Medtronic

Clinical Investigation Plan

Clinical Investigation Plan/Study Title	A prospective, multi-center, single arm study of BiZact™ on children undergoing tonsillectomy.
Clinical Investigation Plan / Study Identifier	MDT17024BZP
Study Product Name	BiZact™
Local Sponsors	Covidien-Medtronic Minimally Invasive Therapies Group Surgical Innovations 5920 Longbow Dr. Boulder, CO 80301 Covidien-Medtronic
Document Version	Version 5.0, 18 March 2019

1. Investigator Statement

Study product Name	BiZact™
Sponsors	Covidien-Medtronic Minimally Invasive Therapies Group Surgical Innovations 5920 Longbow Dr. Boulder, CO 80301 Covidien-Medtronic
Clinical Investigation Plan / Study Identifier	MDT17024BZP
Version Number/Date	5.0, 18 March 2019

I have read the protocol, including all appendices, and I agree that it contains all necessary details for me and my staff to conduct this study as described. I will conduct this study as outlined herein and will make a reasonable effort to complete the study within the time designated.

I agree to comply with the applicable regulatory guidelines under which the study is being conducted, I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the evaluation and conduct of the clinical investigation without the prior written consent of Medtronic. Additionally, I will commit to:

- conduct the investigation in accordance with the agreement, the investigational plan, FDA 21 CFR Part 812 and other applicable FDA regulations, and conditions of approval imposed by the reviewing IRB/Ethics Committee, local /regional regulatory requirements;
- supervise all testing of the device involving human subjects; and
- ensure that the requirements for obtaining informed consent are met
- provide sufficient and accurate financial disclosure information and update information if any relevant changes occur during the investigation and for one year following the completion of the study.

I will provide all study personnel under my supervision copies of the protocol and access to all information provided by Medtronic. I will discuss this material with them to ensure that they are fully informed about the products and the study.

Investigator's Signature:	
Investigator's Name:	
Institution:	
Date:	

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2. Glossary

Term	Definition
ADE	Adverse device effect: Adverse event related to the use of an investigational medical device. Note: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation or any malfunction of the investigational medical device. Note: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device. See Clinical Event definition for more information.
AE	Adverse event: Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device. Note: This definition includes events related to the investigational medical device or the comparator. Note: This definition includes events related to the procedures involved. Note: for users or other persons, this definition is restricted to events related to investigational medical devices. See Clinical Event definition for more information.
Assent	An agreement by an individual not competent to legally give valid informed consent generally because of age or mental status
CIP	Clinical Investigation Plan Document that state(s) the rationale, objectives, design and proposed analysis, methodology, monitoring, conduct and recordkeeping of the clinical investigation. Note: The term “protocol” is synonymous with “CIP”. However, protocol has many different meanings, some not related to clinical investigation, and these can differ from country to country. Therefore, the term CIP is used in this International Standard.
EC	Ethics Committee: Independent body whose responsibility is to review clinical investigations in order to protect the rights, safety and well-being of human subjects participating in a clinical investigation. Also known as the Institutional Review Board (IRB). Note: For the purposes of this International Standard, “ethics committee” is synonymous with “research ethics committee,” “independent ethics committee” or “institutional review board”. The regulatory requirements pertaining to ethics committees or similar institutions vary by country or region.
eCRF/CRF	(Electronic) Case Report Form: A paper or electronic data collection form, designed to collect information on each subject as required by the Study Protocol /Clinical Investigation Plan.
ENT	Ear, nose and throat, a subspecialty of medicine dealing with the diagnosis and management of medical conditions related to the ears, nose, and throat, also referred to as otolaryngology or otorhinolaryngology
FLACC behavioral pain assessment scale	Face, Legs, Activity, Cry, Consolability behavioral pain assessment scale: A validated pain measurement instrument to assess pain for children age 2 months to seven (7) years of age. The scale has five (5) criteria with 0 representing behavior with no pain and 2 representing the most pain.
GCP	Good Clinical Practice: A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical studies that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of study subjects are protected.
Hemostasis	The arrest of bleeding, whether it be by normal vasoconstriction (the vessel walls closing temporarily), by an abnormal obstruction (such as a plaque) or by coagulation or surgical means (such as ligation).
Intra-operative Bleeding	Bleeding that occurs during the course of the surgical operation.

Term	Definition
IRB	Institutional Review Board: Any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. Also known as Ethics Committee (EC).
LAR	Legally Authorized Representative: Individual or judicial or other body authorized under applicable law to consent, on behalf of a prospective subject, to the subject's participation in the clinical investigation. LAR may be the subject's parent or parental guardian. For the purposes of this protocol LAR will be used, but may be synonymous with parent in cases where a parent is the LAR.
Likert Scale	A psychological measurement device that is used to gauge attitudes, values, and opinions, generally using a 5-point rating system.
Peritonsillar abscess	A formation of pus within the peritonsillar space (beside the tonsil) generally formed as the result of bacterial infection within the loose connective tissue found in the area.
SAE	Serious Adverse Event: Adverse event that: a) Led to a death, b) Led to a serious deterioration in the health of the subject, that either resulted in: 1) Resulted in a life-threatening illness or injury, or 2) Resulted in a permanent impairment of a body structure or a body function, or 3) In-patient or prolonged hospitalization, or 4) Medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function, or Led to fetal distress, fetal death or a congenital abnormality or birth defect. Note: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.
SADE	Serious Adverse Device Effect: Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Tonsillectomy	A surgical procedure to remove the tonsils
US	United States
USADE	Unanticipated Serious Adverse Device Effect: 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 CIP or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety or welfare of subjects.
Wong-Baker FACES® Scale	An illustrated pain scale ranging from a happy face at 0 "No Hurt" to a crying face at 10 "Hurts Worst"

3. Synopsis

Title	A prospective, multi-center, single arm study of BiZact™ on children undergoing tonsillectomy
Clinical Study Type	Pre-market Pivotal / IDE Study
Product Name	BiZact™ (BZ4212)
Sponsor	Medtronic, Minimally Invasive Therapies Group, Surgical Innovations
Local Sponsors	Covidien-Medtronic Minimally Invasive Therapies Group Surgical Innovations 5920 Longbow Dr. Boulder, CO 80301 Covidien-Medtronic
Indication under investigation	Tonsillectomy in children (age 2-12 at the time of the procedure, inclusive)
Investigation Purpose	The purpose of this study is to assess safety and performance with the use of the BiZact™ device in tonsillectomy procedures in children.
Product Status	• Food and Drug Administration (FDA) cleared for adult ENT procedures including tonsillectomy • Therapeutic Goods Administration (TGA) License for ENT procedures including tonsillectomy in adults, children and adolescents.
Primary Objective(s)	The primary objective of this study is to assess safety and performance with the use of the BiZact™ device in children (ages 2-12 at the time of the procedure, inclusive) tonsillectomy procedures.
Study Design	A prospective, multi-center, single arm, study of BiZact™ on children undergoing tonsillectomy.
Primary Endpoint(s)	Intra-operative blood loss: The study will be considered a success if the mean intra-operative blood loss is less than the mean intra-operative blood loss associated with conventional tonsillectomy in a large meta-analysis (Alexiou *et al.* 2011). See the Statistics section below for more details.

Secondary Endpoint(s)	Study will analyze and describe device performance and patient response related to the following: ○ Ability to dissect tonsils with investigational medical device via Likert Scale (Very Good, Good, Acceptable, Poor, Very Poor) ○ Usability Challenges ○ Ability to achieve hemostasis (arrest of bleeding, as assessed by visual inspection of the Investigator) without the use of other interventions (e.g. energy device or sutures) ○ Evaluation of post-operative pain incidence and severity measured using the Wong-Baker FACES® Pain Rating Scale and FLACC behavioral pain assessment scale ○ Analgesic consumption (standard of care) and concomitant medications (via patient diary)
Sample Size	A minimum of sixty (60) completed procedures, with at least 40% study wide in the age range of 2-5 years of age, will be undertaken at a minimum of 2 sites in US. When 36 procedures with subjects ⩾6 years of age have been completed (60% of total minimum enrollment), enrollment for this age group will close. Power considerations are detailed in the Statistics section below.
Inclusion/Exclusion Criteria	Inclusion Criteria: 1. Children subjects 2-12 years of age at time of procedure, inclusive 2. Scheduled to undergo tonsillectomy 3. The subject and subject's Legally Authorized Representative (LAR) is willing to participate and consents to participate, as documented by signed informed consent form and/ or assent form (as applicable) Exclusion Criteria:

	1. Subjects undergoing: a. Tonsillectomy as a result of cancer b. Unilateral tonsillectomy 2. Subjects with: a. Known Bleeding disorders b. History of peritonsillar abscess c. Craniofacial disorders d. Down's syndrome (Trisomy 21) e. Cerebral palsy f. Major heart disease (including but not limited to; right-sided heart failure, left-sided heart failure, congestive heart failure, coronary artery disease, arrhythmias, chronic heart failure, acute heart failure, etc.) g. Current tobacco use 3. Subjects unable to comply with the required study follow-up visits 4. Female subjects pregnant at time of procedure 5. The subject has comorbidities which, in the opinion of the Investigator, will not be appropriate for the study or the subject has an estimated life expectancy of less than 6 months. 6. The subject is participating or has participated in any drug or device research study within 30 days of enrollment.
Study Procedures and Assessments	Pre-operative & Operative Assessments: • Demographics • Histories: Medical, Surgical, Medication • Urine pregnancy test for females of child bearing potential • Type of admission • AE/SAE Assessment • Pre-operative physical exam (abbreviated) • Intra-operative bleeding volume (excluding other fluids) ○ Operative field irrigant volume ○ Presence of gastric fluids ○ Volume of stomach juices and blood in suction container ○ Differential weight of any sponges applied to tonsil bed to absorb blood • Surgical performance parameters ○ Operative time - time from the first incision to complete hemostasis (arrest of bleeding as assessed by visual inspection of the Investigator) of the tonsillar bed (excluding time for closing)

	○ Device ease of use ○ Usability challenges ○ Alternate device(s) use (if any) ○ Ability to dissect tonsil with device graded via Likert Scale (Very Good, Good, Acceptable, Poor, Very Poor) ○ Tonsil size measurement (mL) • Concomitant Medications • Device accountability Follow-up Assessments (Forms filled out by subject or parent/LAR on post-operative days 1-7, 10, 14 and 28 see full protocol for assessment windows): • Pain level • Analgesic consumption • Ability to return to normal diet (via Patient Diary) • Ability to return to normal activity (via Patient Diary) • Incidence of post-operative hemorrhage - any primary (≤24 hours) requiring medical intervention and secondary (>24 hours) bleeding requiring medical intervention (e.g., cautery, admission for observation, or re-operation) • Incidence of post-operative readmission
Safety Assessments	Safety will be assessed as the proportion of subjects with: 1. Post-operative hemorrhage - any primary (≤24 hours) requiring medical intervention and/or secondary (>24 hours) bleeding requiring medical intervention (e.g., cautery, admission for observation, or re-operation) 2. Post-operative readmission 3. Evidence of glossopharyngeal nerve damage (e.g., prolonged pain or difficulty swallowing) as diagnosed by the surgeon 4. Other intra/post-operative complications (complications related to device deficiencies) 5. Other adverse events (e.g., post-operative dehydration, fever, etc.) 6. Localized Infection a. Infection confined to a single organ or tissue The study will assess the observed rates of device related serious adverse events.

Statistics	The analysis technique will be a 1-sample t-test (or Wilcoxon ranked sign if nonparametric test is desired), with a one-sided type I error rate (α) of 0.025. A sample size of 60 is selected to ensure that multiple surgeons participate and to create an opportunity for a range of subject ages to be enrolled. Statistical power for a sample size of 60 exceeds 99%. The primary hypotheses of this study are: H0: Mean intra-operative blood loss = 31 mL HA: Mean intra-operative blood loss < 31 mL The performance goal of 31 mL derives from a meta-analysis comparing modern technology to conventional techniques (i.e. electrocautery and cold steel) (Alexiou *et al*. 2011). This paper included a total of 3139 patients included in thirty-three published studies. The values from all of the studies that reported intra-operative bleeding were combined to calculate a mean blood loss. This value encompasses a variety of techniques and technologies and a number of different studies to capture a realistic value for comparison. Intraoperative blood loss during tonsillectomy with BiZact™ is expected to be low. The expected mean value for the BiZact™ device is a conservative estimate derived from data for LigaSure™ and other vessel sealing systems in the Alexiou meta-analysis. The expected standard deviation is the average of the standard deviation values for all studies that reported blood loss in the meta-analysis. Expected mean for BiZact™: 10 mL Expected standard deviation: 15.1 mL Additionally, descriptive statistics for blood loss will be reported for different age groups (ages 2-5 and ages 6-12) as well as for different sites, surgeons, and countries. Secondary endpoints will be evaluated with descriptive statistics. For continuous variables, the mean, median, and standard deviation will be reported, along with a 95% confidence interval for the mean where appropriate. For categorical data, proportions will be reported, along with 95% confidence intervals where appropriate.

4. Introduction

4.1. Background

4.1.1. Tonsillectomy Procedure

Tonsillectomy is one of the most frequently performed otorhinolaryngologic procedures. Aside from the conventional technique of cold steel and electrocautery dissection, the introduction of numerous energy based tools and techniques allows for the simultaneous dissection and sealing of vessels, potentially improving safety and reducing the complications of the procedure (1-3). Generally thought of as safe and effective, energy based devices such as laser, Shaw scalpel, electrosurgical devices (needle, scissor, or knife), radiofrequency needle ablation device, thermal welding, and Coblator™, use heat energy to denature protein, leading to vascular tamponade and hemostasis (arrest of bleeding). Unfortunately, a byproduct of using this energy during surgery is the lateral heating of the surgical area, which can damage adjacent structures, delay wound healing, increase post-operative pain, and increase the subject's time to return to normal diet and activity (4).

In order to address these concerns, Medtronic has developed BiZact™, a bipolar electrosurgical instrument intended for use in open surgical procedures, such as tonsillectomies, where ligation and division of vessels, tissue bundles, and lymphatics is desired. BiZact™ is designed as a pistol grip radiofrequency (RF) sealer/dissector for use with vessels up to and including 3mm. Compatible with the already in use Valleylab™ (LS10, FT10, ForceTriad™) energy platforms, BiZact™ employs bipolar electrosurgical RF energy and pressure to ligate vessels interposed between its jaws which can then be transected using the built-in knife deployed by the device trigger. Based off of Ligasure™ technology, bipolar electrosurgical devices have demonstrated utility for tonsillectomy procedures, providing hemostasis while minimizing postoperative pain (5, 6, 8, 9).

4.1.2. BiZact™ Device

Animal model studies have found BiZact™ to be able to achieve hemostasis and minimize lateral thermal spread potentially resulting in reduced post-operative pain. Details of preclinical testing can be found within the BiZact™ instructions for use (IFU) and in the Investigator's Brochure. Additionally, the performance of the BiZact™ device is also being evaluated in an adult tonsillectomy pilot study in the US and Europe (ClinicalTrials.gov Identifier: NCT02876575).

4.2. Purpose

The purpose of this study is to assess safety and performance of the BiZact™ device in tonsillectomy procedures in children. Sixty (60) pediatric subjects (ages 2-12 inclusive) will be treated for tonsillectomy with BiZact™ enrolled at a minimum of 2 clinical sites across the USA with enrollment and completion of the tonsillectomy procedure with the study device not to exceed 36 subjects per site. The study will be considered a success if the mean intra-operative blood loss is less than the mean intra-operative blood loss associated with conventional tonsillectomy in a large meta-analysis (7). At the conclusion of the study, data will be submitted to the FDA for consideration for a pediatric indication and for publication.

5. Objectives and Endpoints

5.1. Objectives

5.1.1. Primary Objective

The primary objective of this study is to assess safety and performance with the use of the BiZact™ device in children (ages 2-12 at the time of the procedure, inclusive) tonsillectomy procedures.

5.2. Endpoints

5.2.1. Primary Endpoint

The primary endpoint of this study is the amount of intra-operative blood loss. The study will be considered a success if the mean intra-operative blood loss is less than the mean intra-operative blood loss associated with conventional tonsillectomy in a large meta-analysis (7). See the Statistical Design and Methods (Section 13) for additional details.

5.2.2. Secondary Endpoints

- Ability to dissect tonsils with investigational medical device (Likert Scale: Very Good, Good, Acceptable, Poor, Very Poor) and Usability Challenges
- Ability to achieve hemostasis (arrest of bleeding, as assessed by visual inspection of the investigator) without the use of other methods (e.g. energy device or sutures)
- Evaluation of post-operative pain incidence and severity measured using the Wong-Baker FACES® Pain Rating Scale or FLACC behavioral pain assessment scale
- Analgesic consumption (standard of care) and concomitant medications (via Patient Diary)

5.2.3. Safety Assessment

The study will assess the observed rates of device-related adverse events. This includes, but is not limited to consideration of the following conditions:

- Post-operative hemorrhage
    - Any primary (≦24 hours) requiring medical intervention and/or secondary (>24 hours) bleeding requiring medical intervention (e.g., cautery, admission for observation, or re-operation)
- Post-operative readmission
- Evidence of glossopharyngeal nerve damage as diagnosed by the investigator via subject assessment
- Other intra/post-operative complications (complications related to device deficiencies)
- Other adverse events (e.g., post-operative dehydration, fever, etc.)
- Localized Infection
    - Infection confined to a single organ or tissue

6. Study Design

6.1. Duration

Including enrollment and follow up time, the current study is estimated to progress for up to 18 months. During this time, subjects will participate for a maximum of 67 days. Subject screening for

eligibility will occur up to 30 days prior to the procedure. Post-procedure, subjects will be assessed for pain and their ability to return to normal diet and activity via a patient diary and either the FLACC behavioral pain assessment scale (age 2) or the Wong Baker Faces® Scale at days 1 through 7, Day 10 (+/-1 day), Day 14 (+/-1 day), and Day 28 (+/-1 day), before returning the FLACC/FACES® scales and Patient Diary during the return to clinic on day 28 (+7). Please see section 9 for study schematic.

6.2. Rationale

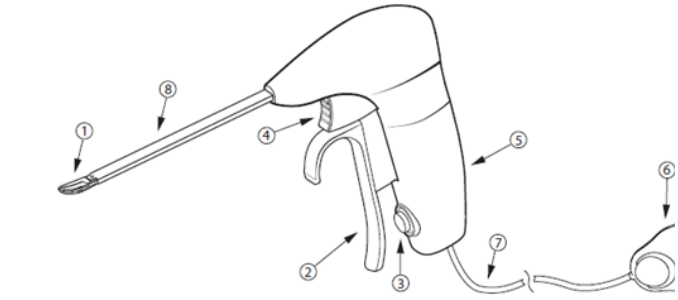
In order to assess the clinical safety and performance of BiZact™ (BZ4212) on a pediatric population, Medtronic is performing a prospective, multi-center, single arm study of BiZact™ on children (2-12 years of age at the time of the procedure, inclusive) undergoing tonsillectomy. Intra-operative blood loss will be assessed as well as post-operative pain and other quality of life aspects for 28 (+7) days following the procedure. Pre-clinical testing has found BiZact™ to satisfactorily achieve hemostasis and currently a multicenter adult tonsillectomy study is underway in the US and Europe. As a study with no comparator, this study does not utilize any randomization or blinding. The BiZact™ device will only be used during the course of the tonsillectomy procedure and subjects will be followed for 28 (+7) days to monitor bleeding, pain and return to normal diet and activity. If any adverse events are identified they will be assessed, reported and documented in the eCRF.

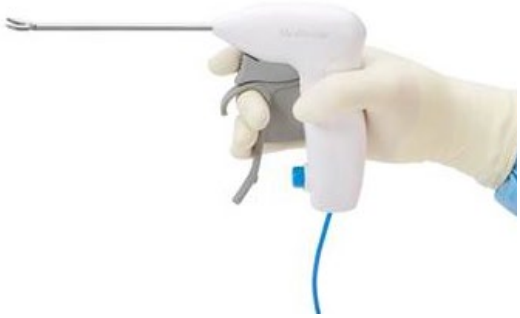
7. Product Description

7.1. General

The BiZact™ is a single use bipolar electrosurgical instrument intended for use in general open surgical procedures. It is also indicated for adult ENT procedures, including tonsillectomy, for the ligation and division of vessels, tissue bundles, and lymphatics 2-3 mm away from unintended thermally sensitive structures.

BiZact™ is a pistol grip RF-based sealer/ dissector similar (design, technology and materials) to current Ligasure™ devices. Akin the commercialized device, LF1212 (Ligasure™ small jaw), BiZact™ includes a jaw, a deploying knife, a lever to open and close the jaws, and a trigger to deploy the knife and inline activation of bipolar energy. The device does not include a rotation knob for rotating the jaws, but the device does allow surgeons to perform procedures by switching hands. BiZact™ is compatible with the Valleylab™ (LS10 with V1.1 or V1.2 software, ForceTriad with v4.0 software, and FT10 with v2.0 software) energy platforms, which are able to recognize the device utilizing radiofrequency identification (RFID) or barcode capabilities. In total, 120 BiZact™ units will be assigned to this study to account for any situations in which more than one device is needed.





① Jaws (gray)
② Lever (white)
③ Activation button (purple)
④ Cutting trigger (gray)
⑤ Handle (white)
⑥ Connector
⑦ Cable
⑧ Outer shaft (metallic)

Figure 1: BiZact™ (BZ4212) schematic diagram (left), and device photo (right)

7.2. Dosage Form and Route of Administration

This instrument creates tissue fusion by application of bipolar electrosurgical RF energy and pressure to vessels/tissue interposed between the jaws of the instrument. The tissue fusion can then be transected using the built in cutting mechanism. The instrument can be used for vessels and lymphatic tissue up to and including 3mm in diameter and tissue bundles. The instrument also incorporates inline RF activation, features for grasping and tips for dissection. The instrument is intended primarily for surgeons performing tonsillectomies. See Instructions for Use (included in Appendix A) for instructional information.

The BiZact™ device has received the following approvals for the ligation and division of vessels, tissue bundles and lymphatics 2-3 mm away from unintended thermally sensitive structures;

- Food and Drug Administration (FDA) indication for adult ENT procedures including tonsillectomy (US)
- Therapeutic Goods Administration (TGA) License for ENT procedures including tonsillectomy in adults, children and adolescents (AUS)

This information is contained in the IFU (Appendix A) but the IFU accompanying the device should always be consulted.

7.3. Manufacturer

BiZact™ is manufactured by Covidien (Covidien LP is an indirect wholly owned subsidiary of Medtronic plc.). The Covidien facility located at 5920 Longbow Drive, Boulder, CO is an FDA registered establishment (1717344) manufacturing US Class 1 and 2 medical devices in accordance with the 21 CFR 820 Quality System Regulation. The site also holds both an ISO 13485 Quality Management Certificate (FM 71825) and Full Quality Assurance System Certificate (CE 00500). Both certificates are issued by Boulder's Notified Body, BSI. BSI holds annual quality assessments to ensure continued compliance to quality processes.

Components used in the assembly of the device are manufactured by several different suppliers. All suppliers undergo a robust qualification process prior to inclusion on Covidien's "Approved Supplier List." Once suppliers are selected, they are audited on a periodic basis per Covidien's procedures to ensure continued adherence to Covidien specifications and standards. Each supplier is assigned a risk rating, and this determines the timetable for subsequent audits that are not for cause.

7.4. Packaging

See Appendix A, Instructions for Use. BiZact™ is provided as a single use disposable product. Each instrument is individually packaged and sealed in a Tyvek ® pouch. Six sealed pouches are packaged in one shipper case.

In the United States, the BiZact™ devices will be labeled as investigational according to regulations: "CAUTION – Investigational Device - Limited by Federal (or United States) Law to Investigational Use."

For Australia, devices for the study will be shipped accompanied by instructions that the devices are indicated for the BiZact™ clinical study use only, to be used by study qualified investigators, and consistent with local requirements.

7.5. Intended Population

The BiZact™ device has received the following approvals or clearances for the ligation and division of vessels, tissue bundles and lymphatics 2-3 mm away from unintended thermally sensitive structures;

- Food and Drug Administration (FDA) indication for adult ENT procedures including tonsillectomy (US)
- Therapeutic Goods Administration (TGA) License for ENT procedures including tonsillectomy in adults, children and adolescents (AUS)
- CE Mark under the Medical Device Directive for use in ENT procedures including tonsillectomy in adults, children and adolescents (EU)

7.6. Equipment

BiZact™ devices are single-use disposable products. If needed, a compatible Valleylab™ generator will be supplied and approved by the hospital biomedical department if applicable. Each site will receive or be assigned to use a different compatible Valleylab generator for this study. BiZact™ is compatible with the Valleylab™ (LS10 with V1.1 or V1.2 software, ForceTriad with v4.0 software, and FT10 with v2.0 software) energy platforms, which are able to recognize the device utilizing radiofrequency identification (RFID) or barcode capabilities after the BiZact™ device is plugged into the Ligasure ™ port of the Valleylab generator. There is no need for any necessary calibration or monitoring of the equipment to enable use with the BiZact™ device.

7.7. Product Use

The BiZact™ device is a bipolar electrosurgical instrument intended for use in open surgical procedures where ligation and division of vessels, tissue bundles, and lymphatics is desired.

The tissue fusion function of the device can be used on vessels (arteries and veins) and lymphatics up to and including 3 mm diameter. The BiZact™ device is indicated for use in open general surgical procedures.

The BiZact™ device has not been shown to be effective for tubal sterilization or tubal coagulation for sterilization procedures, and should not be used for these procedures.

This information is contained in the IFU (Appendix A) but the IFU accompanying the device should always be consulted.

7.8. Product Training Requirements

Each Investigator participating in the clinical study and the associated clinical study staff will receive training on the clinical protocol, as well as the BiZact™ device. Investigators and study staff will be trained on device characteristics, shelf life and storage requirements, device use, and warnings, precautions, contraindications.

7.9. Product Receipt and Tracking

BiZact™ will be shipped to each site with the shipment form (which includes shipping/ dispersal date, the quantity, model, lot, and, serial number and expiration date). Each site will review contents and document on the form the confirmation the shipment information is accurate as well as the date received. The use of the device for a procedure or disposition of the devices (e.g. if returned due to damage upon arrival) will be recorded in the eCRF device tracking section in conjunction with the above information.

BiZact™ will be provided to each site upon Sponsor collection and approval of all required regulatory documentation. Additionally, a Valleylab™ generator will be supplied if necessary (see above).

7.10. Product Storage

Access should be limited to designated study staff only. Study devices should be kept in an area or otherwise contained where only qualified study personnel can access the device (i.e. locked or secured). This area/container should be kept at ambient temperatures without exposure to water with adequate provisions for maintaining ambient temperatures if a loss of power is experienced. Device accountability will be tracked in the electronic case report forms (eCRFs). If the devices are exposed to water or a drastic change in temperature, sites should contact the study team for possible replacement devices.

7.11. Product Return

It is the responsibility of the site to return the Valleylab™ generator to Medtronic within 30 days of the End of Study if one was loaned, along with any unused or expired BiZact™ devices. Sites should follow instructions and complete all appropriate forms provided by the study team for product return.

7.12. Product Accountability

Access should be limited to designated study staff only. Device accountability will be tracked in the electronic case report forms (eCRFs). It is the site's responsibility to document the receipt (which

includes shipping/ dispersal date, the quantity, model, lot, and, serial number and expiration date), disposition of the product (per subject use, including amount used, amount remaining, etc.), transfer (if applicable) and return of all unopened investigational medical devices.

8. Selection of Subjects

8.1. Study Population

A minimum of sixty (60) completed procedures with subjects ages 2-12 (at the time of the procedure inclusive), with at least 40% study wide in the age range of 2-5 years of age, will be undertaken at a minimum of 2 sites in US. When 36 procedures with subjects ⩾6 years of age have been completed (60% of minimum total enrollment), enrollment for this age group will close. A minimum of five surgeons across the 2 sites will participate.

The sample size of 60 was selected to ensure that multiple surgeons participate and to create an opportunity for a range of subject ages to be enrolled. Power considerations are detailed below (Section 13).

8.2. Subject Enrollment

A minimum of 60 subjects will be enrolled in the study at a minimum 2 sites with competitive enrollment not to exceed 36 enrolled subjects per site. Subjects' participation in the study will last 28 (+7) days post procedure. Subjects will be considered for the study if they meet all of the preoperative inclusion criteria and none of the exclusion criteria (Section 8.3, 8.4), and sign the informed consent form.

A subject is considered enrolled in the study when the subject's legally authorized representative signs the informed consent form. However, data will not be collected for the study until the subject has determined to be eligible for the study and the surgical procedure has begun. No adverse event information will be recorded before the procedure has begun. As soon as the tonsillectomy procedure has begun and the study device has contacted the patient, the patient must be followed regardless of whether or not the procedure has been fully completed with the device . See section 9.10.3 for the full definition of enrolled subjects. The procedure will be performed per the institution's standard practice.

8.3. Inclusion Criteria

1. Children subjects 2-12 years of age at the time of the procedure, inclusive
2. Scheduled to undergo tonsillectomy
3. The Subject and Subject's Legally Authorized Representative (LAR) is willing to participate and consents to participate, as documented by signed informed consent form and/ or assent form (as applicable)

8.4. Exclusion Criteria

1. Subjects undergoing:
    a. Tonsillectomy as a result of cancer
    b. Unilateral tonsillectomy
2. Subjects with:
    a. Known bleeding disorders
    b. Current peritonsillar abscess
    c. Craniofacial disorders

d. Down's syndrome (Trisomy 21)
e. Cerebral palsy
f. Major heart disease (including but not limited to; right-sided heart failure, left-sided heart failure, congestive heart failure, coronary artery disease, arrhythmias, chronic heart failure, acute heart failure, etc.)
g. Current tobacco use

3. Subjects unable to comply with the required study follow-up visits
4. Female subjects pregnant at time of procedure.
5. The subject has comorbidities which, in the opinion of the Investigator, will not be appropriate for the study or the subject has an estimated life expectancy of less than 6 months.
6. The subject is participating or has participated in any drug or device research study within 30 days of enrollment.

9. Study Procedures

9.1. Schedule of Events and Study Schematic

The schematic of the study is presented in the table below.

	Screening / Baseline Day -30 to 0	Surgery (Day 0) [1]	Post-Op[6] Day 1 – Day 7, 10 & 14 (Home)	Post-Op[6] Day 28	Return to Clinic Day 28 (+7 days)
	Can be combined			Can be combined	
Informed Consent [1]	X[1]				
Eligibility Criteria	X[1]				
Urine pregnancy test		X [4]			
Demographic data [2]	X				
Medical history	X				
Surgical history	X				
Medication history	X				
Analgesic consumption & Concomitant medications (via patient diary)		X	X	X	
Type of admission		X			
Physical Examination (abbreviated)		X			
Intra-operative bleeding volume		X			
Tonsil measurement		X			
Operation time		X			
Device ease of use		X			
Usability Challenges [2]		X			
Ability to dissect tonsil via Likert scale		X			
Alternate device used (if any)		X			
Post-operative bleeding		X	X	X	X
AE, SAE, ADE, USADE Assessment and device deficiencies [3]		X	X	X	X
Readmission			X	X	X
Record Pain via Wong-Baker FACES® Pain Rating Scale or FLACC behavioral pain assessment scale [5]			X	X	
Patient diary			X	X	
Return pain scales and diary [5]					X
Device accountability		X			
Protocol deviation collection	X	X	X	X	X

[1] Study specific procedures may only be performed after subject has agreed to participate and the signed informed consent form. Screening and informed consent are considered as a process that may occur over multiple days within 30 days prior to procedure. Any new information about the subject's eligibility and willingness to participate must be considered prior to the tonsillectomy with the investigational device.

[2] See protocol and CRF pages for specific data points

[3] Device-related SAEs will be collected from the start of the procedure as soon as the device is in contact with the subject. If any events are ongoing at the last visit Day 28 (+7), they must be followed up to seven (7) days or resolution whichever is first.

[4] A negative urine pregnancy test performed within 24 hours prior to surgery will be acceptable to satisfy eligibility criteria. This will apply to all "females of child bearing potential." Local definition and standard of care for testing of "female of child bearing potential" will be documented and observed for each site.

[5] For participants age 2, parents will evaluate pain using the FLACC behavioral pain assessment scale as validated measurement. All older subjects will utilize the Wong-Baker FACES Pain Rating Scale.

[6] For Days 10,14, and 28, post-operative assessments including pain scales and diary may be completed +/- 1 day but should be returned Day 28 (+7).

9.1.1. Screening / Baseline Visit

A screening/baseline visit will be performed within 30 days up to the day of the scheduled procedure and may be combined with the Procedure Visit. Subjects' legally authorized representative will need to provide consent prior any procedures specific to the study are undertaken. The purpose and all aspects of the study will be explained to the subject and LAR(s). \LAR(s) who agree to study participation must sign and personally date the sponsor and IRB/EC-approved informed consent form prior to participating in any study activities. Additionally, assent forms will be completed and signed as applicable per IRB/EC requirements.

Once informed consent/assent has been obtained according to IRB/EC requirements and eligibility is confirmed, the subject's demographics and medical history will be assessed to include: age, gender, weight, ethnicity and race. Relevant medical history will be assessed and included in the electronic case report form (eCRF).

The following assessments will be performed within 30 days prior to the scheduled surgical procedure and the results recorded on the appropriate subject eCRFs:

- Verification of eligibility criteria
- Demographic data (date of birth, ethnicity, gender height weight)
- Medical history, including comorbidities such as obesity, and underlying conditions that necessitated surgery
- Surgical history
- Medication history (such as during pre-operative period)
- Pregnancy test, if applicable (must be within 24 hours prior to surgery)
- Concomitant medication(s)
  Note: All medications will be coded using the World Health Organization (WHO) drug coding dictionary.

9.1.2. Surgical Procedure (Day 0)

The Study Investigator should perform the surgical procedure according to the appropriate standard procedures and practices at his/her institution using BiZact™. BiZact™, in conjunction with other non-energy surgical tools (e.g. Allis clamp), should be used to complete the entire procedure unless it is medically necessary to use another device. Additionally, the following procedures and assessments will be performed:

- Type of admission (e.g. inpatient/outpatient)
- AE/SAE assessment
- Pre-operative procedure abbreviated physical examination
  - Including assessment of heart/lungs, neurological, ENT, immune system and vital signs (blood pressure, respiration rate, heart rate, temperature)
- Female subjects will undergo a urine pregnancy test, according to institutional and state guidelines on assessment of child-bearing potential. If the test is positive, they will be withdrawn from the study.
- Intra-operative bleeding volume (If completed within conjunction of adenoidectomy, this should be measured prior to adenoidectomy procedure)
  - Record volume of any operative field irrigant used during procedure
  - Record presence of gastric fluids

- Record volume of fluid in suction container (*i.e.* stomach juices and blood) prior to stomach drainage and again after
- Differential weight of any sponges applied to the tonsil bed to absorb blood

- Surgical performance parameters
  - Operative time - time from the first incision to complete hemostasis (arrest of bleeding as assessed by visual inspection of the Investigator) of the tonsillar bed (excluding closing time)
  - Device ease of use (Easy, Moderate, Difficult)
  - Ability to dissect tonsil with device graded via Likert Scale (Very Good, Good, Acceptable, Poor, Very Poor)
  - Usability Challenges (observations of the following):
    - tissue sticking
    - tissue slippage
    - accidental activation
    - visualization of tip
  - Assessment of any complications during the procedure
    - Related to bleeding
      - If there were any transfusions required and if so how much
  - Other non-investigational medical device alternative procedural devices used (if any),
    - Operation time used
    - Tonsil location (Left/Right)
    - Reason for use
  - Tonsil size measurement (volume)
- Device accountability
- Concomitant medications (including anesthesia)
  Note: All medications will be coded using the World Health Organization (WHO) drug coding dictionary.

9.1.3. Post-Operative Follow-up: Days 1 through 7, Day 10, Day 14 and Day 28

Post-operative hospital stay and AE/SAE assessment will take place by delegated study personnel. Additionally, during post-operative days 1 through 7, Day 10 (+/-1 day), Day 14 (+/-1 day), and Day 28 (+/-1 day), the following assessments will be made:

- Pain will be assessed via the FLACC behavioral pain assessment scale (age 2) and the Wong-Baker FACES® Pain Rating Scale (Ages 3-12)
- Analgesic consumption and concomitant medications
- Ability to return to normal diet via patient diary
- Ability to return to normal activity via patient diary
- Incidence of post-operative hemorrhage - any primary (≦24 hours) requiring medical intervention and secondary (>24hrs) bleeding requiring medical intervention (e.g., cautery, admission for observation, or re-operation)
- Incidence of post-operative readmission
- AE/SAE reporting

9.1.4. Assessment Instruments

9.1.4.1. Wong Baker FACES Pain Scale

The Wong Baker FACES pain scale is an instrument validated for ages 3+ to measure pain, by selecting a number on an ordinal 0-10 scale ("0" being no pain and "10" being the worst pain ever). Subjects will receive at least eleven copies of the Wong-Baker FACES® Pain Rating scale (below). Prior to the subject receiving the scale, the subject ID will be written on each page. On post-operative days 1 through 7, Day 10 (+/-1 day), Day 14 (+/-1 day), and Day 28 (+/-1 day), subjects and/or LAR(s) will be instructed to indicate the subject's degree of pain at the same time each morning prior to taking any pain medication by marking and dating the appropriate face.

9.1.4.2. FLACC Behavioral Pain Assessment Scale

The FLACC behavioral pain assessment scale is an instrument validated for use for children ages 2 months 7 years of age to measure pain. A parent or guardian will rate the child's behavior across five (5) domains (Face, Legs, Activity, Crying, and Consolability) on a scale of 0-2 ("0" being no pain behavior and "2" being the highest pain behavior). Subjects will receive at least eleven copies of the FLACC behavioral pain assessment scale. Prior to the subject receiving the scale, the subject ID will be written on each page. On post-operative days 1 through 7, Day 10 (+/-1 day), Day 14 (+/-1 day), and Day 28 (+/-1 day), parent(s)/ will be instructed to indicate the subject's degree of pain at the same time each morning prior to taking any pain medication by rating the child's behavior according to the scale's instructions.

9.1.4.3. Post-Operative Patient Diary

The patient diary will be provided to the subject/subject's LAR. This diary will be used to record any adverse events, or medicines that have been taken relative to the tonsillectomy procedure. The diary will also be used to record return to normal eating and living activities.

9.1.5. Return to Clinic: Day 28 (+7)

On post-operative day 28 (+7) (end of study) the subject will return to the clinic to return their Wong-Baker FACES® pain rating scale(s) or FLACC Behavioral Pain Assessment Sales(s) and the Patient diary. Post-operative day 28 (from section 9.1.3) and Return to Clinic can be combined if both are completed on day 28.

9.2. Prior and Concomitant Medications

Provided that the medications do not conflict with study-related procedures, or are not indicative of an underlying condition that would constitute an eligibility criteria violation, they will follow the normal medication regimen as prescribed by their doctor when proceeding with study participation. No specific post-operative regimen will be required for this study. Medications, including medications for pain, will be recorded as concomitant medications

9.3. Subject Consent

Subjects' legally authorized representatives will need to provide consent to participate in the study prior to any procedures specific to the study are undertaken. Subjects and/or LAR(s) will be provided with a description of the device and procedure; risks, benefits, and alternative procedures; length of participation required; method and amount of compensation, if applicable; and information regarding injury and confidentiality. Written and verbal communication will include non-technical language that is understandable to the subject(s)/LAR(s). Requirements for Informed Consent and, where applicable, Assent from the child will be per local IRB and regulatory requirements. The informed consent discussion(s) will only be conducted by the principal investigators (PIs) and/or his/her designee, provided they are trained in the study. Subjects and/or parent(s)/LAR(s) will be informed that their participation in this study is voluntary and they may refuse to participate or discontinue from the study at any time. PIs or designees will avoid any coercive language and at no time improperly influence or offer improper inducement of subjects to participate or continue participating in the study. At no time will any discussion or written language waive or appear to waive the subject's/ LAR's legal rights. Subjects and parent(s)/LAR(s) will be given ample opportunity to consider the study, read the informed consent form, and ask the investigator questions so that they are adequately informed about the research. Subjects/ LAR(s) will also be informed that after the investigation visits are completed, the subjects will receive the standard medical care, just as they would have, had they not participated in the study. The informed consent form must be personally signed and dated by subject and/or parent(s)/LAR(s) and investigator at time of consent. Additionally, assent forms will be completed and signed as applicable per IRB requirements. The informed consent process will be documented in the source records and a copy of the consent will be provided to the subject and/or parent(s)/LAR(s).

If new information becomes available that may affect a subject's and/or and parent(s)/LAR(s)'s decision to continue to take part in the study, this information will be discussed with the subject and LAR(s) by the investigator and new consent will be obtained in writing. The informed consent form must be personally signed and dated by subject and/or LAR(s) and investigator at time of consent. The informed consent process will be documented in the source records and a copy of the consent will be provided to the subject and/or and LAR(s).

9.4. Randomization and Treatment Assignment

No randomization will occur during the course of the study.

9.5. Medication Compliance

Compliance to the recommended standard of care will be monitored via the at home patient diary. Variations in standard care and patient departures from the standard of care will be recorded and considered in the analysis, but will not be considered a protocol deviation.

9.6. Assessment of Efficacy

Intra-operative blood loss, procedure time, ability to dissect tonsil, ability to achieve hemostasis, analgesic consumption and post-operative pain level will be recorded in the eCRF and used to assess efficacy of the BiZact™ device.

9.7. Assessment of Safety

Safety will be assessed by monitoring the occurrence of adverse events (AEs), serious adverse events (SAEs), death, adverse device effects (ADE), unanticipated serious adverse device effects (USADE), device deficiencies or the presence of localized infection as defined in Section 10. Assessments will take place starting during the procedure as soon as the device is in contact with the subject, through post-operative day 28 (+7) and will be recorded in the eCRF.

9.8. Recording Data

This study will utilize an electronic database and eCRF. All data requested on the eCRF are required. Study visits or measurements not collected and/or recorded will be considered deviations unless otherwise specified. Generally, a source document will be generated for any clinical data points that are required for the study. However, there may be data such as the generation of subject ID, and certain aspects of the Adverse Event (AE) information (e.g. date reported, investigator evaluation) which may be considered as source. The Principal Investigator or authorized designee(s) must ensure the accuracy and completeness of the recorded data and then provide his/her electronic signature on the eCRFs. The Investigator's electronic signature for specific eCRFs will be documented in compliance with local regulations and compliance with the protocol. Changes to data previously submitted to the sponsor will require a new electronic signature by the Investigator to acknowledge/approve the changes.

9.9. Deviation Handling

A study deviation is an event where the Investigator or site personnel did not conduct the clinical study according to the Clinical Investigational Plan or Clinical Investigation Agreement. The Investigator is not allowed to deviate from the above-mentioned documents except under emergency circumstances to protect the rights, safety and well-being of human subjects.

No changes to the protocol will be permitted without the written approval from Medtronic, the IRB/EC and applicable Competent Authority. The investigator must notify Medtronic and the reviewing IRB/EC of any deviation from the Investigational Plan when specific to the protection of the life or physical well-being of a subject in an emergency. The deviation will be recorded in the eCRF and such notice must be given as soon as possible, but in no event later than five (5) working days after the emergency has occurred. Except in such an emergency, prior written approval by Medtronic is required for changes in or deviations from the Plan. If these changes or deviations affect the scientific soundness of the Plan or the rights, safety, or welfare of human subjects the IRB/EC will also be notified. All other deviations will be reported per the site's IRB/EC standard operating procedures. Should any deviations from the Investigational Plan occur, these will be reviewed by Medtronic for their clinical significance and compliance to the protocol. Repetitive or serious investigator compliance issues may result in the need to initiate a corrective action plan, and in some cases, freeze enrolment or ultimately terminate the Investigator's participation in the clinical study.

If any Medtronic representative discovers that an investigator is not complying with the signed Investigator Agreement, the investigational plan, applicable laws, or any conditions of approval imposed by the reviewing IRB/EC, they will report to the clinical study manager and take such steps necessary to promptly secure compliance. If compliance cannot be secured, device shipments to the investigator may be discontinued and the investigator's participation in the investigation terminated. Medtronic shall also require such an investigator to dispose of or return the device, unless this action would jeopardize the rights, safety, or welfare of a subject.

9.10.Subject Status

9.10.1. Screened Subjects

Subjects who are being evaluated for eligibility in the study are considered screened or being screened.

9.10.2. Screen Failures

Subjects whose LAR(s) provide study consent, but then are determined to be ineligible to participate prior to the procedure will be considered screening failures and will not require additional study follow-up visits. The reason for the screening failure will be clearly delineated on the applicable CRFs. If a subject is being screened to participate and the cohort closes during the screening period (see section 9.10.1), the subject should be withdrawn by the investigator, and he/she will not receive the surgery with the device.

9.10.3. Enrolled Subjects

A subject is considered enrolled in the study when the subject's LAR signs the consent. Data will not be captured until the subject is determined to be eligible and the tonsillectomy has begun (Day 0). As soon as the tonsillectomy surgical procedure has begun and the BiZact™ device has been in contact with the subject, the subject must be followed. Subjects who are enrolled, but discontinue the study for any reason prior to the start of the tonsillectomy procedure or usage of the study device, will not be followed unless they are later able to complete the tonsillectomy, See section 9.10.4. These subjects will not count towards the 60-subject enrollment for the study, nor towards the site enrollment maximum (36). In all subject cases where the device was in contact with the subject will be included in the intent-to-treat (ITT) population. The per-protocol population will consist of subjects in the ITT population that did not have a major protocol deviation.

9.10.4. Subject Withdrawal or Discontinuation

Subjects for whom consent has been obtained and are deemed eligible, but later consent is withdrawn will be withdrawn from the study, and their enrollment will not count toward the study enrollment, nor the maximum site enrollment (36). In the event the subject/subject's LAR withdraws consent, the date of withdrawal will be documented.

Subjects whose tonsillectomy has been rescheduled, but still wish to participate may participate if the dates of consent and screening are within 30 days of the new planned tonsillectomy date. If the new tonsillectomy date is more than 30 days after date of screening and/or consent, subjects / LAR(s) who wish to participate should be re-consented and re-screened. In this circumstance, this would be considered a new subject, and the previous consent and screening materials will be considered as a "withdrawn" subject.

If the surgeon has begun the tonsillectomy procedure with the intention of using the investigational medical device, but does not perform the procedure with the investigational medical device for any reason, that subject will not be included in the study nor will their enrollment count toward the maximum number of subjects per site or the total of sixty (60) subjects for the final analysis (section 13.3 Analysis Population). Only procedures where the investigational medical device has come in contact with the subject will be included in the study analysis (see sections 9.10.3 and 13.3 ITT population). If the tonsillectomy procedure has begun, but the investigational device is not used (e.g. generator failure), the subject will be removed from the study, and the reason will be document, including any device deficiencies.

The reason for study exit will be documented on the applicable electronic case report form (eCRF). If the Study Investigator voluntarily removes a subject from further study participation prior to the surgery, supporting documentation must be in place for the rationale and date of removal. Follow-up of subjects withdrawn or discontinued after the surgical procedure will be determined by surgeon, but will respect the rights and wishes of the subject. Every attempt will be made to contact subjects that are noncompliant with study procedures. Subjects will be considered lost to follow-up once the following steps have been taken:

- Two phone calls should be made to the subject/LAR(s). Each attempt should be clearly documented in the source documents and the response or lack thereof should be captured.
- If there is no response to the phone calls, then an official, certified letter should be written to the subject/ LAR(s). A copy of the letter and return or delivery receipts should be retained in the subject's source document.
- Additionally, the site should attempt to reach out to the primary care practitioner to determine the status of the subject and document this in the eCRF.
- When all due diligence attempts to contact have been made, after a period of two (2) weeks, the subject will be considered Lost to Follow-up. The Sponsor should be notified and the End of Study (EOS) form should be completed.

9.11.Selection of Investigators

Surgeons who are qualified by training (board certified in otolaryngology in accordance with USand hospital guidelines), education, and relevant experience appropriate to the use of the product and associated procedures will be considered for participation as investigators in this study. Investigators/sites must have adequate time and resources to conduct the study throughout the duration of the study and have access to an adequate number of eligible subjects. Investigators/sites must be able to comply with applicable Institutional Review Board (IRB) and regulatory requirements. Investigator must not be debarred, disqualified, or working under sanctions in applicable regions. Qualifications are verified through valid CV and current licensing and maintained with study documentation.

10. Risks and Benefits

10.1. Potential Risks

10.1.1. Risks of Investigational Medical Device

The potential risks associated with the standard tonsillectomy procedure include but are not limited to: reaction to anesthesia, swelling, bleeding, infection (including fever), nausea, vomiting, dehydration, velopharyngeal incompetence, and pain.

The potential risks associated with BiZact™ include: unintended cutting, bruising, tearing, thermal burns, or other damage to tissue, arcing, pinching, inadequate/no seal, pain, bleeding, nausea, vomiting, and headache. There is also a risk of electromagnetic interference if the patient has an implantable electronic device.

In the event of unacceptable bleeding, investigators may use alternate means to achieve acceptable hemostasis, just as they would in a typical tonsillectomy procedure. Subjects in the study will be given instruction as to what to do in the event of post-operative bleeding in order to minimize any adverse effects.

The risk analysis is based on the operation of BiZact™ by trained personnel. The overall residual risk after design risk mitigation strategies and/or design control was deemed acceptable for the BiZact™ system.

The instructions for use (IFU) provide instructions on proper use of the device along with warnings and precautions to mitigate risk of misuse and notify the surgeon of potential risks. Surgeons will undergo training on the device prior to participation in the study.

Reproductive and developmental toxicology studies in animals to evaluate the potential for AEs on reproductive ability and effects on the embryo/fetus have not been conducted. As with any device, there is always a risk of a rare or previously unknown side effect developing from the treatment or use of the device.

10.2. Potential Benefits

The potential benefits associated with BiZact™ device usage include, but are not limited to: reduction in pain, blood loss, time to return to normal diet, and activity post tonsillectomy procedure as compared to conventional tonsillectomy; however, there may be no benefits at all.

10.3. Risk Benefit Rationale

Post-operative pain and delayed time to normal diet and activity are common challenges after tonsillectomy procedures. Aside from conventional cold steel and electrocautery dissection, the introduction of numerous energy based tools and techniques allow for the simultaneous dissection and sealing of vessels significantly improving safety and reducing the complications of the procedure (1-3). In most cases however, these energy based devices use heat to establish hemostasis (arrest of bleeding), which can lead to lateral heating and damage to adjacent structures delaying wound healing and increasing post-operative pain (4). Thus, the use of the investigational medical device for

tonsillectomy presents a similar risk profile and minimal if any increase in risk over other commonly used devices.

A positive risk/benefit ratio has been demonstrated with BiZact™ as evidenced by preclinical and biocompatibility testing, and a multicenter adult tonsillectomy is currently underway. There were no apparent adverse systemic or local effects in any of the preclinical studies using animal models. BiZact™ is based off Ligasure™ technology which historically has been shown to be safe and effective for tonsillectomy procedures providing adequate hemostasis (arrest of bleeding) while minimizing postoperative pain.

The product design, as well as the results of internal studies, support BiZact™ as a class 2 FDA cleared for use in adult patients. It is CE-mark and Therapeutic Goods Administration (TGA) Licensed product for use in adult and pediatric patients. There are currently no known interactions between the BiZact™ device and concurrent medical interventions.

11. Adverse Events and Device Deficiencies

Adverse event (AE) definitions used in this study are based on ISO 14155:2011 (Clinical Investigation of Medical Devices for Human Subjects -- Good Clinical Practice).

All AEs and Device Deficiencies will be collected and documented a and Day 0 (after commencement of surgery with BiZact™ to 28 (+7) days follow-up. Device Deficiencies not related to an adverse event (e.g. damaged out of the box) will be collected from when they are first noticed, regardless of usage in a case.

11.1.Definitions and Classifications

11.1.1. Adverse Event (AE)

In alignment with ISO 14155:2011 (Section 3.2), an Adverse Event is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.

This definition includes events related to the investigational medical device and the procedures involved. For users or other persons, this definition is restricted to events related to investigational medical devices.

Adverse Events may include but are not limited to bleeding, tissue injury, and thermal burns.

For study purposes, the following occurrences are considered to be expected observations following surgical procedures (primarily associated with anesthesia) and will not be considered reportable AEs, as long as the event is not associated with significant sequelae, does not prolong hospitalization, and responds to standard medical therapy:

- Postoperative transient nausea determined to be procedure related within the first 24 postoperative hours.
- Postoperative transient emesis determined to be procedure related within the first 24 postoperative hours.

- Postoperative constipation, determined to be procedure and/or medication related for the duration of medication administration for management of pain.
- Postoperative pain that the Investigator considers common and within normal limits for the procedure and is well-managed with medication. Pain that the Investigator considers outside normal, or is not well-managed with medication, as well as pain that severe (score 7 or higher) and ongoing at the end of the study will be captured as an adverse event.

Additionally, the following should not be considered an AE:

- A condition requiring a preplanned procedure unless the condition worsened since enrollment
- A preexisting condition found as a result of screening, unless the condition has worsened since enrollment.

All responses to the above events that require treatment beyond the institution's standard procedures will be reported as AEs.

All AEs observed during the course of this study, regardless of severity or relationship to the device will be recorded on the appropriate eCRF. Adverse events regardless of relatedness will be treated per standard of care at each institution. For example, the management of pain or bleeding will be at the discretion of the treating physician, as he or she is monitoring the patient's condition.

11.1.2. Serious Adverse Events (SAE)

In alignment with ISO 14155:2011 (Section 3.37), a serious adverse event (SAE) is any AE that has:

- led to death,
- led to serious deterioration in the health of the subject that either resulted in
  - a life-threatening illness or injury, or
  - a permanent impairment of a body structure or a body function, or
  - in-patient or prolonged 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
- led to fetal distress, fetal death, or a congenital abnormality or birth defect.

NOTE: Planned hospitalization for a pre-existing condition or a procedure required by the clinical investigational plan, without serious deterioration in health, is not considered an SAE.

11.1.3. Adverse Device Effect (ADE)

In alignment with ISO 14155:2011 (Section 3.1), an Adverse Device Effect is an 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 includes any event resulting from use error or from intentional misuse of the investigational medical device.

Adverse Device Effects will be reported by the Investigator(s). If escalation is required (due to the potential need for reporting) ADEs will be reviewed by Medtronic Medical Affairs. Both confirmed and

possible device related events will be included in the study report. ADE(s) may be anticipated or unanticipated (UADE).

Examples of adverse device effects include but are not limited to: unintended cutting, unintended electrical path, or arcing.

11.1.4. Serious Adverse Device Effect (SADE)

In alignment with ISO 14155:2011 (Section 3.36), a Serious Adverse Device Effect is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

11.1.5. Unanticipated Serious Adverse Device Effect (USADE)

In alignment with ISO 14155:2011 (Section 3.42), an Unanticipated Serious Adverse Device Effect is a serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the current version of the risk analysis report.

NOTE: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report.

11.1.6. Adverse Event Severity Classification

Severity will be defined according to the following criteria:

Mild	Awareness of event, but easily tolerated
Moderate	Discomfort enough to cause some interference with activities of daily living (ADL)
Severe	Incapacitating, with an inability to perform ADL
Death	Death related to AE

An AE can be classified as severe and not deemed an SAE. Similarly, an SAE is not automatically severe in nature.

11.1.7. Adverse Event Relationship Classification

Causality assessments define the relationship between the use of the medical device (including the medical-surgical procedure) and the occurrence of each adverse event, according to MEDDEV (Guidelines on Medical Devices, Clinical Investigations: Serious Adverse Event Reporting). The presence of confounding factors, such as concomitant medication/treatment, the natural history of the underlying disease, other concurrent illness or risk factors shall also be considered.

Each AE will be classified according to five different levels of causality. The sponsor and the investigators will use the following definitions to assess the relationship of the serious adverse event to the investigational medical device or procedures:

Not related: relationship to the device or procedures can be excluded when:

1. the event is not a known side effect of the product category the device belongs to or of similar devices and procedures
2. the event has no temporal relationship with the use of the device or the procedures;
3. the serious event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;

4. the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious event;
5. the event involves a body-site or an organ not expected to be affected by the device or procedure;
6. the serious event can be attributed to another cause (e.g. an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors);
7. the event does not depend on a false result given by the device used for diagnosis, when applicable;
8. harms to the subject are not clearly due to use error;
9. In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

Unlikely: the relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
Possible: the relationship with the use of the device is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases were relatedness cannot be assessed or no information has been obtained should also be classified as possible.
Probable: the relationship with the use of the device seems relevant and/or the event cannot be reasonably explained by another cause, but additional information may be obtained.
Causal relationship: the serious event is associated with the device or with procedures beyond reasonable doubt when:

1. the event is a known side effect of the product category the device belongs to or of similar devices and procedures;
2. the event has a temporal relationship with device use/application or procedures;
3. the event involves a body-site or organ that
    a. the device or procedures are applied to;
    b. the device or procedures have an effect on;
4. the serious event follows a known response pattern to the medical device (if the response pattern is previously known);
5. the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the serious event (when clinically feasible);
6. other possible causes (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;
7. harm to the subject is due to error in use;
8. the event depends on a false result given by the device used for diagnosis, when applicable;
9. In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

The Sponsor and the Investigators will distinguish between the serious adverse events related to the device and those related to the procedures (any procedure specific to the clinical investigation). An adverse event can be related both to procedures and the device. Complications of procedures are considered not related if the said procedures would have been applied to the subjects also in the absence of device use/application.

In some particular cases, the event may be not adequately assessed because information is insufficient or contradictory and/or the data cannot be verified or supplemented. The sponsor and the Investigators will make the maximum effort to define and categorize the event and avoid these situations. Where the sponsor remains uncertain about classifying the serious event, it should not exclude the relatedness and classify the event as "possible".

Particular attention shall be given to the causality evaluation of unanticipated serious adverse (device) events. The occurrence of unanticipated events related to the use of the device (USADE) could suggest that the clinical investigation places subjects at increased risk of harm than was to be expected beforehand.

11.1.8. Adverse Event Outcome Classification

Outcome of the event will be defined according to the following:

- ***Fatal**:* This event is determined to be the cause of death.
- ***Not Recovering/Not Resolved***: The event has retained pathological conditions resulting from the prior disease or injury.
- ***Recovered/Resolved**:* The event has fully resolved at the end of the study.
- ***Recovering/Resolving**:* The event is ongoing at the end of the study.
- ***Unknown***: The event has been unclassified at the end of the study.

11.2. Reporting of Adverse Events

The following events are generally considered reportable during the course of this study and should be reported to the sponsor:

- any ADE, SADE, SAE, or USADE
- any Device Deficiency that might have led to an SADE if
  - suitable action had not been taken or
  - intervention had not been made or
  - circumstances had been less fortunate
- new findings/updates in relation to already reported events.

Events will be reviewed by the sponsor to determine any reporting obligations to regulatory bodies and IRBs/ECs.

The following table captures the reporting requirements for this study. Local and regional regulatory requirements shall be followed in addition to study requirements.

Type of Event	Timeframe	Submit to	Other Reporting Requirements
AE	**As soon as possible** but no more than 10 working days after the day that you become aware of information from any source, thatreasonably suggests that an AE has occurred	Sponsor/ Device Manufacturer	
Any Death	**As soonas practicable** but no more than 10 work days after the day that you become aware of information from any source, thatreasonably suggests that a device has or may have caused or contributed tothe death of a patient of your facility	Sponsor/ Device Manufacturer and Local (IRB/ EC) and regional regulators (FDA)	
UADE	**As soon as possible,** but in no event later than 10 working days afterthe investigator first learns of the effect.	Sponsor / Device Manufacturer and any local/ regionally required regulators	
All Serious Events including SAEs, USADEs, Serious Injuries or Significant Safety Issues	**Within 24 hours, but no later than 10 work days (and/or per local requirements)** after the day that investigator becomes aware of information, from any source,that reasonably suggests that a device has or may have causedor contributed to a serious injury to a patient of your facility.	Sponsor / Device Manufacturer and as per local reporting requirements.	

11.3.Adverse Event Recording

All observed adverse events (ADEs, UADEs and SAEs) will be collected and documented at the time of surgery to 28 (+7) days follow-up. If the adverse event is recorded at the last subject visit and considered serious and device-related, the event should be followed for resolution for up to seven (7) days, or until the resolution of the event, whichever is earliest, even if this falls outside the 28 (+7) day visit window. To ensure consistency of data collection no new events will be recorded after the 28 (+7) day visit window, even if the subject is being followed for resolution of another event. If the adverse event is ongoing at the end of the study, and exceeds the follow up time frame, the patient will continue to receive standard care with their normal physician, and the event will be listed as ongoing.

Assessment of the occurrence of an AE will be based on changes in the subject's physical examination, laboratory results and/or signs and symptoms. Adverse events will be monitored until a subject completes the study unless the Investigator determines the event is related to the device, in which case they will be monitored until resolution if possible. Medical care will be provided, as defined in the informed consent, for any AE related to study participation. Adverse events will be collected on an AE eCRF and applicable source documentation. To the extent possible, the event to be recorded and reported is the event diagnosis as opposed to event symptoms (e.g., fever, chills, nausea and vomiting in the presence of a clinically diagnosed infection is to be reported as infection only). For the purposes of this protocol, only those AEs occurring after enrollment and the commencement of the tonsillectomy with the study device will be recorded.

11.4.Study Contact Information

Questions regarding safety or medical procedures should be directed to Medtronic MITG Medical Affairs. All other questions should be directed to Medtronic MITG Surgical Innovations, Clinical Research. Sponsor internal clinical research team and field monitor contact information will be distributed to sites, to be retained in the study files, and updated as necessary.

Clinical Affairs	Medical Affairs
Stephanie Huston, BS, CCRC Senior Clinical Research Specialist/ Study Manager Medtronic MITG Surgical Innovations 5920 Longbow Dr. Boulder, CO 80301 USA Phone: (303) 763-0813 stephanie.r.huston@medtronic.com	Matthew Savary, MD Director of Medical Affairs Medtronic MITG Surgical Innovations 5920 Longbow Dr. Boulder, CO 80301 USA Phone: 203-530-1395 Matthew.Savary@medtronic.com

11.5. Device Deficiencies

In alignment with ISO14155:2011 (Section 3.15), a Device deficiency is an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labeling.

All BiZact™ device deficiencies will be documented on the Device Malfunction eCRF and the device should be returned to Medtronic for analysis, if possible. Instructions for returning the device will be provided. Device deficiencies should also be documented in the subject's medical record.

Device deficiencies are NOT to be reported as AEs. However, if there is an AE that results from a device deficiency, that specific event would be recorded on the eCRF.

12. Data Review Committees

There will be no use of data review committees in this study. Instead, a steering committee and a safety review committee will monitor the trial's progress including trends of data over time and scientific relevance of the data collected. Please see section 15.10. These groups will provide oversight in terms of scientific validity and the safe conduct of the study.

By nature, this study's focus is about the amount of intraoperative bleeding, which is expected to be low due to the nature of the procedure and the currently available date. Additionally, this is a study of 3 sites and 60 subjects, with no planned interim analysis, and as such, has a lower burden in terms of severity of implications, and degree of data review and analysis compared to a larger study with interim data review needs or a study focusing on severe complications or mortality. Per FDA guidance (OMB Control No 0910-0581 "The Establishment and Operation of Clinical Trial Data Monitoring Committees for Clinical Trial Sponsors" DMCs are "generally recommended for any controlled trial of any size that will compare rates of mortality or major morbidity, but a DMC is not required or recommended for most clinical studies." The guidance goes on to list conditions wherein a DMC may offer additional protections to study participants. Apart from the use in pediatric population, this study does not meet any of the criteria listed wherein a DMC would provide added benefit. Even within this population, the study is small and of short planned duration, so it is unlikely that a DMC would be able to provide added or more rapid benefit than the steering committee or safety review mechanisms.

13. Statistical Design and Methods

13.1. Statistical Test Methods

Continuous variables will be summarized using counts, means, standard deviations, medians, minimum and maximum. Categorical variables will be summarized using frequencies and percentages. Changes to the planned statistical analysis as defined in the protocol will be documented in the statistical analysis plan and clinical study report.

13.2. Sample Size Determination

The analysis technique will be a 1-sample t-test (or Wilcoxon ranked sign if nonparametric test is desired), with a one-sided type I error rate (α) of 0.025. A sample size of 60 subjects is selected to ensure that multiple surgeons participate and to create an opportunity for a range of subject ages to be enrolled. Statistical power for a sample size of 60 subjects exceeds 99%.

13.3.Analysis Population

The intent-to-treat (ITT) population will consist of all enrolled subjects in the study who have undergone tonsillectomy and had contact with the BiZact™ device. The endpoint analyses based on the ITT population will be considered the principal analyses.
The per-protocol (PP) population will consist of all patients in the ITT population who do not have a major protocol violation. Analyses on the PP population will provide supporting evidence to the primary results.

13.4.Statistical Analysis Endpoints

13.4.1. Primary Endpoint

The primary hypotheses of this study are:

H0: Mean intra-operative blood loss =31 mL
HA: Mean intra-operative blood loss < 31 mL

The analysis technique will be a 1-sample t-test, with a one-sided type I error rate (α) of 0.025. If intra-operative blood loss data appear to be non-normally distributed (as evidenced by $p < 0.05$ from a Shapiro-Wilk test), a Wilcoxon signed rank test will also be conducted.

The performance goal of 31 mL derives from a meta-analysis comparing modern technology-assisted to conventional tonsillectomy (i.e. electrocautery and cold steel) (7). This paper included a total of 3,139 patients included in thirty-three published studies. The values from the studies that reported intra-operative bleeding were combined to calculate a mean blood loss. This value encompasses a variety of techniques and technologies and a number of different studies to capture a realistic value for comparison.

Intra-operative blood loss during tonsillectomy with BiZact™ is expected to be low. The expected mean value for the BiZact™ device is a conservative estimate derived from data for LigaSure™ and other vessel sealing systems in the Alexiou meta-analysis (7). The expected standard deviation is the average of the standard deviation values for all studies that reported blood loss in the meta-analysis.

Expected mean intra-operative blood loss for BiZact™: 10 mL
Expected standard deviation: 15.1 mL

Additionally, descriptive statistics for blood loss will be reported for different age groups (ages 2-5 and ages 6-12) as well as for different sites, surgeons, and countries.

13.4.2. Secondary Endpoint

Secondary endpoints will be summarized using descriptive statistics. In addition, 95% confidence intervals will be provided, unless otherwise noted. For continuous variables, the mean, median, and standard deviation will be reported. For categorical data, proportions will be reported. No hypothesis tests are planned

13.5.Statistical Analysis of Safety Endpoints

The safety endpoints will be analyzed using the ITT population. Proportions of the following events will be reported for the study:

- Post-operative hemorrhage

- Any primary (≦24 hours) requiring medical intervention and/or secondary (>24 hours) bleeding requiring medical intervention (e.g., cautery, admission for observation, or re-operation)
- Post-operative readmission
- Evidence of glossopharyngeal nerve damage as diagnosed by the investigator via subject assessment (e.g., prolonged pain or difficulty swallowing)
- Localized Infection
  - Infection confined to a single organ or tissue
- Other serious device-related adverse events

13.6.Handling of Missing Data

No data imputation will be performed for missing data. All practical monitoring and follow-up steps will be taken to ensure complete and accurate data collection. Since primary endpoints are assessed intra-operatively, it is anticipated that there will be minimal missing data for these endpoints.

13.7.Interim Analysis

Currently no interim analysis is planned for this study. Should the need arise for an interim analysis, the protocol will be revised, and statistical plan will be updated accordingly. Periodic data extractions may need to occur in order to provide ongoing feedback for regulatory purposes (e.g. for annual reports), to prepare information for periodic reviews of safety information (e.g. counts of adverse events) or to assist in the ongoing internal review of data to ensure consistency and validity of data. This is considered part of ongoing study management activities, and the endpoints of the study will not be formally analyzed.

13.8. Poolability of Results

Poolability of blood loss data will be assessed for each of the participating investigational sites. Descriptive statistics will be reported separately by site. A one-way ANOVA will test whether there is evidence of a difference in mean blood loss between sites. If this test does not suggest a difference (p-value ≥ 0.15), data will be pooled across sites for inference (i.e., for the primary hypothesis test and 95% confidence interval for mean blood loss). If there is evidence of a difference ($p < 0.15$ from the one-way ANOVA), confidence intervals will be presented separately for each site, and p-values from the hypothesis test in Section 8.4.1 will also be calculated separately for each site. For full details on the planned analysis and poolability, see Statistical Analysis Plan (SAP).

14. Ethics

14.1.Statement(s) of Compliance

This clinical investigation will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and any regional or national regulations such as FDA regulations (US), and ISO 14155:2011 (except conditions specifically excluded as adverse events in Section 11.1.1) as appropriate. All principles of the Declaration of Helsinki have been implemented in this clinical study by means of the subject informed consent process, IRB/EC approval, clinical study training, clinical study registration, publication policy.

The clinical investigation will not begin until all necessary approvals/favorable opinions are obtained from the appropriate IRB/EC or regulatory authority, as appropriate. Should an IRB/EC or regulatory authority impose any additional requirements, they will be followed. If any action is taken by a EC/IRB with respect to the investigation, that information will be forwarded to the sponsor.

Information regarding the study and study data will be made available via publication on clintrials.gov. Additionally, the results of this study will be offered for publication at the conclusion of the study, if participating investigators believe the data warrants publication in an appropriate journal.

15. Study Administration

15.1. Monitoring

Site visits will be conducted by an authorized Medtronic representative to qualify potential sites, conduct site initiation, ensure compliance, assess informed consent process, monitor study data, subjects' medical records, eCRFs, device accountability, device use and storage, IRB/EC submissions, regulatory binder in accordance with current protocol, applicable regulations and standards, and the respective local and national regulations and guidelines (if applicable). The Study Investigator and the investigating site will permit authorized clinical research personnel and clinical monitors from Medtronic or contracted by Medtronic to review completed eCRFs, IRB/EC decisions, and Investigator and clinical site records at regular intervals throughout the study as well as permit study-related monitoring, audits, EC/IRB review, and regulatory inspection(s) by providing direct access to source data/documents. Additionally, subject charts and clinical records will be requested and reviewed so that protocol adherence and source documentation can be verified. In instances where data protection regulations prohibit the direct examination of hospital records by the study Sponsor or designee(s), the Investigator will cooperate in a system of source data verification with the Sponsor. Monitoring may be performed with in person visits or remotely, when applicable.

To ensure the rights, safety, and welfare of study subjects are being maintained, the monitor will maintain assurance that all study staff are trained on the study protocol and use of the investigational medical devices. If the monitor discovers that an investigator is not complying with the signed Investigator Agreement, the investigational plan, applicable laws, or any conditions of approval imposed by the reviewing IRB/EC, the monitor will report to the Sponsor and take such steps necessary to promptly secure compliance. If compliance cannot be secured, device shipments to the investigator may be discontinued and the investigator's participation in the investigation terminated. The monitor shall also require such an investigator to dispose of or return the device, unless this action would jeopardize the rights, safety, or welfare of a subject.

15.2. Data Management

Visual and/or computer data review will be performed to identify possible data discrepancies. In regions where applicable, the investigator will clearly mark or provide a sign/data within clinical record to indicate that the subject is enrolled in this clinical investigation. Where copies of the original source document as well as print outs of original electronic source documents are retained, these shall be signed and dated by a member of the investigation site team with a statement that it is a true reproduction of the original source document. Manual and/or automatic queries will be created in the

Oracle remote data capture (RDC) system and will be issued to the site for appropriate response. The site staff will be responsible for resolving all queries in the database. Medications will be coded under the World Health Organization (WHO) dictionary while Medical History, Surgical History and/or Adverse Events will be coded in Medical Dictionary for Regulatory Activities (MedDRA).

This study will be using a 21 CFR Part 11 compliant electronic data capture system. All system level validation documentation is retained within the Information Systems group.

15.3. Direct Access to Source Data/Documents

Investigator(s)/institution(s) will permit study-related monitoring, audits, IRB/EC review, and regulatory inspection(s), and provide direct access to source data/documents as per local policies and regulations.

15.4. Confidentiality

All records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available.

Subject names will be kept confidential. Only the subject number will be recorded in the eCRF, and if the subject name appears on any other document, it must be obliterated. Study findings stored on a computer will be stored in accordance with local data protection laws. The subjects will be informed in writing that representatives of the sponsor, IRBs/ECs, or Regulatory Authorities may inspect their medical records to verify the information collected, and that all personal information made available for inspection will be handled in strictest confidence and in accordance with local data protection laws. Subjects will also be informed that information regarding the study that does not include subject identifiers will be posted on clinicaltrials.gov.

If the results of the study are published, the subject's identity will remain confidential.
The investigator will maintain a master list to enable subjects' records to be identified.

15.5. Liability

Medtronic maintains appropriate clinical study liability insurance coverage as required under applicable laws and regulations and will comply with applicable local law and custom concerning specific insurance coverage. If required, a clinical study insurance statement/certificate will be provided to the IRB/EC.

15.6. Clinical Investigation Plan (CIP)/Protocol Amendments

A CIP/Protocol amendment will be prepared when there are revisions that are significant changes or corrections, or modifications that impact subject safety, ethical conduct, data integrity or study design. CIP/Protocol amendments must undergo review and approval by the sponsor, IRB/EC and any appropriate regulatory authority, and will be logged in the document version history (Section 17). IRB/EC approval, regulatory authority approval, site training and a new Acknowledgement form will be signed and returned before any new procedures take place.

15.7.Record Retention

The investigator and the sponsor will maintain the records of the study including all pertinent correspondence, the study protocol with any/all amendments, all correspondence with and approval from the IRB/EC, the clinical trial agreement, the Investigator Agreement, device accountability records, individual subject records, and signed informed consent forms. Subject files, other source data and essential documentation kept in the Investigator study files, must be kept for a period of no less than 2 years after the latter of the following two dates: the date on which this investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket application; Medtronic will also retain the study records according to Medtronic policy, whichever prevailing policy or regulation may be longer. Records may need to be maintained by the Principal Investigator for a longer duration if national regulations require or if agreed to in writing with Medtronic. All data and documents should be made available if requested by relevant authorities.

15.8.Publication and Use of Information

The Medtronic Publication and Authorship Policy is aligned with the International Committee of Medical Journal Editors (ICMJE) recommendations (www.icmje.org). Medtronic will seek to publish, in appropriate peer-reviewed journals and scientific conferences, results of clinical studies where human subjects are involved, regardless of outcome. While study results are owned by Medtronic, all data on which a publication is based will be made available to all authors as required for their participation in the publication process. Furthermore, data may be published or used by study investigators provided that such publication or use is in accordance with this protocol, the Medtronic Publication and Authorship Policy, and the Clinical Investigation Agreement. Investigators must submit a copy of all manuscripts and/or abstracts to Medtronic for review and comment 30 days prior to planned submission. Medtronic acknowledges that its right to review and comment shall relate solely to the proprietary, licensing, and/or confidential rights Medtronic may have in such proposed publication, rather than whether such results and/or opinions are favorable to Medtronic.

The publication of post-hoc analyses, regional results, or single-center experiences based on multicenter clinical studies should not precede that of the primary multicenter publication, and should cite the primary publication whenever possible, as required by specific journal and scientific meeting guidelines.

Medtronic involvement in a publication (e.g., funding of the study; sponsor of the study; collection, analysis, and interpretation of data; professional writing assistance) must be disclosed according to journal-specific policies, submission requirements, and prevailing editorial standards, in addition to those specified by International Committee of Medical Journal Editors. Authors must ensure that an acknowledgement/disclosure statement is included in the body of the manuscript for Medtronic to review for accuracy. All authors must also disclose financial or personal affiliations that could be considered conflicts of interest as per journal/conference requirements.

To enable health care providers, payers, and subjects access to the wealth of Medtronic's research, Medtronic will report its scientific data in accordance with the principles outlined in the Guidance Document on Registration and Reporting Results of Company-Sponsored Clinical Trials Under FDAAA 2007 (Title VIII).

15.9.Suspension or Early Termination

Medtronic or appropriate regulatory authorities reserve the right to suspend or discontinue the study at any stage, with written notice to all investigators, all institutions, all reviewing IRBs (US), any investigator(s) in communication with the EC (Australia), all subjects and subjects' personal physicians and any applicable regulatory agencies. Similarly, investigators may withdraw from the study at any time, subject to providing written notification to Medtronic 30 days prior to the date they intend to withdraw from study participation. However, Medtronic and investigators will be bound by their obligation to complete the follow-up of subjects already enrolled in the study. The subjects must be followed according to the clinical protocol, and any additional information obtained during subject follow-up shall be reported to Medtronic on the appropriate eCRF, provided subjects have not withdrawn individually. The above paragraph relates to the withdrawal of a site from the study, not the withdrawal of individual subjects. For individual subject withdrawal, see section 9.10.4.

15.10. Safety Committees

15.10.1. Independent Medical Monitor

The Sponsor will utilize an Independent Medical Monitor to provide medical review and adjudication of pre-specified adverse events in support of protocol defined endpoint data after the site investigator has provided his or her initial assessment of the event. The Independent Medical Monitor will be a qualified, board-certified otolaryngology surgeon that is not affiliated with an investigative center.

Throughout the course of the study and during the review of adverse events, the Independent Medical Monitor will be blinded to the investigational site and Investigator(s) and shall make decisions about relatedness, severity, etc. independent of Medtronic personnel. Adverse events will be provided to the independent medical monitor, at minimum, on a monthly basis to adjudicate.

In alignment with current Medtronic safety policies, the most conservative assessment of the event between the site investigator and the medical monitor will be documented and acted upon as appropriate (i.e. if the medical monitor evaluates an event as not related but the site has considered the event possibly related, the event will remain categorized as possibly related), and reported as such both internally to the internal safety data review committee, to post-market vigilance, and to external agencies as needed.

The medical monitor may be contacted by the internal study team or the internal safety data review team for additional expertise to aid in decision making and recommendations should the need arise.

15.10.2. Steering Committee

The Steering Committee will consist of Investigators participating in this study, as well as relevant members of Medtronic Clinical and Medical Affairs in supportive roles. As noted, investigators for the studies are qualified as part of site qualification procedures and are board-certified otolaryngology surgeons. The role of the Steering Committee is to make recommendations on the design and conduct of the study, the analysis of data, and the communication of results in alignment with the Medtronic Publication and Authorship Policy. The Steering Committee will also be presented with aggregate adverse event data during typical Steering Committee meetings, as described in the Steering Committee Charter; this review will aid in the interpretation of the meaning of the collective data and

potentially help guide study conduct and definitions if additional clarity is needed (e.g. definition of a type of adverse event for consistency across study sites). Because this committee is comprised of investigators from the study, it will not be considered fully impartial, but can make recommendations to the internal safety review team and the internal study team.

15.10.3. Internal Safety Data Review

Internal safety data reviews will consist of a representative of the safety team (registered nurse), an internally employed Medtronic physician, a statistician, the project manager or designee as representative from the study, a member of clinical research leadership for research decision escalation and support as well as representative of quality or post-market vigilance reviews. The independent medical monitor may be consulted if there is a need for clarification of event reviews, for additional expertise is needed for decision making around the conduct of the study, or for additional interpretation of aggregated adverse event information.

The function of this group will be to review safety trends on a periodic basis during the study, as well as any trends or events on an ad hoc basis (e.g. should any unexpected events occur), to monitor subject safety, and to provide guidance regarding the continued safety of enrolled subjects. These meetings are held at least on a quarterly basis during study enrollment, but are also more frequent if necessary (e.g. due to more rapid enrollment), and conducted as urgently as possible in the event of an unexpected frequency or type of adverse event. As this team will have the access to aggregate information on the severity, relatedness, and expectedness of adverse events for the overall study, and between study sites, as well as post-market vigilance data for the product where it is commercially available, this team will have the necessary data and the ultimate responsibility to make decisions regarding holding enrollment at a site or for the entire study or stopping/terminating a study site or the entire study. The procedure by which safety events will be evaluated individually and in aggregate form, is detailed in the Clinical Safety Management and Potential Complaint Plan.

16. References

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17. Version History

Version	Summary of Changes	Author(s)/Title
1.0	• Not Applicable, New Document	Nicholas Paquette, Senior Medical Writer Tianna Aronson, MPH Clinical Project Manager
2.0	• FDA Requested Clarifications including: ○ Clarification related to number of sites ○ Definitions of ITT and per protocol population ○ Inclusion of specific "usability challenges" data collection ○ Updates for consistency and clarity related to risks of procedure and device, as well as the collection period for these events	Tianna Aronson, MPH Clinical Project Manager Greg Sindberg, Senior Medical Writer
3.0	• Removal of subjects age 13 or older to focus study on pediatric population (ages 2-12), along with adjustment of related consent/assent language • FDA requested clarifications including: ○ Adjustments to the assessment of poolability of data ○ Clarification that each site will receive or be assigned to a different generator ○ Clarification on reportable adverse events ○ Clarification on role of data review/ other committees responsible for safety and integrity of data • Minor adjustments to device information and removal of Appendix B, to indicate Investigator's Brochure (IB) will exist as a separate document. • Minor/Administrative changes including: ○ Section numbering and order change due to template revision ○ Updated patient diary sample ○ Updated FLACC scale sample	Tianna Aronson, MPH Clinical Project Manager Greg Sindberg, Senior Medical Writer
4.0	• Clarification to Section 8.2, minor formatting changes	Tianna Aronson, MPH Clinical Project Manager

5.0	• Removal of Australia as a Sponsor Site • Removal of Australia as a clinical site • Decrease from 3 to 2 clinical sites • Increase to 36 from 24 subject per site • Decrease from 6 surgeon investigators to 5 surgeon investigators • Clarification of Adverse Event reporting timeline • Change in Sponsor Contact from Tianna Aronson to Stephanie Huston • Removal of Australian IFU	Stephanie Huston, BS, CCRC Senior Clinical Research Specialist/Study Manager

18. Appendices

18.1.APPENDIX A: Instructions for Use (IFU)

The copies of the IFU contained in this appendix have been inserted from the controlled file. Please note the IFU for the United States and for Australia are included and have different indications. The English version of the IFU for Australia is included herein, directly following the United States IFU. Always refer to the IFU provided with the device itself, in case of any labeling change, and delay in the update in this appendix.

United States IFU

Medtronic

REF BZ4212A

BiZact™

Tonsillectomy Device
Advanced Bipolar Tissue Sealer/Divider

en Instructions for Use

STERILE EO

Rx ONLY

Part No. PT00013974

Covidien llc,
15 Hampshire Street, Mansfield, MA 02048 USA.

Made in USA. Printed in USA.

www.medtronic.com

REV 02/2017

BZ4212A

Compatible with:

FORCETRIAD SW v4.0 or Higher

VLFT10GEN SW v2.0 or Higher

VLLS10GEN SW v1.2 or Higher

United States IFU

en

BiZact™

REF BZ4212A **Tonsillectomy Device Advanced Bipolar Tissue Sealer/Divider 12 mm - 12 cm**

The BiZact Open Sealer/Divider is designed for use with Covidien electrosurgical generators that include vessel sealing capability. Please refer to the cover page for details on compatible generator models and software versions. If the software version on your generator is lower than required, contact Covidien about software updates.

These instructions assume that the operator is knowledgeable about correct setup and operation of the associated Covidien generator. Refer to the generator user's guide for set up information and for additional warnings and cautions.

The instrument creates a seal by application of radiofrequency (RF) electrosurgical energy to blood and lymphatic vessels or tissue bundles interposed between the jaws of the instrument. A cutting blade within the instrument is surgeon-activated to divide tissue.

Maximum rated voltage for the VLLS10GEN: 250 V_{peak}

Maximum rated voltage for the ForceTriad and VLFT10GEN: 288 V_{peak}

Not made with natural rubber latex

Do not use if package is opened or damaged

Type CF applied part

Indications for Use

The BiZact device is a bipolar instrument intended for use in open surgical procedures where ligation and division of vessels, tissue bundles, and lymphatics is desired.

The tissue fusion function of the device can be used on vessels (arteries and veins) and lymphatics up to and including 3 mm diameter. The BiZact device is indicated for use in open general surgical procedures.

It is also indicated for adult ENT procedures, including tonsillectomy, for the ligation and division of vessels, tissue bundles and lymphatics 2-3 mm away from unintended thermally sensitive structures.

The BiZact device has not been shown to be effective for tubal sterilization or tubal coagulation for sterilization procedures. Do not use for these procedures.

Warning

This product cannot be adequately cleaned and/or sterilized by the user in order to facilitate safe reuse, and is therefore intended for single use. Attempts to clean or sterilize these devices without appropriate regulatory authorization may result in bio-incompatibility, infection, or product failure risks to the patient.

This instrument is intended for use ONLY with the Covidien equipment listed on the cover of this document. Use of this instrument with other generators may not result in the desired tissue effect, may result in injury to the patient or surgical team, or may cause damage to the instrument.

Do not use the BiZact system unless properly trained to use it in the specific procedure being undertaken. Use of this equipment without such training may result in serious unintended patient injury.

Use the system with caution in the presence of internal or external pacemakers or other implanted devices. Interference produced by electrosurgical equipment can cause a pacemaker or other device to enter an unsafe mode or permanently damage the device. Consult the device manufacturer or responsible hospital department for further information when use is planned in patients with implanted medical devices.

Contact between an active instrument electrode and any metal objects (hemostats, staples, clips, retractors, etc.) may increase current flow and may result in unintended surgical effects, such as an effect at an unintended site or insufficient energy deposition.

The safe and effective use of RF energy depends on many factors solely under the control of the operator. There is no substitute for properly trained and vigilant personnel. It is important that the operating instructions supplied with this or any other medical equipment be read, understood, and followed.

Precaution

Use caution during surgical cases in which patients exhibit certain types of vascular pathology (atherosclerosis, aneurysmal vessels, etc.). For best results, apply the seal to unaffected vasculature.

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United States IFU

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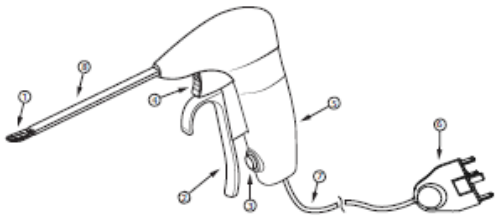
BZ4212A BiZact Open Sealer/Divider



① Jaws (gray)
② Lever (gray)
③ Activation button (blue)
④ Cutting trigger (gray)
⑤ Handle (white)
⑥ Connector (blue and white)
⑦ Cable (blue)
⑧ Outer shaft (metallic)

Setup

Warning

Electric Shock Hazard – Do not connect wet accessories to the BiZact system.

Position instrument cords to avoid contact with the patient or other cords. Do not wrap cords around metal objects. This may induce currents that could lead to shocks, fires, or injury to the patient or surgical team.

Examine all BiZact system and instrument connections before using. Improper connections may result in arcing, sparks, accessory malfunction, or unintended surgical effects.

Confirm proper BiZact system settings before proceeding with surgery.

Do not bend instrument shaft. If the instrument shaft is visibly bent, discard and replace the instrument. A bent shaft may prevent the instrument from sealing or cutting properly.

Inspect the instrument and cords for breaks, cracks, nicks, or other damage before use. Failure to observe this caution may result in injury or electrical shock to the patient or surgical team or cause damage to the instrument. If damaged, do not use.

Warning

Do not use in the presence of flammable anesthetics or oxidizing gases, such as nitrous oxide (N_2O) and oxygen, or in close proximity to volatile solvents (such as ether or alcohol) as explosion may occur.

Because of concerns about the carcinogenic and infectious potential of electrosurgical by-products (such as tissue smoke plume and aerosols), protective eye wear, filtration masks, and effective smoke evacuation equipment should be used.

Connect adaptors and accessories to the electrosurgical unit only when the unit is off or in standby mode. Failure to do so may result in injury or electrical shock to the patient or operating personnel.

Precaution

The performance of this single use device has been tested according to the expected conditions of a single surgical procedure. Subjecting the device to process steps, tools, and/or chemicals commonly used by third-party reprocessors may negatively affect its performance.

Inspect packaging for damage. If damaged, do not use.

1. Open the pouch, remove the device from the pouch and the card.
2. Insert the instrument connector **(6)** of the BiZact device into the LigaSure™ instrument port of the generator. Refer to the generator user's guide for additional set up information.

During Surgery

The BiZact instrument can be used during surgery both to manipulate and dissect tissue, and to seal and cut vessels and tissue bundles. Instructions for use of the instrument during a procedure are provided in this section.

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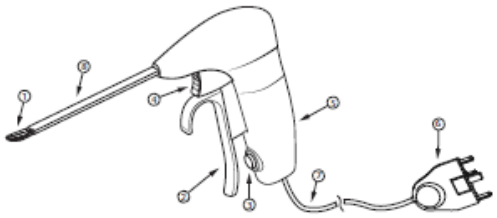
BZ4212A BiZact Open Sealer/Divider



① Jaws (gray)
② Lever (gray)
③ Activation button (blue)
④ Cutting trigger (gray)
⑤ Handle (white)
⑥ Connector (blue and white)
⑦ Cable (blue)
⑧ Outer shaft (metallic)

Setup

Warning

Electric Shock Hazard – Do not connect wet accessories to the BiZact system.

Position instrument cords to avoid contact with the patient or other cords. Do not wrap cords around metal objects. This may induce currents that could lead to shocks, fires, or injury to the patient or surgical team.

Examine all BiZact system and instrument connections before using. Improper connections may result in arcing, sparks, accessory malfunction, or unintended surgical effects.

Confirm proper BiZact system settings before proceeding with surgery.

Do not bend instrument shaft. If the instrument shaft is visibly bent, discard and replace the instrument. A bent shaft may prevent the instrument from sealing or cutting properly.

Inspect the instrument and cords for breaks, cracks, nicks, or other damage before use. Failure to observe this caution may result in injury or electrical shock to the patient or surgical team or cause damage to the instrument. If damaged, do not use.

Warning

Do not use in the presence of flammable anesthetics or oxidizing gases, such as nitrous oxide (N_2O) and oxygen, or in close proximity to volatile solvents (such as ether or alcohol) as explosion may occur.

Because of concerns about the carcinogenic and infectious potential of electrosurgical by-products (such as tissue smoke plume and aerosols), protective eye wear, filtration masks, and effective smoke evacuation equipment should be used.

Connect adaptors and accessories to the electrosurgical unit only when the unit is off or in standby mode. Failure to do so may result in injury or electrical shock to the patient or operating personnel.

Precaution

The performance of this single use device has been tested according to the expected conditions of a single surgical procedure. Subjecting the device to process steps, tools, and/or chemicals commonly used by third-party reprocessors may negatively affect its performance.

Inspect packaging for damage. If damaged, do not use.

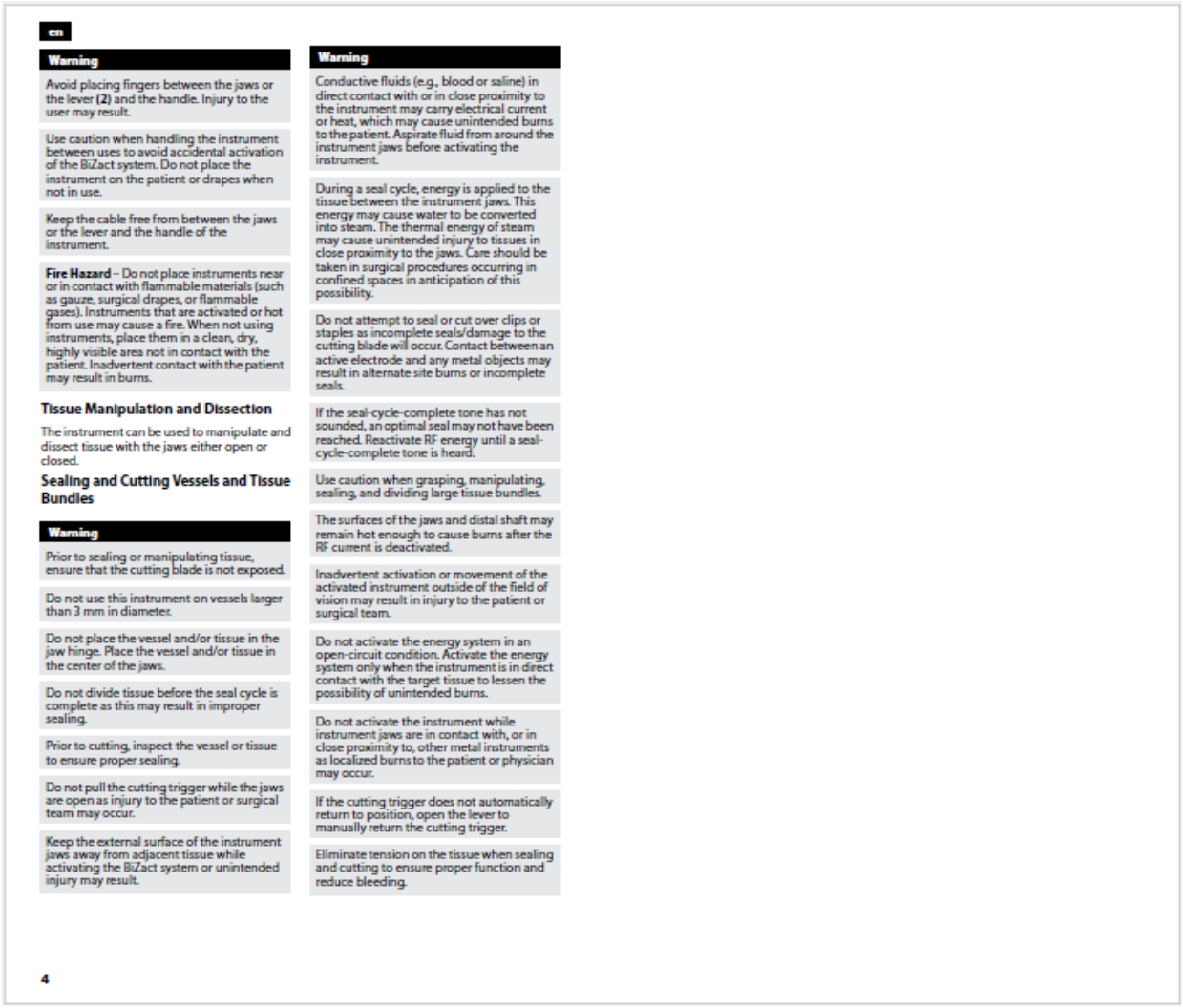
1. Open the pouch, remove the device from the pouch and the card.
2. Insert the instrument connector **(6)** of the BiZact device into the LigaSure™ instrument port of the generator. Refer to the generator user's guide for additional set up information.

During Surgery

The BiZact instrument can be used during surgery both to manipulate and dissect tissue, and to seal and cut vessels and tissue bundles. Instructions for use of the instrument during a procedure are provided in this section.

3

United States IFU



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Warning

Avoid placing fingers between the jaws or the lever (2) and the handle. Injury to the user may result.

Use caution when handling the instrument between uses to avoid accidental activation of the BiZact system. Do not place the instrument on the patient or drapes when not in use.

Keep the cable free from between the jaws or the lever and the handle of the instrument.

Fire Hazard – Do not place instruments near or in contact with flammable materials (such as gauze, surgical drapes, or flammable gases). Instruments that are activated or hot from use may cause a fire. When not using instruments, place them in a clean, dry, highly visible area not in contact with the patient. Inadvertent contact with the patient may result in burns.

Tissue Manipulation and Dissection

The instrument can be used to manipulate and dissect tissue with the jaws either open or closed.

Sealing and Cutting Vessels and Tissue Bundles

Warning

Prior to sealing or manipulating tissue, ensure that the cutting blade is not exposed.

Do not use this instrument on vessels larger than 3 mm in diameter.

Do not place the vessel and/or tissue in the jaw hinge. Place the vessel and/or tissue in the center of the jaws.

Do not divide tissue before the seal cycle is complete as this may result in improper sealing.

Prior to cutting, inspect the vessel or tissue to ensure proper sealing.

Do not pull the cutting trigger while the jaws are open as injury to the patient or surgical team may occur.

Keep the external surface of the instrument jaws away from adjacent tissue while activating the BiZact system or unintended injury may result.

Warning

Conductive fluids (e.g., blood or saline) in direct contact with or in close proximity to the instrument may carry electrical current or heat, which may cause unintended burns to the patient. Aspirate fluid from around the instrument jaws before activating the instrument.

During a seal cycle, energy is applied to the tissue between the instrument jaws. This energy may cause water to be converted into steam. The thermal energy of steam may cause unintended injury to tissues in close proximity to the jaws. Care should be taken in surgical procedures occurring in confined spaces in anticipation of this possibility.

Do not attempt to seal or cut over clips or staples as incomplete seals/damage to the cutting blade will occur. Contact between an active electrode and any metal objects may result in alternate site burns or incomplete seals.

If the seal-cycle-complete tone has not sounded, an optimal seal may not have been reached. Reactivate RF energy until a seal-cycle-complete tone is heard.

Use caution when grasping, manipulating, sealing, and dividing large tissue bundles.

The surfaces of the jaws and distal shaft may remain hot enough to cause burns after the RF current is deactivated.

Inadvertent activation or movement of the activated instrument outside of the field of vision may result in injury to the patient or surgical team.

Do not activate the energy system in an open-circuit condition. Activate the energy system only when the instrument is in direct contact with the target tissue to lessen the possibility of unintended burns.

Do not activate the instrument while instrument jaws are in contact with, or in close proximity to, other metal instruments as localized burns to the patient or physician may occur.

If the cutting trigger does not automatically return to position, open the lever to manually return the cutting trigger.

Eliminate tension on the tissue when sealing and cutting to ensure proper function and reduce bleeding.

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California Proposition 65 Statement

For information regarding California Proposition 65, please refer to www.covidien.com/caprop65.

Precaution

When intending only to grasp or manipulate tissue, ensure pressure from the lever to the button does not activate energy delivery.

During tonsillectomy procedures, stay in the correct surgical plane to prevent damage to critical structures such as the glossopharyngeal nerve.

Keep the instrument jaws clean. Build-up of eschar may reduce the seal and/or cutting effectiveness. Do not activate the instrument while cleaning. Wipe jaw surfaces and edges with a wet gauze pad as needed.

Do not overfill the jaws of the instrument with tissue, as this may reduce device performance.

Hand Activation

Notice

Closing the lever until it clicks activates energy delivery if hand-activation is being used.

1. Ensure hand-activation is enabled on the appropriate port. Refer to the generator user's guide if needed.
2. Grasp the intended vessel and/or tissue in the center of the jaws.
3. Close the lever until you hear or feel the click. At the click, energy is delivered.

   A continuous tone sounds to indicate the activation of RF energy. When the activation cycle is complete, a two-pulsed Seal-Cycle Complete tone sounds and (RF) output ceases.
4. To divide tissue, maintain steady pressure on the lever and pull the cutting trigger (**4**) until a hard stop is reached. Then release the cutting trigger to allow the blade to retract.

Notice

Failure to maintain steady pressure on the lever while cutting could result in inadvertent reactivation of energy.

5. Open the jaws to release tissue.
6. To seal adjacent tissue, overlap the edge of the existing seal. The second seal should be distal to the first seal to increase seal margin.

Footswitch Activation

Important

The LS10 generator does not support footswitch activation.

A footswitch can be used instead of the hand-activation button (**3**). Ensure that the LS0300 footswitch is connected to the footswitch receptacle. Refer to the generator user's guide for additional information.

Warning

Activating energy delivery with a footswitch when the hand-activation button is not fully depressed may result in improper sealing and increase thermal spread to tissue outside the surgical site.

1. Grasp the intended vessel and/or tissue in the center of the jaws.

Notice

If the footswitch is activated with the jaws open, the generator will provide a regrasp alarm indicating the user should regrasp the tissue.

2. Press and hold the lever to the click to ensure appropriate pressure on the grasped tissue.
3. Press and hold the footswitch pedal to activate energy.

   A continuous tone sounds to indicate the activation of RF energy. When the activation cycle is complete, a two-pulsed Seal-Cycle Complete tone sounds and (RF) output ceases.
4. To divide tissue, maintain steady pressure on the lever and pull the cutting trigger until a hard stop is reached. Then release the cutting trigger to allow the blade to retract.
5. Open the jaws to release tissue.
6. To seal adjacent tissue, overlap the edge of the existing seal. The second seal should be distal to the first seal to increase seal margin.

   Note: If both the activation button and the footswitch pedal are activated during the same seal cycle, the vessel sealing system delivers energy from the activation source it detects first.

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Cutting Tissue

Warning

Energy-based devices, such as ES pencils or ultrasonic scalpels that are associated with thermal spread, should not be used to transect seals and sealed tissue.

Notice

Failure to maintain steady pressure on the lever while cutting could result in inadvertent reactivation of energy.

1. To divide tissue, maintain steady pressure on the lever and pull the cutting trigger until a hard stop is reached. Then release the cutting trigger to allow the cutting blade to retract.
2. Open the jaws to release tissue.

Cleaning the Instrument During Use

Warning

Inspect the instrument jaws prior to cleaning to ensure the cutting blade is not deployed.

Do not activate the instrument or cutting trigger while cleaning the jaws. Injury to operating room personnel may result.

1. Ensure the instrument is not plugged into the generator.
2. Wipe jaw surfaces and edges with a sterile, wet gauze pad as needed.

Notice

Do not attempt to clean the instrument jaws by activating the instrument on wet gauze. Product damage may occur.

Remove any embedded tissue from blade track and jaw hinge area.

Do not clean the instrument jaws with a scratch pad or other abrasives.

Troubleshooting

Troubleshooting information	
The following is a list of troubleshooting suggestions for situations encountered when using the instrument with compatible Covidien vessel sealing generators. For details on specific situations, refer to the corresponding generator user's guide or the generator quick reference guide.	
Alert situations	When an alert condition occurs, energy delivery stops, the generator produces a sequence of pulsed tones, and an alert will be displayed on the generator. **Do Not Cut the Vessel.** The user should inspect the seal site and instrument before proceeding. After the alert condition has been corrected, energy delivery will be immediately available.
Troubleshooting steps	1) Release the footswitch pedal or activation button, if still engaged. 2) Open the instrument jaws and inspect for a successful seal. 3) Follow the suggested corrective actions on the generator screen, the generator quick reference card, or in the generator user's guide. 4) If possible, reposition the instrument and regrasp tissue in a location that overlaps the previous seal, then reactivate the seal cycle.
Reasons for alert	**Too little tissue between the jaws** – The user is grasping thin tissue or not enough tissue; open the jaws and confirm that a sufficient amount of tissue is inside the jaws. If necessary, increase the thickness of tissue that is grasped and reactivate the seal cycle. **Too much tissue between the jaws** – The user is grasping too much tissue; open the jaws, reduce the amount of tissue that is grasped, and reactivate the seal cycle. **Activating on a metal object** – Avoid grasping objects, such as staples, clips, or encapsulated sutures in the jaws of the instrument. **Dirty jaws** – Use a wet gauze pad to clean surfaces and edges of instrument jaws. **Excess Fluids in the Surgical Field** – Minimize or remove excess fluids from around the instrument jaws. Activation switch released before seal complete tone – The footswitch or activation button was released before the seal cycle was complete. **Maximum seal cycle time has been reached** – The system needs more time and energy to complete the seal cycle.

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After Surgery

Discard the instrument after use according to the facility's policy for biohazards and sharps. **Do not resterilize.**

Pre-Clinical Studies

Notice

There is no animal data qualified to predict the effectiveness of this device in sealing vessels containing atherosclerotic plaque.

Product performance of the device was established in a chronic in-vivo porcine model. The results showed that no animals studied experienced any hemostatic complications related to the device during the 21-day survival period. A variety of tissue types and vessels was evaluated to demonstrate effective sealing in arteries and veins up to and including 3 mm. The United States clearance of this device was not based on human clinical testing.

In vivo vessel performance (chronic)		
Vessel type	Tissue/Vessel name	**Vessel size range**
A/V bundle	Omentum	up to 1.0 mm
	Gastrosplenic	3.0 mm – 4.0 mm arteries within bundles
	Ovarian Pedicle	4.0 mm – 5.0 mm
	Broad Ligament	1.0 mm – 3.0 mm
	Short Gastric	2.5 mm – 5.0 mm
Isolated vessel (artery, vein)	Splenic	1.5 mm – 4.0 mm

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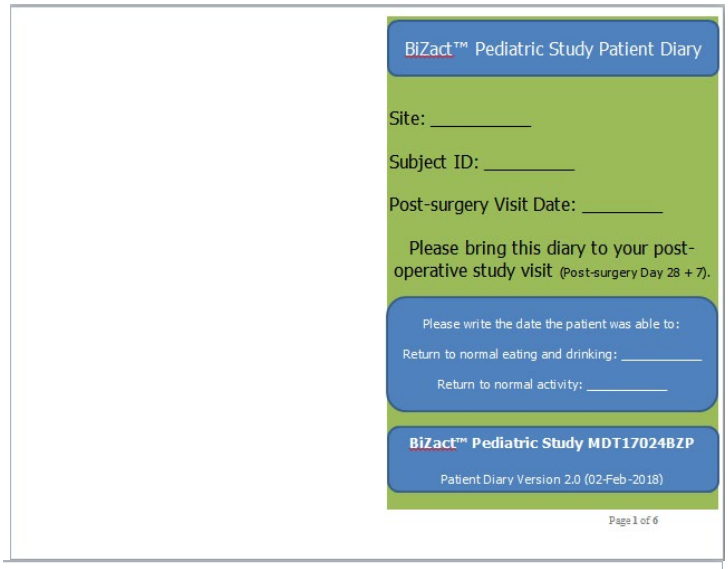
18.2.APPENDIX B: Sample of Post-Operative Patient Diary

The Post-Operative Patient Diary will be kept as a separate document. A sample is provided below, and subject to change.



BiZact™ Pediatric Study Patient Diary

Site: _____

Subject ID: _____

Post-surgery Visit Date: _____

Please bring this diary to your post-operative study visit (Post-surgery Day 28 + 7).

Please write the date the patient was able to:

Return to normal eating and drinking: _____

Return to normal activity: _____

BiZact™ Pediatric Study MDT17024BZP

Patient Diary Version 2.0 (02-Feb-2018)

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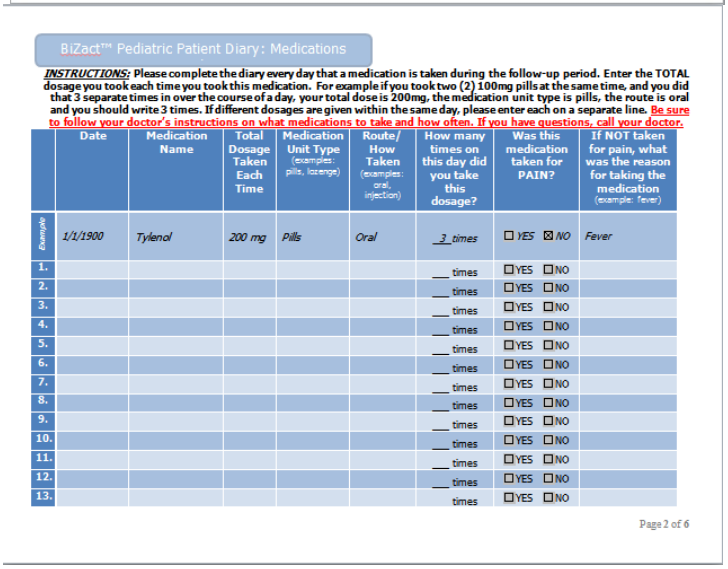

BiZact™ Pediatric Patient Diary: Medications

INSTRUCTIONS: **Please complete the diary every day that a medication is taken during the follow-up period. Enter the TOTAL dosage you took each time you took this medication. For example if you took two (2) 100mg pills at the same time, and you did that 3 separate times in over the course of a day, your total dose is 200mg, the medication unit type is pills, the route is oral and you should write 3 times. If different dosages are given within the same day, please enter each on a separate line. Be sure to follow your doctor's instructions on what medications to take and how often. If you have questions, call your doctor.**

	Date	Medication Name	Total Dosage Taken Each Time	Medication Unit Type (examples: pills, lozenge)	Route/ How Taken (examples: oral, injection)	How many times on this day did you take this dosage?	Was this medication taken for PAIN?	If NOT taken for pain, what was the reason for taking the medication (example: fever)
Example	*1/1/1900*	*Tylenol*	*200 mg*	*Pills*	*Oral*	*_3_ times*	☐ YES ☒ NO	*Fever*
1.						___ times	☐YES ☐NO	
2.						___ times	☐YES ☐NO	
3.						___ times	☐YES ☐NO	
4.						___ times	☐YES ☐NO	
5.						___ times	☐YES ☐NO	
6.						___ times	☐YES ☐NO	
7.						___ times	☐YES ☐NO	
8.						___ times	☐YES ☐NO	
9.						___ times	☐YES ☐NO	
10.						___ times	☐YES ☐NO	
11.						___ times	☐YES ☐NO	
12.						___ times	☐YES ☐NO	
13.						___ times	☐YES ☐NO	

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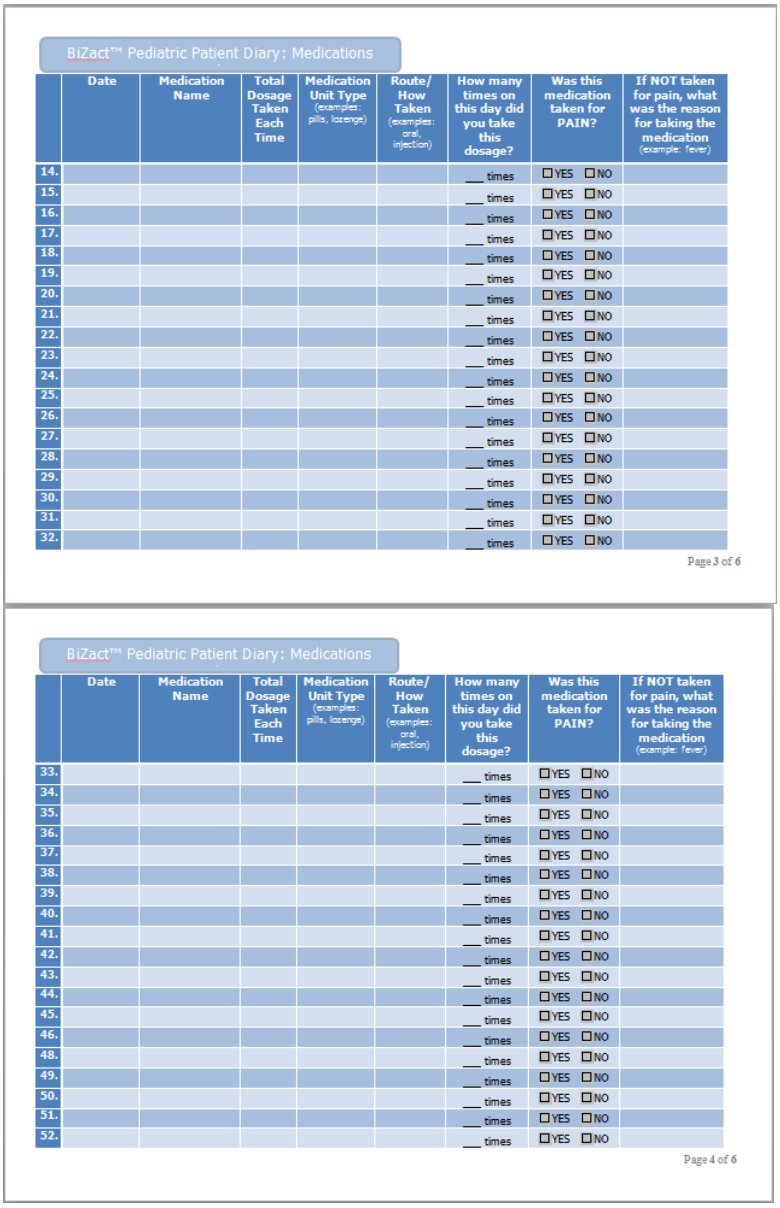

BiZact™ Pediatric Patient Diary: Medications

	Date	Medication Name	Total Dosage Taken Each Time	Medication Unit Type (examples: pills, lozenge)	Route/ How Taken (examples: oral, injection)	How many times on this day did you take this dosage?	Was this medication taken for PAIN?	If NOT taken for pain, what was the reason for taking the medication (example: fever)
14.						___ times	☐YES ☐NO	
15.						___ times	☐YES ☐NO	
16.						___ times	☐YES ☐NO	
17.						___ times	☐YES ☐NO	
18.						___ times	☐YES ☐NO	
19.						___ times	☐YES ☐NO	
20.						___ times	☐YES ☐NO	
21.						___ times	☐YES ☐NO	
22.						___ times	☐YES ☐NO	
23.						___ times	☐YES ☐NO	
24.						___ times	☐YES ☐NO	
25.						___ times	☐YES ☐NO	
26.						___ times	☐YES ☐NO	
27.						___ times	☐YES ☐NO	
28.						___ times	☐YES ☐NO	
29.						___ times	☐YES ☐NO	
30.						___ times	☐YES ☐NO	
31.						___ times	☐YES ☐NO	
32.						___ times	☐YES ☐NO	

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BiZact™ Pediatric Patient Diary: Medications

	Date	Medication Name	Total Dosage Taken Each Time	Medication Unit Type (examples: pills, lozenge)	Route/ How Taken (examples: oral, injection)	How many times on this day did you take this dosage?	Was this medication taken for PAIN?	If NOT taken for pain, what was the reason for taking the medication (example: fever)
33.						___ times	☐YES ☐NO	
34.						___ times	☐YES ☐NO	
35.						___ times	☐YES ☐NO	
36.						___ times	☐YES ☐NO	
37.						___ times	☐YES ☐NO	
38.						___ times	☐YES ☐NO	
39.						___ times	☐YES ☐NO	
40.						___ times	☐YES ☐NO	
41.						___ times	☐YES ☐NO	
42.						___ times	☐YES ☐NO	
43.						___ times	☐YES ☐NO	
44.						___ times	☐YES ☐NO	
45.						___ times	☐YES ☐NO	
46.						___ times	☐YES ☐NO	
48.						___ times	☐YES ☐NO	
49.						___ times	☐YES ☐NO	
50.						___ times	☐YES ☐NO	
51.						___ times	☐YES ☐NO	
52.						___ times	☐YES ☐NO	

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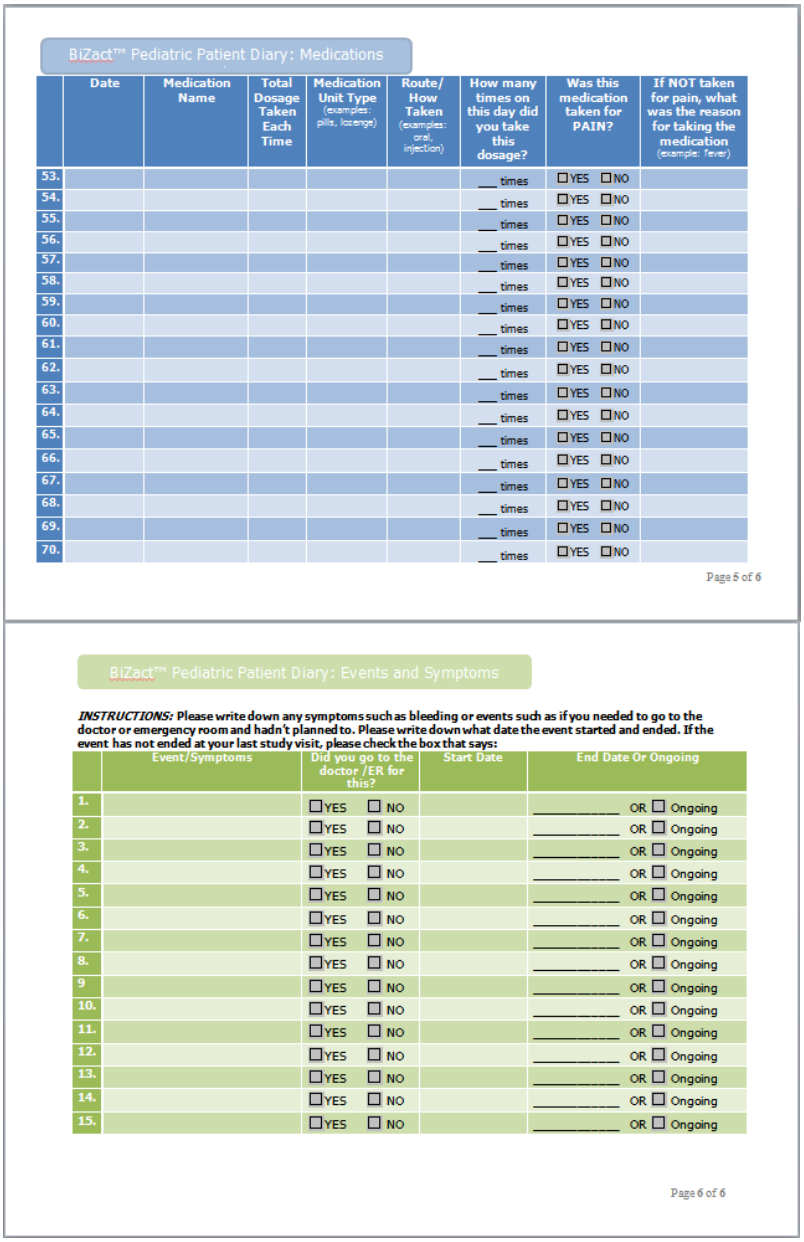

BiZact™ Pediatric Patient Diary: Medications

	Date	Medication Name	Total Dosage Taken Each Time	Medication Unit Type (examples: pills, lozenge)	Route/ How Taken (examples: oral, injection)	How many times on this day did you take this dosage?	Was this medication taken for PAIN?	If NOT taken for pain, what was the reason for taking the medication (example: fever)
53.						___ times	☐YES ☐NO	
54.						___ times	☐YES ☐NO	
55.						___ times	☐YES ☐NO	
56.						___ times	☐YES ☐NO	
57.						___ times	☐YES ☐NO	
58.						___ times	☐YES ☐NO	
59.						___ times	☐YES ☐NO	
60.						___ times	☐YES ☐NO	
61.						___ times	☐YES ☐NO	
62.						___ times	☐YES ☐NO	
63.						___ times	☐YES ☐NO	
64.						___ times	☐YES ☐NO	
65.						___ times	☐YES ☐NO	
66.						___ times	☐YES ☐NO	
67.						___ times	☐YES ☐NO	
68.						___ times	☐YES ☐NO	
69.						___ times	☐YES ☐NO	
70.						___ times	☐YES ☐NO	

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BiZact™ Pediatric Patient Diary: Events and Symptoms

INSTRUCTIONS: **Please write down any symptoms such as bleeding or events such as if you needed to go to the doctor or emergency room and hadn't planned to. Please write down what date the event started and ended. If the event has not ended at your last study visit, please check the box that says:**

	Event/Symptoms	Did you go to the doctor /ER for this?	Start Date	End Date Or Ongoing
1.		☐YES ☐ NO		_____ OR ☐ Ongoing
2.		☐YES ☐ NO		_____ OR ☐ Ongoing
3.		☐YES ☐ NO		_____ OR ☐ Ongoing
4.		☐YES ☐ NO		_____ OR ☐ Ongoing
5.		☐YES ☐ NO		_____ OR ☐ Ongoing
6.		☐YES ☐ NO		_____ OR ☐ Ongoing
7.		☐YES ☐ NO		_____ OR ☐ Ongoing
8.		☐YES ☐ NO		_____ OR ☐ Ongoing
9		☐YES ☐ NO		_____ OR ☐ Ongoing
10.		☐YES ☐ NO		_____ OR ☐ Ongoing
11.		☐YES ☐ NO		_____ OR ☐ Ongoing
12.		☐YES ☐ NO		_____ OR ☐ Ongoing
13.		☐YES ☐ NO		_____ OR ☐ Ongoing
14.		☐YES ☐ NO		_____ OR ☐ Ongoing
15.		☐YES ☐ NO		_____ OR ☐ Ongoing

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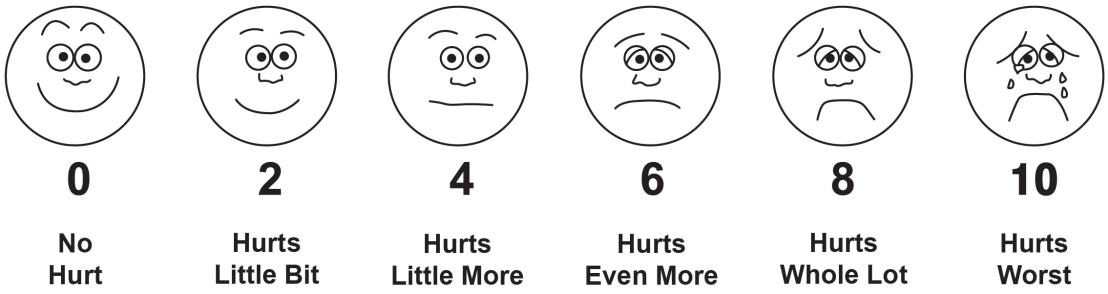
18.3.APPENDIX C: Sample of Wong-Baker FACES® Pain Rating Scale

The Wong Baker FACES pain rating scale will be provided to sites as a separate document. A sample is provided below, and subject to change.

Wong-Baker FACES® Pain Rating Scale



0	2	4	6	8	10
No Hurt	Hurts Little Bit	Hurts Little More	Hurts Even More	Hurts Whole Lot	Hurts Worst

Date of Assessment: _____ Time of Assessment: _____

18.4.APPENDIX D: Sample of FLACC Behavioral Pain Assessment Scale

The FLACC Behavioral Pain Assessment scale will be provided to sites as a separate document. A sample is provided below, and subject to change.

FLACC Behavioral Scale

Categories	Scoring		
	0	1	2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant frown, clenched jaw, quivering chin
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid, or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or being talked to, distractable	Difficult to console or comfort
Each of the five categories (F) Face; (L) Legs; (A) Activity; (C) Cry; (C) Consolability is scored from 0-2, which results in a total score between zero and ten.			

FLACC Behavioral Pain Scale

Patients who are awake: Observe for at least 1-2 minutes. Observe legs and body uncovered. Reposition patient or observe activity, assess body for tenseness and tone. Initiate consoling interventions if needed
Patients who are asleep: Observe for at least 2 minutes or longer. Observe body and legs uncovered. If possible reposition the patient. Touch the body and assess for tenseness and tone.

Face
Score 0 point if patient has a relaxed face, eye contact and interest in surroundings

Score 1 point if patient has a worried look to face, with eyebrows lowered, eyes, partially closed, cheeks raised, mouth pursed

Score 2 points if patient has deep furrows in the forehead, with closed eyes, open mouth and deep lines around nose/lips

Legs
Score 0 points if patient has usual tone and motion to limbs (legs and arms)

Score 1 point if patient has increase tone, rigidity, tense, intermittent flexion/extension of limbs

Score 2 points if patient has hyper tonicity, legs pulled tight, exaggerated flexion/extension of limbs, tremors

Activity
Score 0 points if patient moves easily and freely, normal activity/restrictions

Score 1 point if patient shifts positions, hesitant to move, guarding, tense torso, pressure on body part

Score 2 points if patient is in fixed position, rocking, side-to-side head movement, rubbing body part

Cry
Score 0 points if patient has no cry/moan awake or asleep

Score 1 point if patient has occasional moans, cries, whimpers, sighs

Score 2 points if patient has frequent/continuous moans, cries, grunts

Consolability

Score 0 points if patient is calm and does not require consoling

Score 1 point if patient responds to comfort by touch or talk in ½- 1 minute

Whenever feasible, behavioral measurement of pain should be used in conjunction with self-report. When self-report is not possible, interpretation of pain behaviors and decision making regarding treatment of pain requires careful consideration of the context in which the pain behaviors were observed.

Each category is scored on the 0-2 scale which results in a total score of 0-10
Assessment of Behavioral Score:
- 0 = Relaxed and comfortable
- 1-3 = Mild discomfort
- 4-6 = Moderate pain
- 7-10 = Severe discomfort/pain

18.5.APPENDIX E: Additional records and reports

There are no additional records or reports other than those required in Subpart G of the IDE regulations.

18.6.APPENDIX F: List of Investigators and Institutions

Investigative Sites information including addresses, contact information, Principal Investigators, their respective IRBs/ECs, and will be retained in a separate document from the body of the clinical investigation plan document. This will be provided to investigative sites and updated as necessary.