monitored regularly to ensure that the study is conducted under ISO14155 and 21 CFR Parts 11, 50, 54, 56, 812, the study protocol, IRB requirements, and other applicable regulations. Study monitors will also ensure that the data reported in Electronic Data Capture (EDC) database is accurate, complete, and consistent with the information found in the subject's medical records and source documents as part of source document verification. Monitoring will include assessment of the site's overall enrollment progress, the site's ability to maintain and report accurate, complete, and consistent records and to report study related data, including AEs, complaints, and device malfunctions and deficiencies, to the study sponsor in a timely fashion. In order to appropriately monitor the progress of the study, the monitor will have access to the site source documents and other information necessary to ensure investigator compliance with the protocol and applicable rules and regulations and to assess the progress of the clinical investigation.

The study monitors will maintain personal contact with investigators and study coordinators by phone, e-mail, mail and on-site/remote visits. Monitoring will be performed periodically during the period of subject enrollment through final database lock. The schedule of monitoring at individual clinical sites will be determined based on factors such as enrollment number and rate, presence of new clinical investigators, training needs, protocol compliance and individual clinical site needs. The monitor will complete a monitoring report for each visit which will be provided to the sponsor.

Letters documenting the visit and relevant findings will be provided to the site. Monitoring will ensure continued protocol compliance and accurate reporting of data, AEs, complaints, device deficiencies and malfunctions, protocol deviations and product accountability.

Appropriate source data verification will be performed on efficacy and safety data for each subject enrolled in this study.

19.7 Data Management Responsibilities

Data management will be performed by the sponsor.

Electronic data capture

An EDC system will be utilized to capture study data and compliant with 21 CFR Part 11 and under the guidance of 'FDA Guidance for Industry: Computerized Systems Used in Clinical Investigations'. The EDC will be validated and verified prior to use, and validation and verification and release documentation will be maintained on file by the study sponsor. Data entry will be performed by site personnel after completing an appropriate training. Modifications to the EDC will be made if deemed necessary by the study sponsor.

Data cleaning

The database will be subject to initial inspection for omitted data, gross data inconsistencies, and deviations. Any deficiencies or deviations will be reviewed, and any necessary action determined (e.g., data query, communication with the study center).

Intermittent data review will be performed, and any discovered errors will be reported to the study site using the electronic query process (as necessary). The study site will be expected to review and complete the query. The data cleaning cycle will be repeated until all data are considered clean.

Data back-up, confidentiality and security

Incremental data back-up will be performed on a regular basis by the EDC system vendor. All media will be stored in a secure location. Passwords will be issued to appropriate personnel to ensure confidentiality and protection of data.

19.8 Investigator Responsibilities

General responsibilities

- Each investigator is responsible for ensuring that an investigation is conducted per the signed investigator statement (Investigator Agreement/Commitment), the study protocol, and applicable regulations; for protecting the rights, safety, and welfare of study subjects under the investigator's care and for the control of drugs/devices under investigation.
- The investigator shall assure the accuracy, completeness, legibility and timeliness of the data reported to the sponsor on the CRFs and in all required reports.
- Each investigator shall obtain informed consent of each patient to whom the treatment is administered in accordance with provisions of 21 CFR Part 50 and ISO14155.
- Each investigator (designee) is responsible for all applicable IRB requirements under 21 CFR Part 56 and ISO14155.
- Each investigator is responsible for disclosure of financial obligations/conflict of interest to the sponsor in accordance with provisions of 21 CFR Part 54.
- The study will be conducted under 21 CFR 11, 50, 54, 56, 812 and ISO14155. Investigators will be trained on their responsibilities.
- To ensure proper execution of the study protocol, each investigator will identify a study coordinator(s) for this study. Working with and under the oversight of the principal investigator, the study coordinator(s) ensures that all study requirements are fulfilled.
- Each investigator will allow monitoring and auditing of their clinical investigation procedure(s) by the sponsor or designee.

Control and disposition of the study devices

An investigator shall administer the EXPAND study devices only to subjects under the clinical investigator's personal supervision. The investigator shall not supply the EXPAND study device

to any person not authorized to receive it. An investigator (or designee) is required to maintain adequate records of the disposition of the study devices, including dates, quantity, and use by subjects. All unopened unused devices must be returned to the sponsor.

Required documents from study centers

At a minimum, the following documents will be provided by the study center to the study sponsor:

- IRB study approval letter
- IRB approved informed consent
- Fully executed clinical trial agreement (CTA)
- Investigator agreement/commitment for the participating investigator(s)
- Financial disclosure form for the participating investigator(s)
- Curriculum vitae (CV) for the participating investigator(s)
- Current medical license for the participating investigator(s)
- Principal investigator protocol acknowledgement form

A site may not begin active enrollment of patients until the documentation for the site principal investigator has been provided to the sponsor and the sponsor has provided written approval to begin enrollment.

To ensure proper execution of the study protocol, each investigator should identify a study coordinator for this study. Working with and per delegated authority of the principal investigator, the study coordinator assures that study requirements are fulfilled.

The investigator will permit collection and review of the site's standard operating procedure(s) by monitors, as well as on-site/remote auditing of the clinical study upon request.

Maintenance of Study Records

The investigator is responsible for maintaining medical and study records for every subject participating in the clinical study (including information maintained electronically such as digital imaging), from enrollment through study exit. The investigator will also maintain ***original*** source documents from which study-related data are derived, which may include, but are not limited to:

- Clinic progress notes recording subject's medical history and medications
- Medical charts with operative reports and condition of subject upon discharge
- Medical records regarding AEs, including treatment and clinical outcome
- Results of diagnostic examinations
- Imaging (e.g., x-rays, CT scans)

- Notes of phone calls and/or correspondence indicating investigational site's attempts to follow study subjects at the required follow-up visits until subject's participation in the study is complete or terminated
- Records relating to subject death (e.g., death certificate, autopsy report)
- Printouts of source data generated by technical equipment (e.g., CT, MRI) must be filed with the subject's records.

The study investigator must ensure that all study subject records and study regulatory documentation pertaining to the clinical study are stored per regulatory body requirements. To avoid error, the study site should contact the study sponsor prior to the destruction of study records to ensure that they no longer need to be retained. In addition, the Sponsor should be contacted if the investigator plans to leave the study site so that arrangements can be made for the handling or transfer of study records.

19.9 Protection of Subject Confidentiality

In all clinical studies, confidentiality of protected health information may be breached due to study-related activities beyond those of routine clinical care. This risk will be minimized by not collecting personally identifying information on CRFs or other study related documentation to be provided to the study sponsor. It is the sponsor's policy to redact any subject's personally At all times throughout the clinical investigation, confidentiality will be observed by all parties involved. All data shall be secured against unauthorized access. Privacy and confidentiality of information about each subject shall be preserved in the reports and in any publication. Each subject participating in this study will be assigned a unique identifier. All database forms and source documents sent to the sponsor will be tracked, evaluated, and stored using only this unique identifier.

Clinical investigators will maintain confidential study subject lists identifying all enrolled subjects. The clinical investigators bear responsibility for keeping these lists current and confidential. These lists will not be provided to the study sponsor.

Monitors and auditors will have access to the study screening and enrollment logs and other personally identifying information of study subjects to ensure that data reported in the EDC corresponds to the person who signed the ICF and the information contained in the original source documents. Such personal identifying information may include, the subject's name, address, date of birth, gender, race, and medical record number.

The subject's name, medical record number or address will not be recorded in the monitor's visit report or the database. Demographic data that may be recorded include age, race, and gender. Any source documents copied for monitoring purposes by the sponsor will be identified by using the assigned subject's unique identifier in an effort to protect subject confidentiality. All personally identifiable information will be redacted from source documents.

19.10 Study Suspension or Early Termination

The study can be discontinued at the discretion of the investigator or study sponsor for reasons including, but not limited to, the following:

- Occurrence of AEs unknown to date in respect to their nature, severity, or duration, or the unexpected incidence of known AEs
- Obtaining new scientific knowledge that shows that the study is no longer valid or necessary
- Insufficient recruitment of subjects
- Unanticipated adverse device effect (UADE) or unanticipated serious adverse device effect (USADE) presenting an unreasonable risk to subjects (sponsor may terminate the study immediately)
- Persistent non-compliance with the protocol
- Persistent non-compliance with applicable ethics committee or regulatory requirements
- Sponsor decision to terminate study

If the study is discontinued or suspended prematurely, the sponsor shall promptly inform all clinical investigator(s)/study center(s) of the termination or suspension and the reason(s) for this. The IRB shall also be informed promptly and provided with the reason(s) for the termination or suspension by the sponsor or by the clinical investigator/investigation center(s). Regulatory authorities and the personal physicians of the subjects may also need to be informed if deemed necessary and provided any blinding information to assist with patient care.

19.11 Site Closeout

At the time of the site close-out, the monitor will have ensured all outstanding study documents are reconciled, the investigator's files are accurate and complete, have reviewed record retention requirements with the investigator, made a final accounting of all study supplies, and ensured that all applicable requirements are met for the study. Any specific observations and actions made at this visit may be documented in a final monitoring report.

19.12 Quality Assurance and Supervision by Authorities

All documents and data shall be produced and maintained in such a way to assure control of documents and data to protect the subject's privacy as far as reasonably practicable. The sponsor and representatives of the FDA, IRB or other regulatory authorities are permitted to inspect the study documents (e.g., study protocol, CRFs, and original study-relevant medical records/files) as needed. All attempts will be made to preserve subject confidentiality.

The study centers are subject to audit by study sponsor personnel or designee for protocol adherence, accuracy of CRFs and compliance with applicable regulations. The sponsor will communicate to the site any patterns of non-compliance. The sponsor will work with the site to

determine any necessary corrective action, as applicable. The sponsor will continue to monitor the site until compliance has been secured. If the site continues to display non-compliance, further and more serious action may be taken by the study sponsor.

The study protocol, data-recording procedures, data handling as well as study reports are subject to an independent clinical Quality Assurance audit by the Sponsor, its designee, or health authorities.

19.13 Approved ICF and Protection of Study Subject

An IRB must review and approve an informed consent form (ICF) specific to this study, prior to consent of a study subject. Sponsor will provide the sites with an ICF template, which the site may modify to include site-specific contact information and site-specific IRB requirements. Sponsor must approve all site-modified informed consent forms prior to use in consenting a subject. IRB approvals and approval renewals of all versions of the site ICF will be provided to sponsor and maintained by the site for the duration of the study. The original, signed and dated ICF for each subject should be retained by the site for monitoring.

Subjects will be informed both verbally and in writing (i.e., ICF) about the nature of the study, the anticipated risks and benefits involved and the discomfort to which they will be exposed. They will be instructed about their right to discontinue their participation at any time without prejudice or jeopardy to future medical care. They must confirm consent in writing prior to any screening procedures. A copy of the informed consent will be provided to the subject.

19.14 IRB Approval

The study protocol and ICF must be approved prior to study commencement under 21 CFR Part 56. A justification of the non-significant risk determination of the study and any supporting information, as necessary, will be provided to the IRB under 21 CFR 812.2(b). Clinical investigators must also obtain renewal of IRB approval throughout the duration of the study. Clinical investigators are responsible for fulfilling any conditions of approval imposed by the reviewing IRB, such as regular reporting, study timing, etc. Clinical investigators will provide the study sponsor with copies of such approvals and reports.

19.15 Other Investigator Reports

The investigator is responsible for the generation of the following reports according to the following schedule:

Type of Notification	**Timeline**
Withdrawal of IRB Approval	Initial report within 24 hours followed by a written report within 5 working days
Informed Consent Not Obtained	written report within 24 hours of identification

NOTE: Reports must be redacted of any personal identification information to protect subject's confidentiality.

19.16 Final Clinical Study Report

A final clinical study report (CSR) will be prepared by the study sponsor and provided to the regulatory agency, as needed.

20 PUBLICATION POLICY

At the conclusion of the study, an abstract reporting the results will be prepared and may be presented at a scientific meeting(s). A manuscript may also be prepared for publication in a peer-reviewed scientific journal. Co-authorship will be granted to the National PI and those site PIs from the top enrolling sites. Consistent with "Recommendations for the Conduct, Reporting, and Publication of Scholarly Work in Medical Journals", every author should meet the following for authorship:

- Substantial contributions to the conception or 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.

The study will also be registered in publicly accessible databases (e.g., ClinicalTrials.gov) per applicable regulation.

21 COVID -19 CONTIGENCY MEASURES

This section identifies contingency measures for the study procedures and various aspects of study management to address limitations to study site visits imposed by the COVID-19 pandemic in accordance with "FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency" (March 2020, updated on August 30th, 2021).

21.1 Study Procedures During COVID-19

- The implementation of contingency measures should be consistent with the protocol to the extent possible, and sponsor and clinical investigators should document the reason for any contingency measures implemented.
- Informed consent and Screening: The ICF may be sent to prospective subjects for review and discussed remotely via phone contact or virtual visit but it must be signed and dated during on-site visit prior to and on the same day as the protocol-required screening assessments to confirm initial eligibility and obtain baseline values. In the event that new information requires a subject be re-consented, the updated ICF may be sent to the subject electronically or via mail for review and discussed remotely via phone contact or virtual visit. The consent form can be signed, scanned and returned electronically to the site, returned by mail using a

prepaid envelope provided by the site, or returned in person. COVID-19 screening procedures that may be mandated by the clinical sites do not need to be entered into EDC. If a potential subject tests positive for COVID-19, the subject is considered screen failure.

- Follow-up Visit: If COVID-19 restrictions or subject's health status prevent the subject from attending a protocol-required on-site visits, those visits can be conducted remotely. The protocol-required CT and endoscopic assessment on baseline and follow-up visits shall be conducted on-site to maintain data quality and integrity for the primary and key secondary efficacy endpoints. If a subject completes the follow up visits out of window because of COVID-19, this will be reported as a protocol deviation with COVID-19 as a reason. The data from these late visits can be leveraged based on scientifically based rationale and clinical judgement.
- CT and endoscopy assessment: If the CT or endoscopy assessment cannot be completed within the visit window, they can either be completed within reasonable (< 30 days) from the visit window or be left as not done. These will be reported as a protocol deviation with COVID-19 as a reason.
- SNOT-22, RSI and CRS side-specific symptom questionnaire: The study staff can mail the paper questionnaires to the subject's home for completion during a virtual study visit. The completed and initialed questionnaires can be returned to the site in person or using envelopes provided by the study site. The visit type will be recorded in the EDC.
- Reporting of any AEs, device deficiencies and change in concomitant medications: These can be completed during virtual visit and documented in the EDC.

21.2 Contingency Measures for Study Management

- SIV training: The required training can be completed through web-based self-training or in person through video conferencing. The training must be documented.
- Data monitoring: In the event an in-person study site visit is not permissible, CRAs will perform remote monitoring. Remote monitoring will include remote source data verification and collection of essential documents. Remote performance of source data verification will require the site research coordinator to redact, scan and send certified copies of source documents to a secure, cloud-based portal or through email. Redacted copies should be kept in the investigator's site master file with records of their communication to the monitor. Uploaded source documents will be accessed by site monitors for source verification with entries in EDC. Issues identified and their resolution will be tracked through annotations made in EDC. Discrepancies between source and EDC will be managed and documented through the EDC query resolution process. Once source data verification is complete, the CRA will securely destroy any copy made locally and provide a certificate of destruction to the trial site.

- EMR system: If local study site policies allow access to the site EMR system, collection of electronic medical records may be completed using the same process. If local study site policies allow access to the site EMR system, the CRA should be provided with secure, read-only access, including all modules relevant for review. This access should be restricted to the records of only those patients who participate in the trial. A list of the monitors to whom remote access has been granted should be maintained. In order to prevent unauthorized access, access rights should be revoked once remote SDV tasks have been completed for the trial. The EMR system should have an audit trail and be able to log information on who accessed data and when. Remote access to the EMR should only be possible using a two-factor authentication. It should not be possible to make local copies of trial participants' health records. Users should be aware of the automatic creation of temporary files on their computer when reviewing trial participant data and should securely delete such files immediately after each source data verification session.
- Situations where CRAs were unable to access or had delayed monitoring of a clinical site shall be documented, including whether identification of deviations or GCP non-compliance was delayed due to postponed monitoring findings and action items resulting from remote monitoring can be discussed with PI and site coordinator via teleconference. Monitoring activities shall be documented per normal procedure.
- Reporting of protocol deviations: When a deviation is the result of a COVID-19 limitation, the deviation report shall include the specific limitation imposed by COVID-19 leading to the inability to comply with the protocol.

22 REFERENCES

Bugten V, Nordgård S, Steinsvåg S. The effects of debridement after endoscopic sinus surgery. Laryngoscope. 2006;116:2037-43.

Chandra RK, Palmer JN, Tangsujarittham T, Kennedy DW. Factors associated with failure of frontal sinusotomy in the early follow-up period. Otolaryngol-HNS. 2004;131:514-8.

Davies RJ, Nelson HS. Once-daily mometasone furoate nasal spray: efficacy and safety of a new intranasal glucocorticoid for allergic rhinitis. Clinical Ther. 1997;19:27-38; discussion 2-3.

Drouin M, Yang WH, Bertrand B, et al. Once daily mometasone furoate aqueous nasal spray is as effective as twice daily beclomethasone dipropionate for treating perennial allergic rhinitis patients. Ann Allergy, Asthma & Immunol. 1996;77:153-60.

Graft D, Aaronson D, Chervinsky P, et al. A placebo- and active-controlled randomized trial of prophylactic treatment of seasonal allergic rhinitis with mometasone furoate aqueous nasal spray. J Allergy Clin Immunology. 1996;98:724-31.

Hebert JR, Nolop K, Lutsky BN. Once-daily mometasone furoate aqueous nasal spray (Nasonex) in seasonal allergic rhinitis: an active- and placebo-controlled study. Allergy. 1996;51:569-76.

Kennedy DW, Wright ED, Goldberg AN. Objective and subjective outcomes in surgery for chronic sinusitis. Laryngoscope. 2000;110:29-31.

Kyrmizakis DE, Papadakis CE, Lohuis PJ, et al. Acute candidiasis of the oro- and hypopharynx as the result of topical intranasal steroids administration. Rhinol. 2000;38:87-9.

Luong A, Ow RA, Singh A, et al. Safety and effectiveness of a bioabsorbable steroid-releasing implant for the paranasal sinus ostia: a randomized clinical trial. JAMA Otolaryngol-HNS. 2018;144:28-35.

Mandl M, Nolop K, Lutsky B. Comparison of once daily mometasone furoate (Nasonex) and fluticasone propionate aqueous nasal sprays for the treatment of perennial rhinitis. Ann Allergy, Asthma & Immunol. 1997;79:370-8.

McCormack PL, Plosker GL. Inhaled mometasone furoate: A review of its use in persistent asthma in adults and adolescents. Drugs. 2006; 66:1151-68.

Mygind N, Andersson M. Topical glucocorticosteroids in rhinitis: clinical aspects. Acta Oto-laryngol. 2006;126:1022-9.

Naidoo Y, Wen D, Bassiouni A, et al. Long-term results after primary frontal sinus surgery. IFAR. 2012;2:185-90.

Nayak AS, Settipane GA, Pedinoff A, et al. Effective dose range of mometasone furoate nasal spray in the treatment of acute rhinosinusitis. Ann Allergy, Asthma & Immunol. 2002; 89:271-8.

Orlandi RR, Kingdom TT, Smith TL, et al. International consensus statement on allergy and rhinology: rhinosinusitis 2021. Int Forum Allergy Rhinol. 2021 Mar;11(3):213-739.

Ramadan HH. Surgical causes of failure in endoscopic sinus surgery. Laryngoscope. 1999;109:27-9.

Rickham PP. Human experimentation. Code of ethics of the World Medical Association. Declaration of Helsinki. British Med J. 1964;2:177.

Schenkel E. Features of mometasone furoate nasal spray and its utility in the management of allergic rhinitis. Expert Opinion Pharm. 2003;4:1579-91.

Singh A, Luong AU, Fong KJ, et al. Bioabsorbable steroid-releasing implants in the frontal sinus ostia: a pooled analysis. Int Forum Allergy Rhinol. 2019; 9:131-9.

Van Cauwenberge P, Van Hoecke H, Vandenbulcke L, et al. Glucocorticosteroids in allergic inflammation: clinical benefits in allergic rhinitis, rhinosinusitis, and otitis media. Immunol & Allergy Clinics. 2005; 25:489-509.

Vogt FC. The incidence of oral candidiasis with use of inhaled corticosteroids. Ann Allergy. 1979; 43:205-10.

Internal Document

CP-00038 Radiographic Evaluation Protocol for P500-1220 (The EXPAND Study), Rev 2.0, 18 May 2022

APPENDIX I: LIST OF CORTICOSTEROID MEDICATIONS

Trade Name (alphabetical order)	**Generic Name**	**Route of Administration**
Budesonide Pulmicort Respules	Budesonide	Nasal (e.g., irrigations, rinses)
Decadron Dexasone	Dexamethasone	Intramuscular Oral
Depo Medrol Medrol Medrol Dosepak Methylprednisolone	Methylprednisolone Methylprednisolone Acetate	Oral Parenteral routes (e.g., intra-articular, intra-cervical)
Flovent Flonase Xhance	Fluticasone Propionate Fluticasone Propionate w/Salmeterol	Nasal irrigations Intranasal sprays
Kenalog	Triamcinolone Triamcinolone Acetonide	Intramuscular Subcutaneous Submucosal
Nasonex	Mometasone furoate	Nasal irrigations Intranasal sprays
Deltasone Prednicot Sterapred	Prednisone	Intramuscular Oral